The conformational behaviour of free \( \text{d-glucose} \)—at last†

José L. Alonso,† María A. Lozoya, Isabel Peña, Juan C. López, Carlos Cabezas, Santiago Mata and Susana Blanco

The conformational behaviour of isolated \( \text{d-glucose} \) has been revealed in this work using Fourier transform microwave spectroscopy coupled with laser ablation of crystalline \( \alpha \)- and \( \beta \)-glucopyranose samples. Four conformers of \( \alpha \)-\( \text{d-glucopyranose} \) and three of \( \beta \)-\( \text{d-glucopyranose} \) have been unequivocally identified on the basis of the spectroscopic rotational parameters in conjunction with ab initio predictions. Stereoelectronic hyperconjugative factors, like those associated with anomeric or gauche effects, as well as the cooperative OH⋯O chains extended along the entire molecule, are the main factors driving the conformational behaviour. The most abundant conformers exhibit a counter-clockwise arrangement (cc) of the network of intramolecular hydrogen bonds.

Introduction

\( \text{d-glucose} \) (\( \text{C}_6\text{H}_{12}\text{O}_6 \), see Fig. 1a) is one archetypical monosaccharide having a critical role in energy metabolism of many living organisms,\(^1\) its residues being components of important polysaccharides, and representing the major building block for many carbohydrate systems.\(^2\) Like other six-carbon monosaccharides, it may exist in either linear or cyclic, pyranose or furanose, forms.\(^3\) In aqueous solution, NMR studies have shown that the pyranose form is the dominant one.\(^4,5\) The nucleophilic addition of the \( \text{C}_5 \) hydroxyl group to the aldehyde group generates a hemiacetal, possessing a chiral center \( \text{C}_1 \). The cyclization leads to the occurrence of two anomeric species, \( \alpha \) and \( \beta \), according to the position of the OH group (see Haworth diagram in Fig. 1b). For the pyranose forms, the chair configuration \( ^4\text{C}_1 \) \((^4\text{C}_1 \) refers to a chair configuration where the \( \text{C}_4 \) carbon is above the reference plane \( \text{C}_2\text{C}_3\text{C}_5\text{O} \) and \( \text{C}_1 \) carbon is found below it, as depicted in Fig. 1c) is dominant, with all substituents but the \( \text{C}_1 \) hydroxyl group (which assumes an axial orientation in the \( \alpha \) anomer) in equatorial orientation.

It is commonly believed that the \( \alpha \) anomer is more stable than the \( \beta \) anomer due to the stereoelectronic anomeric effect.\(^4\) However, when \( \text{d-glucose} \) is dissolved in water, the \( \alpha \) and \( \beta \) anomers are present in a 40 : 60 ratio in the \( ^4\text{C}_1 \) ring conformation. The observed abundance of the \( \beta \) anomer in water could only be explained by taking into consideration strong solvation effects, that overcome the preference for the \( \alpha \) anomer.\(^5\) Moreover, the glucopyranose’s hydroxymethyl group conformation must be considered in terms of three staggered conformers, designated G+, G− and T (see Fig. 1d), associated to the \( \text{C}_6\text{O}_6\text{C}_5\text{O}_3 \) torsional angle, which assumes values of ca. 60°, −60° or 180°, respectively. Experimental observations in both solid phase\(^6\) and solution\(^7\) display approximately equal populations of G+ and G− conformers, with an almost complete absence of the T conformer. This propensity in glucopyranosides to adopt gauche conformations is known as a gauche effect,\(^8\) generally accepted as a solvent-dependent phenomenon.\(^9\) Finally, the structural analysis of \( \text{d-glucose} \) requires the consideration of intramolecular hydrogen bonding between adjacent OH groups. Plausible formation of hydrogen bond networks reinforces their stability due to hydrogen bond cooperativity effects.\(^10\) The orientation of the hydroxyl groups is relevant to distinguish between the different conformers of \( \text{d-glucose} \). A subtle variation in hydroxyl orientation is thought to account for differences in chemical and physical properties of this biologically relevant biomolecule.\(^11,12\)

