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Theoretical Studies on the Conformation of Saccharides

I. Conformational Flexibility of the Pyranose Ring

Tibor Kožár and Igor Tvaroška
Institute of Chemistry, Slovak Academy of Sciences, CS-809 33 Bratislava, Czechoslovakia

Conformations of 2-methoxytetrahydropyran as a model for the six-membered ring in aldopyranosides have been calculated by the PCILO method using the algorithm of the conjugated gradient to optimize the geometry. The calculated geometry of the fourteen basic forms of 2-methoxytetrahydropyran was found to be in agreement with the available data obtained by X-ray diffraction of pyranosides. The results indicate differences in the geometry of 2-methoxytetrahydropyran resulting from the change of the axial vs. equatorial position of the methoxyl group. These changes are particularly meaningful in the values of bond angles and they are in agreement with the anomeric and exoanomeric effects. The experimentally found differences in the energies of an axial ($^4C_1$) and equatorial ($^1C_4$) conformer, $\Delta G = 2.9$–3.7 kJ/mol, and the dipole moment, $\mu = 1.20 \pm 0.05$ D (1D = $3.33\ 10^{-30}$ mAs) agree well with the calculated values $\Delta E = 3.18$ kJ/mol and $\langle\mu\rangle = 1.18$ D which, in turn, suggest that the axial conformer is preferred over the equatorial one by a ratio $a{:}e = 78{:}22$.

Key words: 2-Methoxytetrahydropyran – Saccharides, conformation of ∼ – Pyranose ring, flexibility of ∼

1. Introduction

Conformational properties and electronic structure of biomolecules have been recently described in numerous quantum-chemical works. Although carbohydrates and polysaccharides belong to the most important biomolecules, from this point of view they have received but little attention [1–5]. Owing to the complexity of their structure some of the conformational properties of these substances, e.g. anomeric and exoanomeric effects, have been studied using acyclic model compounds [6–9]. The next logical step to be undertaken to clarify conformational properties of sugar

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by quantum-chemical work is the study of the pyranose ring and particularly of its conformational properties. As far as we are aware no such quantum-chemical studies are available in the literature on this type of compound which would involve the optimization of the geometry.

It is generally assumed that the most stable form of pyranose sugars is the so-called chair conformation. Since the six-membered ring may adopt also lower-symmetry forms, other conformations, e.g. boat and skew, are known as well. The flexible forms exist near the absolute minimum on the conformational space of the molecule and, as a result of pseudorotation, they can change one to another. As far as pyranose sugars are concerned, the geometry of these less abundant forms and the course of the potential energy along the pseudorotation path is unknown. Although no direct proof about the existence of some of the flexible forms of pyranose sugars have been presented, some of the recent results [10] indicate that, at least in solution, a low percentage of units in a polysaccharide might be present in other than chair conformation. It is also probable that the hexopyranose ring of sugars involved in biological processes has other than the chair conformation. An example of these phenomena enzymatic hydrolysis may be mentioned, during which process the chair form of sugar moieties in the active centrum of the hydrolysis is deformed [11]. The aim of the present work is the calculation of energy, geometry and charge distribution of various forms of the hexopyranose ring along the pseudorotation pathway. Attention will be also focussed on the conformational equilibrium of the two chair forms having axially and equatorially oriented methoxyl group. The results presented are hoped to extend our knowledge about pyranosides and should make it possible to understand more precisely their behavior in higher structural units such as polysaccharides, glycoproteins, glycolipids, etc.

2. The Model and the Method of Calculation

2-Methoxytetrahydropyran (MTHP), which might also be considered as deoxyhexopyranose, was chosen as a model for the study of the flexibility of the hexopyranose ring in sugars for several reasons. Firstly, it contains the main conformational features of the pyranose ring and the glycosidic linkage and, secondly, by the substitution of hydrogen atoms for hydroxyl groups the large number of degrees of freedom, which has to be taken into account in the optimization of geometry, is reduced. Thirdly, in the literature there is a sufficient amount of data obtained experimentally with a wide spectrum of solvents on conformational equilibrium of the two chair forms in solution. The MTHP molecule (for numbering of the atoms see Fig. 1) was studied in fourteen conformations of which two were chair, six were boat and six were skew. The individual conformers are named according to Rules for Conformational Nomenclature for Five- and Six-membered Rings in Monosaccharides and their Derivatives [12].

