Vibrational Raman and Raman Optical Activity Spectra of D-Lactic Acid, D-Lactate, and D-Glyceraldehyde: Ab Initio Calculations

Magdalena Pecul*

Department of Chemistry, University of Warsaw, Pasteura 1, 02-093 Warsaw, Poland, and Istituto per i Processi Chimico-Fisici[†] del C.N.R., Area della Ricerca di Pisa, Via Moruzzi 1, I-56124 Pisa, Italy

Antonio Rizzo[‡]

Istituto per i Processi Chimico-Fisici del CNR, Area della Ricerca di Pisa, Via Moruzzi 1, I-56124, Pisa, Italy

Jerzy Leszczynski

Computational Center for Molecular Structure and Interactions, Department of Chemistry,
Jackson State University, Jackson, Mississippi 39217

Received: April 22, 2002; In Final Form: August 12, 2002

Vibrational Raman and Raman optical activity (VROA) spectra have been obtained ab initio for various conformations of D-lactic acid, D-lactate, and D-glyceraldehyde. The calculations have been carried out at the linear response self-consistent field level. The VROA spectra have been found to be very sensitive to the conformational changes. The VROA parameter of the stretching vibration of the carbonyl group is shown to be a promising parameter for structural investigations because it changes sign when a short internal hydrogen bond OH···OC is formed. Raman spectra do not exhibit such sensitivity to the molecular conformation, although an analysis of the stretching vibrations of the hydroxyl group can also be helpful in localizing internal hydrogen bonds.

I. Introduction

Vibrational Raman optical activity (VROA), until recently a scientific curiosity, is now receiving much attention as a probe of molecular conformation, in particular for biomolecules.[1,2] VROA spectroscopy, in contrast to conventional Raman spectroscopy, discriminates between individual enantiomers and as such it is suitable for the study of optically active molecules, to which class the building blocks of living matter belong. Nowadays the advancement in laser technology enables us to collect spectra of biologically interesting molecules (such as peptides and nucleotides) in an aqueous environment.[1,2]

The ab initio calculation of VROA spectra is a difficult and time-consuming computational task. To predict a VROA spectrum, it is necessary to evaluate the geometric derivatives of the dynamic electric dipole−electric dipole polarizability α, of the optical activity tensor $\mathbf{G}'$, and of the electric dipole−electric quadrupole polarizability $\mathbf{A}$. Such computations are in general time-consuming, especially when the derivatives are taken numerically. Moreover, as it is usual in the case of calculations of properties involving magnetic dipole and electric quadrupole moment operators, the problem of origin dependence of the results arises. As a consequence, most of the theoretical studies of the VROA effect have been focused on the smallest molecules exhibiting vibrational optical activity, such as CFHDT, H_2O_2, and methyloxirane.[3,4] There are also several theoretical studies in the literature predicting the VROA spectrum of alanine,[5−7] the smallest chiral amino acid. Recently, the VROA spectrum of a model peptide has been simulated by means of the sum-over-states density functional theory (SOS-DFT) method.[8] The spectrum of L-alanyl-L-alanine dipeptide has been also calculated.[9] However, to our knowledge, no ab initio calculations of the VROA spectra of carbohydrates, the other important class of biologically active molecules, have been reported in the literature.

In this paper we try to fill this gap. Frequency-dependent linear response self-consistent field calculations of the Raman and VROA spectra of lactic acid (also in its deprotonated form) and glyceraldehyde have been carried out. Gauge invariant atomic orbitals (GIAO) are employed. The two molecules play a primary role in metabolism and are at the same time the simplest examples of chiral carbohydrate and chiral aldaric acid, respectively. Spectra have been calculated for several conformers of each molecule and, additionally, for the lactic acid anion. We hope that the analysis of the influence of molecular conformation on the Raman and VROA spectra of these biologically active compounds will contribute to the development of VROA spectroscopy as a tool for structural studies.

To our knowledge no experimental VROA spectra of the molecules investigated here are available in the literature. The Raman spectra of lactic acid and sodium lactate have been collected in aqueous solution.[10,11] It is difficult to investigate glyceraldehyde, present in most solvents in the form of dimers, by means of spectroscopic methods. However, the Raman and IR spectra of solutions containing glyceraldehyde have been reported in the literature,[12,13] and some of the bands have been ascribed to monomeric glyceraldehyde. It should be noted that hydration breaks internal hydrogen bonds in these molecules, changing significantly the molecular conformation,[13] so the

---

* Corresponding author. E-mail: magda@joanna.chem.uw.edu.pl. Permanent address: University of Warsaw.

[†] Formerly Istituto di Chimica Quantistica ed Energetica Molecolare.

[‡] E-mail: rizzo@icqem.pi.cnr.it.

10.1021/jp021030m CCC: $22.00

comparison of the theoretical predictions with the experimental spectra would be problematic even if more experimental data were available. However, the main task of the paper is to get some insight into the influence of the molecular conformation (and in particular of the presence of internal hydrogen bonds) on the VROA spectra using glyceraldehyde and lactic acid as model compounds, rather than to predict the actual spectra of these molecules.

In the next section the theory underlying the calculation of VROA is briefly outlined and the computational details are given. The results of the calculations are reported in section III. First, the optimized structures of the molecules under study are described, then the Raman and VROA spectra are discussed. Finally, the calculated spectra are compared, when possible, with experiment. The paper ends with a summary.

II. Theory and Computational Details

A. VROA. The VROA effect is usually described by means of the absolute difference between scattered intensities with linear α-polarization for right- and left-circularly polarized incident light, $I_\alpha^R - I_\alpha^L$, or by means of the relative dimensionless circular intensity difference (CID) Δ_α[14]

$$\Delta_\alpha = \frac{I_\alpha^R - I_\alpha^L}{I_\alpha^R + I_\alpha^L} \tag{1}$$

We shall present here the absolute VROA parameter $I_\alpha^R - I_\alpha^L$ for backscattering configuration, Δ(180°), which for Rayleigh optical activity is proportional to[14]

$$\Delta(180°) \sim 24\left[\beta(G')^2 + \frac{1}{3}\beta(A)^2\right] \tag{2}$$

For linearly polarized incident light in the backscattering configuration the Rayleigh intensity I is proportional to[15]

$$I \sim 90\alpha^2 + 8\beta(\alpha)^2 \tag{3}$$

Here α, $\beta(\alpha)$, $\beta(G')^2$, and $\beta(A)^2$, are invariants of the electric dipole−electric dipole polarizability tensor **α**, the optical activity tensor **G′** tensor, and the electric dipole−electric quadrupole polarizability **A** tensor, respectively, i.e.

$$\alpha = \frac{1}{3}\alpha_{\alpha\alpha} \tag{4}$$

$$\beta(\alpha)^2 = \frac{1}{2}(3\alpha_{\alpha\beta}\alpha_{\alpha\beta} - \alpha_{\alpha\alpha}\alpha_{\beta\beta}) \tag{5}$$

$$\beta(G')^2 = \frac{1}{2}(3\alpha_{\alpha\beta}G'_{\alpha\beta} - \alpha_{\alpha\alpha}G'_{\beta\beta}) \tag{6}$$

$$\beta(A)^2 = \frac{1}{2}\omega\alpha_{\alpha\beta}\epsilon_{\alpha\gamma\delta}A_{\gamma,\delta\beta} \tag{7}$$

Greek subscripts denote Cartesian components whereas repeated suffixes indicate summation over tensor components. $\epsilon_{\alpha\gamma\delta}$ denotes the Levi−Civita symbol, and ω is the laser frequency.

