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Author(s):
Jetzki, Martin; Signorell, Ruth

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The competition between hydrogen bonding and chemical change in carbohydrate nanoparticles

Martin Jetzki and Ruth Signorell

Institut für Physikalische Chemie, Universität Göttingen, Tammannstr. 6, D-37077 Göttingen, Germany

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Broad band Fourier transform infrared spectroscopy was used to study the competition between hydrogen bonding and conformational and chemical changes in molecular nanoparticles. Particles of small carbohydrates (dihydroxyacetone, glyceraldehyde, fructose, and glucose) with sizes between 20 and 100 nm served as model systems. The variation of the preparation conditions allowed to control the chemical composition of the particles. For dihydroxyacetone, the particle generation in an electrospray is accompanied by the formation of intermolecular hemiketals. In contrast, particles generated directly from the vapor phase in a collisional cooling cell consist exclusively of the monomeric form. Quantum chemical simulations demonstrate that conformational changes upon particle formation can be understood to a good approximation on a molecular level. In contrast to that, the characteristic band shape observed for all carbohydrates studied is determined by the interaction of the whole ensemble of OH-oscillators. These contributions could be described within a continuum model. © 2002 American Institute of Physics. [DOI: 10.1063/1.1510744]

I. INTRODUCTION

The spectroscopic investigation of particulate matter of molecular substances leads to one central question: Which properties of the particles can be described on a molecular level and which are inherently ensemble properties? One of the most important factors in this context is certainly the kind of intermolecular interactions (hydrogen bonds, dispersion forces) present in the particles. The best investigated systems held together by hydrogen bonds and dispersion forces are H₂O¹⁻⁶ and CO₂/N₂O⁷⁻¹⁴ respectively. Both systems have been studied over a wide size range from nanometer-sized particles up to particles with radii in the micrometer region. In this size range a wealth of different phenomena appears, the analysis of which is still under current investigation. For instance, the complex band shape observed in the infrared spectra of CO₂ and N₂O particles above about 50 nm is assumed to arise from extended excitation. They originate in the coupling of transition dipole moments and include the whole ensemble of molecules.¹⁵¹⁶ More local effects have been found in small ice particles by Devlin, Buch, and co-workers.⁴⁻⁶ Ice particles below about 20 nm show a layer structure which leads to characteristic absorption in the infrared spectra. In addition, these spectra exhibit a characteristic OH-stretching band near the corresponding band of the free water molecule. This is a local effect which arises from the molecules lying directly on the particle surface.

The present work focuses on the properties of carbohydrate nanoparticles with diameters between 20 and 100 nm. Particles of small carbohydrates are ideal model systems to study the interplay between hydrogen bonding, conformational dynamics, and also chemical changes upon the aggregation of the molecules.¹⁷⁻¹⁹ Recently, we have started to generate particles of nonvolatile substances in an electrospray.²⁰²¹ In the case of dihydroxyacetone,²¹ the particle generation is accompanied by the formation of the intermolecular cyclic hemiketal 2,5-dihydroxymethyl-2,5-dihydroxy-1,4-dioxane. We have interpreted the characteristic band shape in the OH-stretching region in the spectra of these amorphous particles to arise from a certain degree of local order of the dioxane rings in the particles. In the present study, we extend the electrospray generation to other small carbohydrates (glyceraldehyde dimer, fructose, glucose) which enables us to compare the hydrogen bond dynamics in similar particulate systems. The corresponding results are summarized in Sec. IV A.

An important aspect of this contribution is the use of two different techniques for the particle formation, i.e., electrospray generation and collisional cooling (Sec. IV B). In the case of dihydroxyacetone, this allows us to control the chemical composition of the nanoparticles. In addition, the collisional cooling directly from the gas phase leads to interesting conformational changes upon particle formation which can be understood on a molecular level. We conclude in Sec. IV C with a comparison with bulk spectra.

II. EXPERIMENT

The experimental setup for the infrared spectroscopic investigation of the aerosols generated in the electrospray (Sec. IV A) has been described in more detail previously.²⁰²¹ In short, the aerosols are generated in an electrospray (TSI 3480) from aqueous solutions. The particles leave the electrospray supported in synthetic air. To measure the particle number size distribution simultaneously with the infrared spectra, one part of the aerosol flow is guided through a Scanning Mobility Particle Sizer (TSI 3080N, 3022A). The mean diameter of the particles can be varied between 20 and...
100 nm. Typically, the particle size distributions have geometric standard deviation between 1.3 and 1.8 and a total number concentration of about $10^6 \text{cm}^{-3}$. A detailed description of the particle size distributions can be found in Refs. 20 and 21. The remaining aerosol flow enters a multi-reflection cell (see below) for the spectroscopic investigation. The optical path-length amounted to $h = 16 \text{ m}$. The electrospray and the cell were operated at room temperature. The infrared spectra were recorded at a resolution of 2 cm$^{-1}$ with a Bruker IFS 66v/S spectrometer equipped with a Globar light source, a KBr beam splitter, and a MCT detector.