In order to describe completely the conformation of a hexopyranose ring in the internal coordinates it is necessary that, in addition to the bond lengths between the atoms A and B, r(A–B), also the bond angles among the three atoms A–B–C as $\alpha(i) = \alpha$(A–B–C) and for the system of four atoms A–B–C–D the torsional angles

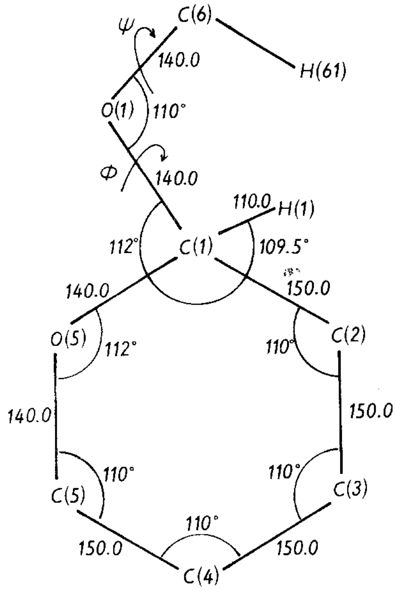

Fig. 1. The numbering of the atoms and the initial geometrical parameters for 2-methoxytetrahydropyran

$\nu(i) = \nu(\text{A–B–C–D})$ [13], be specified. The indices for our case have been assigned according to Eq. (1).

$$\begin{aligned}
\alpha(1) &= \alpha[\mathrm{O(5)–C(1)–O(1)}]\\
\alpha(2) &= \alpha[\mathrm{C(1)–C(2)–C(3)}]\\
\alpha(3) &= \alpha[\mathrm{C(2)–C(3)–C(4)}]\\
\alpha(4) &= \alpha[\mathrm{C(3)–C(4)–C(5)}]\\
\alpha(5) &= \alpha[\mathrm{C(4)–C(5)–O(5)}]\\
\alpha(6) &= \alpha[\mathrm{C(1)–O(5)–C(5)}]\\
\alpha(7) &= \alpha[\mathrm{O(5)–C(1)–H(1)}]\\
\nu(1) &= \nu[\mathrm{O(5)–C(1)–C(2)–C(3)}]\\
\nu(2) &= \nu[\mathrm{C(1)–C(2)–C(3)–C(4)}]\\
\nu(3) &= \nu[\mathrm{C(2)–C(3)–C(4)–C(5)}]\\
\nu(4) &= \nu[\mathrm{C(3)–C(4)–C(5)–O(5)}]\\
\nu(5) &= \nu[\mathrm{C(4)–C(5)–O(5)–C(1)}]\\
\nu(6) &= \nu[\mathrm{C(5)–O(5)–C(1)–C(2)}]
\end{aligned}\tag{1}$$

To describe the conformation of the glycosidic linkage it is of advantage to define, in addition to the commonly used torsional angles Φ, Ψ and the glycosidic angle β, also the third torsional angle Θ (Eq. (2)).

$$\begin{aligned}
\Phi &= \Phi[\mathrm{O(5)–C(1)–O(1)–C(6)}]\\
\Psi &= \Psi[\mathrm{C(1)–O(1)–C(6)–H(61)}]\\
\Theta &= \Theta[\mathrm{C(5)–O(5)–C(1)–O(1)}]\\
\beta &= \beta[\mathrm{C(1)–O(1)–C(6)}]
\end{aligned}\tag{2}$$