Although the discussion of all of the above factors goes back many years, a clear dissection of these factors in archetype representative \( \text{d-glucose} \) has not been possible. The experimental results obtained in condensed phases by NMR\(^4\) and vibrational spectroscopy,\(^13\) as well as the X-ray and neutron diffraction,\(^14\) seem to indicate that a subtle balance between intrinsic and environmental effects governs the conformational preferences of \( \text{d-glucose} \). To separate these contributions is crucial to obtain data of the isolated glucose in the gas phase. This highlights the importance of generating glucose in isolated conditions free from the influence of environmental effects to determine its intrinsic conformational properties. This is also relevant to understand its biological activity and to rationalize...
the structure of more complex polysaccharides, cyclodextrines or glycoproteins. Apart from the number of theoretical studies on D-gluco-
pyranose, there are no structural studies of this benchmark molecule in the gas phase, free from solvent influence. Only one vibrational spectroscopic study of \( \alpha \)-D-glucopyranose isolated in an Ar matrix has been reported. The IR signatures were interpreted with the help of \( \text{ab initio} \) computations in terms of the predominance of the three most stable predicted conformers. No comparable work has been reported for \( \beta \)-D-glucose. Laser spectroscopy through UV-UV and IR-UV double-resonance techniques has contributed to the description of the conformations of some \( \beta \)-phenylglucopyranosides and their hydrates. These studies are limited to vibrational resolution and the structural conclusions are not transferable to \( \nu \)-glucose because of the electronic chromophore at the anomeric position. Hence, among the relevant chemical compounds whose structures have been determined, the structure of free \( \nu \)-glucose has remained unknown until now.

In recent years, it has become possible to explore the architecture of solid biomolecules in the gas phase through the development of techniques which combine laser ablation (LA) for transferring them into the gas phase with Fourier transform microwave (FTMW) spectroscopy in a molecular beam (MB). The rotational spectrum is extremely sensitive to the molecular geometry, so conformers can be discerned as totally different species. The shape of drugs such as aspirin\(^{10}\), paracetamol\(^{11}\) and nicotine\(^{12}\) has been also revealed. Recently, this experimental approach has been successfully extended to the monosaccharides \( \nu \)-ribose, 2-deoxy-\( \nu \)-ribose, d-xyllose\(^{15}\) and d-fructose.\(^{16}\)

In this work we have examined for the first time the gas phase structure of \( \nu \)-glucose using this LA-MB-FTMW experimental technique. The low-temperature environment of a supersonic expansion provides the ideal medium for preparing individual conformers of \( \alpha \) and \( \beta \)-D-glucopyranose in virtual isolation conditions ready to be interrogated by a short burst of microwave radiation. The Fourier transformation of the temporal profile of the emanating radiation yields rotational spectra of superb resolution and sensitivity. A comparison of experimental spectroscopic constants with those predicted by high level \( \text{ab initio} \) computations enables us to conclusively identify four conformers for \( \alpha \)-D-glucopyranose and three for \( \beta \)-D-glucopyranose. All factors contributing to stabilization of the observed species have been discussed. Details of the investigation are given in the next sections.

**Methods**

The rotational spectra of \( \alpha \) and \( \beta \)-D-glucose (m.p. = 153 and 157 °C, respectively) have been investigated using our LA-MB-FTMW spectrometer, the details of which are described elsewhere. Solid rods of commercial \( \alpha \) and \( \beta \)-D-glucose samples, were formed by pressing fine powders mixed with minimum quantities of a binder, which were ablated by using a Nd:YAG picosecond laser (35 ps, 10 mJ per pulse). The desorbed products were seeded in Ne (stagnation pressure 15 bar) and expanded adiabatically to form a supersonic jet into a Fabry–Pérot resonator. The delay time between opening the pulsed valve and the laser trigger was adjusted to optimize the amount of neutrals in the supersonic expansion. A short microwave radiation pulse (0.3 \( \mu \)s) in the range 3 to 10 GHz was then applied to macroscopically polarize the vaporized molecules. The microwave transient free-induction decay associated to molecular relaxation was registered in the time domain and

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**Fig. 1** (a) Fisher projection of \( \alpha \)-glucose. (b) Haworth projections of \( \alpha \) and \( \beta \) anomers. (c) \( ^{1}C_{1} \) chair conformations. (d) Newman projections of the plausible conformations of the hydroxymethyl group around C5–C6 and C6–O6 bonds.

