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1 **Unravelling the structural features of the monosaccharide**
2 **glyceraldehyde upon mono-hydration by quantum chemistry and**
3 **rotational spectroscopy**

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8 **ABSTRACT**

9 Water is a fundamental molecule for life, and investigating its interaction with monosaccharides
10 is of great interest in order to understand its influence on their conformational behavior. In this
11 study, we report on the conformational landscape of monosaccharide glyceraldehyde, the
12 simplest aldose sugar, in the presence of a single water molecule in the gas phase. This
13 investigation was performed using a combination of Fourier transform microwave spectroscopy
14 and theoretical calculations. Out of the nine calculated conformers, only the lowest energy
15 conformer was experimentally observed and characterized. Interestingly, the presence of water
16 was found to induce structural features in the lowest energy conformer of the glyceraldehyde
17 monomer, with water positioned between the alcohol groups. To analyze this interaction further,
18 Non-Covalent Interaction (NCI) plots were employed to map the intermolecular interactions in
19 the observed species. Additionally, Natural Bond Orbital (NBO) analysis was conducted to study
20 the effects of charge transfer in the monohydrate system. Furthermore, topological analysis

21 based on Bader's Atoms in Molecules theory was performed to gain insights into the observed
22 complex. The results of all three analyses consistently showed the formation of relatively strong
23 hydrogen bonds between water and glyceraldehyde, leading to the formation of a seven-
24 member ring network.

25 **INTRODUCTION**

26 The presence of water and organic compounds was a necessary condition for the emergence of
27 life on early Earth.¹ Water plays a pivotal role in sustaining the functions of living organisms,
28 making it an indispensable element for life. The deep comprehension of its interactions with
29 organic molecules at the molecular level remains of utmost importance in the field of
30 biochemistry.² Additionally, gaining insight into water's impact on gas-phase reactivity, along
31 with its hydrogen complexes that can act either catalysts or inhibitors, has been the focus of
32 numerous recent research studies.³⁻⁵ Carbohydrates fulfill crucial roles in biological systems,
33 serving as both energy storage and metabolic intermediates. Among carbohydrates, sugars are
34 considered one of the most vital molecules for living organisms.⁶ They are indispensable for
35 metabolism and the synthesis of other essential organic compounds such as amino acids and
36 nucleotides. Additionally, sugars are integral components of nucleic acids, namely DNA and RNA.⁷
37 The origin and evolution of life on Earth remain captivating and mysterious, with various models
38 proposed. It has been suggested that biomolecules, including sugars, were initially synthesized
39 through complex chemical processes on early Earth, leading to the production of abiotic sugars.⁸
40 Over two centuries ago, A. Bulterov reported the synthesis of sugars from formaldehyde under
41 basic conditions, a reaction known as the formose reaction.⁹ The synthesis of sugars from basic

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42 building blocks holds great significance in understanding the development of complexity in
43 organic molecules. It is widely believed that sugars were likely formed on the prebiotic Earth
44 through a chemical process known as the formose reaction.¹⁰ Monosaccharides, with the general
45 formula ($C_nH_{2n}O_n$, $n=3-6$), comprise the simplest category of carbohydrates. They are
46 characterized as polyhydroxy aldehydes or ketones containing three or more carbon atoms.¹¹
47 Among monosaccharides, glyceraldehyde ($CH_2OHCHOHCHO$, GA) is the simplest aldotriose which
48 is considered as the first and simple sugar with a chemical molecular formula of $C_3H_6O_3$.¹²
49 Glyceraldehyde has a single asymmetric carbon, and as a result, there are two stereoisomers of
50 this sugar.¹²

51 GA plays a significant role in various processes related to the synthesis of complex organic
52 molecules and the origin of life. It has been proposed as an alternative to formaldehyde in the
53 formose reaction for the production of large sugars.^{13,14} GA also serves as a precursor for the
54 formation of other essential organic molecules essential for life.^{8,15} It can act also as a source of
55 molecules relevant to abiotic synthesis when exposed to ionizing radiation, and leading to sugar
56 and sugar-like molecules such as ketohexose.¹⁶ In carbohydrate metabolism, GA acts as an
57 intermediate compound.¹⁷ Recently, new synthetic experimental approaches have
58 demonstrated that ribonucleotides, essential building blocks for RNA, could potentially originate
59 from simple precursors, including GA, yielding to the formation of pentose aminooxazoline.^{8,18}