For convenience of the description of the shape of the ring, puckering parameters of Cremer and Pople [14] Q, Θ_2, φ_2, q_2 and q_3 will be used. The pseudorotation cycle of the flexible forms of MTHP and the position of the chair conformers on the conformational sphere of the parameters Q, Θ_2 and φ_2 is in Fig. 2. The three puckering parameters Q, Θ_2 and φ_2 define unambiguously the position of the individual forms of MTHP on the conformational sphere. Characteristic of the chair conformers is their position at the poles of the sphere, viz. position for which $\Theta_2 = 0°$ or $180°$. All twelve flexible forms are located at the equator and boat conformers have $\varphi_2 = 0, 60, 120, 180, 240$ and $300°$, whereas the skew conformers are characterized by $\varphi_2 = 30, 90, 150, 210, 270$ and $330°$.

For optimization of the geometry of all conformers the same initial bond angles and bond lengths were used as shown in Fig. 1. The angles in the C—C—H and O—C—H bonds were assumed to be tetrahedral and the value 110 pm was used as initial for all C—H bonds. Values given by Goebel [15] were used as initial for the endocyclic dihedral angles characteristic of the individual ring forms.

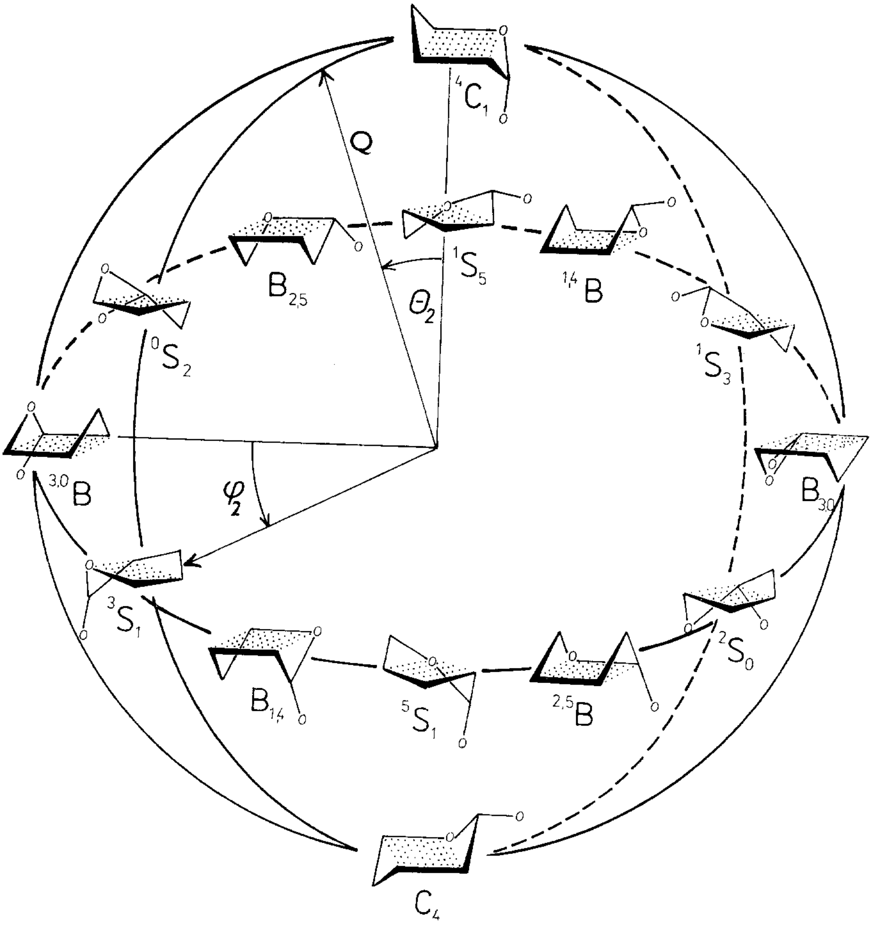

Fig. 2. Conformations of 2-methoxytetrahydropyran and their position on the conformational sphere defined by the Q, Θ_2 and φ_2 parameters

