J. Phys. Chem. A **2005,** *109,* 8617−8623

Magnitude of Zero-Point Vibrational Corrections to Optical Rotation in Rigid Organic Molecules: A Time-Dependent Density Functional Study

Brendan C. Mort and Jochen Autschbach*

Department of Chemistry, University at Buffalo, State University of New York, Buffalo, New York 14260-3000

Received: April 2, 2005; In Final Form: July 15, 2005

The zero-point vibrational corrections (ZPVCs) to the optical rotation of 22 rigid organic molecules have been calculated using time-dependent density functional theory with the B3LYP hybrid functional. We outline an implementation for calculating ZPVCs that can be applied with a variety of quantum chemistry programs and methods. It is shown that the ZPVCs to optical rotation have a wide range of values and can be quite significant depending on the molecule. On average, it has been determined that vibrational corrections can account for about 20% of the optical rotation for the equilibrium value. It is also concluded that vibrational effects alone cannot be the only factor in improving the calculated values of optical rotation with respect to experimental data measured in solution.

1. Introduction

Vibrational averaging has become an important factor in improving the accuracy of first-principles molecular property calculations to predict or confirm experimental data. The goal here is to augment the accuracy of calculated values by including the effects due to the motion of the nuclei on a molecular property. A number of studies have shown that vibrational effects can be quite significant.[1] Calculations of polarizabilities,[2,3] hyperpolarizabilities,[4,5] magnetizabilities,[6,7] hypermagnetizabilities,[8] NMR isotropic shielding constants,[9−15] and spin−spin coupling constants[16,17] have all benefited from vibrational corrections to the corresponding calculated values at a fixed equilibrium geometry. Continuing with the theme of electric and magnetic perturbations, it is not surprising that optical activity is also subjected to significant vibrational effects.[18,19]

Vibrational averaging of properties is not a new subject. It has been known for a long time that experimental results represent an averaging of the molecular property over a range of geometries. Traditionally, such an averaging of calculated property values has been met with some rather sophisticated analytical derivations.[20−26] These methods, along with a desire to simplify the calculations by exploiting symmetry, have often been applied to diatomics, small molecules, or highly symmetric systems. With massively parallel computers and computing farms becoming available to most researchers, energy and property calculations at the number of molecular geometries necessary for obtaining vibrationally averaged properties of polyatomic molecules by numerical derivative methods are no longer the daunting task that they once were. Much of the current work in this field benefits from applying relatively straightforward numerical methods to the calculation of derivatives of the energy and/or the property with respect to normal coordinates.[16,27−30]

In this work, we investigate the zero-point vibrational corrections to optical rotations for a test set of optically active molecules using time-dependent density functional theory (TDDFT) with a hybrid functional. On the basis of Hartree−Fock calculations on two chiral molecules, Ruud and co-workers have shown that zero-point vibrational corrections (ZPVCs) to optical activity are potentially significant.[18] This work has been cited a number of times to support the argument that the vibrational correction to optical rotation *might* be an important factor in obtaining accurate optical rotation calculations.[31−36] Recently, the case of methyloxirane was reinvestigated by Ruud and Zanasi to show that ZPVCs are critical for explaining experimental trends.[19] However, it is not yet quite clear what a typical magnitude of ZPVCs in rigid organic systems is and how strongly these corrections vary between different systems. The demand for vibrational corrections to optical rotation calculations continues to increase as investigations of other corrective factors, such as electron correlation, gauge invariance, basis set dependence, and solvent effects, continue.[31,36−38] We extend previous work in the calculation of ZPVCs of optical activity to density functional theory and provide a larger set of optically active rigid organic molecules for investigation. We will show that vibrational corrections to optical rotation can be significant and are very much dependent on the molecular structure.

In section 2, background information on the optical rotation and vibrational averaging calculations is given. Next, the computational details of the work are described (section 3), followed by the presentation of the data (section 4). Finally, in section 5, conclusions are drawn and an outlook is given for future work.

2. Methodology

2.1. Optical Rotation. The development of the theory of optical rotation in a framework of molecular quantum mechanics dates back to Rosenfeld's paper in 1928.[39] The coupling between the electric field induced polarization and the time-dependent magnetic field of electromagnetic radiation provides the theoretical basis for a change in light polarization that is observed as optical rotation. From perturbation expansions of the electric or magnetic dipole moments in the presence of a time-dependent magnetic or electric field, respectively,[40] one obtains the electric

---

* Corresponding author. E-mail: jochena@buffalo.edu.

10.1021/jp051685y CCC: $30.25

dipole−magnetic polarizability tensor **G′**given by the equation (in atomic units)[41]

$$G'_{\alpha\beta} = -2\omega \sum_{n\neq 0} \mathrm{Im} \frac{\langle\psi_0|\hat{\mu}_\alpha|\psi_n\rangle\langle\psi_n|\hat{m}_\beta|\psi_0\rangle}{{\omega_{n0}}^2 - \omega^2} \tag{1}$$

Here, ω is the frequency of the incident light, ψ_0 is the ground-state wave function, ψ_n are the excited-state wave functions, and $\hat{\mu}_\alpha$ and $\hat{m}_\beta$ are components of the electric and magnetic dipole operators, respectively.