60 All these studies show the importance of GA and its derivatives, particularly in their role as
61 fundamental chiral asymmetric building blocks, from which enantiomerically enriched
62 oligonucleotide intermediates were synthesized in a prebiotic RNA World.¹⁹ The gas-phase
63 structure and hydrogen bond networks of the GA monomer has been already reported by *Lovas*

64 *et al.*²⁰ Three conformers have been observed: Conformer I, which is the most stable, Conformer
 65 II with a relative energy of 5.7 kJ.mol⁻¹, and Conformer III with a relative energy of 9.8 kJ.mol⁻¹.
 66 These conformers are stabilized by intramolecular hydrogen bonds. Conformers I and II feature
 67 two such bonds, while Conformer III has one, formed between a hydrogen atom of a hydroxyl
 68 group and an oxygen atom of a carbonyl group.

69 Glycolaldehyde (C₂H₄O₂) and its clusters have been extensively studied leading to the
 70 characterization of the hydrogen bond network involved in the stabilization of the observed
 71 species such as its complexes with water^{21,22} and dimers of glycolaldehyde with water.²³ To our
 72 knowledge, there is no experimental study on the hydration of the C3 monosaccharide
 73 glyceraldehyde in the gas phase. Examining systems stabilized by hydrogen bonds (HB) is very
 74 interesting because HB plays a pivotal role in chemical reactivity, solvation, and the assembly of
 75 materials.²⁴ HB also plays a fundamental role in shaping the structure of biomolecules, upon
 76 which their biological functions ultimately depend. For the glyceraldehyde-water complexes it is
 77 necessary to understand its behavior and the possible structural changes upon hydration. In this
 78 paper, we report the gas phase mono-hydration of simple sugar glyceraldehyde (GA-1w). GA is
 79 very flexible molecules and its interaction with water results in large variety of conformers.
 80 Among the different calculated structures of the monohydrate, the lowest energy conformer has
 81 been observed experimentally. The structural features upon hydration are also discussed. This
 82 study could be of great interest in the understanding of the first step of the chemical prebiotic
 83 evolution at molecular scale of such an important organic sugar, glyceraldehyde.

84 **METHODS**

85 **THEORETICAL CALCULATIONS**

86 Theoretical calculations have been used to predict the conformational landscape of the
87 glyceraldehyde-water complex and consequently facilitate the search of the detectable
88 conformers. Molecular mechanics at the semi-empirical AM1²⁵ level were first performed to find
89 a starting set of low energy conformers of GA-1w. A rich conformational landscape with thirty-
90 two different structures were found by molecular mechanics. GAUSSIAN16 software package²⁶
91 was then used to obtain more precise equilibrium geometries and energetic aspects of the lowest
92 energy conformers. Full geometry optimizations were carried out using different theoretical
93 methods. *Ab initio* second-order perturbation theory Møller-Plesset (MP2)²⁷ and DFT methods
94 M06-2X²⁸ and ω B97xD²⁹ were all performed with the Pople split-valence triple-zeta basis set
95 augmented with diffuse and polarization functions on all atoms (the 6-311++G(d,p) basis set).³⁰
96 The rotational constants and the electric dipole moment components are necessary for the
97 analysis, and they were obtained from calculations. Natural bond analysis (NBO)³¹ of the
98 intermolecular charge transfer involved in the stability of the observed of GA-1w complex was
99 also performed using the MP2/6-311++G(d,p) level of theory. Non-covalent Interaction (NCI)³²
100 analysis was performed to map of the Non-covalent hydrogen bond interactions of the observed
101 GA-1w conformer using Multiwfn software³³ from MP2/6-311++G(d,p) level output. In the main
102 text only MP2/6-311++G(d,p) results are presented, all the other calculations results are
103 presented in the supplementary material.