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Fourier-transformed to the frequency domain. The pulsed molecular beam was introduced parallel to the axis of the Fabry–Pérot resonator so each observed transition appears as a Doppler doublet. The resonance frequency is determined by the arithmetic mean of the two Doppler components. The estimated Doppler doublet. The resonance frequency is determined by the spectroscopic constants. The agreement between the experimental and theoretical values of stable conformers of \( \alpha \) and \( \beta \)-\( \text{D-glucose} \) is based on the cation of the observed species is based on the 

Thus, we considered the most-stable conformers of \( \alpha \)– and \( \beta \)-\( \text{D-glucose} \) obtained previously from \textit{ab initio} methods, to predict\textsuperscript{25} the rotational constants and the electric dipole moment components relevant for the analysis of the spectra. A summary of these calculations for \( \alpha \) and \( \beta \)-\( \text{D-glucose} \) is given in Tables 1 and 2, respectively. We have used the same notation described before\textsuperscript{123} to label the different conformers. The standard letters \( \alpha \) or \( \beta \) are used to describe the anomer type. The next symbols, describe the configuration of the hydroxymethyl group. The symbol in capital letters, \( G^+ \), \( G^- \) or \( T \), describe the torsion angle \( O_6-C_6-C_5-O_3 \) (see Fig. 1d) of about 60°, \(-60°\) or 180°, respectively. The lower case symbol \( g^+ \), \( g^- \), or \( t \), describe in the same way the torsion angle \( H_6-O_6-C_6-C_5 \) (see Fig. 1d). These symbols are

Table 1  Molecular properties predicted \textit{ab initio}\textsuperscript{a} for the most stable conformers (below 600 cm\textsuperscript{-1}) of \( \alpha \)-\( \text{D-glucopyranose} \)

<table>
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<th>Parameter</th>
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\textsuperscript{a} \textit{Ab initio} calculations (MP2-6-311++G(d,p)). \textsuperscript{b} \( A \), \( B \) and \( C \) are the rotational constants. \textsuperscript{c} Planar inertial moment \( P_x = 0.5(I_x + I_y - I_z) = \sum m_i r_i^2 \), where the sum is extended to all atoms, \( m_i \) is the mass of atom \( i \) and \( r_i \) is its corresponding principal inertial axis \( c \) coordinate. Conversion factor: 505379.1 MHz \( \text{Å}^2 \). \textsuperscript{d} \( \mu_x, \mu_y \) and \( \mu_z \) are the electric dipole moment components (1 D \( = 3.3356 \times 10^{-30} \text{ C m} \)). \textsuperscript{e} Relative electronic energies calculated at MP2/6-311++G(d,p) level of theory. \textsuperscript{f} Gibbs energies calculated at 298 K.

Table 2  Molecular properties predicted \textit{ab initio}\textsuperscript{a} for the most stable conformers (below 600 cm\textsuperscript{-1}) of \( \beta \)-\( \text{D-glucopyranose} \)

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<td>367</td>
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\textsuperscript{a} \textit{Ab initio} calculations (MP2-6-311++G(d,p)). \textsuperscript{b} \( A \), \( B \) and \( C \) are the rotational constants. \textsuperscript{c} Planar inertial moment \( P_x = 0.5(I_x + I_y - I_z) = \sum m_i r_i^2 \), where the sum is extended to all atoms, \( m_i \) is the mass of atom \( i \) and \( r_i \) is its corresponding principal inertial axis \( c \) coordinate. Conversion factor: 505379.1 MHz \( \text{Å}^2 \). \textsuperscript{d} \( \mu_x, \mu_y \) and \( \mu_z \) are the electric dipole moment components (1 D \( = 3.3356 \times 10^{-30} \text{ C m} \)). \textsuperscript{e} Relative electronic energies calculated at MP2/6-311++G(d,p) electronic energies. \textsuperscript{f} Gibbs energies calculated at 298 K.
followed by a slash and the symbol cl or cc describing respectively the clockwise (cl) or counterclockwise (cc) arrangement of the cooperative network of intramolecular hydrogen bonds. Then, after the slash, the last symbol, $g^+$, $g^-$, or $t$, gives the value of the torsion angle $\mathrm{H}_1-\mathrm{O}_1-\mathrm{C}_1-\mathrm{C}_3$ that describes the orientation of the anomeric hydroxyl group hydrogen atom.