The multi-reflection cell mentioned above can also be used as a collisional cooling cell. The cell and its operation have been described previously. Briefly, the particles are formed by injecting a molecular gas into a cold buffer gas, where, due to the supersaturation, nucleation and condensation take place. In the present investigation, we have used liquid-nitrogen as the cooling medium and helium as the buffer gas. To generate particles also of less-volatile substances, the cell was equipped with a heatable gas inlet. It consists of a heatable sample gas reservoir and a heatable stainless steel tube which projects into the cold cell. The hot sample gas (dihydroxyacetone in He at $T<440 \text{ K}$) was injected through a magnetic valve into the cell by a single gas pulse. Immediately after the gas pulse, three separate infrared spectra were recorded with 30 scans at a resolution of 1 cm$^{-1}$.

The gas phase infrared spectrum of dihydroxyacetone was measured in a heatable three meter long single path glass cell. Thin layers of dihydroxyacetone were prepared by deposition of gas phase dihydroxyacetone on a KBr window. The FTIR spectra of the crystalline carbohydrates were recorded in the form of KBr pellets. The KBr pellets were prepared by grinding KBr with the sample and subsequent evacuating (10 min) and pressing (10 min at 10 tons/cm$^2$) of the mixture. All of these spectra were measured with a Bruker Vector 22 FTIR spectrometer, a mid-infrared Globar light source, and a DTGS detector at a resolution of 2 cm$^{-1}$.

All substances used here were of research grade Fluka puriss. and were used without further purification [(L)-glyceraldehyde dimer (C$_6$H$_{12}$O$_6$), dihydroxyacetone dimer (C$_6$H$_{14}$O$_8$), D-glucose (C$_6$H$_{12}$O$_6$), D-fructose (C$_6$H$_{12}$O$_6$), D-erythrose (C$_6$H$_{10}$O$_4$)].

III. CALCULATIONS

All quantum chemical calculations were performed with the Gaussian program package on the B3LYP/6–31G** or MP2/aug-cc-pVDZ level of theory. Equilibrium geometries, electronic energies, and harmonic vibrational frequencies have been calculated. The density functional theory (DFT) calculations employed integration grids of 50 radial shells with 194 angular points each, pruned to about 7500 grid points per atom. The second-order Moller–Plesset (MP2) calculations included only valence orbitals (frozen core approximation). In the case of 1,3-dihydroxy-2-propanone, we have compared the Becke three parameter Lee–Yang–Parr (B3LYP) with the MP2 calculations for six different conformers to check the reliability of the B3LYP method used for the description of the larger sugars and the hydrogen bonded clusters. This comparison reveals a reasonably good agreement for frequencies and intensities justifying the use of B3LYP for larger systems.

For the band shape analysis in Sec. IV A, we have described the optical properties of the particles with a model of damped harmonic oscillators. This so-called Lorentz model leads to the Kramers–Heisenberg dielectric function

$$
\varepsilon = \varepsilon_1 + \varepsilon_2 = \varepsilon_* + \sum_x \frac{\tilde{\nu}_x f_x}{\tilde{\nu}_x^2 - \nu^2 - i \gamma_x \nu},
$$

and

$$
\eta = \frac{\sqrt{\varepsilon_1^2 + \varepsilon_2^2 + \varepsilon_1}}{2}, \quad \kappa = \frac{\sqrt{\varepsilon_1^2 + \varepsilon_2^2 - \varepsilon_1}}{2}.
$$

$\varepsilon$ is the complex dielectric function and $\varepsilon_*$ is its value at frequencies high compared with the vibrational excitations considered but low compared with electronic excitations. $\gamma_x$ has been held fixed at the value of 2.25$^{21,26}$ The relation between the dielectric function and the complex index of refraction $(n, k)$ is given in Eq. (2). Equation (1) sums over all oscillators in the spectral region of interest which are characterized by their resonance wavenumber $\tilde{\nu}_x$, their reduced oscillator strength $f_x$, and a damping width $\gamma_x$. The Lorentz parameters are optimized in a nonlinear least squares refinement to fit the experimentally observed absorbance between about 800 and 4000 cm$^{-1}$. In these refinements, we have employed the Mie theory$^{25}$ to calculate the frequency dependent extinction cross sections $C_j$ for spherical particles of diameter $d_j$. The Mie theory gives the solutions for the scattering and absorption of light by spherical particles. We assume a spherical shape to be an adequate model for our amorphous particles. With the experimental particle size distribution determined independently as described in Refs. 20 and 21, the absorbance $A_{calc}$ is obtained by summing over all different diameters

$$
A_{calc} = -h \sum_j N_j C_j.
$$

$h$ is the optical path length and $N_j$ corresponds to the number of particles per cm$^3$ aerosol in the size interval $j$. The refractive index of the surrounding medium was set to unity in these calculations.

The absorbance $A_{calc}$ for transmission spectra through thin layers of dihydroxyacetone monomer and dimer in Sec. IV C has been calculated approximately according to:

$$
A_{calc} = a \cdot k/\lambda.
$$

This equation neglects all effects due to reflexions at the different surfaces.$^{25}$ $a$ is an arbitrary scaling factor. Its value is unknown because the thickness of the layer is unknown. $\lambda$ stands for the wavelength and $k$ represents the imaginary part of the complex refractive index. The values of $k$ were derived from the experimental particle spectra exploiting the Kramers–Kronig relation between the real $(n)$ and imaginary $(k)$ part of the refractive index. Details are explained in Ref. 21. This procedure is independent of any particular model for the optical constants.
IV. RESULTS
A. Electrospray generation

In an electrospray, particles of nonvolatile substances are formed by spraying their aqueous solution in a high voltage field and subsequent evaporation of the solvent. We have shown in a previous publication that for the carbohydrate dihydroxyacetone the particle formation in an electrospray is accompanied by a chemical reaction, namely the formation of the intermolecular hemiketal 2,5-dihydroxymethyl-2,5-dihydroxy-1,4-dioxane in Fig. 2. The infrared spectra of these particles exhibit broad bands with little structure in Fig. 1, upper traces. This is an indication of the amorphous nature of the particles.