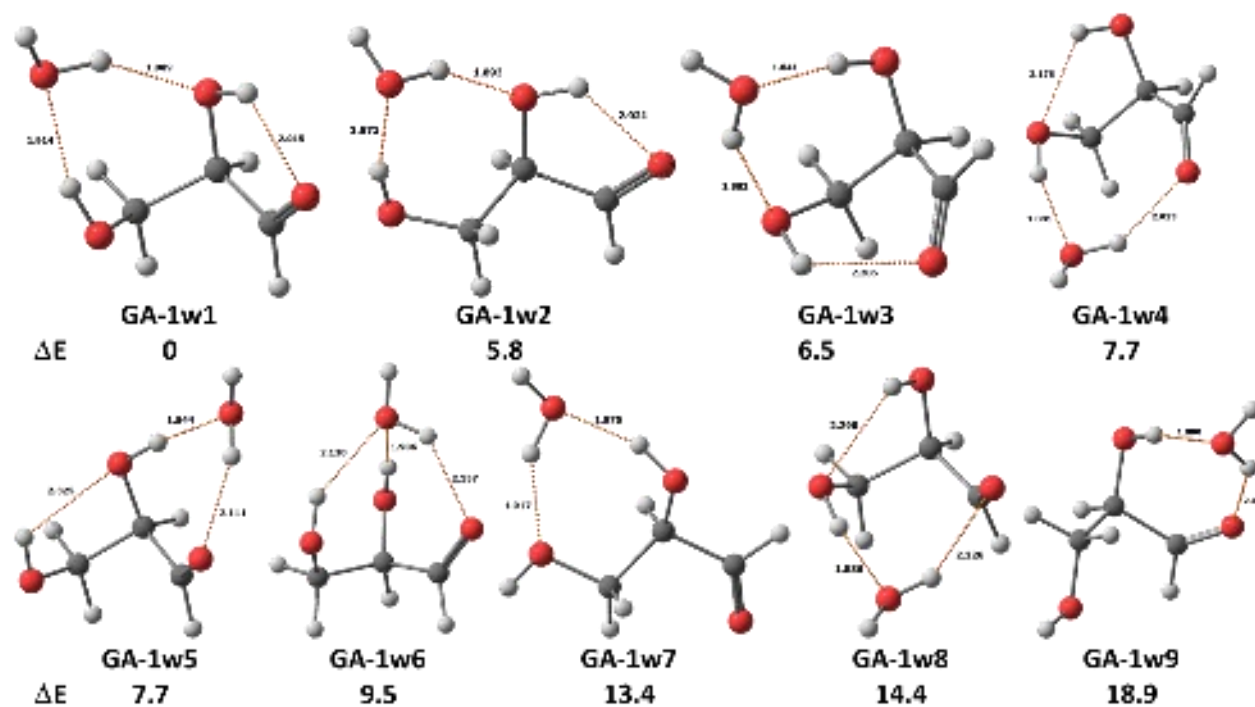
104 **EXPERIMENTAL**

105 The pure rotation spectra of GA-1w have been recorded in the 5–20 GHz frequency range using
 106 impulse Fabry–Pérot supersonic jet Fourier transform microwave (FTMW) spectrometers in Lille,
 107 which have been described in details elsewhere.^{34–36} A commercial sample of Glyceraldehyde
 108 dimer (fluka, 97%) was used with no further purification, placed into nozzle and heated at 370 K.
 109 To create the supersonic expansion a pressure of 3.5 bars of Neon were mixed with the sample.
 110 There was no need to add water, since the thermal decomposition of GA produces water, as
 111 validated by the strong signals of the water dimer. Afterward, the gas mixture was injected into
 112 the Fabry-Pérot cavity, precisely along the optical axis, through a 1 mm diameter pinhole. This
 113 injection was accomplished using a pulsed nozzle, operating at a repetition rate of 2 Hz. The
 114 rotational temperature of the molecules in the supersonic jet is estimated to be about few Kelvin.
 115 To polarize the molecules, microwave power pulses of 2 μ s were employed and Free-Induction
 116 Decay (FID) signal was acquired and digitized at 120 MS/s. To achieve spectra with optimal signal-
 117 to-noise ratios, between 100 and 2000 FID signals were co-added and the experimental precision
 118 is estimated to be approximately 2 kHz.

119 **RESULTS AND DISCUSSION**

120 GA-1w presents a rich conformational landscape governed by a series of hydrogen bonds, as
 121 presented in Fig. 1. All the three series of performed theoretical calculations agreed that only
 122 one lowest energy conformer (GA-1w1) is expected to be observed in the gas phase, since the
 123 second one (GA-1w2) is relatively high in energy (5.8 kJ.mol⁻¹).

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124

125 **FIG 1.** Equilibrium structures of the nine most stable conformers of the GA-1w complex. ΔE represents
126 the relative energies given kJ.mol⁻¹ calculated at MP2/6-311++G(d,p) level of theory. Hydrogen bond
127 lengths are given in Å.

128 The obtained theoretical molecular parameters of interest for rotational spectroscopy (rotational
129 constants, electric dipole moments and relative energies) for the nine conformers are reported
130 in Table I.