For Raman scattering, the tensors **α**, **G′**, and **A** are replaced by corresponding vibrational Raman transition tensors. In the approach employed in this paper the Placzek[15] and harmonic approximations are used, which means that the vibrational Raman transition tensors are approximated by geometric derivatives (with respect to normal coordinates) of **α**, **G′**, and **A**. For more information concerning the mechanism of VROA, see refs 4, 14, and 16.

B. Computational Details. Equilibrium structures of lactic acid, lactate, and glyceraldehyde have been found by an unconstrained geometry optimization at the SCF level. After that, the optimization has been repeated at the MP2 level, starting from the SCF minimum structure. It is possible that there are also other minima on the potential energy surface of the molecules under investigation, but we believe that the lowest lying ones are all accounted for. The issue will be addressed in some detail in the next section. The calculations have been performed using the Dunning's aug-cc-pVDZ basis set on carbon and oxygen and cc-pVDZ on the hydrogen atoms.[17−20] The same basis set has been used for geometry optimization and later for calculations of the Raman and VROA spectra.

Spectra have been calculated for molecular structures optimized at the SCF level. The **α**, **G′**, and **A** tensors, which in the notation of modern response theory can be written as[21]

$$\alpha_{\alpha\beta}(-\omega;\omega) = -\langle\langle\mu_\alpha;\mu_\beta\rangle\rangle_\omega \tag{8}$$

$$G'_{\alpha\beta}(-\omega;\omega) = -i\langle\langle\mu_\alpha;m_\beta\rangle\rangle_\omega \tag{9}$$

$$A_{\alpha,\beta\gamma}(-\omega;\omega) = \langle\langle\hat{\mu}_\alpha;\Theta_{\beta\gamma}\rangle\rangle_\omega \tag{10}$$

are computed by means of the linear response self-consistent field (SCF) (or random phase approximation) approach. Above μ_α, m_β, and $\Theta_{\beta\gamma}$ are tensor components of the electric dipole moment, magnetic dipole moment and electric quadrupole moment operators, respectively. Unless otherwise stated, magnetic field-dependent GIAO orbitals[22−26] have been used for calculation of the **G′** and **A** tensors. The frequency employed corresponds to the wavelength of 514.5 nm, the green line of the Ar laser, which has been used for collecting Raman spectra of the molecules under study[10−13] and is commonly used also in VROA spectroscopy.

The Raman and VROA spectra are obtained from the responses, eqs 8−10, by numerical differentiation with respect to nuclear geometric coordinates. A three-point formula with displacements of $\pm 10^{-4}$ atomic units from the original geometry, as described in ref 4, was employed. The SCF force field was used. All reported frequencies are unscaled. The theory underlying the ab initio calculations of the VROA parameters at the linear response SCF level with magnetic field-dependent London atomic orbitals is described in detail in ref 4.

Geometry optimization has been performed using the GAUSSIAN98[27] package. For all the calculations of Raman and VROA spectra, the DALTON package[28] has been used. The vibrational modes have been analyzed using the VEDA program.[29]

III. Results and Discussion

A. Geometric Structures. The structures of D-lactic acid (I and II) and D-lactate (III), optimized at the SCF level, are presented in Figure 1. Those of D-glyceraldehyde, IV−IX, can be seen in Figure 2. Table 1 contains the energies ΔD_0 of D-lactic acid and D-glyceraldehyde relative to the most stable conformation of each molecule, i.e., I and IV, respectively, the relative energies with zero-point vibrational corrections ΔD_ν, and the hydrogen bond lengths.

1. D-Lactic Acid and D-Lactate Anion. The molecule of lactic acid has four bonds around which free rotation is possible. This results in a large number of local minima. However, the assumption of the existence of an internal hydrogen bond limits considerably the number of possible structures. Without the

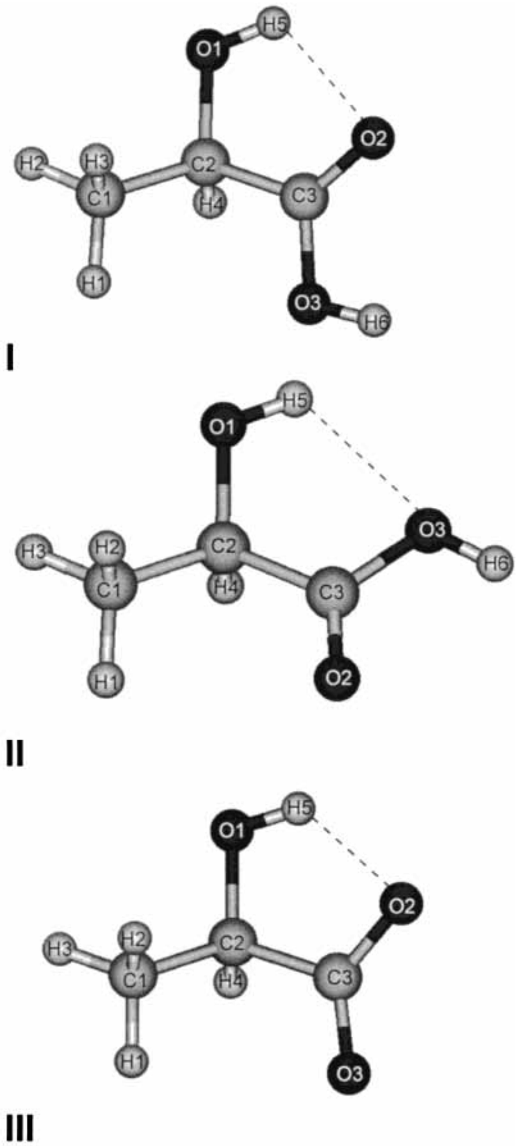

Figure 1. SCF-optimized structures of D-lactic acid and D-lactate. Dashed lines indicate the presence of hydrogen bonds.

stabilizing influence of the internal hydrogen bond, the other minima should be much higher in energy.

Two stable minima have been found for lactic acid at the SCF level, both with an internal hydrogen bond between the proton H5 of the hydroxyl group and the carboxyl group. In structure I the carbonyl oxygen atom O2 acts as a proton acceptor, whereas in structure II the oxygen atom O3 of the hydroxyl group carries out this function. I, with a shorter hydrogen bond and an almost planar structure of the five-membered ring containing it, is significantly lower in energy than II.

The conformation of the lactate anion III is similar to that of structure I of the protonated form. As expected, the internal hydrogen bond is shorter in the anion (1.897 Å, to be compared with 2.130 Å in the protonated form) and is closer to linearity (the O1H5O2 angle is 124.7° in the anion and 114.9° in the protonated form).