Owing to a large number of calculations required in the present study the *ab initio* method could not be used even in the minimum basis. Therefore, the semiempirical PCILO method [16, 17], which proved to be useful in the conformational studies, was selected. The calculations were carried out using the standard version of the PCILO method as adopted for the optimization of the geometry according to Powell–Zangwill's [18, 19] algorithm through internal parameters. The polarity of all bonds has been optimized throughout the overall calculation. Of the geometrical parameters, bond lengths, bond angles and torsional angles of all atoms, except those of the atoms of hydrogen linked to C(2), C(3), C(4), C(5) and C(6), i.e. together 21 geometrical parameters, were optimized. The required accuracy during the optimization of the geometry was 0.1 pm for the bond lengths, 0.05° for the bond angles and 0.5° for the torsional angles.

3. Results and Discussion

3.1. Geometry

The assignment of the optimized structures of MTHP to the individual pyranose ring forms on the conformational sphere (Fig. 2) can be accomplished using puckering parameters according to the above-given conditions. It can be seen from the puckering parameters (Table 1) that for the flexible forms Θ_2 is close to 90° and that the value of φ_2 varies according to its correspondence to the skew or boat forms. The values of puckering parameter Θ_2 (3.6 and 175.6) show deviations of the $^4C_1$ and $^1C_4$ conformations from the ideal chair forms of cyclohexane. These

Table 1. Relative energies (kJ/mol), dipole moments (D) and puckering parameters (deg, pm) of fourteen conformers of 2-methoxytetrahydropyran and standard α- and β-*D*-glucose residues

Conformer (i)	ΔE_i	μ_i	Q	q_2	q_3	Θ_2	φ_2
$^4C_1$	0.0	0.28	57.4	3.6	57.3	3.61	201.81
$^1C_4$	3.14	2.13	57.1	4.4	−56.9	175.58	28.35
$B_{1,4}$	17.10	0.43	71.6	71.5	4.0	93.24	59.68
$^5S_1$	7.66	0.86	67.9	67.9	0.2	90.13	90.20
$^{2,5}B$	22.10	1.44	74.7	74.7	−0.4	90.30	122.59
$^2S_0$	5.60	1.76	68.7	68.6	3.2	87.35	147.94
$B_{3,0}$	15.79	2.10	76.0	75.9	4.2	86.87	177.70
$^1S_3$	6.07	2.23	68.5	68.6	2.0	88.36	209.64
$^{1,4}B$	19.40	2.15	71.6	71.5	4.1	86.69	239.95
$^1S_5$	9.84	1.98	67.3	67.3	0.4	89.66	270.55
$B_{2,5}$	24.06	1.47	74.4	74.4	0.6	89.52	303.07
$^0S_2$	5.64	1.03	68.7	68.6	−2.7	92.23	328.82
$^{3,0}B$	13.90	0.29	76.1	76.1	−3.7	92.82	358.08
$^3S_1$	4.55	0.32	68.9	68.9	−1.8	91.47	29.85
α-Glc			56.8	2.4	56.8	2.41	23.54
β-Glc			57.6	3.6	57.5	3.58	13.50