However, the characteristic band shape of the OH-stretching band has been interpreted to arise from some degree of short range order of the molecules in the amorphous particles due to the presence of strong intermolecular hydrogen bonds. These observations for dihydroxyacetone have raised the question whether such effects are only specific for the particular system or whether they are more general phenomena. To find out more about this, we have investigated nanoparticles of various small carbohydrates which have been generated in an electrospray: D,L-glyceraldehyde (C\textsubscript{3}H\textsubscript{6}O\textsubscript{3}), D-glucose (C\textsubscript{6}H\textsubscript{12}O\textsubscript{6}), D-fructose (C\textsubscript{6}H\textsubscript{12}O\textsubscript{6}), and D-erythrose (C\textsubscript{4}H\textsubscript{8}O\textsubscript{4}).

1. Glyceraldehyde

Glyceraldehyde is an isomer of dihydroxyacetone. In contrast to the latter it exists in two enantiomeric forms, i.e., D(+) and L(−). As outlined in the following, glyceraldehyde and dihydroxyacetone show a similar behavior in the crystalline state as well as in the gas phase. We have measured gas phase infrared spectra of glyceraldehyde and dihydroxyacetone, respectively. Structures (2a) and (1a) in Fig. 2, respectively, in the gas phase. From an x-ray diffraction study we determined that glyceraldehyde exists in the monomeric form 2,3-dihydroxypropanal and 1,3-dihydroxy-2-propanone, and glyceraldehyde monomer [(2a) and (2b): 2,3-dihydroxypropanal], and glyceraldehyde dimer [(2c) and (2d): 2,5-dihydroxymethyl-3,6-dihydroxy-1,4-dioxane, (2e): Five-membered ring]. O, C, and H atoms are represented by dark, medium, and light gray spheres, respectively.

FIG. 1. Upper traces: Experimental infrared spectra of nanoparticles with the empirical formula C\textsubscript{6}H\textsubscript{12}O\textsubscript{6}. The particles were generated in the electrospray. Lower traces: Experimental infrared spectra of the corresponding crystalline substances in KBr [(a) 2,5-dihydroxymethyl-2,5-dihydroxy-1,4-dioxane; (b) 2,5-dihydroxymethyl-3,6-dihydroxy-1,4-dioxane; (c) β-D-fructopyranose; (d) α-D-glucopyranose]. The absolute extinction values apply to the particle spectra. The KBr pellet spectra are scaled to the particle spectra near 1100 cm\textsuperscript{-1}.

FIG. 2. Calculated equilibrium geometries (B3LYP/6–31G**) of different isomers of dihydroxyacetone monomer [(1a) and (1b): 1,3-dihydroxy-2-propanone], dihydroxyacetone dimer [(1c) and (1d): 2,5-dihydroxymethyl-2,5-dihydroxy-1,4-dioxane], glyceraldehyde monomer [(2a) and (2b): 2,3-dihydroxypropanal], and glyceraldehyde dimer [(2c) and (2d): 2,5-dihydroxymethyl-3,6-dihydroxy-1,4-dioxane, (2e): Five-membered ring]. O, C, and H atoms are represented by dark, medium, and light gray spheres, respectively.
TABLE I. Electronic energies ($E$) and vibrational zero point energies (ZPE) with respect to the most stable structures (1a) for the monomeric substances and (1c) for the dimers (see Fig. 2). The electronic energy of the structure (1a) amounts to $-343.584 \pm 0.00 \text{E}_r$, and its ZPE is $20.688 \text{cm}^{-1}$. The electronic energy of the structure (1c) amounts to $-687.188 \pm 0.01 \text{E}_r$, and its ZPE is $43.399 \text{cm}^{-1}$. The dimerization energy ($\Delta H^0_2$; including zero-point correction) for the reaction $1a + 1a = 1c$ is $-2430 \text{cm}^{-1}$ and that for the reaction $2a + 2a = 2c$ amounts to $-2799 \text{cm}^{-1}$. The calculations were performed on the B3LYP/6-31G** level.

<table>
<thead>
<tr>
<th>Substance</th>
<th>Structure (Fig. 2)</th>
<th>$\Delta E(\text{hc} \cdot \text{cm}^{-1})$</th>
<th>$(\Delta E + \Delta \text{ZPE})(\text{hc} \cdot \text{cm}^{-1})$</th>
</tr>
</thead>
<tbody>
<tr>
<td>dihydroxyacetone monomer</td>
<td>(1a)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>(1b)</td>
<td>1582</td>
<td>1748</td>
</tr>
<tr>
<td>glyceraldehyde monomer</td>
<td>(2a)</td>
<td>917</td>
<td>1134</td>
</tr>
<tr>
<td></td>
<td>(2b)</td>
<td>1311</td>
<td>1492</td>
</tr>
<tr>
<td>dihydroxyacetone dimer</td>
<td>(1c)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>(1d)</td>
<td>184</td>
<td>355</td>
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<tr>
<td>glyceraldehyde dimer</td>
<td>(2c)</td>
<td>1857</td>
<td>1899</td>
</tr>
<tr>
<td></td>
<td>(2d)</td>
<td>2000</td>
<td>2068</td>
</tr>
<tr>
<td></td>
<td>(2e)</td>
<td>3622</td>
<td>3561</td>
</tr>
</tbody>
</table>