**Results**

**Rotational spectrum of $\alpha$-$D$-glucopyranose**

The microwave spectrum of $\alpha$-$D$-glucopyranose was investigated first. Our spectroscopic searches were guided by the estimated values of rotational constants and dipole moment components for each of the six plausible conformers below 600 cm$^{-1}$ shown in Table 1. All conformers are predicted as prolate asymmetric tops with a-type $R$-branch lines, appearing to form regularly spaced bands of $R$-branch transitions at $B=0$ intervals. After completing a wide frequency scan, it became possible to assign the rotational spectra of three different rotamers of $\alpha$-$D$-glucopyranose labelled as $A_3$, $B_3$ and $C_3$. Fig. 2 shows a small section of the recorded spectra showing individual transitions of the detected rotamers. They can be independently studied in the supersonic expansion by their rotational spectra, just as in the case of a mixture of stable species. Following an iterative process of fitting and prediction, new assignments for $\mu_a$-type and $\mu_b$-type $R$-branch spectra for rotamer $A_a$ but only $\mu_a$-type spectra for $B_a$ and $C_a$ rotamers were completed. After discarding the spectra of the observed rotamers, a new set of $\mu_b$-type $R$-branch transitions, belonging to another rotamer $D_a$, was discovered. A rigid rotor model was sufficient to fit the measured frequencies given in the ESI (Table S1†) with residuals smaller than the estimated accuracy of frequency measurements. The obtained spectroscopic constants are collected in Table 3.

The analysis of the experimental inertial data alone provided the first piece of evidence about the shape of $\alpha$-$D$-glucopyranose rotamers. In this molecule the anomeric OH group is always in the axial position and for the most stable predicted conformers the OH groups bonded to $C_2$, $C_3$ or $C_4$ atoms are in the equatorial position (see Fig. 1c). Since the $ab$ inertial plane lies close to the pyranose ring atoms, the planar moment $P_a = \frac{1}{2}(I_a + I_b - I_c) = \Sigma m_i c_i^2$, which gives the mass extension out of the $ab$ inertial plane, could allow distinction between the axial and equatorial arrangement of the oxygen atom of the hydroxymethyl, $-\mathrm{CH}_2\mathrm{OH}$, group. Thus, it has been calculated that rotamers $A_a$ and $D_a$ have $P_a$ planar moments of 82.77 µÅ$^2$ and 76.52 µÅ$^2$, while rotamers $B_a$ and $C_a$ have similar values of 49.15 µÅ$^2$ and 51.83 µÅ$^2$, clearly indicating that the oxygen atom of the hydroxymethyl group is axial to the pyranose ring in conformers $A_a$ and $D_a$, while in conformers $B_a$ and $C_a$ it assumes an equatorial orientation. Ascription now becomes possible: rotamers $A_a$ and $D_a$ can be ascribed to the conformers, $G^-/g^+/cc/t$ and $G^-/g^+/cl/g^-$, while rotamers $B_a$ and $C_a$ could be either $G^-/g^--/cc/g^+$ or the $T$-type conformers of Table 1.

Conformers $G^-/g^+/cc/t$ and $G^-/g^+/cl/g^-$ differ only in opposite-site arrangements of the OH groups; their absolute values of the rotational constants do not allow discrimination between them. However, changing the orientation of the OH groups (from counterclockwise in $G^-/g^+/cc/g^+$, towards clockwise in $G^-/g^+/cl/g^-$) induces small changes in the values of rotational constants of both conformers. Hence, the predicted changes in rotational constants $\Delta A = -17$ MHz, $\Delta B = -3$ MHz, and $\Delta C = 6$ MHz are

![Table 3](Image)

**Experimental spectroscopic constants for the observed rotamers of $\alpha$-$D$-glucopyranose and $\beta$-$D$-glucopyranose**

