Density Functional Calculation of Structural and Vibrational Properties of Glycerol

Riccardo Chelli, Francesco L. Gervasio, Cristina Gellini, Piero Procacci, Gianni Cardini, and Vincenzo Schettino*

Università di Firenze, Dipartimento di Chimica, Via Gino Capponi 9, 50121 Firenze, Italy, and European Laboratory for Nonlinear Spectroscopy (LENS), Largo E. Fermi 2, 50125 Florence, Italy

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The conformational distribution of glycerol is still an open question both in gas and in liquid phase. Density functional calculations on different conformers of glycerol are reported and compared to the experimental infrared spectra of the gas and of the liquid. The experimental infrared spectra of gas and liquid glycerol are fitted by a linear combination of the single conformer ab initio spectra, obtaining the relative conformer concentrations. For the gas the results are in agreement with electron diffraction experiments and with molecular dynamics simulation data. The conformational distribution of glycerol in liquid phase is less accurate but always indicative. Some results about the role of the intramolecular hydrogen bonding in stabilization and in structural features of the conformers are discussed.

I. Introduction

Glycerol (1,2,3-propanetriol) has been the object of numerous investigations for its important role in biochemical reactions.1 Glycerol, although being a molecule without asymmetric carbons, is metabolized asymmetrically.2 This important property must be connected with conformational energetics that render the molecule prochiral.1,2 The molecule is characterized by a high degree of flexibility and, due to the presence of three hydroxyl groups, can give rise to intra- and/or intermolecular hydrogen bonds (H-bonds). Each CH₂OH group can rotate around a CC covalent bond, giving three possible staggered conformations labeled by Bastiansen3 as α, β, and γ. As illustrated in Figure 1, in the α conformation the end oxygen atom is in trans position with respect to the opposite end carbon; in the β conformation, the two oxygen atoms of the CH₂OH and CHOH groups are in trans position; finally, in the γ conformation the oxygen atom of the CH₂OH group is in trans position with respect to the aliphatic hydrogen atom of the CHOH group. Hence six different backbone structures, namely αα, αβ, αγ, ββ, βγ, and γγ, can be identified irrespective of the hydroxyl hydrogen positions. Conformational distribution can be different for different aggregation states, due to the possibility to form intra- and intermolecular H-bonds. In fact, different conformers or mixtures of them have been identified or suggested as predominant in gas,3,4 liquid,5,6 and glassy7 phases. The conformational structure of glycerol has been unambiguously identified only in the crystalline state, where X-ray diffraction4 revealed the presence of only αα backbone conformers. For all other phases, the available experimental and theoretical data are contradictory. Several ab initio studies5,9,10 on the isolated molecule agree to indicate the γγ conformation as the most energetically stable implying, therefore, that in the gas phase glycerol exhibits mainly this conformation. These results seem to be confirmed by a recent experimental study where the gas phase rotational spectrum4 of glycerol has been found consistent with a conformational distribution consisting

Figure 1. Newman projections of glycerol backbone conformations.

* To whom correspondence should be addressed. E-mail: schettin@chim.unifi.it.

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many cases\textsuperscript{18--23} it was shown that this approach is able to accurately reproduce vibrational properties.

Ab initio computed spectra referring to monomer glycerol are here used to evaluate the conformational distribution in the gas phase by performing a fit of the experimental spectra. Furthermore, combined DFT data of monomers and dimers and experimental measurements can yield reliable indications on the conformational distribution of the liquid as well.

The layout of this paper is as follows: in section II some insights on the computational details are given. In section III structural features, related to H-bonding formation, are discussed. In the same section, the main results on the conformational distribution of glycerol in gas and liquid phases are given. Finally, conclusive remarks appear in section IV.

II. Calculations

As previously stated, the most stable backbone structures of glycerol in all phases involve the $\alpha$ and/or $\gamma$ conformations. We have therefore chosen to study 10 different backbone conformers of $\alpha\alpha$, $\alpha\gamma$, and $\gamma\gamma$ kind. The starting structures were taken from previous ab initio studies.\textsuperscript{2,10} For completeness we have also included three structures involving the $\beta$ conformation ($\alpha\beta$, $\beta\beta$, and $\beta\gamma$), for a total of 13 structures. The ab initio calculations have been performed using B3-LYP exchange-correlation functional,\textsuperscript{15,16} as implemented in the Gaussian98 package.\textsuperscript{24} Basis set selection is a key issue in our study because of the high computational cost required in the calculation of the IR and Raman spectra for many different minima. Based on our past experience,\textsuperscript{19} we have used the standard split valence basis set 6-31G(d).\textsuperscript{17} In fact, the combined use of this basis set and of the B3-LYP functional in DFT calculations has been proven\textsuperscript{20,21} to provide an excellent compromise between accuracy and computational efficiency for large and medium-size molecules.