deviations are not surprising since the substitution of one methylene group in cyclohexane with the electronegative atom of oxygen alters the electronic distribution in the six-membered ring. This, in turn, manifests itself as a change of the bond and torsional angles, as well as of bond lengths. Consequently, the shape of the conformers of the six-membered ring thus produced must differ from the ideal forms of cyclohexane. The Θ_2 values for the chair forms of MTHP are close to those calculated for standard *D*-glucose residues [20] ($\Theta_2 = 2.41$ and 2.58 for the α- and β-anomers, respectively). Also, the Θ_2 values indicate an effect of the orientation of the methoxyl group at the anomeric position upon the geometry of the pyranose ring resulting from the delocalization of the free electron pairs of both oxygen atoms in both conformers [21]. The situation is the same in the case of the flexible conformers, where the distortions from the ideal boat and skew forms are expressed by the deviations from the ideal values of Θ_2 and φ_2 puckering parameters. The maximum deviation of both parameters is 3.5°. The transition of one hexopyranose ring form to another results in a change of dihedral ring angles. Since every six-membered ring has to fulfil six equations of constraint (ring closure conditions), the internal geometrical parameters are not independent. Therefore, every single change of the torsional angle of the ring results in a change of bonding angles and bond lengths, and vice versa. Nevertheless, the force constant of the bond lengths deformations are much greater than those of bond and torsional angles. When a set of potential functions [22] is used, by which the equilibrium conformations of *D*-glucose are well reproduced, a change of the torsional angle by 4–5° from its equilibrium value of 60 or 180° requires roughly the same energy as a deformation of the bonding angle by 1–1.5°, or stretch of the bond length by 1 pm. It can therefore be reasonably expected that the changes of the bond lengths resulting from the change of the ring conformation will be less pronounced compared to the bond angles. The torsional and bond angle values for the optimal structures of individual MTHP conformers are given in Tables 2 and 3. It follows from our calculations that the bond lengths are practically independent of the ring conformation. The bond lengths of the individual types of bond are within a range of 149.5–150.1 and 139.1–140.2 pm for the C—C and C—O bonds, respectively. Since no experimental literature data on the geometry of MTHP are available, the calculated geometrical parameters can be compared only with experimental values obtained for saccharides in the chair conformation. Based on analyses of available X-ray diffraction data for carbohydrates and polysaccharides, Arnott and Scott [20] have determined the so-called standard α- and β-*D*-glucose ring geometrical parameters which have often been used successfully in the determination of the crystal structure of polysaccharides. The bond and torsional angle values obtained for standard *D*-glucose units as well as those of puckering parameters are very close to the values calculated for $^4C_1$ and $^1C_4$ conformers of MTHP (Tables 1–3). The calculated bond lengths also agree rather well with those given by Arnott and Scott [20] for standard *D*-glucose residues. However, in most cases the calculated bond lengths are shorter compared to the experimental values; the maximum deviation, 3 pm, does not exceed 3%. The difference between the experimentally found and the calculated values is not very large considering the fact that the ranges of C—C and C—O lengths within which the experimental values fall are 150.8–153.9 pm and 139.2–144.3 pm, respectively,

Table 2. Torsional angles (deg) of fourteen conformers of 2-methoxytetrahydropyran and of standard α- and β-*D*-glucose residues

Conformer (i)	Θ	Φ	$\nu(1)$	$\nu(2)$	$\nu(3)$	$\nu(4)$	$\nu(5)$	$\nu(6)$
$^4C_1$	65.97	63.04	57.00	−56.89	−57.70	−59.14	59.09	−57.88
$^1C_4$	178.53	58.19	−55.95	56.73	−57.96	59.30	−58.78	56.82
$B_{1,4}$	73.80	63.13	50.51	3.71	−55.10	56.97	−1.68	−51.97
$^5S_1$	95.01	60.42	59.63	−27.29	−27.32	60.02	−29.49	−28.77
$^{2,5}B$	128.70	57.80	52.27	−53.93	2.17	56.02	−61.03	5.61
$^2S_0$	149.48	55.66	32.03	−59.59	28.56	29.85	−60.75	27.28
$B_{3,0}$	177.43	56.91	3.92	−58.56	56.21	0.89	−58.49	55.91
$^1S_3$	184.76	58.61	−28.96	−29.22	58.79	−28.74	−30.73	62.46
$^{1,4}B$	172.81	58.33	−50.52	−3.62	55.06	−57.15	2.10	51.76
$^1S_5$	150.76	56.36	−58.82	27.14	27.08	−59.79	29.86	27.89
$B_{2,5}$	117.12	58.08	−51.55	53.83	−2.44	−55.80	61.41	−6.39
$^0S_2$	96.26	58.80	−30.75	59.16	−28.87	−29.61	61.29	−28.59
$^{3,0}B$	67.97	61.38	−3.14	58.12	−56.29	−0.76	58.75	−56.74
$^3S_1$	61.07	63.48	29.49	28.95	−58.84	22.88	30.93	−63.96
α-Glc	57.85		56.86	−53.53	52.48	−54.82	61.38	−61.98
β-Glc	179.88		57.49	−53.22	52.23	−55.98	62.40	−62.76