The optical rotatory parameter β is related to the rotational average of **G′** by

$$\beta = -\frac{1}{3\omega}\sum_{\alpha} G'_{\alpha\alpha} \tag{2}$$

The specific rotation at frequency $\bar{\nu}$ (in cm^{-1}) can be determined from the optical rotatory parameter using the equation,

$$[\alpha]_{\bar{\nu}} = 1.343 \times 10^{-4}\frac{\beta\bar{\nu}^2}{M} \tag{3}$$

where β is in atomic units and M is the molar mass of the molecule of interest in g/mol. In the present work, we used the Na D-line frequency (589.3 nm or 16 969 cm^{-1}) in all calculations.

The sum in eq 1 extends over an infinite number of excited electronic states. As a result, more practical implementations of optical rotation calculations are necessary. For instance, in density functional theory, **G′** is calculated using analytical derivative techniques.[37,42−47] For the present work, we have employed the implementations of the Turbomole[48] package. The relevant information for the optical rotation calculations is given in the references.[47]

2.2. Vibrational Averaging. To determine the ZPVC of a molecular property, it is first necessary to compute the normal modes of vibration. This procedure is a standard task for most quantum chemistry codes. Generally, the mass-weighted Hessian **U** is constructed and then diagonalized to yield the eigenvector matrix **L** and the eigenvalues Λ such that

$$\mathbf{UL} = \mathbf{L}\Lambda \tag{4}$$

The eigenvector matrix **L** is the representation of the normal modes in mass-weighted Cartesian displacement coordinates. Because we are interested in computing molecular properties at the varying geometries incurred from the vibrational motion of the molecule, the normal modes can be expressed in terms of Cartesian displacement coordinates. Removing the mass weighting from the elements in **L** transforms the mass-weighted Cartesian coordinates to nonmass-weighted Cartesian coordinates. Dividing each row by the square root of the mass of the corresponding atom destroys the normalization of the column vectors. As a result, the vectors can be renormalized and the normalization constant for each vector is identified with the reduced mass μ_j for normal mode j.[48,49] Once the mass weighting has been removed and the eigenvectors are renormalized, a matrix, **S**, of column vectors containing the Cartesian displacements for each x, y, and z component of each atom is formed.

The derivation for the zero-point vibrational correction for a molecular property using a perturbation expansion with respect to normal coordinates has been quoted in a convenient general form by Sauer and Packer[1] and is based on the technique introduced by Kern et al.[22,23,50] We adopt their equation and modify it slightly by adding factors of reduced mass, μ. Including these factors in the equation allows one to adapt the output of a variety of computational chemistry programs to calculate vibrational corrections readily because most programs report the Cartesian displacements as normalized vectors for a given normal mode. Formulas that are based on normal coordinates are dependent on the way the coordinates are defined. This is due to the fact that normal modes can be expressed in different coordinate systems: Cartesian, mass-weighted Cartesian, with and without normalization factors, etc. Our formula assumes that we easily have available normalized (within a given normal mode) Cartesian displacements and reduced masses, which is related to the normalization factor of the corresponding vector in the **S** matrix. With these values at hand, the zero-point vibrational correction, ZPVC, of a molecular property P is readily calculated from the equation

$$\mathrm{ZPVC} = -\frac{1}{4}\sum_{i=1}^{m}\frac{1}{{\omega_i}^2\sqrt{\mu_i}}\left(\frac{\partial P}{\partial Q_i}\right)\sum_{j=1}^{m}\frac{k_{ijj}}{\omega_j\mu_j\sqrt{\mu_i}} + \frac{1}{4}\sum_{i=1}^{m}\frac{1}{\omega_i\mu_i}\left(\frac{\partial^2 P}{\partial {Q_i}^2}\right) \tag{5}$$

where m represents the number of normal modes, ω_i is the frequency of the ith normal mode, and μ_i is its reduced mass, all expressed in atomic units. The property derivatives are taken with respect to the normal coordinates Q_i for a given normal mode i. k_{ijj} represents the anharmonic cubic force constant, which is defined as the mixed third-energy derivative,

$$k_{ijj} = \frac{\partial^3 E}{\partial Q_i \partial {Q_j}^2} \tag{6}$$

at the equilibrium geometry. Finally, ZPVC is the zero-point vibrational correction to the property evaluated at the equilibrium geometry.