infrared study,\textsuperscript{32} it is known that the crystalline state of D, L-glyceraldehyde consists of cyclic dimers \[\text{[2,5-dihydroxymethyl-3,6-dihydroxy-1,4-dioxane; structures (2c) and (2d) in Fig. 2] due to hemiacetal formation between a D- and a L-monomer. This behavior is again analogous to that of crystalline dihydroxyacetone. The infrared spectra in KBr of both substances are shown in the lower traces of Figs. 1(a) and 1(b). Due to the dimerization no carbonyl-stretching band is visible in these spectra. In crystalline D,L-glyceraldehyde dimer, the OH and CH$_2$OH groups are in equatorial positions [see structures (2c) and (2d) depicted in Fig. 2] and the OH and CH$_2$OH groups of the different molecules are connected through hydrogen bonds forming an infinite chain.\textsuperscript{31} Kobayashi et al.\textsuperscript{32} have suggested to assign the two bands at 3128 and 3386 cm$^{-1}$ in the KBr spectrum in Fig. 1(b) to the OH-stretching vibration of the hemiacetal OH group and to the OH-stretching mode of the CH$_2$OH group, respectively. In contrast to crystalline D,L-glyceraldehyde dimer, the pure enantiomers are viscous liquids at room temperature, but they also consist of dimers. The present investigation focuses on the racemic compound.

The extinction spectrum of glyceraldehyde aerosol between 800 and 4000 cm$^{-1}$ is shown in the upper trace in Fig. 1(b). The corresponding measured particle size distribution has a maximum diameter of about 95 nm and a total particle volume fraction of $2.4 \cdot 10^{12} \text{nm}^3/\text{cm}^3$. As in the case of dihydroxyacetone aerosol,\textsuperscript{21} no unusual size-dependence of band intensities or band positions for particles between 20 and 100 nm has been detected, neither for glyceraldehyde nor for the other carbohydrates investigated here. In analogy to dihydroxyacetone [Fig. 1(a)],\textsuperscript{21} we interpret the much broader absorption features in the aerosol spectrum of glyceraldehyde compared to the spectrum of the crystalline state as a clear indication of the amorphous nature of these particles. To underpin this interpretation, we have compared our spectra with the aerosol spectrum of D-erythrose (not shown here) which is a viscous liquid at room temperature and does not crystallize.\textsuperscript{33} Indeed, we have found very similar broad absorption features. Apart from the phase, the chemical composition of the glyceraldehyde particles has to be considered. In the electrospray, the particles are formed from aqueous solutions (17 wt%). In aqueous solution, the following species might be present:\textsuperscript{34–37} (1) The chemically bound glyceraldehyde dimer or other hemiacetal rings. (2) The glyceraldehyde monomer, which can easily be detected in solution due to the characteristic carbonyl-stretching band near 1740 cm$^{-1}$. (3) The hydrated form of glyceraldehyde. (4) The enediol which is an intermediate for the interconversion of glyceraldehyde and dihydroxyacetone monomer. (5) Following from point (4), dihydroxyacetone monomer, its hydrated form, and dihydroxyacetone dimer. However, the lack of any carbonyl-stretching band in the aerosol spectrum [Fig. 1(b)] clearly demonstrates that the particles do obviously not contain any monomeric forms. It is also not plausible that they contain significant amounts of the enediol (unstable intermediate) or the hydrated forms (unstable upon drying). Therefore, one expects the particles to be composed of intermolecular hemiacetal or hemiketal rings of glyceraldehyde or dihydroxyacetone. If one assumes equilibrium conditions in the solution before particle formation, the relative concentrations of glyceraldehyde and dihydroxyacetone dimer [$(G_{\text{dim}}/D_{\text{dim}})$] and monomer [$(G_{\text{mon}}/D_{\text{mon}})$] can be roughly estimated from the quantum chemical calculations of the most stable conformers of the isolated molecules listed in Table I [structures (1a), (2a), (1c), and (2c) in Fig. 2; $kT$ is set to be $210 \text{cm}^{-1}$]:

\[
[G_{\text{dim}}]/[D_{\text{dim}}] = e^{-\Delta E_{\text{dim}}/kT} = 1.2 \cdot 10^{-4},
\]

\[
[G_{\text{mon}}]/[D_{\text{mon}}] = e^{-\Delta E_{\text{mon}}/kT} = 4.5 \cdot 10^{-3}.
\]

In these calculations, we have only included the zero point energies and neglected the influence of the solvatization and of other conformers. With the additional assumption of a fast dimerization during the particle formation, Eq. (6) predicts that particles formed from equilibrium solutions should mainly contain dihydroxyacetone dimers even when the solutions had been prepared from pure glyceraldehyde. However, the particle spectrum in Fig. 1(a) is not identical with the particle spectrum in Fig. 1(b). Both spectra have been measured several days after the preparation of the solutions. This observation together with Eq. (6) indicates that equilibrium conditions between glyceraldehyde and dihydroxyacetone have not been established during this time. Consistently with this, we have not found significant differences...
between the particle spectrum in Fig. 1(b) and a corresponding particle spectrum recorded half an hour after the preparation of the solution (not shown here). Both agree within the uncertainty of the measurement. From the difference spectrum of these two spectra, we estimate that the portion of dihydroxyacetone rings in the glyceraldehyde particle spectrum in Fig. 1(b) is clearly less than 15%. Therefore, the particles are very likely to consist mainly of glyceraldehyde dimer.