The geometric parameters obtained at the MP2 level do not differ substantially from those obtained at the SCF level. The reoptimization at the MP2 level confirms the stability of the two structures of lactic acid and their relative energy. However, the MP2 optimization leads to the shortening of the internal hydrogen bond with respect to the SCF results. This effect has been frequently reported in the literature.[30]

2. D-Glyceraldehyde. Glyceraldehyde has also four bonds around which the rotation is allowed, but there are more possibilities to form internal hydrogen bonds than in lactic acid. Therefore there are more low-lying minima on the potential energy surface. The conformation space map calculated at the SCF/3-21G level[13] contains 27 local minima for an aqueous environment in the continuum model, the lowest 14 having their counterparts in the gas phase.

The five lowest structures from ref 13 have been used as starting points for our calculations. All of them remain minima both at the SCF level and in the MP2 calculations with the aug-cc-pVDZ basis set (cc-pVDZ on the hydrogen atoms). These minima are denoted as IV−VIII. Additionally, our calculations have led also to IX, not reported in ref 13, a structure that is characterized by a significantly larger energy than the first five (see Table 1). It also appears as a minimum on the MP2 potential energy surface. All the structures are shown in Figure 2. Again, there are more minima on the potential energy surface, but they have much higher energy, as ref 13 indicates.

In IV, the global minimum, there are two internal hydrogen bonds, one between the hydroxyl proton H5 and the oxygen O3 from the carbonyl group and a second one, significantly longer, between the hydroxyl proton H1 and the hydroxyl oxygen O2.

V, slightly higher in energy with respect to IV, has the same pattern of hydrogen bonds and it can be obtained from IV through an internal rotation by 60° around the C1−C2 bond and by a rearrangement of the H1 proton.

VI has a different arrangement of internal hydrogen bonds than the first two structures: the cabonyl oxygen O3 is an acceptor of the hydroxyl proton H1, whereas the proton H5 forms the hydrogen bond with the hydroxyl oxygen O1. This results in one six-membered and one five-membered ring formed by internal hydrogen bonds. These hydrogen bonds are longer than those in IV (see Table 1), and VI lies higher in energy than IV.

In VII there is again a hydrogen bond between H5 and O3, forming a five-membered ring. Formally, there is no second internal hydrogen bond, but this structure receives additional stabilization from the hydrogen bond-like interaction between the aldehyde proton H6 and the hydroxyl oxygen O1. Interestingly enough, the zero-point vibrational corrections in VI and VII are large enough to reverse their relative stability at both SCF and MP2 levels of theory (see Table 1).

Structure VIII resembles IV because it has a hydrogen bond between H5 and O3, but there is no second internal hydrogen bond and, consequently, this structure has a higher energy than IV. However, the relatively small energy gap between VIII and IV suggests that VIII is stabilized by a reduction of the torsional tension.

Structure IX, significantly higher in the energy than the other five, has a bifurcated hydrogen bond: the hydroxyl proton H5 is close to both the oxygen O3 from the carbonyl group and the oxygen O1 from the other hydroxyl group. The H5−O3 and H5−O1 distances are similar, especially at the MP2 level.

Similarly as for lactic acid, optimization at the correlated level shifts the relative energies of the conformers of glyceraldehyde, but it does not cause major qualitative changes in the sequence of conformers on the energy scale.

The conformations of glyceraldehyde were also studied in ref 31 at the SCF, MP2, and DFT levels, but using a smaller basis set. Three of the structures reported there have been found

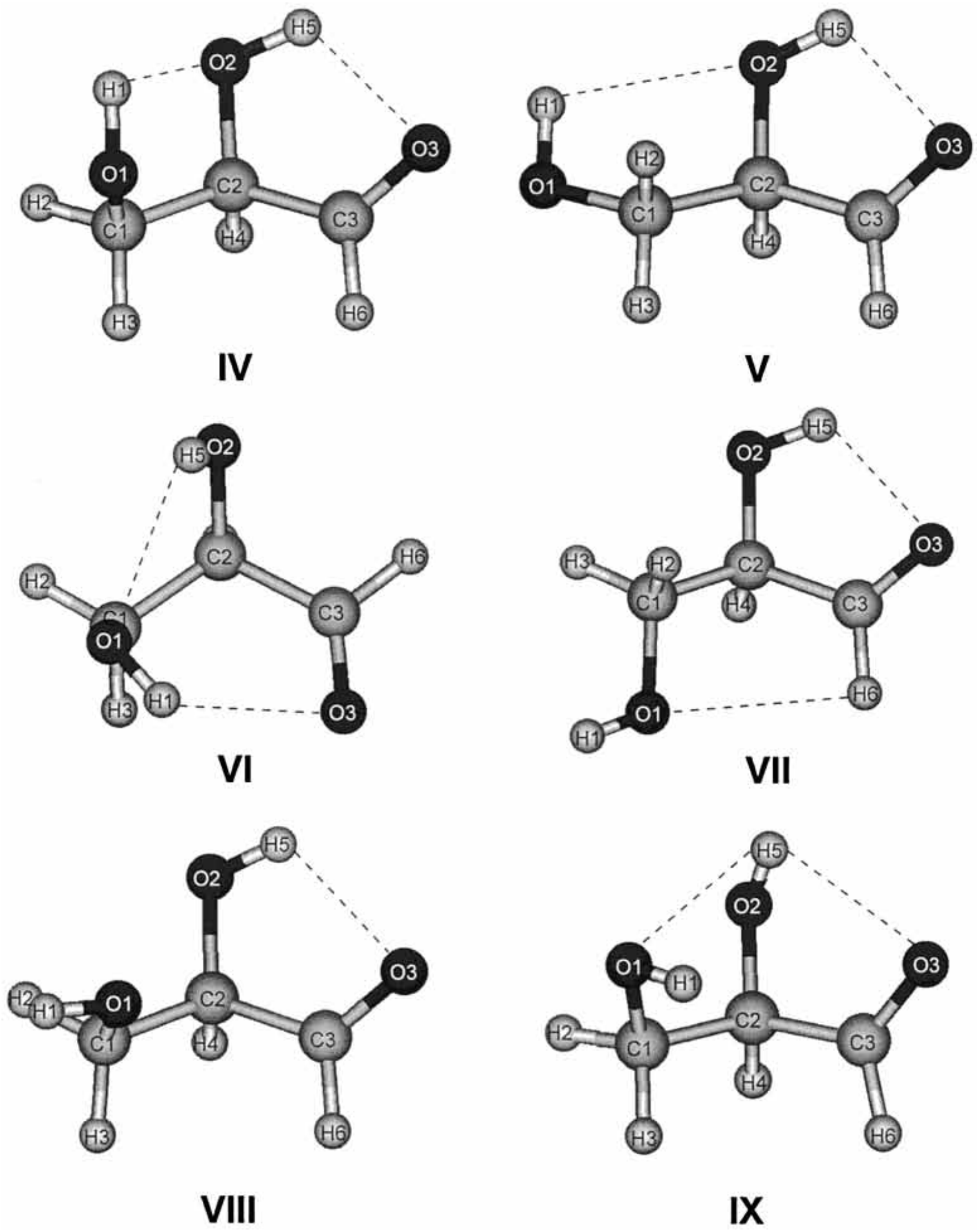

Figure 2. SCF-optimized structures of D-glyceraldehyde. Dashed lines indicate the presence of hydrogen bonds.