131 The lowest energy conformer disposes a μ_c dipole moment component as can be observed from
132 Table I. Surveys were performed to find R-branch c-type transitions. Many lines were observed
133 during the scan. Most of the strong lines are belonging to decomposition products of GA. As
134 mentioned in the paper of Lovas et al.²⁰ the spectra of *t*-methyl Glyoxal, 2-hydroxy-2-propanone
135 and formic acid have been observed. In our study, we made notable observations regarding the
136 prominent transitions associated with glycolaldehyde and formaldehyde. It is widely recognized

137 that the aldol reaction involving glycolaldehyde and formaldehyde can result in the formation of
138 glyceraldehyde³⁷. Evidently, heating is retransforming GA to glycolaldehyde and formaldehyde.
139 Moreover, water clusters such as dimer were found to be very intense also during the survey.
140 Finally, after removing all the known lines, we could identify 18 unknown rotational lines which
141 then were successfully assigned to the glyceraldehyde-water cluster. They were fitted with a
142 Watson's Hamiltonian³⁸ in the *A*-reduction and *I'* representation using SPFIT/SPCAT suits of
143 program.³⁹ As illustrated in Fig. 2, those lines are relatively weak. All were assigned to c-type and
144 b-type transitions.

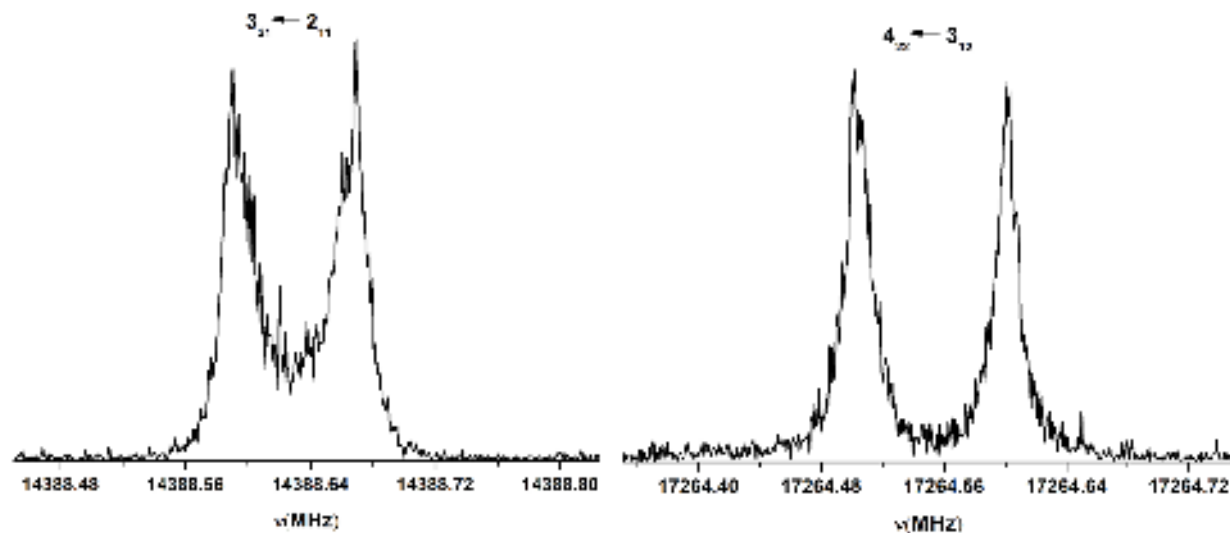
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TABLE I. Spectroscopic parameters of the nine GA-1w conformers as predicted by MP2/6-311++G(d,p) level of theory.									
	GA-1w1	GA-1w2	GA-1w3	GA-1w4	GA-1w5	GA-1w6	GA-1w7	GA-1w8	GA-1w9
<i>A</i> ^a	3407.7	3889.8	2696.3	3264.7	4042.5	2505.6	3916.4	2978.7	3052.7
<i>B</i>	1650.7	1451.2	1864.3	1812.4	1452.9	2155.3	1425.5	1968.9	1599.9
<i>C</i>	1407.7	1130.4	1708.9	317.5	1249.9	1777.8	1148.1	1429.8	1449.7
$ \mu_a $	0.2	1.1	0.3	0.9	1.4	0.4	3.1	2.6	0.5
$ \mu_b $	0.7	0.5	0.8	0.6	0	0.1	2.1	0.1	0.9
$ \mu_c $	1.8	0.9	1.1	0.9	1.9	0.1	0.7	2.2	1.5
ΔE ^b	0	5.8	6.5	7.7	7.7	9.5	13.4	14.4	18.9

^a *A*, *B*, and *C* are the rotational constants in MHz; absolute values of μ_a , μ_b , and μ_c of the electric dipole moment components in Debye. ^b ΔE are the relative electronic energies in $\text{kJ}\cdot\text{mol}^{-1}$ with respect to the global minima calculated at MP2/6-311++G(d,p) level. Only conformers with ΔE below $20 \text{ kJ}\cdot\text{mol}^{-1}$ are reported in the table.