Of which kind are the ring structures present in the glyceraldehyde dimer particles and which are the predominant conformations? From the experimental spectrum, neither question can be answered conclusively. However, there are two hints which would at least favor six-membered hemiacetal rings. One hint is the observation that the overall intensity distribution in the region between 1500 and 800 cm\(^{-1}\) is very similar in the aerosol and in the KBr spectrum [Fig. 1(b)] [The same is also true for dihydroxyacetone dimer in Fig. 1(a)]. The other indication comes from quantum chemical calculations of the isolated molecules. The calculated spectra of the six-membered rings [structure (2c) and (2d) in Fig. 2] agree better with the experimental spectrum than that of the five-membered ring [structure (2e) in Fig. 2] in the region below 1500 cm\(^{-1}\). In addition, six-membered rings also seem to be preferred energetically (see Table I). For different conformers of six-membered rings, the differences in their infrared spectra and their energetics are rather small. So we cannot decide whether a particular conformer predominates in the particles and if so which conformer this could possibly be. At this point we can still conclude that the particles generated from glyceraldehyde solutions most probably consist of six-membered hemiacetal rings formed from two monomers.

2. Fructose–glucose

Dihydroxyacetone dimer, glyceraldehyde dimer, fructose, and glucose are all isomers with the empirical formula \(\text{C}_{6}\text{H}_{12}\text{O}_{6}\). The discussed dimerization in dihydroxyacetone and glyceraldehyde is the intermolecular analogue of the hemiketal and hemiacetal formation in fructose and glucose, respectively. Thus, it is not surprising that the aerosol spectra of fructose and glucose depicted in the upper traces of Figs. 1(c) and 1(d), respectively, have several features in common with the spectra of dihydroxyacetone and glyceraldehyde. They show similar hardly structured bands which is an expression of the amorphous nature of the aerosol particles. The fact that glucose crystallizes notably better than fructose does not lead to significant differences in the phase behavior of these small particles on the time scale of the experiment (within minutes). The absence of the characteristic carbonyl-stretching band around 1740 cm\(^{-1}\) again indicates that no significant amounts of the open forms (ketone–aldehyde) are present in the particles. However, for these two carbohydrates this is not surprising because neither the crystalline forms\(^{38–40}\) nor aqueous solutions (<1%, see Table II,\(^{36,41–48}\)) do contain appreciable amounts of the open forms. The dominance of ring forms in solution, in the crystal, and in our particle spectra seems to originate in particular from the lowering of the energy on ring formation. This finding is also supported by the quantum chemical calculations of the isolated molecules in Table II. For dihydroxyacetone and glyceraldehyde, the dimeric ring forms, at least for isolated molecules, are also preferred energetically (Table I). Therefore, the observation of appreciable amounts of monomeric form in aqueous solution but not in the solid state for these two substances is likely to be a consequence of entropy.

The question about the kind of ring structures present in the aerosol particles of fructose and glucose cannot be answered conclusively from the spectra in Figs. 1(c) and 1(d) as it is the case for glyceraldehyde. Some hints, however, come from the situation in aqueous solutions, in the crystalline state, and from quantum chemical calculations of the isolated molecules. This is outlined in the following for fructose.

(1) Aqueous solutions of fructose consist mainly of the \(\beta\)-D-fructopyranose (\(\beta\)-D-fructopyranose: 70\% and \(\beta\)-D-fructofuranose: 23\%;\(^{42–47}\) and Table II). (2) In the usual crystalline state, fructose exists also as \(\beta\)-D-fructopyranose.\(^{38}\) Here, the molecules are linked together through infinite chains of hydrogen bonds with several hydroxyl groups acting both as donor and as acceptor. The KBr spectrum of crystalline \(\beta\)-D-fructopyranose is depicted in the

### Table II. Electronic energies (\(E\)) and vibrational zero point energies (ZPE) with respect to the most stable structures (3d) for fructose substances and (4a) for glucose (see Fig. 4). The electronic energy of the structure (3d) amounts to \(-686.9886\) E\(_h\) and its ZPE is 43 336 cm\(^{-1}\). The electronic energy of the structure (4a) amounts to \(-687.1901\) E\(_h\) and its ZPE is 43 607 cm\(^{-1}\). The calculations were performed on the B3LYP/6–31G** level.