TABLE 1: Relative Energies (kcal/mol) and the Internal Hydrogen Bond Distances R_1(O···H) and R_2(O···H) (Å) for Various Conformations of D-Lactic Acid and D-Glyceraldehyde

	ΔD_0		ΔD_ν		R_1(O···H)		R_2(O···H)	
	SCF	MP2	SCF	MP2	SCF	MP2	SCF	MP2
				D-Lactic Acid				
I	0	0	0	0	2.130[a]	2.096[a]		
II	1.84	1.88	1.93	1.88	2.300[b]	2.248[b]		
III (anion)	0	0	0	0	1.897[a]	1.794[a]		
				D-Glyceraldehyde				
IV					2.149[b]	2.072[b]	2.520[c]	2.434[c]
V	1.19	1.35	1.03	1.24	2.144[b]	2.084[b]	2.436[c]	2.364[c]
VI	1.43	1.88	1.53	2.02	2.400[d]	2.301[d]	2.526[e]	2.369[e]
VII	1.40	2.38	1.14	2.11	2.121[b]	2.055[b]	2.647[f]	2.650[f]
VIII	2.62	2.82	2.15	2.38	2.148[b]	2.087[b]		
IX	4.22	4.25	3.73	3.69	2.444[b]	2.482[b]	2.722[d]	2.581[d]

[a] H5O2. [b] H5O3. [c] H1O2. [d] H5O1. [e] H1O3. [f] H6O1.

also in the present paper (cf. structures IV, V, and VII) but their relative stabilities differ. The global minimum is the same but, according to ref 31, VII, instead of V, is the second lowest local minimum. This demonstrates the importance of the basis set quality for this type of calculations. The other two structures found in ref 31 are much higher in energy and belong to the manifold of those not considered in the present paper.

B. Raman and VROA Spectra. *1. D-Lactic Acid and D-Lactate.* The calculated Raman spectra of D-lactic acid and D-lactate are presented in Figure 3. Due to the large differences between the Raman intensities of the bands of the high-frequency stretching modes and the remaining bands, the spectra are shown separately for the 0−2100 and 2900−4500 cm^{-1} regions (there are no vibrations in the 2100−2900 cm^{-1} range). The same arrangement has been adopted for the VROA spectra of D-lactic acid and D-lactate (Figure 4) and later on for the calculated Raman and VROA spectra of D-glyceraldehyde (Figures 5−8). All the spectra have been simulated by assigning a fixed arbitrary bandwidth of 8 cm^{-1} to each Lorentzian band. In the absence of experimental data for the bandwidth, the same value as used in ref 32 was employed.

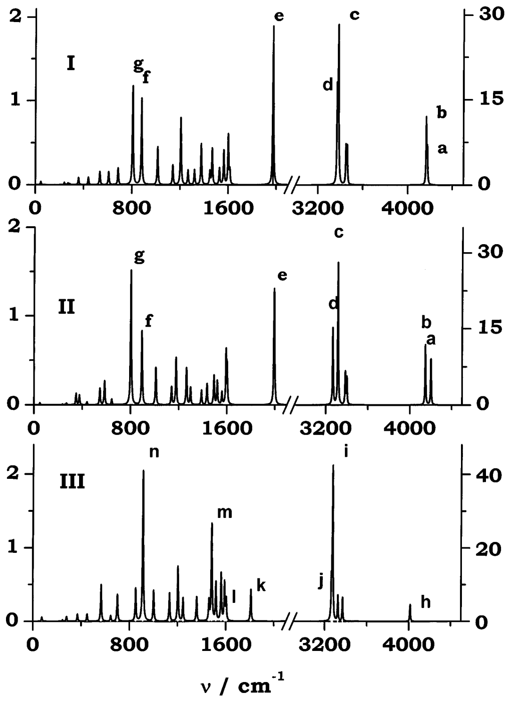

Figure 3. Calculated Raman spectra of D-lactic acid and D-lactate: (a) ν_1(O—H); (b) ν_2(O—H); (c) $\nu_s(CH_3)$; (d) ν(C—H); (e) ν(C=O); (f) ν(C—C); (g) ν(C—C); (h) ν(O—H); (i) $\nu_s(CH_3)$; (j) ν(C—H); (k) $\nu_{as}(CO_2^-)$; (l) $\delta_{as}(CH_3)$; (m) $\nu_s(CO_2^-)$; (n) $\nu(C—CO_2^-)$.

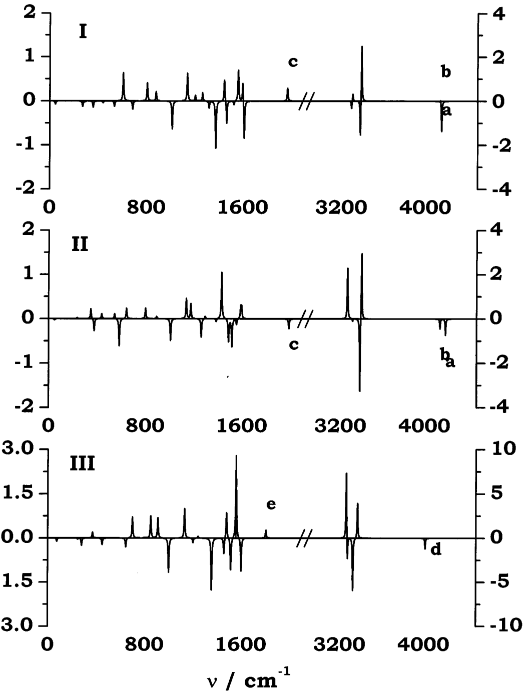

Figure 4. Calculated VROA spectra of D-lactic acid and D-lactate: (a) ν_1(O—H); (b) ν_2(O—H); (c) ν(C=O); (d) ν(O—H); (e) $\nu_{as}(CO_2^-)$.

The Raman spectroscopy does not differentiate strongly between conformers: the Raman spectra for structures I and II of lactic acid are similar. The most noticeable difference is the larger Raman intensity of the first mode, ν_1(O—H) (a), corresponding to the O5—H1 stretching, in the spectrum of II. This is probably due to the weaker hydrogen bond of proton H1 in II than in I, because the formation of a hydrogen bond decreases the polarizability of the OH bond, and therefore causes a decrease in the Raman intensity of the corresponding stretching vibration. In contrast to that, mode e corresponding to the C=O bond stretching is more intense in I than in II. The other difference between the two spectra is that for I two vibrations in the 800—900 cm^{-1} range (f and g corresponding to stretching of the CC bonds) have a similar and relatively substantial Raman intensity, whereas for II vibration g with lower frequency has a much larger Raman intensity than f.