The ZPVC (eq 5) can be analyzed as an equation that contains two terms:

$$\Delta P_1 = -\frac{1}{4}\sum_{i=1}^{m}\frac{1}{{\omega_i}^2\sqrt{\mu_i}}\left(\frac{\partial P}{\partial Q_i}\right)\sum_{j=1}^{m}\frac{k_{ijj}}{\omega_j\mu_j\sqrt{\mu_i}} \tag{7}$$

and

$$\Delta P_2 = \frac{1}{4}\sum_{i=1}^{m}\frac{1}{\omega_i\mu_i}\left(\frac{\partial^2 P}{\partial {Q_i}^2}\right) \tag{8}$$

The ΔP_1 term considers the anharmonicity of the potential energy surface. The anharmonic cubic force constants contribute to the degree in which a change in energy occurs with respect to a change in the geometry from the equilibrium position. The anharmonicity term ΔP_1 accounts for the fact that the zero-point averaged geometry of the molecule, and therefore P, differ from the equilibrium value if the potential energy surface is anharmonic. The ΔP_2 term is due to curvature of the property surface, i.e., the change in the slope of the property with respect to normal coordinates. Both of these terms can contribute to the ZPVC of a molecular property. Higher-order “cross terms” between anharmonicity and property curvature are not considered in this approach. Because this work is focused on zero-point vibrational corrections, we will neglect the thermal population of vibrational states. The extension of this work to the temperature dependence of vibrational corrections is conceptually rather straightforward but will be left for future investigations.

Once the normal modes for the molecule are expressed in Cartesian displacement coordinates, a set of molecular geometries corresponding to the vibrational modes can be constructed. A numerical parameter, δ, is chosen to represent a reasonable size of displacement for the atoms. Because **S** is normalized, it is necessary to take a reasonable and consistent fraction of each atom's displacement for the purpose of obtaining a computationally feasible displaced geometry. The size of these displacements for calculating force constants and other energy derivatives has been discussed in the literature.[51-53] In our program, we take a fraction δ of **S** that allows for the average displacement over the entire **S** matrix of each atom to be equal to a value of 0.04 a_0. Thus, the δ value is calculated directly from **S**, the number of nuclei n, and normal modes m in the molecule:

$$\delta = 0.04\frac{nm}{\sqrt{3}d} \tag{9}$$

where

$$d = \sum_{j=1}^{m}\sum_{i=1}^{n}\sqrt{\sum_{\alpha=1}^{3}(S_{3(i-1)+\alpha,j})^2} \tag{10}$$

It is important to note that this value of average displacement works well for energy derivatives but may not automatically yield desirable results for property derivatives. A brief analysis of the δ dependence of our calculations is given later to address this issue.

The computations proceed as follows: In the first step, the equilibrium geometry is determined with high numerical accuracy and the normal modes and frequencies are calculated. Next, we calculate the property $P_{+/0/-}$ as well as the analytic energy gradients $\partial E_{+/0/-}/\partial Q_j$ at positively (+) and negatively (−) displaced geometries along the normal coordinates, as expressed in the form of the matrix **S**. The equilibrium values (0) are also needed. The energy gradients expressed in terms of the normal modes are obtained from the Cartesian energy gradients as

$$\frac{\partial E_{+/0/-}}{\partial Q_j} = \sum_{\alpha=1}^{3n}\frac{\partial E_{+/0/-}}{\partial x_\alpha}S_{\alpha j} \tag{11}$$

The x_α represents the x, y, or z component of the atomic positions.

The anharmonic cubic force constant is obtained from a three-point finite difference numerical derivative,

$$k_{ijj} = \frac{\partial^3 E}{\partial Q_j^{\,2}\partial Q_i} = \frac{\partial^2}{\partial Q_j^{\,2}}\left(\frac{\partial E}{\partial Q_i}\right) \approx \frac{\frac{\partial E_+}{\partial Q_i} - 2\frac{\partial E_0}{\partial Q_i} + \frac{\partial E_-}{\partial Q_i}}{\delta^2} \tag{12}$$

It would be desirable to work with analytic second derivatives of energy instead, but these are not available for some quantum chemistry codes and/or computational methods. By using analytic first derivatives of energy only, our program has a larger range of applications.

Because eq 5 requires the calculation of the first and second derivatives of the property with respect to the normal coordinates, two-point and three-point numerical finite difference schemes are adopted to calculate the first- and second-property derivatives in our program.

$$\frac{\partial P}{\partial Q_i} \approx \frac{P_+ - P_-}{2\delta} \tag{13}$$

$$\frac{\partial^2 P}{\partial Q_i^{\,2}} \approx \frac{P_+ - 2P_0 + P_-}{\delta^2} \tag{14}$$