<table>
<thead>
<tr>
<th>Substance</th>
<th>Structure (Fig. 4)</th>
<th>In solution %(^{a})</th>
<th>(\Delta E/(h\cdot c\cdot m^{-1}))</th>
<th>((\Delta E + \Delta\text{ZPE})/(h\cdot c\cdot m^{-1}))</th>
</tr>
</thead>
<tbody>
<tr>
<td>D-fructose</td>
<td>(3a) 2</td>
<td>1144</td>
<td>1394</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(3b) 70</td>
<td>-77</td>
<td>61</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(3c) 5</td>
<td>1060</td>
<td>984</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(3d) 23</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(3e) &lt;1</td>
<td>1749</td>
<td>1485</td>
<td></td>
</tr>
<tr>
<td>D-glucose</td>
<td>(4a) 38</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(4b) 62</td>
<td>667</td>
<td>513</td>
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<td></td>
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<td></td>
<td>(4e) 0.3</td>
<td>2617</td>
<td>1986</td>
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</table>

\(^{a}\)References 42–47.

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Assignments of the observed bands are given in Refs. 47 and 49. The good overall agreement of the intensity distribution in the KBr and in the particle spectrum below 1500 cm\(^{-1}\) again points to \( \beta\)-D-fructopyranose. According to the quantum chemical calculations, the \( \beta\)-anomers are the energetically preferred structures in the isolated state (Table II). Figures 3(b)–3(e) show the corresponding calculated infrared gas phase spectra for different isomers of fructose [structures (3a)–(3d) in Fig. 4]. It is clear that the calculated gas phase spectra cannot be compared with the experimental aerosol spectrum (trace a) in the OH-stretching region which is very sensitive to intermolecular interactions. However, the region between 1500 and 600 cm\(^{-1}\) is in general expected to be less sensitive to intermolecular interactions. Under this assumption, a comparison of the calculated with the experimentally observed intensity distribution in this region indicates that the particles consist rather of pyranoses than of furanoses. In summary, point (3) together with points (1) and (2) clearly support a predominance of \( \beta\)-D-fructopyranose in the aerosol particles generated from aqueous solutions of fructose [particle spectrum in Fig. 3(a)].

The spectrum of the glucose particles is depicted in the upper trace of Fig. 1(d). The arguments concerning the ring structures present in the particles are analogous to those made for fructose. Furanose rings are not likely to be present in the glucose particles: They do not significantly contribute to aqueous solutions (Table II; 36,42–44,48) or to the crystalline state [lower trace in Fig. 1(d);39,50–64]. In addition, the quantum chemically calculated infrared spectra for the pyranoses agree better with the experimental spectrum than those of the furanoses [structures (4a)–(4d) in Fig. 4]. As shown for fructose in Fig. 3, the furanose forms of fructose, glucose, and of glyceraldehyde dimer all exhibit a strong absorption band between 1300 and 1500 cm\(^{-1}\) which is not present in the experimental particle spectra. However, because the normal modes are mixtures of many local modes,51,54,63,64 we could not identify one simple origin for these bands. The calculated infrared spectra of \( \alpha\)-D-glucopyranose and \( \beta\)-D-glucopyranose are very similar and do not allow to distinguish between them. The \( \alpha\)-anomer is slightly preferred in the isolated state (Table II) and it is also the preferred anomer upon crystallization. Thus, we can conclude for the glu-
cose particles that they are likely to consist of D-glucopyranose and that a preference of the α–form is at least not in contradiction with the above observations.

3. Hydrogen bonding

The four carbohydrates discussed above are built from similar molecular subunits, most likely from six-membered rings. Nevertheless, their spectra in Fig. 1 exhibit characteristic bands between 1500 and 800 cm\(^{-1}\) which clearly allow to distinguish between them. In the region of the OH-stretching vibrations around 3300 cm\(^{-1}\), however, all four spectra show an almost identical, very broad and unstructured band, which is shaded towards lower frequencies. This is best seen in Fig. 5(a) where the spectra of the four substances are plotted together. This spectral region is dominated by the effects of intermolecular hydrogen bonds in the particles. In the crystalline state, distinct kinds of hydrogen bonds lead to distinct absorption peaks for the four carbohydrates, also at room temperature.\(^{58}\) In the amorphous particles, the OH-stretching region has become unspecific for the four substances in comparison with the crystalline state due to the increase in the inhomogeneous line broadening. The characteristic band shape in Fig. 5(a) thus reflects a more general behavior which is common to all four carbohydrates.

To elucidate this phenomenon, we have performed a band shape analysis assuming a damped harmonic oscillator model (Lorentz model) for the optical properties of the particles (see Sec. III). The Lorentz model leads to the Kramers–Heisenberg dielectric function given in Eq. (1) or alternatively to the complex index of refraction given in Eq. (2).\(^{24,25}\) To calculate the extinction spectra from the refractive index data, we have employed Mie theory for spherical particles [Eq. (3)]. As an example, Fig. 5(b) shows the experimental (full line) and the calculated (dashed line) particle spectrum for glucose. The oscillator strengths (\(\tilde{f}_s\)) and the damping widths (\(\gamma_s\)) of the different oscillators with resonance wave numbers (\(\tilde{\nu}_s\)) are depicted in Figs. 5(c) and 5(d), respectively. The corresponding Lorentz parameters are listed in Table III. Here, we are mainly interested in the OH-stretching region, which is described within our model by a total of six oscillators (see discussion in Ref. 21). The sequence of oscillator strengths and widths found in this region for the particle spectra reveals a hierarchy of hydrogen bonds: Large redshifts (\(\tilde{\nu}_s\)) of OH-stretch transitions are accompanied by an increase of the transition intensity (\(\tilde{\nu}_s^2\tilde{f}_s\)) and a stronger coupling to the environment (\(\gamma_s\)). In analogy to previous results,\(^{23}\) we interpret this observation as a result of a certain degree of short range order in the amorphous solid particles. The nearly identical OH-stretching band observed for the four carbohydrate particles hints at similarities in the kind of short range order for these substances. Taking into account that all these particles are built from similar, rather unflexible rings, a similar hierarchy in hydrogen bonding seems plausible. Another hint for the importance of the rings in this context comes from spectra of particles and layers of dihydroxyacetone which contain dimeric rings as well as monomers (Secs. IV B and IV C). This point will be discussed in Sec. IV C.