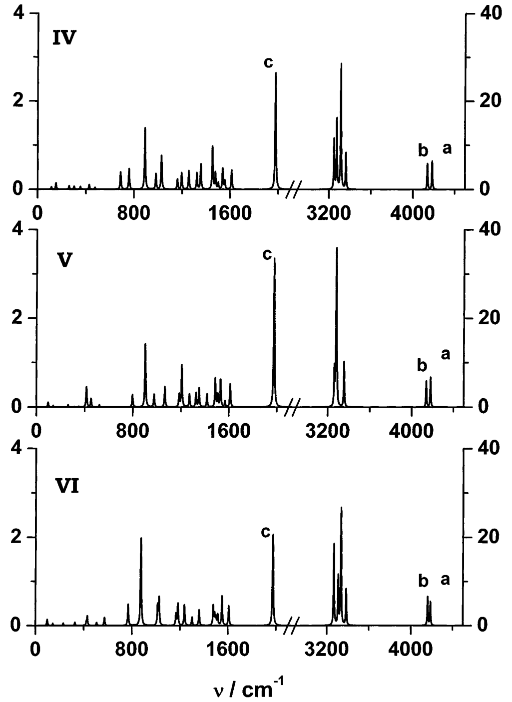

Figure 5. Calculated Raman spectra of D-glyceraldehyde, IV—VI: (a) ν_1(O—H); (b) ν_2(O—H); (c) ν(C=O).

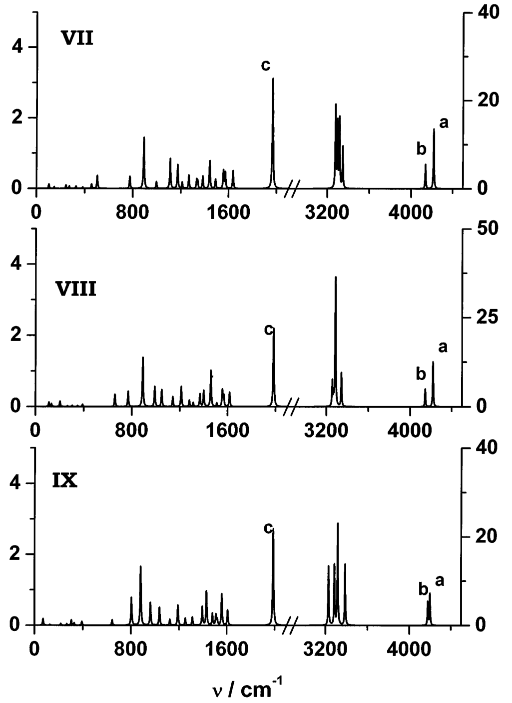

Figure 6. Calculated Raman spectra of D-glyceraldehyde, VII—IX: (a) ν_1(O—H); (b) ν_2(O—H); (c) ν(C=O).

The VROA spectra of D-lactic acid and the D-lactate anion are shown in Figure 4. The absolute VROA effect is larger for the high-frequency vibrations, especially for the C—H stretching modes, than for the low-frequency vibrations. However, this is only a consequence of higher Raman intensity of the high-

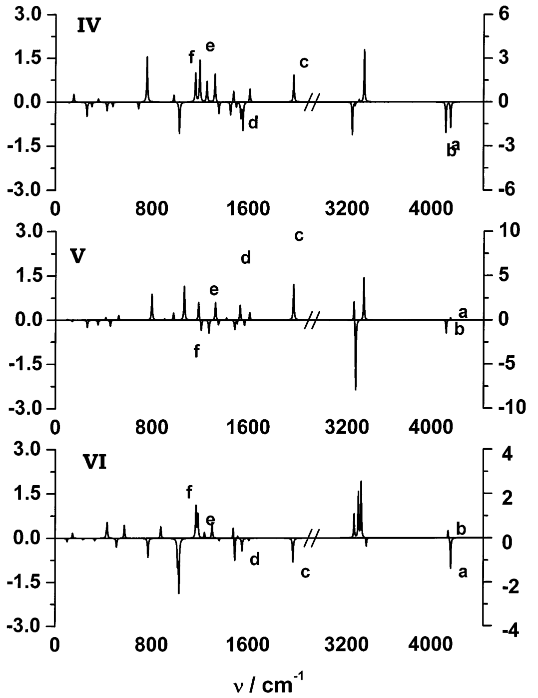

Figure 7. Calculated VROA spectra of D-glyceraldehyde, IV−VI: (a) ν_1(O−H); (b) ν_2(O−H); (c) ν(C=O); (d) δ(O−H); (e) ν(C−O); (f) ν(C−O).

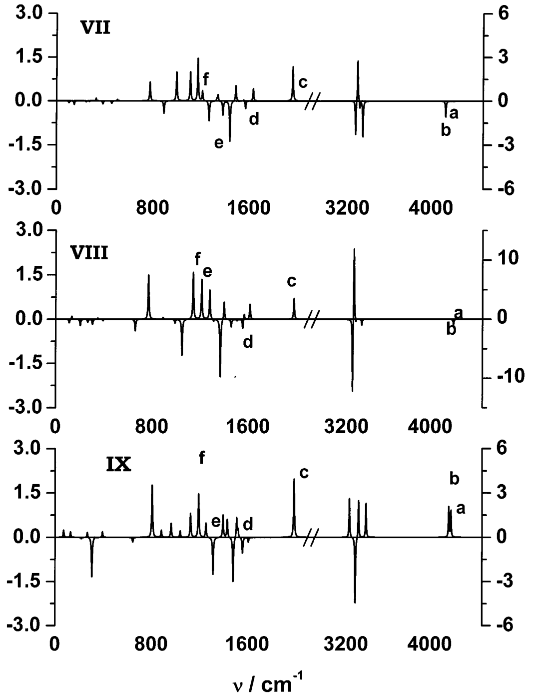

Figure 8. Calculated VROA spectra of D-glyceraldehyde: VII−IX: (a) ν_1(O−H); (b) ν_2(O−H); (c) ν(C=O); (d) δ(O−H); (e) ν(C−O); (f) ν(C−O).

frequency vibrations because the relative CID values are, as usual,[33] much larger for low-frequency than for high-frequency vibrations. Unlike the Raman spectra, the VROA spectra differ considerably for the two conformers.

In the high-frequency region, the ν_1(O−H) (a) stretching mode of the O1H5 bond, attached to the center of chirality, has a relatively high Raman optical activity. The negative VROA of this vibration is larger for structure I and the anion III, where H5 interacts with the carbonyl group, than in II with the hydrogen bond of H5 to the oxygen O3 from the OH group.

The VROA of the stretching ν(C=O) (c) mode is small, but it exhibits a remarkable variation in the two conformers of lactic acid under investigation: it is positive for I, with the carbonyl group engaged in the hydrogen bond, and negative for II, where the carbonyl group is free. For lactate the asymmetric stretching vibration of the CO_2^- group $\nu_{as}(CO_2^-)$ (e) has a positive and relatively significant VROA, both absolute and relative, which corresponds to the strong hydrogen bond of the carbonyl group.