- $A_b$ and $C$ are the rotational constants. $^b$ Planar inertial moment $P_c = \frac{1}{2}(I_a + I_b - I_c) = \Sigma m_i c_i^2$, where the sum is extended to all atoms, $m_i$ is the mass of atom $i$ and $c_i$ is its corresponding principal inertial axis $c$ coordinate. Conversion factor: 50379.1 MHz u Å$^2$. $^c$ Observation of $a_-, b_-$, and $c_-$ type transitions for each structure. $^d$ Number of measured transitions. $^e$ RMS deviation of the fit. $^f$ Standard errors are shown in parentheses in units of the last digit.
consistent with those $\Delta \omega = -14.3$ MHz, $\Delta \beta = -1.84$ MHz, and $\Delta \gamma = 4.28$ MHz derived from the experimental values of Table 3, thus allowing a conclusive identification of rotamer A$_b$ to G–g+/cc/t and rotamer D$_a$ to G–g+/cl/g–. Notice that rotational spectroscopy is able to track these subtle structural changes that are not accessible for other spectroscopic techniques. In addition, the different arrangements in the orientation of OH groups, cc and cl, give rise to dramatic changes in the values of the dipole moment components and consequently, in the type of the observed transitions, which can serve as an additional support, confirming the conformational assignment. Taking this into account, the observation of only $\mu_b$-type transitions in the rotamer D$_a$ spectra is consistent with the near-zero values of the electric dipole moment components $\mu_a$ and $\mu_c$ for conformer G–g+/cl/t, whereas the observation of c-type transitions in rotamer A$_b$ spectra is also consistent with a predicted value of $|\mu_c| = 1.3$ D for conformer G–g+/cc/t.

The identification of B$_a$ and C$_a$ rotamers as conformers G$+$g–/cc/t and Tg$+$cc/t, respectively, has been based on the excellent agreement between the ab initio and experimental rotational constants in Tables 1 and 3. The observation of $\mu_a$ and $\mu_b$-type spectra and the lack of observation of $\mu_c$-type spectra for both B$_a$ and C$_a$ rotamers is only consistent with the predicted electric dipole moment components for conformers G–g–/cc/t and Tg$+$cc/t, further supporting the identification. Scale factors ranging from 1.002 up to 1.007 brings the ab initio values of the rotational constants for the G–g+/cc/t, G$+$g–/cc/t, Tg$+$cc/t and G–g+/cl/g– conformers nearly into coincidence with the experimental values for rotamers A$_b$, B$_b$, C$_b$ and D$_a$, respectively. This fact clearly shows the global consistency of the conformational assignment. Further searches using predicted rotational constants, corrected by the above scale factors, for the remaining higher-energy conformers Tg$+$cl/g– and Tg–/cl/g– in Table 1, failed to observe any spectroscopic signatures belonging to these conformers.

Taking into account all the above, the ab initio structures (see Table S3 of ESI†) can be taken as a good description of the actual structures of the $\alpha$-$\beta$-glycopyranose conformers depicted in Fig. 3. Their relative abundances in the supersonic jet have been estimated by intensity measurements of selected rotational transitions. These are proportional to their number density in the jet and the corresponding electric dipole moment taken from the ab initio values listed in Table 1. Relative populations of G–g+/cc/g+:G$+$g–/cc/g+:Tg$+$cc/g+:G–g+/cl/g– = 1:0.9(2):0.5(1):0.4(2) are in reasonable agreement with those calculated from the Gibbs free energies in Table 1 of 1:0.90:0.30:0.26. Gauche $^4$C$_1$ glucopyranose forms with a counter clockwise arrangement of OH groups dominate the conformational panorama of $\alpha$-$\beta$-glucose.

**Rotational spectrum of $\beta$-$\alpha$-glucopyranose**

In $\beta$-$\alpha$-glucopyranose, the anomic hydroxyl group adopts an equatorial configuration, so all OH groups bonded to the ring atoms are in the equatorial position. This change with respect to $\alpha$-$\beta$-glycopyranose should be reflected in a different mass distribution along the principal inertial axes of the molecule. The predicted low-energy conformers of $\beta$-$\alpha$-glucopyranose in Table 2 present sizeable values of the $\mu_a$ dipole moment component. We first searched for the most intense $\mu_a$-type $R$-branch transitions with low $K_a$ values. Wide frequency scans soon revealed the presence of three rotamers, which were initially labelled as A$_b$, B$_b$ and C$_b$. $\mu_a$, $\mu_b$ and $\mu_c$-type transitions were measured for rotamer A$_b$, while $\mu_a$- and $\mu_b$-type were collected for rotamer B$_b$. Only $\mu_a$-type lines were observed for rotamer C$_b$. The spectroscopic constants listed in Table 3 were derived from a rigid rotor analysis of the measured transitions (see Table S2 of the ESI†).