3. Computational Details

The geometries of 22 rigid organic molecules (Figure 1) were optimized using Turbomole 5.7.[48] The aug-cc-pVDZ basis set[54-56] was used along with the B3LYP hybrid functional.[57,58] The choice of this basis set and hybrid functional is common for many optical rotation calculations. Because Turbomole 5.7 and older versions do not make use of gauge-including atomic orbitals (GIAOs),[59] similar distributed origin techniques, or a dipole−velocity formalism,[60] the values obtained for optical rotation are origin dependent. The use of the aug-cc-pVDZ basis set attempts to mitigate this error.[43,46,61] Geometry optimization was carried out until the norm of the gradients converged to a value better than $10^{-6}E_h\cdot a_0^{-1}$. The program must have a highly optimized starting geometry to obtain accurate vibrational corrections. It has been suggested that gradient residuals should be less than $10^{-7}E_h\cdot a_0^{-1}$.[53] We adopt a criterion of $10^{-6}E_h\cdot a_0^{-1}$ for the norm of the gradient because of the computational cost of optimizing all structures in Figure 1 and the complications introduced by a diffuse basis set. Furthermore, DFT calculations require numerical integration of exchange-correlation terms which introduces some numerical noise. The Turbomole NumForce script was used to obtain the frequencies and normal modes for the vibrations. A locally modified copy of this script was created to remove the basis set restrictions imposed by one of the Turbomole modules. The required changes were minor and were only necessary for the molecules in Figure 1 that contain sulfur or heavier elements. The vibrational averaging program that we have written uses the normal modes to construct displaced geometries and to calculate the gradients and optical rotation of the equilibrium and displaced geometries. The escf module for the version of Turbomole used in this work printed the incorrect sign for the trace of the **G′** tensor. After verification of this behavior, we adjusted all results by multiplying by a factor of −1.

Molecules **1** and **3** were also optimized with Turbomole 5.7 in a similar manner at the Hartree−Fock level using the aug-cc-pVDZ basis set. These molecules were chosen so that comparisons with previously reported literature values could be made.[18] Our vibrational averaging program was applied to these two molecules to obtain the vibrational corrections to optical rotation for **1** and **3**.

4. Results and Discussion

Table 1 shows the results for the vibrational corrections to optical rotation for the 22 organic molecules using the B3LYP functional. For each molecule, we have computed an optimal δ value and the equilibrium geometry optical rotation ($[\alpha]_D^{eq}$) at the sodium D-line transition frequency of 589.3 nm using an optimized geometry for B3LYP. The vibrational correction for each optical rotation (ZPVC) is also given, along with the percent of correction from the equilibrium value. The breakdown of the contributions from the anharmonicity of the potential (ΔP_1) and the curvature of the property surface (ΔP_2) is also presented for each molecule. For reference comparisons, experimental values for the optical rotations are also given. They have been taken from the compilations in the literature.[42,43] All optical rotations are given in units of $\text{deg}\cdot\text{cm}^3\cdot\text{dm}^{-1}\cdot\text{g}^{-1}$.

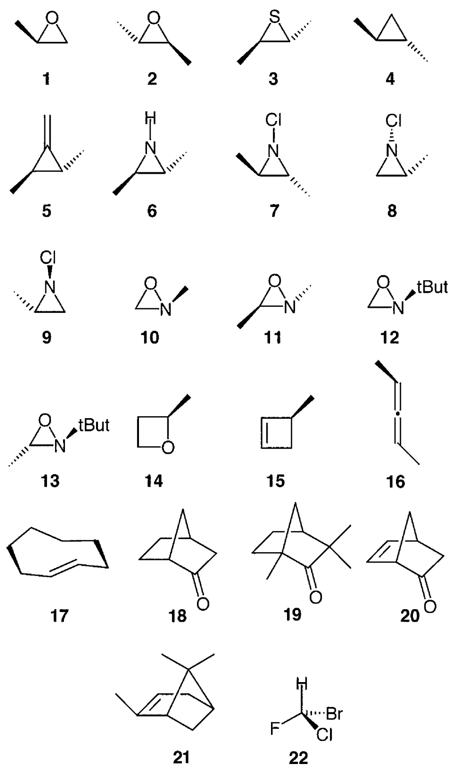

Figure 1. Twenty-two molecules of the test set and their stereochemical configurations for which the computations have been carried out.

TABLE 1: Results of the Optical Rotations and the Zero-Point Vibrational Corrections (ZPVCs) Calculated at the Equilibrium Geometry for the 22 Molecules in Figure 1[a]

molecule	δ	$[\alpha]_D^{eq}$	ΔP_1	ΔP_2	ZPVC	%|ZPVC|	$[\alpha]_D^{exptl\ b}$
1	0.10	18.16	0.25	−7.01	−6.76	37.2	18.7
2	0.11	−78.06	−2.28	4.12	1.84	2.3	−58.8
3	0.11	174.27	5.31	25.15	30.46	17.5	129.0
4	0.12	54.82	1.55	5.35	6.90	12.6	42.0
5	0.13	11.69	−4.92	23.14	18.21	155.8	57.6
6	0.12	111.61	3.69	4.32	8.01	7.2	103.8
7	0.12	−32.92	−1.92	−4.66	−6.58	20.0	−16.8
8	0.11	76.99	1.13	0.74	1.88	2.4	78.2
9	0.11	124.02	2.97	10.54	13.51	10.9	103.4
10	0.10	−131.35	−4.59	−0.63	−5.22	4.0	N/A[c]
11	0.11	198.31	2.97	5.40	8.37	4.2	N/A[c]
12	0.12	−9.08	−1.39	5.75	4.36	48.0	−34.5
13	0.13	−86.28	−1.54	−0.07	−1.61	1.9	−37.1
14	0.12	−76.49	−0.08	−8.10	−8.18	10.7	−34.0
15	0.12	−166.15	−0.34	−4.22	−4.57	2.8	−176.0
16	0.11	−93.13	0.52	3.33	3.85	4.1	−81.0
17	0.14	−322.65	−13.33	−37.81	−51.14	15.8	−430.0
18	0.14	12.00	−0.10	1.98	1.89	15.8	29.0
19	0.17	−57.13	0.35	0.52	0.87	1.5	−50.5
20	0.13	−1216.07	−0.32	−52.83	−53.16	4.4	−1146.0
21	0.18	41.15	0.11	5.02	5.13	12.5	51.6
22	0.07	1.60	0.17	−0.23	−0.06	3.8	1.8