2. D-Glyceraldehyde. The Raman spectra calculated for the conformers of D-glyceraldehyde are shown in Figures 5 and 6. Similarly as for lactic acid, the spectra calculated for different structures look similar at a first glance, except for the shifts in vibrational frequencies. However, there are also some subtle effects on the intensities, similarly as for lactic acid. The Raman intensities of the stretching vibrations of the OH bonds, ν_1(O−H) (a) (of O1−H1) and ν_2(O−H) (b) (of O2−H5), are smaller when the protons are engaged in a strong hydrogen bond. This difference between bands corresponding to stretching vibrations of the free and hydrogen-bonded OH groups is particularly pronounced in the spectra of structures VII and VIII, where only one of the hydroxyl groups forms a hydrogen bond, and the band corresponding to the stretching vibration of this group is significantly smaller than the other one. The Raman intensity of the stretching vibration of the carbonyl group (c) is similar for all the conformers (slightly smaller only for VI and VIII). As far as the other vibrations are concerned, there are some effects when the conformation changes but they are difficult to analyze.

The VROA spectra of six structures of D-glyceraldehyde are shown in Figures 7 and 8. Like for lactic acid, the spectra of various conformations look completely different. Their analysis is difficult but we are able to give guidelines for correlating VROA spectra and molecular structure.

The most localized vibrations are the stretching modes of the hydroxyl groups (a and b), and one may suppose that the Raman optical activity of these vibrations may bring some structural information. However, it turns out that correlating the VROA of these vibration with the molecular conformation is problematic. The VROA of the OH stretching vibration is in most cases negative when the group is engaged in a hydrogen bond, and it tends to assume larger negative values when the hydroxyl group acts as both proton donor and proton acceptor (see, for example, ν_2(O−H) (b) for structure IV, ν_2(O−H) for V, ν_1(O−H) (a) for VI). This was also seen for lactic acid above. However, ν_2(O−H) (b) (of the O2H5 bond) in structure VIII has a positive VROA, even though this OH group forms a strong hydrogen bond with the carbonyl group. The VROA of ν_1(O−H) (a) in V (the stretching vibration of O1H1 bond) is also positive. VROA parameters are also positive for both hydroxyl stretching vibrations in IX, but here the internal hydrogen bonds are very weak.

The VROA of the stretching vibration of the carbonyl group ν(C=O) (c) exhibits a feature similar to that seen in the lactic acid: it is positive for all structures where the carbonyl group is engaged in a strong hydrogen bond forming a five-membered ring and it is negative for structure VI, which is characterized by a six-membered ring where the hydrogen bond is much weaker (judging from the proton-oxygen distance). It seems therefore that the stretching mode of the C=O group could be utilized for locating hydrogen bonds. It is in fact well suited for this purpose, because of the local nature of the vibration. According to our results for glyceraldehyde and lactic acid, the stronger the hydrogen bond of the carbonyl group, the more positive VROA of the stretching mode of the C=O bond for

TABLE 2: Comparison of the Δ(180°) Circular Intensity Difference Calculated for Structure I of D-Lactic Acid with GIAOs and with Conventional Atomic Orbitals, Given in Terms of the Relative Difference Δ (%)

mode	freq (cm^{-1})	Δ (%)
1	4118	1.9
2	4107	−2.4
3	3279	−0.2
4	3265	−4.5
5	3186	−1.1
6	3173	32.0
7	1974	7.2
8	1613	0.7
9	1600	1.7
10	1563	−6.0
11	1527	−13.9
12	1466	−1.8
13	1447	−2.9
14	1375	−2.2
15	1319	11.3
16	1265	−2.5
17	1205	−8.0
18	1139	−0.5
19	1013	−6.7
20	879	−4.2
21	806	0.3
22	685	9.1
23	607	0.0
24	533	6.4
25	439	−11.6
26	358	−0.4
27	286	−8.4
28	271	−3.6
29	241	−93.1
30	45	0.0

D-enantiomers. However, the other structural features also contribute to the VROA parameter of the ν(C=O) vibration (for example, in structure IX the VROA is substantial despite a relatively weak hydrogen bond) and more studies of this subject would be welcome.

Significant optical activity is exhibited by the stretching vibrations of C−H bonds, the stretching vibrations of single C−O bonds (the bands e and f in the 1150−1280 cm^{-1} range), by the bending modes of OH groups (d) and of the C2H4 bond (1300−1550 cm^{-1}), by the torsional motion around the CO bonds (bands in the range 300−500 cm^{-1}), and for some of the conformations, by the bending and torsional vibrations of the aldehyde group. However, we do not see any consistent pattern correlating their magnitude to the molecular conformation.

3. Role of GIAO Orbitals. The basis set used for the calculations of the VROA spectra is rather small, although it contains the diffuse functions necessary for this type of calculations.[4] Some assessment of the error introduced by the basis set incompleteness can be obtained by comparing VROA calculated with gauge invariant atomic orbitals with that given by conventional atomic orbitals (with gauge origin at the center of mass of the molecule), because the use of GIAOs not only ensures origin invariance but also improves the quality of the basis set.

The relative differences between VROA parameters for structure I of D-lactic acid obtained with the conventional basis set and those obtained with the use of London's orbitals are collected in Table 2. The differences between the two sets of results are minor. The discrepancy is usually below 3%, in particular for all the modes with significant VROA. The difference is larger than 10% for a few vibrations only, all of them corresponding to VROA parameters close to zero. It suggests that the basis set employed, although of moderate size, is in fact appropriate for the calculations.

C. Comparison with Experiment. *1. D-Lactic Acid and D-Lactate.* The Raman spectra of lactic acid and sodium lactate have been collected in aqueous solutions,[10,11] which makes the comparison of theoretically predicted and experimental spectra very complicated. To illustrate some of the difficulties associated with that, we present in Table 3 the calculated Raman spectrum

TABLE 3: Comparison of the Calculated and Experimental[a] Raman Spectrum of Lactate Anion