### B. Collisional cooling

As mentioned in the previous section, the aqueous solutions used for the electrospray generation of dihydroxyac-
acetone and glyceraldehyde contain an appreciable amount of the monomeric forms. In the spectra of the resulting aerosol particles, however, the characteristic carbonyl-stretching band of the open forms could not be detected. Consequently, the dimerization of the monomers is complete on the time scale of aerosol formation, viz. within seconds. In line with semi-quantitative kinetic studies, the dimerization must be efficiently catalyzed in the protic environment of the aqueous solution. Thus, working under totally aprotic conditions it should be possible to generate a condensed phase of dihydroxyacetone which only contains monomers. The aerosol formation directly from the gas phase, where dihydroxyacetone exists as monomer, fulfills this requirement. The aprotic conditions do not only prevent the formation of intermolecular hydrogen bonds. In the region below 2000 cm$^{-1}$, the two spectra agree astonishingly well, with one exception: The strong band at 1290 cm$^{-1}$ in the gas phase spectrum (labeled with an asterisk) has disappeared in the particle spectrum. One possible explanation is a change in the molecule’s conformation upon aggregation. Thus, the formation of intermolecular hydrogen bonds could lead to a break-up of intramolecular hydrogen bonds. The simulation of the gas phase spectra of different conformers suggests that this is exactly what happens in the case of dihydroxyacetone. The strong band at 1290 cm$^{-1}$ only appears for conformers with an intramolecular hydrogen bond to the carbonyl oxygen. According to the calculations this characteristic band corresponds to the OH-bending motion of the OH-group involved in this hydrogen bond combined with the CH$_2$-wagging motion. This observation is exemplified by the two conformers (1a) and (1b) of Fig. 2, the calculated spectra of which are depicted in Figs. 6(c) and 6(d). In addition, a comparison of traces b and c reveals that the conformer (1a) is primarily present in the gas phase at 373 K from which the particles are formed. From these arguments and from the good overall agreement of the spectra below 2000 cm$^{-1}$ in Figs. 6(a) and 6(b), we conclude that the particles formed in the collisional cooling cell mainly consist of monomeric dihydroxyacetone. The spectrum shows no detectable amount of the dimeric form, for instance through its strong band near 1070 cm$^{-1}$. The dimerization is thus negligible under these conditions.

Quantum chemical calculations for small hydrogen bonded clusters can at least give a hint to the conformers and types of hydrogen bonds present in the amorphous particles. Calculated infrared spectra for different hydrogen bonded dimers of dihydroxyacetone in the region between 2000 and 700 cm$^{-1}$ are depicted in Figs. 7(b)–7(e). For comparison, trace a again shows the experimental particle spectrum. As it is expected from the arguments outlined above, none of the calculated spectra exhibit the prominent band near 1290 cm$^{-1}$. This is in line with the picture that the two intramolecular hydrogen bonds formed in the gas phase are replaced by intermolecular hydrogen bonds in the condensed phase. The overall intensity distribution of the experimental spectrum is best reproduced by the calculated spectra of the two chain-fragments in Figs. 7(b) and 7(c). The agreement for the two ring forms in Figs. 7(d) and 7(e) is slightly worse. However, in view of the level of calculations and the fact that simulations for dimers are compared with condensed phase spectra this observation should not be stressed to much.

Some insight into the spectral changes to be expected when going from dimers to the condensed phase can come from calculations for larger clusters. One example is depicted in Fig. 8. The experimental particle spectrum and the dimer spectrum of Fig. 7(b) are again shown in Figs. 8(a) and 8(b), respectively. Figure 8(c) contains the spectrum of the corresponding trimer and Fig. 8(d) that of the tetramer. In all three clusters, chains of successive (cooperative) hydro-
gen bonds are formed which become stronger for longer chains (larger clusters) due to the cooperative effect. Inter- and intramolecular hydrogen bonds alternate in these chains as can be seen from the molecular structures in Fig. 8. The comparison of the three different calculated spectra reveals that the spectra in the region below 2000 cm$^{-1}$ remain very stable with increasing chain length. The bands in the OH-stretching region become more intense and are redshifted for longer chains due to the cooperative effect. This is consistent with a corresponding decrease in the calculated hydrogen bond lengths. For example, the shortest hydrogen bond in the trimer amounts to 1.773 Å and that in the tetramer to 1.745 Å. For both cases, the OHO bond angle lies around 174°. We conclude at this point that the above simulations are in agreement with the picture of amorphous particles which consist of hydrogen bonded chains containing different numbers of monomers.