As for $\alpha$-$\beta$-glycopyranose conformers, the $P_c$ planar moment can be used to establish the axial or equatorial position of the oxygen atom of the hydroxymethyl group of $\beta$-$\alpha$-glycopyranose. Planar moments of 51.55 u $\AA^2$ for the A$_b$ rotamer and 22.75 u $\AA^2$ and 23.96 u $\AA^2$ for B$_b$ and C$_b$, respectively, allow us to locate the oxygen atom of the hydroxymethyl group in an axial configuration for A$_b$ rotamer ($G$– type conformer) and in its equatorial configuration for B$_b$ rotamer ($G$+ type). The comparison of the experimental rotational constants (see Table 3) with those calculated ab initio (see Table 2) allows definitive identification, ascribing rotamer A$_b$ as being G–g+/cc/t, B$_b$ as being G$+$g–/cc/t and C$_b$ as being Tg+cc/t. The types of observed spectra are in

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**Fig. 3** The four observed conformers of $\alpha$-$\beta$-glycopyranose showing the intramolecular hydrogen bond distances in $\AA$. 
accordance with \textit{ab initio} dipole moment components. Scale factors ranging from 1.002 to 1.005, bringing the \textit{ab initio} values of the rotational constants into coincidence with the experimental ones, reflect the excellent match between theory and experiment (better than 0.6%). Hence, the \textit{ab initio} structures (see Table S4 of ESI†) can be taken as a good approximation of the actual structures of the three \(\beta\)-glucopyranose conformers depicted in Fig. 4. Their relative abundances \(G_{\text{g+}}/\text{cc/t}:G_{\text{g-}}/\text{cc/t}:G_{\text{tg+}}/\text{cc/t} = 0.9(2):1.0:2.1(1)\) obtained by relative intensity measurements\(^{27}\) are in good agreement with those 1:0.90:0.20 derived from the calculated Gibbs free energies of Table 2. Following the same procedure used in \(\alpha\)-glucopyranose, no spectral signatures attributable to other low-energy conformers of \(\beta\)-D-glucopyranose were observed.

Additional spectroscopic searches were conducted with \(\alpha\)- and \(\beta\)-D-glucose samples. No traces of the identified \(\alpha\)-glucopyranose conformers (see Table 3 and Fig. 3) were found in the rotational spectrum of \(\beta\)-D-glucose. No spectral signatures of \(\beta\)-D-glucopyranose conformers (see Table 3 and Fig. 4) were found in the rotational spectrum of \(\alpha\)-D-glucose either. This is a strong indication that the rotational spectrum of laser ablated crystalline samples of \(\alpha\)- and \(\beta\)-D-glucose reflect the \(\alpha\)- or \(\beta\)-D-glucopyranose forms found in the X-ray crystalline studies\(^{8}\) and that no interconversion between \(\alpha\) and \(\beta\) anomers occurs during the laser ablation experiment. This phenomenon takes place through a mutarotation reaction, which is a solvent mediated process, which would not occur that easily especially if the sample is completely dry.\(^{30}\)

**Discussion**

The relative stability among the different conformers of both \(\alpha\)- and \(\beta\)-D-glucopyranose (Fig. 3 and 4) can be rationalized in terms of different contributing factors. These mainly include stereoelectronic effects (gauche and anomeric effects) and intramolecular hydrogen bonding between vicinal OH groups. The \textit{gauche effect}\(^{7}\) is associated with the stabilization of the syncinal (gauche) conformation of two vicinal electonegative groups bonded to a two carbon unit, \textit{e.g.} HO–C–C–OH. In all the observed conformers of \(\alpha\)- and \(\beta\)-glucopyranose, all the adjacent OH groups bonded to the ring carbon atoms adopt a gauche or syncinal configuration.

As mentioned above, crystalline samples of \(\alpha\)- and \(\beta\)-D-glucose do not generate a gas phase equilibrium mixture of \(\alpha\)- and \(\beta\)-D-glucopyranose forms. Although \textit{in vacuo} \textit{ab initio} calculations predict that the \(\alpha\)-D-glucopyranose conformer (432 cm\(^{-1}\)) is more stable than \(\beta\)-D-glucopyranose conformer,\(^{25}\) there is no experimental way to test these predictions. Hence, the results reported here for \(\alpha\) or \(\beta\) anomer forms could only be discussed separately.