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146

147 **FIG. 2.** High-resolution rotational transitions of the detected complex GA-1w1. Each transition is split by
148 the Doppler effect and labeled with the corresponding quantum numbers $J'_{K'_a K'_c} \leftarrow J_{K_a K_c}$.

149 The experimental rotational parameters are reported in the Table II and their values are
150 compared to those obtained theoretically for the five lowest energy forms of GA-1w. As evident
151 from the results, the observed rotational constants are in excellent agreement with those
152 obtained for the conformer GA-1w1. Furthermore, the experimental microwave polarization
153 power applied to detect b-type rotational transitions was notably higher than that used for c-
154 type transitions. This observation is consistent with theoretical calculations indicating a higher
155 dipole moment component, μ_c , for the GA-1w1 conformer as compared to μ_b . Notably, no a-type
156 transitions were observed, in agreement with theoretical calculations predicting a very small
157 dipole moment component, μ_a . Therefore, the observed species is unambiguously identified and
158 assigned to the lowest energy conformer GA-1w1.

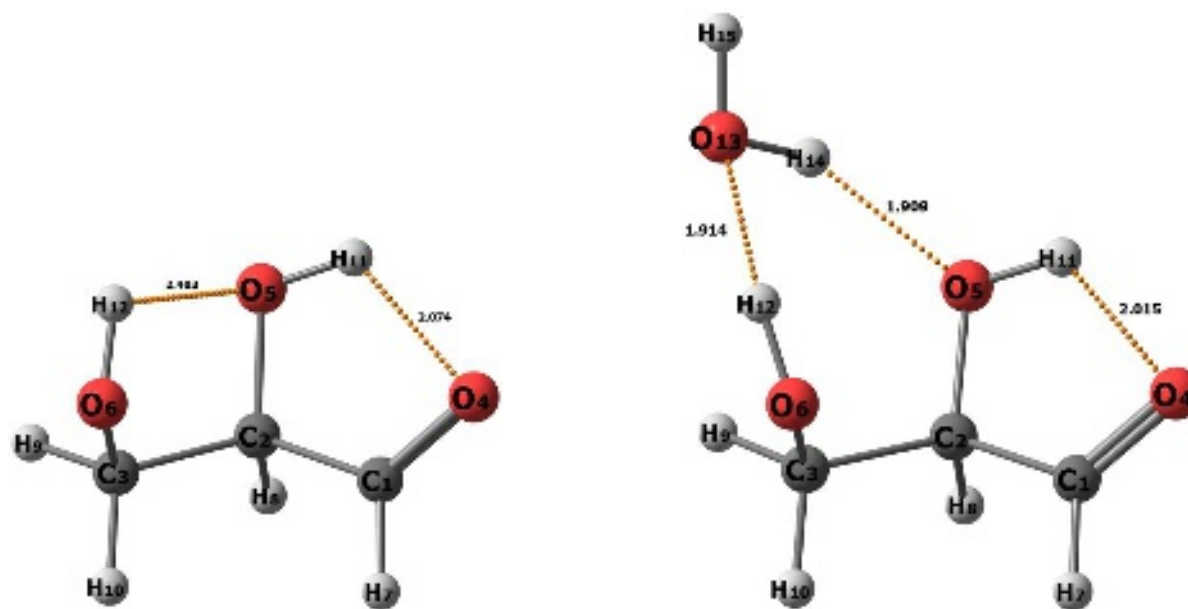
TABLE II. Experimental spectroscopic parameters for the observed monohydrated conformer of glycerinaldehyde-water complex compared with those obtained from MP2/6-311++G(d,p) for the lowest five conformers.

	Exp.	GA-1w1	GA-1w2	GA-1w3	GA-1w4	GA-1w5
A^a	3368.3478(18)	3407.7	3889.8	2696.3	3264.7	4042.5
B	1629.25231(84)	1650.7	1451.2	1864.3	1812.4	1452.9
C	1389.99074(86)	1407.7	1130.4	1708.9	1317.5	1249.9
Δ_J	0.816(16)	0.780	0.381	2.474	0.665	0.438
Δ_{JK}	-3.41(11)	-2.83	-0.128	-9.25	-1.55	0.69
Δ_K	12.97(14)	10.10	5.06	12.0	6.01	4.93
rms^b	5.2	-	-	-	-	-
N^c	18	-	-	-	-	-
$ \mu_a $	Not observed	0.2	1.1	0.3	0.9	1.4
$ \mu_b $	Observed	0.7	0.5	0.8	0.6	0.0
$ \mu_c $	Observed	1.8	0.9	1.1	0.9	1.9
ΔE^d	-	0	5.8	6.5	7.7	7.7
$\Delta(E+ZPE)^e$	-	0	5.4	7.6	6.7	6.0