The coordinates of the optimized structures, their frequencies, and corresponding assignment along with IR and Raman intensities are available upon request to the authors.

III. Results and Discussion

A. Structural Properties. The optimized structures of the analyzed conformers are displayed in Figure 2 and labeled with two Greek letters that identify the backbone conformation followed by a number to discriminate, in order of increasing energy, among conformers having the same backbone arrangement and different OH orientations. The energies of the conformers are reported in Table 1 along with those obtained at the MP2 level by Teppen et al.\textsuperscript{10} The energy ordering of the various conformations is not much different in the DFT and

Figure 2. Computed structures of glycerol.
When the oxygen is H-acceptor as well as H-donor (for instance increases on average to 1.427 Å. In fact, in the length markedly depends on the hydrogen donor (H-donor) or respectively.

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<th>TABLE 1: Energies of the Conformers shown in Figure 2</th>
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* Entries in column 2 refer to absolute energies (atomic units) using DFT/B3-LYP method. Entries in columns 3 and 4 are the relative DFT/B3-LYP energies (kJ mol$^{-1}$) with respect to the most stable conformer ($\gamma\gamma1$) without ($\Delta E_{DFT}$) or with ($\Delta E_{DFT-L}$) Lennard-Jones corrections (see text), respectively. MP2 results (column 5) are taken from ref 10.

MP2 calculations. In fact, excluding conformers involving $\beta$ arrangements, one can distinguish three subsets of conformations ($\alpha\gamma1, \gamma\gamma2, \alpha\gamma2, \alpha\gamma3, \alpha\alpha1, \alpha\alpha3, \alpha\alpha4, \alpha\alpha5$), and ($\alpha\alpha3$) with very similar energy above the most stable $\gamma\gamma1$ conformer. The discrepancy is probably due to the absence of the dispersive contribution to the total energy in gradient-corrected DFT calculations. In fact, the DFT energies have been corrected by adding an empirical Lennard-Jones atom—atom contribution based on the standard AMBER force field. As can be seen from Table 1, for most of the conformers the energy difference between the MP2 and the Lennard-Jones corrected DFT values is within 1 or 2 kJ mol$^{-1}$, with the only exception of the $\gamma\gamma2$ conformer whose corrected energy is much too high. This conformer, however, is characterized by a very short O3–O2 distance (2.73 Å) and hence by a strongly repulsive Lennard-Jones (6.305 kJ mol$^{-1}$) contribution, very likely overcorrecting the corresponding DFT energy. In agreement with previous ab initio calculations, the $\beta\beta$ conformer is found with an energy much higher than $\alpha\alpha, \gamma\gamma, \alpha\gamma$ forms. A similar behavior was found for the $\alpha\beta$ and $\beta\gamma$ conformers. This fact is not surprising, as $\beta\gamma, \beta\beta, \alpha\beta$, unlike the others, have only one intramolecular H-bond as can be observed in Table 2 (we arbitrarily assume that an H-bond is established when the O–H distance is shorter than 2.5 Å).

In agreement with MP2 calculations, the most stable conformer is $\gamma\gamma1$. This structure is characterized by the presence of three H-bonds, two of them being relatively strong with a H–O distances of 2.09 Å (H6–O3) and 2.05 Å (H8–O2), respectively (see Table 2). We note that the formation of the shortest H-bonds always occurs in conformers with a typical closed six-membered ring arrangement ($-C-C-O-O-H-O-C-\ldots$). In the $\gamma\gamma2$ and $\beta\gamma$ conformers, for instance, the H8–O2 ($\gamma\gamma2$) and H7–O3 ($\beta\gamma$) H-bonds, belonging to the six-membered ring $-C2-C3-O2-H8-O3-C1-\ldots$ and $-C2-C1-O3-H7-O2-C3-$, have a length of 1.96 and 1.97 Å, respectively.