C. Comparison with bulk spectra

To compare the aerosol spectra with bulk data, we have recorded Fourier-transform infrared (FTIR) spectra of aqueous dihydroxyacetone solutions (35–75 wt%) and thin layers. The layers have been prepared by deposition of gas phase dihydroxyacetone on a KBr window in the vacuum and by rapid evaporation of saturated dihydroxyacetone–methanol solutions on a NaCl window. The three types of spectra look very similar with the exception of the additional water absorptions in the solution spectra. As an example, the spectrum of the layer obtained by gas phase deposition is depicted in Fig. 9. The two prominent bands at 1738 and 1006 cm$^{-1}$ makes one think of the particle spectrum of the monomeric form in Fig. 6, whereas the broad band around 1070 cm$^{-1}$ draws to the particle spectrum of the dimeric form in Fig. 1.

We have extracted the real ($n$) and the imaginary ($k$) part of the complex refractive index from the particle spectra of Figs. 1(a) and 6(a) using the Kramers–Kronig inversion and Mie theory (see Sec. III). Transmission spectra for layers have then been calculated from the values of $k$ according to Eq. (4). The corresponding calculated spectra are depicted in Figs. 9(b) and 9(a) for a monomeric and for a dimeric layer of dihydroxyacetone, respectively. A comparison between particle and layer spectra reveals only small frequency shifts and changes in the band shapes between the two types of spectra. This is also consistent with the lack of long-range
interactions in these amorphous substances. Figure 9(c) contains the sum of the two calculated spectra in Figs. 9(a) and 9(b). The comparison with Fig. 9(d) reveals a strikingly good agreement from which we conclude that layers and solutions are built up from a mixture of the two chemically different forms of dihydroxyacetone, i.e., monomers and chemically bound dimers. The formation of the dimeric form upon deposition of monomeric gas phase dihydroxyacetone may be astonishing at first sight. However, in contrast to the particle formation with collisional cooling there are always small traces of water present on the KBr window which are able to catalyze the dimerization.

Though the overall intensity distribution in Figs. 9(c) and 9(d) is very similar, the agreement is not perfect. There are several reasons for this. First, we have neglected reflections at the surfaces in the calculations of the layers (Sec. II) as well as the difference in temperature for Fig. 9(b). In addition, we have assumed Fig. 9(c) to be the sum of Figs. 9(a) and 9(b). A mixture of two substances, however, is not simply the superposition of its components because, for instance, different intermolecular interactions can lead to different conformational arrangements. Such effects could be the reason for the observed difference in the band shape of the OH-stretching band in Figs. 9(c) and 9(d). This brings us back to the discussion of the hydrogen bonding in Sec. IV A, where we have found almost identical OH-stretching band shapes for particles consisting of molecular rings with the empirical formula C₆H₁₂O₆. Figure 9(b) finally demonstrates that the band shape for particles consisting of monomers (C₅H₈O₃) clearly differs from those containing dimeric rings [Fig. 9(a)]. From temperature dependent spectra recorded in the collisional cooling cell between 80 and 290 K it is clear that the difference between Figs. 9(b) and 9(a) cannot be explained only by temperature effects. Rather these differences must arise from changes in hydrogen bonding due to the different molecular composition—the conclusion already reached in Sec. IV A.

V. SUMMARY

In the present study, we have investigated the properties of carbohydrate nanoparticles with sizes between 20 and 100 nm. The combination of two different preparation methods (electrospray generation and collisional cooling) with broad band FTIR spectroscopy has allowed us to study the competition between hydrogen bonding, and conformational and chemical changes.

In the case of dihydroxyacetone, we have demonstrated that the chemical composition of the particles can be carefully directed by the variation of the preparation conditions. The particle generation from aqueous solutions in an electrospray is accompanied by the formation of intramolecular hemiketals, i.e., the chemically bound dimers. In contrast to that, the particle growth directly form the vapor in the collisional cooling cell (aprotic conditions) leads to particles which consist of monomeric dihydroxyacetone. A comparison with spectra of the crystalline forms reveals that independent of the preparation method used the particles are amorphous. From a band shape analysis in the OH-stretching region in terms of a Lorentz model, we can further conclude that strong intermolecular hydrogen bonds lead to some degree of short range order in the otherwise amorphous particles. The kind of short range order turns out to be very similar for carbohydrates with similar molecular structure. This has been demonstrated for dihydroxyacetone dimer, glyceraldehyde dimer, glucose, and fructose which all consist of similar molecular rings with the empirical formula C₆H₁₂O₆.

The formation of intermolecular hydrogen bonds can also lead to a preference in the conformation of the mol-
species present in the condensed phase. This has been shown here for dihydroxyacetone monomer particles generated in the collisional cooling cell. The particle formation is accompanied by the break-up of the intramolecular hydrogen bonds present in the isolated molecule. The formation of new intermolecular bonds most probably leads to hydrogen bonded chains with different numbers of monomers. We have simulated the spectra below 2000 cm$^{-1}$ with quantum chemical methods for different hydrogen bonded conformers. These simulations essentially demonstrate that conformational changes can be understood to a good approximation on a molecular level. In contrast to that, the band shape in the OH-stretching region is determined by the whole ensemble of OH-oscillators through homogeneous and inhomogeneous line broadening. These contributions are well described with the continuum model discussed above. The investigation of the temperature dependence of the smallest sugarlike substances, currently under way in our laboratory, will further contribute to a more detailed understanding of the conformational dynamics in particulate matter.

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