Table 3. The bond angles (deg) of fourteen conformers of 2-methoxytetrahydropyran and of standard α- and β-*D*-glucose residues

Conformer (i)	$\alpha(1)$	$\alpha(2)$	$\alpha(3)$	$\alpha(4)$	$\alpha(5)$	$\alpha(6)$	β
$^4C_1$	110.54	109.32	108.27	108.55	111.67	111.93	108.79
$^1C_4$	106.56	109.60	108.41	108.31	111.75	112.36	108.52
$B_{1,4}$	110.67	112.36	108.52	110.28	112.23	114.60	108.65
$^5S_1$	109.25	111.69	110.93	111.79	113.41	115.02	108.50
$^{2,5}B$	107.97	109.87	109.90	109.97	110.74	112.68	108.00
$^2S_0$	106.80	110.20	110.04	111.89	113.73	113.47	108.33
$B_{3,0}$	106.64	108.75	107.96	109.46	112.29	111.38	108.68
$^1S_3$	106.44	111.40	110.14	111.32	114.19	113.19	108.86
$^{1,4}B$	106.07	112.15	108.74	110.13	112.28	114.59	108.54
$^1S_5$	106.61	111.91	111.07	111.89	113.42	115.20	108.26
$B_{2,5}$	108.02	110.01	110.01	110.00	110.71	112.67	108.19
$^0S_2$	108.69	110.30	110.15	111.88	113.65	113.18	108.76
$^{3,0}B$	110.24	108.73	107.80	109.53	112.01	111.30	109.07
$^3S_1$	110.18	111.48	110.00	111.32	114.10	113.07	109.16
α-Glc	111.60	110.48	110.43	110.19	109.85	113.90	
β-Glc	107.30	110.53	110.30	110.17	110.16	112.27	

and that the standard deviations are within 0.8–1.1 pm. On the other hand, the fact that the deviations shift the bond lengths mainly to smaller values might reflect a certain property of the PCILO method as far as the prediction of the bond lengths is concerned. Recently, when studying α- and β-forms of *D*-glucose, Kildeby *et al.* used the simple force field method [22] involving optimization of geometry. It follows from their work that the bond lengths and bond angles are independent of the ring conformation. From the comparison of the calculated and experimental values obtained for the $^4C_1$ conformers of α- and β-*D*-glucose the following root mean square deviations have been calculated: 1.1 pm for bond lengths, 1.5° for bond angles and 2.6° for torsional endocyclic angles. It should be noted, however, that the force field parameters were fitted to comply with these experimental data. A comparison of torsional angles calculated during this work with those obtained by the force field method shows that whereas they are almost identical for the chair conformation, in the case of skew conformers the torsional angle values calculated by the PCILO method differ considerably from those obtained by the force field method. Owing to the pronounced flexibility of the skew forms the torsion angles calculated for these species of MTHP and saccharides can be expected to differ more than in the case of rigid chair forms, as a result of the presence of hydroxyl groups.