We observe in general that in all conformations the CO bond length markedly depends on the hydrogen donor (H-donor) or acceptor (H-acceptor) character of the oxygen atom. The C3–O2 average distance is, e.g., about 1.416 Å when O2 is H-donor ($\alpha\alpha1, \alpha\alpha2, \alpha\alpha3, \alpha\alpha4, \alpha\alpha2$), while it increases to 1.433 Å when O2 behaves as H-acceptor ($\gamma\gamma2, \alpha\gamma3$). When the oxygen is H-acceptor as well as H-donor (for instance O1 in the $\gamma\gamma1, \alpha\gamma1, \alpha\gamma2, \alpha\gamma3, \alpha\alpha1, \alpha\gamma4$, and $\alpha\alpha2$ conformers), the H-acceptor effect is dominating and the CO bond length increases on average to 1.427 Å. In fact, in the $\alpha\beta$ conformer, where the H8–O3 hydroxyl group is not involved in H-bonding, the C1–O3 covalent bond is 1.4207 Å.

From Tables 1 and 2, we can observe that the energetically favored $\gamma\gamma$ and $\alpha\gamma$ conformations are often characterized by strong (i.e., short) H-bonds. However, the H-bond length is not the only driving factor for energy stabilization: the $\alpha\gamma2$ conformer is less stable than $\alpha\gamma1$, despite the fact that its H-bonds (H6–O3 and H7–O1) are shorter and hence presumably stronger than in $\alpha\gamma1$. From the analysis of the optimized structures it emerges that an important structural feature for energy stabilization in intramolecular H-bonding is the orientation of the lone pair of the H-acceptor oxygen. For example, in the most stable $\alpha\gamma$ conformer ($\alpha\gamma1$) the H6–O3–H8 angle is 105.4° (very close to the ideal sp$^3$ hybridization value), which means that H6 is pointing toward the O3 lone pair. In $\alpha\gamma2$ the short O3–H6 H-bond forms an angle of 131.3° with the O3–H8 bond, missing by more than 20° the lone pair.

It is indeed remarkable that the most stable backbone conformer of $\alpha\alpha$ type, i.e., $\alpha\alpha1$, has a relatively high energy. We recall that crystalline glycerol is made exclusively by $\alpha\alpha$ conformers and in the liquid and glassy phases the $\alpha\alpha$ conformation, together with the $\gamma\gamma$, is believed predominant. The energy stabilization of $\alpha\alpha$ conformers (as well as $\gamma\gamma$) in the condensed phases should be attributed to the formation of intermolecular H-bonds. This is certainly true in the crystal phase where each glycerol molecule is involved in six intermolecular H-bonds, with three oxygen atoms acting as H-donors and three as H-acceptors.

**B. Vibrational Spectra. 1. Gas Phase.** As stated in the Introduction, there is no agreement on the conformational distribution in the gas phase. Comparison of the gas phase experimental IR spectrum of glycerol to the calculated individual spectra of the various conformers may be of great help in resolving the matter of the conformational composition.
in the gas phase. To this aim, we have computed the vibrational frequencies along with IR and Raman intensities for the conformers of \( \alpha\alpha, \alpha\gamma, \) and \( \gamma\gamma \) types (the Raman intensities have been computed only for \( \alpha\alpha, \alpha\alpha, \alpha\gamma, \alpha\gamma, \gamma\gamma \), and \( \gamma\gamma \) conformers). To put these considerations in a quantitative assessment, the glycerol gas phase spectrum has been calculated as an overlap of the monomer spectra

\[
S_{\text{calc}}(\omega) = \sum_i \sum_j C_{ij}(\omega) e^{-\left(\omega - \omega_{ij}\right)} w^2
\]  

where \( i \) and \( j \) label the normal modes and the conformers, respectively, \( \omega_{ij} \) and \( I(\omega_{ij}) \) are the calculated frequencies and intensities, \( C_{ij} \) is the fractional concentration of the \( j \)th conformer, and \( W \) (common to all the conformers) is related to the band width \( \Gamma \) by the relation \( \Gamma = 2W/\ln2 \). The fit to experiments of the calculated spectrum (3.1) has been estimated through the quantity

\[
F = \frac{\int_{\omega_{\text{min}}}^{\omega_{\text{max}}} S_{\text{exp}}(\omega) S_{\text{calc}}(\omega) d\omega}{\left[ \int_{\omega_{\text{min}}}^{\omega_{\text{max}}} S_{\text{exp}}^2(\omega) d\omega \right]^{1/2}}
\]