The four observed conformers of \(\alpha\)-glucopyranose, depicted in Fig. 3, are stabilized by an anomeric effect; they have a \(1\)\textsubscript{C\text{I}} ring configuration with the anomeric OH group towards the axial position. The hydroxyl groups located at equatorial positions are able to form chains of hydrogen bonds, strongly reinforced by sigma-hydrogen bond cooperativity. This phenomenon is associated with chains or cycles of hydrogen bonds between groups that act simultaneously as proton donors and acceptors. The most abundant \(\alpha\) conformers, \(G_{\text{g+}}/\text{cc/t}\) and \(G_{\text{g-}}/\text{cc/t}\), present a counterclockwise arrangement of the OH groups with a chain of four cooperative hydrogen bonds \(\text{O}_2\text{H} \cdots \text{O}_3\text{H} \cdots \text{O}_4\text{H} \cdots \text{O}_5\text{H} \cdots \text{O}_7\text{H} \cdots \text{O}_9\text{H} \cdots \text{O}_{12}\text{H}\) and an additional \(\text{O}_4\text{H} \cdots \text{O}_5\) interaction with the \(\text{G-} \) or \(\text{G+}\) configuration of the hydroxymethyl side chain, respectively. The least abundant \(\alpha\)-D-glucopyranose conformer presents a clockwise arrangement of three cooperative hydrogen bonds \(\text{O}_2\text{H} \cdots \text{O}_3\text{H} \cdots \text{O}_4\text{H} \cdots \text{O}_5\text{H}\) and one non-cooperative \(\text{O}_4\text{H} \cdots \text{O}_5\text{H} \cdots \text{O}_7\text{H}\). The \(\text{O}_4\text{H} \cdots \text{O}_5\text{H}\) interaction does not take place in the clockwise oriented network, explaining its low abundance. \(\text{D-Xylose, which is the aldopentose analogue to D-glucose, presents similar hydrogen bond networks.}\(^{24}\) Hence, the most abundant conformer of \(\text{D-xylene}\) shows a counterclockwise arrangement of the vicinal hydrogen bonds, while the least abundant conformer exhibits a clockwise arrangement. The two most abundant \(\beta\) conformers \(G_{\text{g+}}/\text{cc/t}\) and \(G_{\text{g+}}/\text{cc/t}\) exhibit the same conformational shape as those observed in \(\alpha\) forms with the obvious differences in the anomeric OH group.

The observation of conformers with an anti orientation of the dihedral angle (\(\text{O}_6\text{C}_5\text{C}_4\text{C}_3\text{O}_3\)) constitutes a remarkable fact. Numerous experimental studies on \(\alpha\) and \(\beta\)-D-glucopyranosides, both in solid\(^{\text{I}}\) and solution phases,\(^{24}\) have shown that the dihedral angle (\(\text{O}_6\text{C}_5\text{C}_4\text{C}_3\text{O}_3\)) displays a preference for \(\text{G-}\) and
G+ gauche configurations, which has been attributed to the gauche effect.⁷ This feature was exemplified in a statistical analysis of X-ray structures of glucopyranosyl derivatives,⁸ yielding a rotamer population of 40:0:60 (G+/T/G⁻). In contrast to previous results, our gas-phase experiment revealed the existence of trans conformations in α-Tg⁺/cc/t and β-Tg⁺/cc/t conformers. In agreement with ab initio calculations, these forms have a higher energy and are less abundant in the jet. Both conformers exhibit a chain of five cooperative hydrogen bonds O₅H···O₄H···O₃H···O₂H···O₁H oriented counter-clockwise involving the hydroxymethyl group. Therefore, the structure and relative stability of isolated α- and β-D-glucopyranose are different from their counterparts in condensed phases.

Conclusion

The present study provides the first experimental information on υ-glucose in the gas phase which has led to the determination of its intrinsic conformational landscape. Four rotamers have been detected for α-glucopyranose and three for β-glucopyranose for which the rotational parameters and relative abundances have been determined. The data provided by LA-MB-FTMW spectroscopy and the fact that they are directly comparable with those of high level ab initio calculations constitute an unmatched tool to achieve the unambiguous identification of the conformers observed. As found for related sugars (ref. 14 and references therein), the glucose conformers are stabilized by the interplay of stereoelectronic hyper-conjugative forces, like those associated with anomeric or gauche effects, and the cooperative OH···O chains extended along the entire molecule. The most stable conformers for α-glucopyranose and β-glucopyranose have practically the same configurations and relative energies, with the exception of the axial (α) or equatorial (β) configuration of the anomeric OH group. This significant change, however, is sufficient to give different physical properties for both species.

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Notes and references

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