3.2. Conformational Energy and the Charge Distribution

It can be seen from Table 1 that the boat forms possess the highest energy and that the chair forms of MTHP are the most stable ones. Energetically most favored is the $^4C_1$ conformer having the methoxyl group axially oriented. The chair $^1C_4$ conformer bearing an equatorially oriented methoxyl group has energy higher by 3.14 kJ/mol. This value is in excellent agreement with experimental values determined in non-polar solvents (2.9–3.7 kJ/mol) [23–26]. The energetical difference corresponds to the ratio of axial and equatorial MTHP forms of 78:22. Unfortunately, no literature data are available allowing a direct comparison of the energetical differences between the chair, boat and skew MTHP conformers. Infrared and Raman spectral data obtained with tetrahydropyran (THP) reveal, however, the presence of several ring distortion modes, manifested by bands below 500 cm^{-1}, which suggests a relatively free pseudorotation path of the six-membered ring of THP [27–28]. Based on their results, the authors of the cited study assume that the least stable flexible THP form is by about 27 kJ/mol over the chair conformation. A comparison with data observed for cyclohexane shows that this difference is smaller by 9 kJ/mol. Although the course of pseudorotation potential energy of THP will be different as in the case of MTHP, owing to the presence of the acetal segment, it can serve as a basis for the comparison of results obtained during this work. The calculated conformational energies for skew and boat forms are in a reasonable agreement with the conclusions obtained from the analysis of the THP. Whereas the values of conformational energies obtained for boat forms seem reasonable also from the quantitative point of view, the skew form energies seem too low. Although their correctness cannot be *a priori* excluded, they disagree with the results of ^{1}H-NMR studies [23–26]. Several explanations can be offered for the relatively low energy values of the skew forms obtained for MTHP. The complexity of the multidimensional conformational space permits the possibility that the optimized forms do not correspond to the skew forms but to local minima near to chair forms. Another possibility is in the approximations used in the PCILO method itself, most probably because of an underestimation of repulsive terms. Based upon the puckering parameter values (Table 1), by which these species are unambiguously characterized as skew forms, we support the latter of the explanations given above.

An important degree of freedom in MTHP constitutes the rotation about the C(1)–O(1) bond by which the conformation of the glycosidic segment and, thus, the stability of the individual MTHP conformers, is determined. The anomeric and exoanomeric effects postulate the preference of synclinal (*sc*) vs. antiperiplanar (*ap*) conformations during the rotation around the central bonds in the acetal segment. In agreement with the exoanomeric effect in the all ring forms of MTHP (Table 2), the most stable conformation of the methyl group, characterized by the angle Φ, is the *sc* conformation. In the case of angle Θ the value of which is fixed according to the ring shape, and in agreement with the anomeric effect, the more stable of the individual pairs of conformers is the synclinal arrangement, e.g. the $^4C_1$ conformer is more stable than the $^1C_4$ one.

In addition to energetical consequences, the change in the conformation of the acetal segment results also in the change of its geometry. The mutual dependency of the torsion angles Θ and Φ with other geometrical parameters is particularly pronounced for the angle O(5)–C(1)–O(1), the value of which varies in the range of 106.2–110.5° (Table 3) depending upon angles Θ and Φ characteristic of the conformation of the acetal segment in carbohydrates. These questions will be discussed in greater detail in our subsequent work dealing with conformational properties of the glycosidic linkage.

Figure 3 shows the distribution of electronic charges in MTHP for two chair ring conformations. The important information which can be extracted from Fig. 3 are the different charges at the atoms involved in the acetal segment in its different conformations. The charge transfer from the oxygen atoms to the antibonding orbitals of the C(1)–H(1) and C(1)–C(2) bonds is much more pronounced in the $^1C_4$ conformation (the Θ angle is close to the antiperiplanar arrangement) than in the $^4C_1$ conformation (the Θ angle is close to the synclinal arrangement) due to the conformational dependence of the delocalization of lone electron pairs at the oxygen atoms by through-space and through-bond mechanism [21]. At the oxygen atoms there is then in the $^4C_1$ conformation a larger, and at H(1) and C(2) a smaller charge than in the $^1C_4$ conformation.