[a] Calculations were done with the B3LYP hybrid functional and the aug-cc-pVDZ basis set. δ has been determined with eq 9. ΔP_1 and ΔP_2 are defined by eqs 7 and 8, respectively. The ZPVC is a sum of these two terms. All optical rotations and ZPVCs are given in units of deg·cm^3·dm^{-1}·g^{-1}. [b] Experimental values have been taken from the compilations in the literature.[42,43] In some cases, the experimental value has been measured for the optical antipode and is consequently multiplied by −1. [c] Data are not available in the compilations cited above.

TABLE 2: A Statistical Analysis of the Zero-Point Vibrational Corrections from Table 1[a]

molecule	$[\alpha]_D^{eq}$	$[\alpha]_D^{ZPA\ b}$	$[\alpha]_D^{exptl}$	$\|\Delta^{eq}\|^c$	$\%\|\Delta^{eq}\|^d$	$\|\Delta^{ZPA}\|^e$	$\%\|\Delta^{ZPA}\|^f$
1	18.16	11.40	18.7	0.5	2.9	7.3	39.0
2	−78.06	−76.22	−58.8	19.3	32.8	17.4	29.6
3	174.27	204.73	129.0	45.3	35.1	75.7	58.7
4	54.82	61.72	42.0	12.8	30.5	19.7	47.0
5	11.69	29.90	57.6	45.9	79.7	27.7	48.1
6	111.61	119.62	103.8	7.8	7.5	15.8	15.2
7	−32.92	−39.50	−16.8	16.1	96.0	22.7	135.1
8	76.99	78.87	78.2	1.2	1.5	0.7	0.9
9	124.02	137.53	103.4	20.6	19.9	34.1	33.0
12	−9.08	−4.72	−34.5	25.4	73.7	29.8	86.3
13	−86.28	−87.89	−37.1	49.2	132.6	50.8	136.9
14	−76.49	−84.67	−34.0	42.5	125.0	50.7	149.0
15	−166.15	−170.72	−176.0	9.9	5.6	5.3	3.0
16	−93.13	−89.28	−81.0	12.1	15.0	8.3	10.2
17	−322.65	−373.79	−430.0	107.4	25.0	56.2	13.1
18	12.00	13.89	29.0	17.0	58.6	15.1	52.1
19	−57.13	−56.26	−50.5	6.6	13.1	5.8	11.4
20	−1216.07	−1269.23	−1146.0	70.1	6.1	123.2	10.8
21	41.15	46.28	51.6	10.5	20.3	5.3	10.3
22	1.60	1.54	1.8	0.2	10	0.3	10
avg				26.0	40.0	28.6	45.0

[a] Only results that have experimental data available have been included here. All optical rotations and ZPVCs are given in units of deg·cm^3·dm^{-1}·g^{-1}. [b] $[\alpha]_D^{ZPA}$ is the zero-point averaged quantity and is equal to $[\alpha]_D^{eq}$ + ZPVC. [c] $|[\alpha - [\alpha]_D^{exptl}|$. [d] $100|([\alpha]_D^{eq} - [\alpha]_D^{exptl})/[\alpha]_D^{exptl}|$. [e] $|[\alpha]_D^{ZPA} - [\alpha]_D^{exptl}|$. [f] $100|([\alpha]_D^{ZPA} - [\alpha]_D^{exptl})/[\alpha]_D^{exptl}|$.

TABLE 3: A Comparison Between Literature Values[18] (lit.) and This Work for the Zero-Point Vibrational Corrections for Molecules 1 and 3[a]

molecule	δ	$[\alpha]_D^{eq}$	$[\alpha]_D^{lit.}$	ZPVC	ZPVC$^{lit.}$	%|ZPVC|	%|ZPVC|$^{lit.}$
1	0.10	11.37	9.98	−4.14	−3.62	36.4	36.3
3	0.11	165.37	154.48	27.33	32.97	16.5	21.3

[a] All optical rotations and ZPVCs are given in units of deg·cm^3·dm^{-1}·g^{-1}. δ has been determined by eq 9. All calculations presented here were done at the Hartree−Fock level with the aug-cc-pVDZ basis set. Note that the optical rotation and its corresponding zero-point vibrational correction reported in the literature have been multiplied by a factor of −1 to correspond with the optical antipode that was used in this work.