frequency		intensity		frequency	intensity	
SCF	MP2	SCF		exp	exp	
3963	3385	51.6	ν(O−H)			
3255	3166	72.2	ν_{as}(CH$_3$)	2985	s	ν_{as}(CH$_3$), ν_s(CH$_3$)
3207	3138	76.8	ν_{as}(CH$_3$)	2935	vs	ν_{as}(CH$_3$), ν_s(CH$_3$)
3151	3048	461.4	ν_s(CH$_3$)	2900	sh	ν_{as}(CH$_3$), ν_s(CH$_3$)
3138	3030	112.0	ν(C−H)	2885	s	ν(C−H)
1810	1662	4.8	ν_{as}(CO$_2^-$)	1590 (1585)[b]	m	ν_{as}(CO$_2^-$)
1604	1499	3.2	δ_{as}(CH$_3$)	1470	sh	δ_{as}(CH$_3$)
1590	1490	5.8	δ_{as}(CH$_3$)	1455	s	δ_{as}(CH$_3$)
1562	1440	7.2	δ(O−H)	1420	s	ν_s(CO$_2^-$)
1518	1380	5.8	ν_sCO$_2^-$	1390	sh	δ_sCH$_3$
1482	1350	14.8	ν_sCO$_2^-$	1365	m	δ_sCH$_3$
1460	1340	3.0	δ(C−H)	1315	m	δ(C−H)
1357	1237	3.8	δ(C−H)	1285	m	δ(C−H)
1245	1128	3.6	ν(C−O)	1270	s	δ(O−H)
1203	1123	8.4	ν(C−CH$_3$)	1125	m	r(CH$_3$), ν(C−O)
1133	1046	4.4	ν(C−O), δ(C−COH)	1085 (1090)[b]	s	ν(C−O)
1001	917	4.6	ν(C−O), ν(C−CO$_2^-$), ν(C−CH$_3$)	1045	s	ν(C−CH$_3$)
911	834	23.0	ν(C−CO$_2^-$), ν(C−CH$_3$), δ(CO$_2^-$)	930	m	r(CH$_3$)
852	764	5.0	r(CH$_3$)	860	vs	ν(C−CO$_2^-$)
700	720	4.0	ν(C−CO$_2^-$), δ(CO$_2^-$)	775	m	δ(CO$_2^-$)
645	640	0.8	δ(C−COH)	660	m	δ(C−COH)
565	520	5.6	w(CO$_2^-$)	540	s	w(CO$_2^-$)
449	412	1.2	r(CO$_2^-$)	430	m	r(CO$_2^-$)
370	345	1.0	w(CO$_2^-$)	350	w	δ(CCC)
280	254	0.8	δ(CCC)	280	m	τ(CCC)
246	234	0.2	τ(CCC)			
75	79	0.6	τ(CO$_2^-$)			

[a] Experimental Raman spectrum in aqueous solution.[10] [b] IR frequencies in parentheses.

of the lactate anion and the experimental spectrum of sodium lactate, taken in an aqueous solution.[10]

The picture is relatively clear for the high-frequency region. According to our results, the largest Raman intensity corresponds to the symmetric stretching vibration of the CH_3 group; the band corresponding to the stretching vibration of the OH group was not determined experimentally due to the Raman scattering of water. However, for the lower frequencies, especially in the region below 1200 cm^{-1}, it is difficult to assign theoretically obtained frequencies to a given experimental band. In most cases the vibrational energy is evenly distributed among several internal coordinates, which makes it impossible to discuss the vibrations in terms of characteristic modes, as it was done in the experimental paper.[10] Solvent effects, which can be assumed to be substantial, additionally complicate the comparison. It is rewarding that the stretching vibration of the C2C3 bond, $\nu(C-CO_2^-)$ (denoted as n in Figure 3), dominating the experimental Raman spectrum in the region of low frequencies, has also a substantial Raman intensity predicted theoretically. The relatively large Raman intensity of the $\nu_s(CO_2^-)$ (m) vibration is also reproduced theoretically. However, the large intensity of the asymmetric bending modes $\delta_{as}(CH_3)$ (e.g., l in Figure 3) is not. As expected, the MP2 frequencies are much closer to the experiment than the SCF results, for both lactate and lactic acid.

We shall not discuss in detail the Raman spectrum of the protonated form of the lactic acid because the picture is basically similar as in the case of lactate. The experiment was performed for a 40% aqueous solution,[10,11] so strong solvent effects are expected.

The largest Raman intensity of the CH stretching vibrations in lactic acid are exhibited by $\nu_s(CH_3)$ and $\nu(C-H)$ (stretching of the H4C2 bond). A substantial Raman intensity of the C=O stretching vibration (e) is reproduced by our calculations, although its frequency is slightly overestimated even at the MP2 level (1777 cm^{-1} for I and 1793 cm^{-1} for II, whereas the experiment yields 1725 cm^{-1}). The experimental spectrum exhibits also the intense line at 830 cm^{-1}, attributed to the $\nu(C-COOH)$ stretching vibration. This is also in agreement with our theoretical predictions (when taking into account the overestimation of the vibrational frequencies by the SCF method). What our calculations do not predict is the substantial Raman intensity for the out-of-plane vibration at approximately 520 cm^{-1}.

It is not possible to assess which structure occurs in the solution on the basis of the Raman spectra because of the solvent effects and partial polymerization, not accounted for in our calculations. Moreover, some of the bands are obscured by water scattering and, as said above, the Raman spectrum is insensitive to the conformational changes. The spectra calculated for structures I and II are very similar and both seem close to the experimental spectrum, although the equilibrium structures predicted for the gaseous phase in all probability differ considerably from those present in aqueous solution.

2. D-Glyceraldehyde. The experimental vibrational Raman study of glyceraldehyde was focused on the stretching vibration of the carbonyl group,[13] and there is no trace in the literature of results of investigations of the other regions of the spectrum. The comparison of the theoretical and experimental frequencies of this mode is presented in Table 4. There is an experimentally established difference between this frequency in water and triethylamine, which in ref 13 was ascribed to the structures with five-membered and six-membered rings, respectively. In a way our calculations confirm this, because the global minimum with a five-membered ring, IV, has indeed a higher frequency than VI, with a six-membered ring, and the frequency values obtained at the MP2 level are in amazingly good agreement with experiment. However, this is most probably coincidental, considering the approximations made and the fact that the other predicted five-membered ring structures have different frequencies for this vibration.

TABLE 4: Comparison of the Calculated and Experimental[a] C=O Stretching Frequency of Glyceraldehyde (cm^{-1})

	SCF	MP2
IV	1979	1730
V	1977	1721
VI	1975	1722
VII	1967	1717
VIII	1983	1735
IX	1988	1730
exp five-membered ring[b] (in water)	1730	
exp six-membered ring[b] (in triethylamine)	1724	

[a] Reference 13. [b] Assignment of ref 13.

IV. Summary

We have presented the results of the linear response SCF calculations of Raman and vibrational Raman optical activity spectra for D-lactic acid (two conformers), D-lactate, and D-glyceraldehyde (six conformers). The main conclusions can be summarized as follows.

Raman spectroscopy does not discriminate strongly between various conformers of the same molecule, although it has been shown to be applicable for analysis of the mixture of various carbohydrates.[34] A discernible feature is a decrease in the Raman intensity of the OH stretching vibration when the hydroxyl group is a proton donor to an internal hydrogen bond. Unfortunately, this observation cannot be employed in practice, at least not in aqueous solutions, because OH stretching bands are likely to be obscured by the Raman scattering of water. The structural effects on the Raman intensities of the other vibrations are small and difficult to analyze.

The vibrational Raman optical activity spectra change profoundly when the molecule assumes a different conformation. In many cases even the sign of the circular intensity difference changes when the conformation is changed. The relative CID values are large for the bending and out-of-plane vibrations, but their analysis is difficult. The stretching vibrations are localized and therefore best suited for the purpose of structural investigation.

The Raman optical activity of the $\nu(C=O)$ stretching mode, although small, may be employed to localize hydrogen bonds. The VROA of this vibration is positive when the carbonyl group is engaged in the internal hydrogen bond and its value seems to correlate with the strength of the bond, although other factors are also likely to contribute. When the carbonyl group is free, or the hydrogen bond is weak, the VROA is negative.