^a Same parameter definition as in Table I; Δ_J , Δ_{JK} , and Δ_K are the quartic centrifugal distortion constant given in kHz; ^b standard deviation of the fit in kHz. ^c Number of fitted lines. ^d ΔE are the relative electronic energies and in $\text{kJ}\cdot\text{mol}^{-1}$ with respect to the global minima; ^e $\Delta(E+ZPE)$ relative electronic energies including zero-point energy correction in $\text{kJ}\cdot\text{mol}^{-1}$.

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159

160 **FIG. 3.** The calculated structures of the mono-hydrated GA-1w1 (on the right) and of the lowest energy
161 conformer of GA (on the left) observed in ref. ²⁰. Both structures were optimized at MP2/6-311++G(d,p)
162 level of theory. It could be seen clearly the affected hydroxyl group O6H12 upon mono-hydration.

163 The second observation reveals that the angle C1-C2-C3-O6 is smaller in the case of the
164 monohydrate, being approximately 7°, which implies that the water molecule is causing the H12-
165 O6 hydroxyl group to tilt in order to accommodate the water molecule. Additionally, we noticed
166 that the angle H11-O5-C2-C3 is larger by approximately 3° in the monohydrate case. However, it
167 is worth noting that the other geometrical parameters remain very similar in both cases.

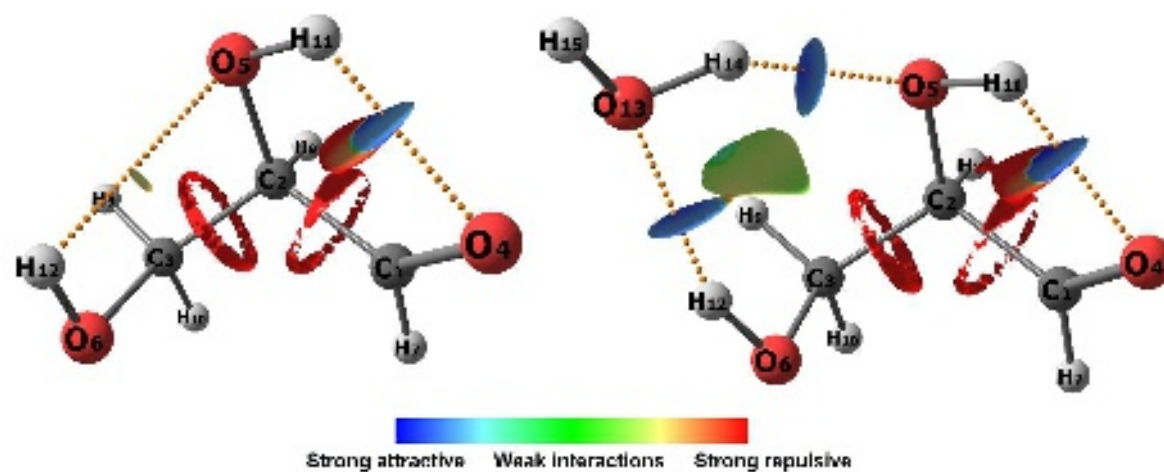
168 As illustrated in Fig. 3, the geometrical structure of the observed complex seems to be similar to
169 the most stable monomer of glyceraldehyde.²⁰ However, many structural features are present
170 upon mono-hydration, affecting the hydroxyl groups and mainly the atoms O6-H12. The complex
171 is characterized by very strong hydrogen bonds formed between water and GA. Water molecule
172 forces the hydroxyl group to adapt its structure. The first observation is the changing of the H12-

173 O6-C3-H9 dihedral angle by about 30° in the case of the hydrate. The insertion of water molecule
174 breaks the intramolecular hydrogen bond O6-H12...O5-H11, forming instead two new hydrogen
175 bonds between water and GA: O6-H12...O13 where water is acting as acceptor, and O13-
176 H14...O5 where water is acting as receptor. The presence of water induces an alteration in the
177 hydroxyl O6-H12 orientation forcing it to adapt its structure upon hydration. This alteration of
178 hydroxyl functional group upon mono-hydration has been observed in some alcohol
179 molecules.^{40,41} Furthermore, a similar phenomenon has been observed in phenyl-substituted
180 monosaccharides such mannose, galactose, and glucose.⁴² In these cases, a water molecule
181 inserts itself into the carbohydrate at a position where it can replace a relatively weak
182 intramolecular interaction forming two stronger intermolecular hydrogen bonds. This
183 substitution results in significant alterations in the conformational preferences of these
184 carbohydrates.^{42,43} Notably, this effect is evident even in the case of the smallest isolated
185 monosaccharide, glyceraldehyde. It is therefore of importance to quantify for benchmark its
186 structural and energy changes for comparisons.