Table 2 gives an analysis of the vibrational corrections for the results that have experimental data available. For each molecule, we report the difference between the calculated and experimental values excluding Δ^{eq} and including Δ^{ZPA} vibrational corrections. The percent difference of the calculated value from the experimental value with and without vibrational correction is also shown. The percent of ZPVC is calculated as the absolute value of the correction divided by the equilibrium value of the optical rotation, as has typically been done in the literature for percent of ZPVC.[1,3,7,9,12,18] The average values are reported in the last row of Table 2. The average values of the absolute vibrational corrections are given, along with the average values of the percentage of absolute vibrational correction.

Our implementation of vibrational averaging differs slightly from the one developed by Ruud, Åstrand, et al.[27,28,62] because we use a method based on a perturbation expansion around the equilibrium geometry, as opposed to an effective geometry. As a verification on the validity of our method with respect to calculating vibrational corrections to optical rotations, we made a comparison with previous work with Hartree−Fock calculations and the aug-cc-pVDZ basis.[18] Table 3 shows that there is good agreement between previously reported values and the values that are obtained with the method presented here. Any differences are most likely due to slightly different equilibrium geometries and numerical noise.

Recently, Wiberg et al. have provided a series of studies on the conformational effects on optical rotation by analyzing substituted 1-butenes.[29,30] In these works, the vibrational correction to optical rotation for the substituted 1-butenes was

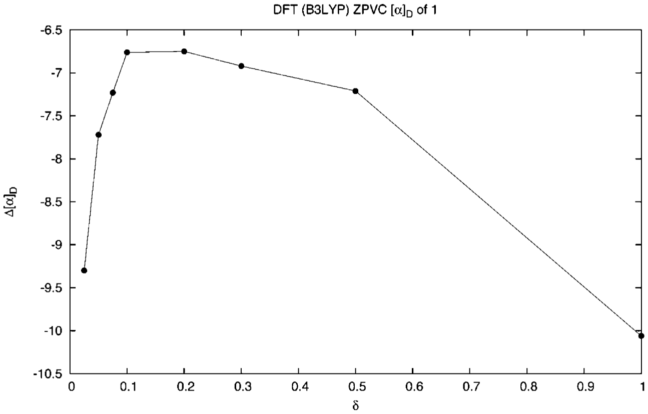

Figure 2. Numerical stability of the zero-point vibrational correction for molecule **1** as a function of the parameter δ.

calculated using a perturbation expansion around the equilibrium geometry, similar to the method used here. However, Wiberg et al. did not consider anharmonic effects and limited their treatment of vibrational effects to the contributions of the curvature of the property surface. In addition, temperature-dependence effects on vibrational corrections were built into the definition of displacement amplitudes that is used in their work. As a result, effects from higher vibrational modes are included in their study. Because the focus of this work is zero-point vibrational effects, we exclude temperature-dependence effects and contributions from higher vibrational states. The anharmonic term in eq 5 makes a noteworthy contribution to the overall vibrational correction, and the exclusion of this term by Wiberg et al. is justified in light of the much larger effects due to conformation in the specific case of the substituted 1-butene molecules. However, optical rotations of molecules that are not subjected to conformational effects may have significant vibrational corrections that are dependent on both the anharmonicity of the potential energy and the curvature of the property surface.

To see how the choice of value for the δ parameter affects the zero-point vibrational correction (ZPVC) of optical rotation in our program, we have analyzed the numerical stability of these corrections with respect to the size of the displacement of the atoms from the equilibrium geometry. A plot of the ZPVC vs δ for molecule **1** is given in Figure 2.

Molecule **1** was chosen for our numerical stability analysis because of its large relative correction that detracts the calculated value from the experimental value. It is important to realize that calculations of ZPVC to optical activity as conducted in this study require a highly optimized geometry and an accurate frequency and normal mode calculation at the beginning. The normal modes are used to construct $2(3n - 6)$ geometries (for nonlinear molecules), which are used to produce a total of $2(3n - 6)$ energy gradient calculations and $2(3n - 6)$ optical rotation calculations, where n is the number of atoms in the molecule. Although the number of coarse grained parallel calculations scales only as $O(n)$, the computation of each one of the energy gradients and optical rotations at a given displaced geometry scales, formally, approximately as $O(n^3)$ for pure DFT and as $O(n^4)$ for hybrid DFT. Better scaling might be obtained by the use of "linear scaling" techniques and efficient integral prescreening. As a result, the numerical stability analysis in this work has been restricted to a small molecule, whose ZPVC has been calculated in previous work.[18]