The parameter 3.2 will range from 1, when the two spectra are identical, to 0, when there is no overlap between the two spectra. By minimizing the function \( F = 1 - F \) with respect to the adjustable parameters \( C_j \) (\( W \) was fixed to 30 cm\(^{-1}\)) and using \( \omega_{\text{min}} = 550 \text{ cm}^{-1} \) and \( \omega_{\text{max}} = 1600 \text{ cm}^{-1} \), we obtained the best fit to the observed IR spectrum \( (F = 0.96) \) shown in Figure 4. The obtained parameters were \( C_{\alpha\alpha} = 0.83, C_{\alpha\gamma} = 0.15, \) and \( C_{\gamma\gamma} = 0.02. \) The agreement with experiments is satisfactory, and the fit gives the conformational composition at the temperature of the experiment, i.e., 498 K.
Our results are consistent with indications from MD simulation of gas glycerol and agree with previous electron diffraction studies. Since the IR spectrum of the liquid, recorded at 300 K, has many similarities with the experimental gas spectrum in the 750–1600 cm$^{-1}$ region, the conformational composition should not vary dramatically with temperature in the range 300–500 K in going from the gas to the liquid phase.

2. Liquid Phase. Both the IR and Raman spectra of liquid glycerol are available. The Raman spectrum has been obtained in this work and is shown in Figure 5 (see caption to figure for experimental details) compared with the ab initio calculated spectra of some conformers.

Derivation of the conformational distribution in the liquid phase using the same procedure as in the gas phase poses some problems. In fact, in the gas phase it could safely be assumed that the experimental spectrum was the superposition of contributions from spectra of the various conformers since formation of associated species (dimers, trimers, etc.) is unlikely in the gas. On the contrary, in the liquid one should expect strong intermolecular H-bonds are formed which are associated with novel intermolecular bands and with significant shift or increased intensities of the fundamentals. These effects are more likely to occur in the low-frequency region of the spectrum ($\omega < 700$ cm$^{-1}$) and in the OH stretching region.

For these reasons, before proceeding to a fit of the liquid spectra, we decided to verify the actual effect of intermolecular association to the vibrational spectra. For this purpose the ab initio IR and Raman spectra of $\alpha\alpha\cdots\alpha\alpha$, $\alpha\alpha\cdots\alpha\gamma$, and $\alpha\gamma\cdots\alpha\gamma$ dimers were calculated optimizing the structures of the dimers to allow for a distortion of $\alpha\alpha1$, $\alpha\alpha2$, $\alpha\gamma1$, and $\alpha\gamma2$ monomers. In the dimers multiple and strong intermolecular H-bonds are formed (three H-bonds for each dimer) with O–H bond distance ranging from 1.76 to 1.94 Å. In Figures 6 and 7 the dimer spectra are compared with the sum spectra of the monomer partners. From the figures it can be seen that both in the low-frequency region and in the OH stretching region the dimer spectrum drastically differs from the monomer sum spectrum. This is most clearly evident from the low values of the $F$ factor calculated according to eq 3.2. It is therefore evident that these spectral regions are not suitable for a fit of the liquid spectrum in terms of monomers’ contributions. However, it can also be seen from Figures 6 and 7 that in the 750–1500 cm$^{-1}$ frequency region the association effect in the dimers is not much pronounced and, in fact, the $F$ factor is higher than 0.89. Therefore, this spectral region can be confidently used also in the liquid phase to sort out a conformational distribution from a fit of the observed spectra to a superposition of monomer spectra. We consider this to be reliable at a semiquantitative level in view of the fact that the association effects on the

**Figure 5.** Calculated Raman spectra of monomers (see text for details) compared to the experimental Raman spectrum of liquid glycerol, measured using the 514.5 nm line of an Ar$^+$ laser with resolution 2 cm$^{-1}$.

**Figure 6.** Calculated IR spectra of the dimers (full line) and sum spectra of the corresponding partners (dashed line). The $F$ factors are defined in eq 3.2.
spectra, certainly important in the liquid state, can only be crudely evaluated by our calculation on tightly H-bonded dimers.