187 **NCI ANALYSIS**

188 To understand the role of hydrogen bond interactions induced by the single water molecule in
189 the structural modification of GA monomer, a Non-Covalent Interaction (NCI) analysis³² of the
190 electron density and its derivative has been performed. Multiwfn software³³ has been used to
191 map the hydrogen bond interaction using the MP2/6-311++G(d,p) level of theory output for both
192 the monomer and the complex with water. The analysis, shown in Fig. 4, is very interesting and
193 permits to compare the monomer and the hydrate of GA. Regarding the monomer of GA, it can
194 be seen clearly that two different interactions are present. The first one is a strong hydrogen

195 bond O5-H11...O4 and a second weak dispersive interaction O6-H12...O5. In the monohydrate
196 the weak dispersive interaction O6-H12...O5 is broken leading to the formation of strong
197 hydrogen bonds between water and GA monomer. These two strong hydrogen bonds are linking
198 O6-H12...O13 and O13-H14...O5. A dispersive interaction is also present and contributes to the
199 stabilization of the hydrate and formed between H15-O13 ...H9.



200

201 **FIG. 4.** NCI map of the lowest energy conformer I of glyceraldehyde and its water complex GA-1w1. The
202 NCI iso-surfaces are showed, for values of $\text{sign}(\lambda_2)\rho$ ranging from -0.04 to $+0.04$ a.u. Blue indicates strong
203 attractive interactions, green indicates weak attractive interactions, and red indicates strong repulsive
204 interactions.

205 **NBO ANALYSIS**

206 NBO analysis is a reliable tool to derive information about the atomic charges, which reflect the
207 relative importance of electrostatic interactions associated with the observed species. To
208 rationalize the transfer of electronic charges of the intra- and inter-molecular interactions of both
209 species, the monomer and complex, natural bond orbital (NBO) analysis³¹ has been performed
210 at the MP2/6-311++G(d,p) level theory. The first general result of the NBO calculations is that the

211 intermolecular interactions can be explained in terms of about 99.3% of Lewis structure and
 212 about 0.7% of non-Lewis structure in both species. The observed values suggest a considerable
 213 degree of charge delocalization within the intermolecular hydrogen bond, which plays a crucial
 214 role in stabilizing the structure. In the case of the monohydrate, the first intermolecular
 215 interaction occurs between a lone pair (LP) of the oxygen atom O13 of water and the anti-bonding
 216 (BD*) orbitals of the O9–H12 bond of GA, directed towards the former with an energy of 36.3
 217 kJ.mol⁻¹. The second intermolecular interaction is formed between a lone pair (LP) of the oxygen
 218 atom O5 of GA and the anti-bonding (BD*) orbitals of the O14–H13 bond of water pointing
 219 toward the former with an energy of 21.8 kJ.mol⁻¹. The intra molecular interaction of GA between
 220 a lone pair (LP) of the oxygen atom O4 of GA and the anti-bonding (BD*) orbitals of the O5–H11
 221 bond of GA pointing toward the former with an energy of 15.5 kJ.mol⁻¹. In the monomer of GA,
 222 the important intramolecular interaction is between a lone pair (LP) of the oxygen atom O4 of
 223 GA and the anti-bonding (BD*) orbitals of the O5–H11 bond of GA pointing toward the former
 224 with an energy of ~11 kJ.mol⁻¹. From those results, we deduced that the intermolecular
 225 interactions between water and glyceraldehyde are very strong and even stronger than the
 226 intramolecular interaction in the monomer. The presence of water increases further the
 227 intramolecular interaction of GA of about 4 kJ.mol⁻¹ which explain the structural feature in the
 228 complex discussed above. Both NCI and NBO analysis are in good agreement and demonstrate
 229 that intermolecular hydrogen bond interaction in the complex are very strong.