Numerical stability of the ZPVCs as a function of the parameter δ is dependent on the molecule. A relatively large range of numerical stability is demonstrated by molecule **1** and may be indicative of a large range in overlap in the energy and property derivative stabilities. It can be seen that the numerical accuracy deteriorates for the parameter values $\delta < 0.1$. We have confirmed this for a few other molecules. Because of inaccuracies of the cubic force constants and property derivatives when δ is large, it is desirable to work with a δ as small as possible. We have confirmed that in all our calculations the actual nuclear displacement was significant enough to yield numerically significant differences in the gradients and properties. As an improvement over the current implementation of our program, a situation can be imagined where the program selects an ideal value for δ for property derivatives that may or may not be equal to an ideal value of δ for the energy derivatives. This method would require four displacements for each normal mode. In addition, a prescribed δ for each normal mode may also help reduce numerical instability. The number of geometry displacements along the normal modes could perhaps be reduced by making use of the symmetry of the molecule. However, the molecules in our test set have low or no symmetry and we are more interested to see first whether the magnitudes of the ZPVCs to the optical rotations would be significant, rather than implementing the most efficient approach.

From Table 1, it is quite evident that there is a large range in percentage of vibrational corrections. Molecule **19** has the smallest percent ZPVC, whereas molecule **5** affords a ZPVC to the optical rotation as large as 156%.

In general, it appears that ΔP_2 contributes more significantly to the ZPVC of a molecule than ΔP_1. As a result, the curvature of the property surface generally has a greater affect on the ZPVC to optical rotation than does the anharmonicity of the potential energy surface. This generalization may be true for many of the molecules presented in Figure 1, but there are notable exceptions. For example, molecule **10** has a ΔP_1 equal to -4.59 and a ΔP_2 equal to -0.63. For molecule **13**, it is -1.54 for the anharmonic contribution and -0.07 for the property curvature contribution. It does seem that molecules with large vibrational corrections tend to get a majority of their corrections from ΔP_2, but the first term ΔP_1 can indeed be significant. Calculating the gradients at each one of the displaced geometries is usually not as computationally demanding as calculating the properties at each one of the displaced geometries. So, the additional computational cost of calculating the gradients at the displaced geometries is affordable and leads to a greater legitimacy of the ZPVCs.

Because the ZPVC equation (eq 5) consists of factors of reciprocal frequencies, it is easy to imagine that low-level frequencies of vibration would have the greatest effect on the ZPVCs to the optical rotation of the molecules presented in Figure 1.[63] Although this statement may be true for some molecules, an analysis of the contributions to the ZPVC for each normal mode indicates that this is not always the case. For example, normal mode 32 (3139 cm^{-1}) of molecule **3** contributes the most, with 11.24 to the ZPVC value of 30.46. There are also cases where the largest correction (-2.78) such as normal mode 36 (3125 cm^{-1}) of molecule **4** is overwhelmed by the sum of the positive contributions from many of the other normal modes. For corrections involving only the zero-point, low-level frequencies do not seem to present as much of a problem as they do when higher states are considered or temperature effects are included. Identifying each vibration that makes the greatest contribution to the ZPVC to optical rotation is beyond the scope of this work as it is presented. This article is primarily concerned with demonstrating the size and range of ZPVCs to optical rotation for a general set of molecules.

It appears that vibrational correction to optical rotation is on average about 20% of the calculated equilibrium value. This is consistent with the 20−30% value reported by Ruud and coworkers[18] from their studies at the Hartree−Fock level with two of the molecules given in Figure 1 (viz. **1** and **3**). Our much larger data set and our correlation-including calculations at the DFT level with a commonly used basis set (aug-cc-pVDZ) reaffirm their conclusion. There is a wide range of values for the absolute value of the correction. We have observed ZPVCs between 1.5 and 156% for the molecules given in Figure 1.

It is likely that inclusion of vibrational effects alone in optical rotation calculations is not sufficient for reproducing experimental data that has been measured in solution. As evidenced from Table 2, including vibrational corrections in the calculated values results in an average percentage difference between the calculated values with the vibrational effects and the experimental numbers that is slightly worse than the average percentage difference between the calculated values without the vibrational effects and the experimental values (45 vs 40%, respectively). This is not too alarming because it has been discussed previously that solvent effects are influential, just as vibrational effects are.[31,32,36,64,65] Ruud et al.[18] noticed that the vibrational corrections for dimethyloxirane (**1**) and dimethylthiirane (**3**) shift the calculated values of the optical rotation away from the experimental number. They attribute this phenomenon to a missing treatment of solvent effects. Of course, the approximate treatment of electron correlation by the B3LYP functional is another source of error.[66]