By using the same procedure as in the gas phase, a single and well-defined global minimum was obtained for the $C_j$ parameters (see eq 3.1) from the IR spectrum. By contrast, the fit of the Raman spectrum yielded multiple and high valued minima for the $g$ function with disparate and unreliable values of the $C_j$ coefficient. The failure of the fitting procedure in the case of the Raman spectrum can be due mainly to a poor reliability of the calculated Raman intensities. In fact, it is now well established that electronic polarizability is very sensitive to the basis set size and therefore the 6-31G* basis set may not be entirely reliable for predicting Raman activity.

The best fit of the IR spectrum yields $F = 0.938$ (eq 3.2), a value slightly lower than in the gas phase. The resulting fractional concentrations are $C_{\alpha\alpha} = 0.74$, $C_{\alpha\gamma} = 0.07$, and $C_{\gamma\gamma} = 0.19$ (with $W = 30.0$ cm$^{-1}$). We remark that the $\gamma\gamma$ contribution is entirely given by the $\gamma\gamma2$ form. This form in the calculated monomer IR spectrum shows a well-defined absorption band at about 650 cm$^{-1}$ that does not seem to have a counterpart in the experimental spectrum. Furthermore, the presence of a significant quantity of $\gamma\gamma$ in the liquid is unlikely from both theoretical and experimental indications. If we perform the fit by arbitrarily excluding the $\gamma\gamma2$ conformer from eq 3.1, we find a result similar to that found in the gas phase, i.e., $F = 0.93$, $C_{\alpha\alpha} = 0.70$, $C_{\alpha\gamma} = 0.27$, and $C_{\gamma\gamma} = 0.03$. Such a result is in agreement with MD simulations on liquid glycerol.

It can therefore be concluded that on the basis of DFT calculations, even if quantitative conclusions on the conformational composition of the liquid glycerol cannot be drawn, the liquid composition should be similar to that in the gas phase and in particular that $\alpha\alpha$ conformer is the more abundant.

**IV. Conclusions**

We have performed ab initio calculations of the structural and vibrational properties of glycerol in order to obtain information on the conformational equilibria in the gas and liquid phases. By comparing calculated intensities to available experimental data, we have gathered convincing evidence that gaseous glycerol basically exists in two forms, the $\alpha\alpha$ and the $\alpha\gamma$ structures, and all other forms, including the very stable $\gamma\gamma$ form, have a negligible concentration. The strong similarity of the experimental spectra of the gas and of the liquid in the 750—1600 cm$^{-1}$ spectral region implies that the conformational composition of the liquid is similar to that of the gas phase. As there is widespread agreement in the literature on the fact that in condensed phase the $\alpha\alpha$ form is prevalent, the similarity of the gas and liquid IR spectra can be used as further evidence of the existence of the $\alpha\alpha$ form in the gas phase. Our combined ab initio and experimental approach confirms the prediction of a recent MD investigation on glycerol, where conformational distribution of the gas and liquid phases were found to be very similar and weakly dependent on temperature in the range 300—400 K and consisting mainly of $\alpha\alpha$ and $\alpha\gamma$ conformers. Our results are also in agreement with earlier electron diffraction studies on the gas phase of glycerol and on more recent neutron scattering measurements in liquid phase.

It seems that these conclusions are not in agreement with the rotational spectrum obtained by Maccaferri et al. on free jet expanded glycerol, which could be interpreted considering that only the $\gamma\gamma$ and $\alpha\gamma$ conformers are present in the gaseous sample. In the assumption that the conformational distribution at the temperature of the preexpanded gas (423 K) is fully quenched during the expansion, the $\alpha\alpha$ conformer should be revealed in the rotational spectrum, since its dipole moment is similar in magnitude to those of $\gamma\gamma$ and $\alpha\gamma$, and the rotational constants of the various conformers differ appreciably (as is reported in the additional material available from the authors).
However, it is well-known\textsuperscript{29,30} that when the interconversion energy barriers are low, as it is the case for glycerol,\textsuperscript{11} a structural relaxation occurs during the expansion. This relaxation can be particularly effective if argon is the carrier gas as in the experiment by Maccaferri et al.\textsuperscript{4} If this is the case, the difference from Maccaferri’s results can be explained.

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References and Notes