230 QTAIM ANALYSIS

231 Bader's quantum theory of atoms in molecules (QTAIM)⁴⁴ analysis is one of the theoretical
 232 methods proposed to uncover the existence of hydrogen bond interactions. Theses analyses

233 reveal the structure by examining the stationary points of the electron density function $\rho(r)$ and
 234 the electron density gradient paths connecting these points. By localizing maxima, it becomes
 235 possible to identify the positions of atoms, whereas saddle points that exist between the maxima,
 236 referred to as bond critical points (BCP), define and characterize chemical bonds. Hydrogen bond
 237 formation occurs when a bond critical point (BCP) exists between the hydrogen atom of the
 238 donor group and the acceptor atom, connected by the associated bond path. As in the case of
 239 NCI and NBO analyses, QTAIM analysis reveals the existence of three critical points corresponding
 240 to three hydrogen bonds in the monohydrated glyceraldehyde, as depicted in Fig. 5. The energies
 241 of the hydrogen bonds, E_{HB} , could be estimated from the electronic potential energy density,
 242 $V(r)$, at the corresponding BCP as $E_{HB} \approx \frac{1}{2}V(r)$, as proposed by *Espinosa et al.*⁴⁵ Using this
 243 approximation we determined for the observed hydrate GA-1w1 the following values for the
 244 hydrogen bonds: the first hydrogen bond O6-H12...O13 has $E_{HB} \approx 28.9$ kJ.mol⁻¹, the second one
 245 O13-H14...O5 has $E_{HB} \approx 29.5$ kJ.mol⁻¹. The intramolecular interaction O5-H11...O4 has an energy
 246 of $E_{HB} \approx 28.9$ kJ.mol⁻¹. For the monomer, a single intramolecular hydrogen bond O5-H11...O4 is
 247 present, having an energy of $E_{HB} \approx 26.5$ kJ.mol⁻¹ which is slightly lower than in the complex. The
 248 QTAIM analysis of charge density showed that the observed GA-1w1 satisfies the criteria of
 249 hydrogen bonding interaction.

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251

252 **FIG. 5.** Graphical representations of molecular structures displaying the results obtained from the
253 QTAIM analysis of the lowest energy conformers of GA monomer (left) and of its water complex
254 GA-1w (right). Critical points are distinguished by various colors: magenta is used for the (3,-3)
255 maxima locating the atoms, orange for the (3,-1) bond critical points (BCP), and yellow for the
256 (3,1) ring critical points (RCP) Brown lines denote bond paths (BP). The equilibrium structures
257 used were computed using the MP2/6-311++G(d,p) level of theory. As observed, one bond
258 critical point (BCP) is observed, indicating the presence of hydrogen bonds between OH and
259 ketone groups in the monomer (right). In contrast, the GA-1w1 complex (left) exhibits two
260 additional BCPs, suggesting hydrogen bonds between water and glyceraldehyde.

261

CONCLUSION

262 The conformational landscape of hydrogen bounded triose sugar glyceraldehyde to water has
263 been investigated through a combination of Fourier transform microwave spectroscopy and
264 quantum chemical calculations. The experimental data have allowed for the unambiguous
265 assignment of the observed rotamer to the lowest energy conformer glyceraldehyde...water
266 complex. It corresponds to the lowest energy conformer of glyceraldehyde forming a hydrogen

267 bond with water. Theoretical molecular parameters of this lowest energy conformer are in very
268 good agreement with the experimental data. In this complex, water acts as both a proton donor
269 and acceptor, forming two hydrogen bonds with the hydroxyl groups of glyceraldehyde. To
270 further understand the hydrogen bonding interactions in the GA-1w1 conformer, analyses such
271 as NCI (Non-Covalent Interactions), NBO (Natural Bond Orbital), and QTAIM (Quantum Theory of
272 Atoms in Molecules) have been employed. These analyses have revealed the presence of
273 relatively strong intermolecular hydrogen bonds that stabilize the observed species. Notably, our
274 results highlight the influence of water in inducing structural modifications of glyceraldehyde,
275 particularly in the hydroxyl group located at the C3 position of the sugar, during the formation of
276 hydrogen bonds. This study provides valuable insights into the nature of the interactions
277 between water and a monosaccharide glyceraldehyde at the molecular level and offers a deeper
278 understanding of the behavior of such systems.

279 **SUPPLEMENTARY MATERIAL**

280 The Supplementary Material contains the calculated parameters of the M062X and ω B97xD with
281 6-311++G(d,p) basis set. In addition, all the fitted lines for the observed GA-1w1. It contains also
282 the cartesian coordinates of the calculated GA-1w geometries.

283 **CONFLICTS OF INTEREST**

284 The authors have no conflicts to declare

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