In the first approximation the dipole moment (μ_i) of the individual forms of the MTHP ring (Table 1) is the vector sum of the two partial dipoles of the C(5)–O(5)–C(1) and C(1)–O(1)–C(6) segments. As a result, the dipole moments of MTHP forms depend almost exclusively upon the conformation of the glycosidic segment. Since in all the conformers the methyl group takes a synclinal position, the determining factor is the conformation of the segment C(5)–O(5)–C(1)–O(1) characterized by the angle Θ. According to the magnitude of the angle Θ all the ring forms

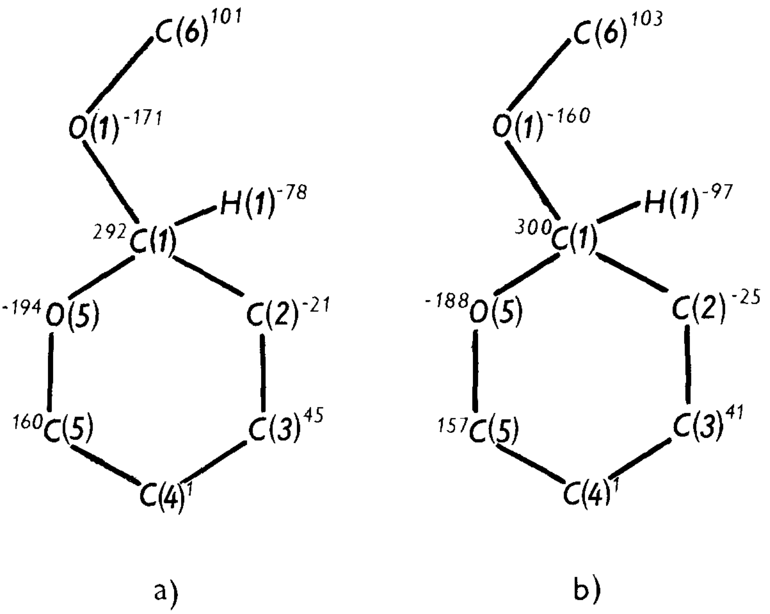

Fig. 3. The distribution of net atomic charges (10^{-3} *e*) in chair conformations of 2-methoxytetrahydropyran having the methoxyl group oriented axially (a) and equatorially (b)

and also their dipole moments can be divided into two groups. To the first group belong forms in which the torsional angle Θ has a value close to that corresponding to the synclinal arrangement with the dipole moments of the segment C(5)–O(5)–C(1) and C(1)–O(1)–C(6) oriented almost antiparallelly. The dipole moment of MTHP forms of this group is therefore small. A change of Θ into the antiperiplanar position results in a change of the orientation of the dipole moment of the C(5)–O(5)–C(1) segment. As a consequence, the dipole moment value is about 2 D. The mean value of the dipole moment (μ = 1.18 D), calculated for MTHP using energy values and dipole moments of the individual conformers (Table 1), is in very good agreement with the experimental value [23] in tetrachloromethane and benzene (1.21 D and 1.23 D, respectively).

4. Conclusions

Conformational energies, geometries and electron distributions for two chair and twelve flexible pyranose forms of 2-methoxytetrahydropyran have been calculated using the PCILO semiempirical quantum-chemical method. The observed values, ΔG = 2.9–3.7 kJ/mol and μ = 1.20 ± 0.05 D, are very satisfactorily reproduced by the values ΔE = 3.14 kJ/mol and $\langle\mu\rangle$ = 1.18 D. As a result of the energetical difference the axial conformer of MTHP with the methyl group in *sc* position is preferred which is also in agreement with the anomeric and exoanomeric effect. Both these effects manifest themselves also in the calculated geometries of the MTHP conformers which depend upon the conformation of the acetal segment of the substance. The dependence of the geometrical parameters upon the torsional angles of the acetal segment is particularly pronounced in the case of the angle O(5)–C(1)–O(1). The comparison of the geometries found for the chair conformers of MTHP with the geometrical parameters of the standard *D*-glucose residues, together with previous results, shows the suitability of the PCILO method for studies of this type, constituting thus a convenient alternative to the more expensive *ab initio* method.

The work described herein is the first quantum-chemical study involving optimization of geometry of the pyranose ring. Although the use of MTHP as the model compound may have given calculated energies and geometries somewhat different from those of saccharides, the results may serve as a starting point for further studies with respect to the flexibility of carbohydrate derivatives. Such a study, together with data on the effect of the solvent upon the conformational equilibrium of MTHP conformers, will be published in our subsequent papers.

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