Acknowledgment. We express our gratitude to Kenneth Ruud for his insightful comments. This work was supported by the European Research and Training Network: "Molecular Properties and Molecular Materials" (MOLPROP), Contract No. HPRN-CT-2000-00013, Grant No. 120-501/68/BW-1522/17/2001 (M.P.), Grant ONR No. N00014-98-1-0592, and Grant NSF-CREST No. 9805465 (J.L.).

References and Notes

(1) Bell, A. F.; Hecht, L.; Barron, L. D. *J. Am. Chem. Soc.* **1998**, *120*, 5820.

(2) Barron, L. D.; Hecht, L.; Bell, A. F. *Appl. Spectrosc.* **1996**, *50*, 619.

(3) Polavarapu, P. L. *J. Phys. Chem.* **1990**, *94*, 8106.

(4) Helgaker, T.; Ruud, K.; Bak, K. L.; Jørgensen, P.; Olsen, J. *Faraday Discuss.* **1994**, *99*, 165.

(5) Barron, L. D.; Gargaro, A. R.; Hecht, L.; Polavarapu, P. L. *Spectrochim. Acta* **1991**, *47a*, 1001.

(6) Yu, G.-S.; Freedman, T. B.; Nafie, L. A.; Deng, Z.; Polavarapu, P. L. *J. Phys. Chem.* **1995**, *99*, 835.

(7) Jalkanen, K. J.; Nieminen, R. M.; Frimand, K.; Bohr, J.; Bohr, H.; Wade, R. C.; Tajkhorshid, E.; Suhai, S. *J. Comput. Chem.* **2001**, *265*, 125.

(8) Bouř, P. *J. Comput. Chem.* **2001**, *22*, 426.

(9) Bouř, P.; Kapitaán, J.; Baumruk, V. *J. Phys. Chem. A* **2001**, *105*, 6362.

(10) Cassanas, G.; Morssli, M.; Fabrégue, E.; Bardet, L. *J. Raman Spectrosc.* **1991**, *22*, 409.

(11) Cassanas, G.; Kister, G.; Fabrégue, E.; Morssli, M.; Bardet, L. *Spectrochim. Acta A* **1991**, *49*, 271.

(12) Kobayashi, Y.; Igarashi, T.; Takahashi, H.; Higasi, K. *J. Mol. Struct.* **1976**, *35*, 85.

(13) Yaylayan, V. A.; Harty-Majors, S.; Ismail, A. A. *Carbohydr. Res.* **1999**, *318*, 20.

(14) Barron, L. D.; Buckingham, A. D. *Mol. Phys.* **1971**, *20*, 1111.

(15) Placzek, G. In *Handbuch der Radiologie*; Marx, E., Ed.; Akademische Verlagsgesellschaft: Leipzig, 1934; Vol. 6, p 205.

(16) Barron, L. D. *Molecular light scattering and optical activity*; Cambridge University Press: Cambridge, U.K., 1982.

(17) Dunning, T. H. *J. Chem. Phys.* **1989**, *90*, 1007.

(18) Kendall, R. A.; Dunning, T. H.; Harrison, R. J. *J. Chem. Phys.* **1992**, *96*, 6796.

(19) Woon, D. E.; Dunning, T. H. *J. Chem. Phys.* **1993**, *98*, 1358.

(20) Woon, D. E.; Dunning, T. H. *J. Chem. Phys.* **1994**, *100*, 2975.

(21) Olsen, J.; Jørgensen, P. In *Modern Electronic Structure Theory, Part II*; Yarkony, D. R., Ed.; World Scientific: Singapore, 1995.

(22) London, F. *J. Phys. Radium* **1937**, *8*, 397.

(23) Ditchfield, R. D. *J. Chem. Phys.* **1972**, *56*, 5688.

(24) Wolinski, K.; Hinton, J. F.; Pulay, P. *J. Am. Chem. Soc.* **1990**, *112*, 8251.

(25) Helgaker, T. U.; Jørgensen, P. *J. Chem. Phys.* **1991**, *95*, 2595.

(26) Ruud, K.; Helgaker, T.; Bak, K. L.; Jensen, H. J. A.; Jørgensen, P. *J. Chem. Phys.* **1993**, *99*, 3847.

(27) Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Zakrzewski, V. G.; Montgomery, J. A.; Stratmann, R. E.; Burant, J. C.; Dapprich, S.; Millam, J. M.; Daniels, A. D.; Kudin, K. N.; Strain, M. C.; Farkas, O.; Tomasi, J.; Barone, V.; Cossi, M.; Cammi, R.; Mennucci, B.; Pomelli, C.; Adamo, C.; Clifford, S.; Ochterski, J.; Petersson, G. A.; Ayala, P. Y.; Cui, Q.; Morokuma, K.; Malick, D. K.; Rabuck, A. D.; Raghavachari, K.; Foresman, J. B.; Cioslowski, J.; Ortiz, J. V.; Stefanov, B. B.; Liu, G.; Liashenko, A.; Piskorz, P.; Komaromi, I.; Gomperts, R.; Martin, R. L.; Fox, D. J.; Keith, T.; Al-Laham, M. A.; Peng, C. Y.; Nanayakkara, A. A.; Gonzalez, C.; Challacombe, M.; Gill, P. M. W.; Johnson, B. G.; Chen, W.; Wong, M. W.; Andres, J. L.; Head-Gordon, M.; Replogle, E. S.; Pople, J. A. *Gaussian 98*, Revision A.1; Gaussian, Inc.: Pittsburgh, PA, 1998.

(28) Helgaker, T.; Jensen, H. J. A.; Jørgensen, P.; Olsen, J.; Ruud, K.; Ågren, H.; Auer, A. A.; Bak, K. L.; Bakken, V.; Christiansen, O.; Coriani, S.; Dahle, P.; Dalskov, E. K.; Enevoldsen, T.; Fernandez, B.; Hättig, C.; Hald, K.; Halkier, A.; Heiberg, H.; Hettema, H.; Jonsson, D.; Kirpekar, S.; Kobayashi, R.; Koch, H.; Mikkelsen, K. V.; Norman, P.; Packer, M. J.; Pedersen, T. B.; Ruden, T. A.; Sanchez, A.; Saue, T.; Sauer, S. P. A.; Schimmelpfenning, B.; Sylvester-Hvid, K. O.; Taylor, P. R.; Vahtras, O. Dalton, an ab initio electronic structure program, release 1.2 2001. See http://www.kjemi.uio.no/software/dalton/dalton.html.

(29) Jamróz, M. H. *Vibrational Energy Distribution Analysis VEDA 3*; Drug Institute: Warsaw, 2000.

(30) Chałsiński, G.; Szczęśniak, M. M. *Chem. Rev.* **2000**, *100*, 4227.

(31) Łożyński, M.; Rusińska-Roszak, D.; H.-G. Mack. *J. Phys. Chem. A* **1998**, *101*, 1542.

(32) Ruud, K.; Helgaker, T.; Bouř, P. *J. Phys. Chem. A* **2002**, *106*, 7448.

(33) Buckingham, A. D. *Faraday Discuss.* **1994**, *99*, 1.

(34) Arboleda, P. H.; Loppnow, G. R. *Anal. Chem.* **2000**, *72*, 2093.