There has been recent interest in examining the difficult case of obtaining accurate optical rotations for methyloxirane in the literature. Recently, Ruud and Zanasi have shown that the observed change in sign in the optical rotation of (*S*)-methyloxirane as the wavelength is varied from 589.3 to 355 nm is due to vibrational corrections.[19] Gas-phase measurements of optical rotation by cavity ring-down polarimetry[64] have shown that the optical rotation of (*S*)-methyloxirane differs in sign from what is experimentally observed in solution. These measurements were taken at 355 nm, and unfortunately, no gas-phase experimental data for the optical rotation of (*S*)-methyloxirane at 589.3 nm are available. However, it should be noted that the experimental values for the optical rotation of (*S*)-methyloxirane at 589.3 nm vary from −30.6 to +4.3 in a series of solvents from C_6H_{12} to H_2O.[65] It is interesting to note that the vibrational correction in Table 1 to the calculated gas-phase (*R*)-methyloxirane optical rotation favors the direction of the opposite configuration. Clearly, more research that includes vibrational corrections and solvent effects simultaneously at a high level of theory is necessary to resolve this issue. For instance, as concluded in ref 19, current approaches to the calculation of ZPVCs to optical rotation is limited due to low excitation energies and the difficulty of a local-mode approximation. Thus, more research in the improvement of calculating vibrational corrections is certainly desirable.

5. Conclusions

It is quite evident that vibrational effects to optical rotation are sizable and need to be included in any attempt to accurately reproduce experimental data. However, including vibrational effects alone is likely not sufficient enough in obtaining experimental values. Solvent effects appear to be substantial when comparing gas-phase calculations with optical rotations measured experimentally in solution, as vibrational corrections alone cannot yield calculated values that correlate better with a variety of experimental data. It is hoped that a follow-up study invoking both vibrational and solvent effects into calculated values for optical rotation will result in better agreement between theory and experiment.

On a side note, it has been pointed out recently that optical rotation calculations at one frequency might not be reliable enough for assigning absolute configurations to chiral molecules.[67] Apparently, one may not be able to obtain accurate values for optical rotations at a given frequency unless all of the known influences (correlation, gauge origin, solvent, vibrational, etc.) are considered. It has been suggested that one should refer to the optical rotatory dispersion curves for assignment of absolute configurations.[33] This may be true at the current understanding of theory and the current limitations of implemented methods and available computational resources.

In addition to providing evidence of the significance of zero-point vibrational corrections (ZPVCs) to optical activity calculations at the equilibrium geometry, we have outlined the details of a simple program that can calculate the ZPVC to optical rotation. Our program is easily adapted to a variety of quantum chemistry packages and is available from the authors free of charge. Because *P* can be any property of interest that is geometry dependent, our program is not limited to calculating ZPVCs of optical rotations.

Acknowledgment. The authors would like to acknowledge support from the Center for Computational Research (CCR) at the University at Buffalo for computational resources. B.C.M. thanks the United States Department of Defense for support through a National Defense Science and Engineering Graduate (NDSEG) Fellowship. J.A. is grateful for financial support from the ACS Petroleum Research Fund and from the CAREER program of The National Science Foundation.

References and Notes

(1) Sauer, S. P. A.; Packer, M. J. The ab initio calculation of molecular properties other than the potential energy surface. In *Computational Molecular Spectroscopy*; Bunker, P. R., Jensen, P., Eds.; John Wiley & Sons: London, 2000.

(2) Bishop, D. M.; Kirtman, B. *J. Chem. Phys.* **1991**, *95*, 2646−2658.

(3) Russell, A. J.; Spackman, M. A. *Mol. Phys.* **1995**, *84*, 1239−1255.

(4) Bishop, D. M.; Kirtman, B.; Kurtz, H. A.; Rice, J. E. *J. Chem. Phys.* **1993**, *98*, 8024−8030.

(5) Bishop, D. M.; Sauer, S. P. A. *J. Chem. Phys.* **1997**, *107*, 8502−8509.

(6) Åstrand, P.-O.; Mikkelsen, K. V. *J. Chem. Phys.* **1996**, *104*, 648−653.

(7) Ruud, K.; Åstrand, P.-O.; Taylor, P. R. *J. Phys. Chem. A* **2001**, *105*, 9926−9930.

(8) Ruud, K.; Jonsson, D.; Taylor, P. R. *Phys. Chem. Chem. Phys.* **2000**, *2*, 2161−2171.

(9) Bishop, D. M.; Cybulski, S. M. *J. Chem. Phys.* **1994**, *101*, 2180−2185.

(10) Fukui, H.; Baba, T.; Narumi, J.; Inomata, H.; Miura, K.; Matsuda, H. *J. Chem. Phys.* **1996**, *105*, 4692−4699.

(11) Sundholm, D.; Gauss, J.; Schäfer, A. *J. Chem. Phys.* **1996**, *105*, 11051−11059.

(12) Ruud, K.; Åstrand, P.-O.; Taylor, P. R. *J. Am. Chem. Soc.* **2001**, *123*, 4826−4833.

(13) Åstrand, P.-O.; Ruud, K. *Phys. Chem. Chem. Phys.* **2003**, *5*, 5015−5020.

(14) Buhl, M.; Imhof, P.; Repisky, M. *Phys. Chem. Chem. Phys.* **2004**, *5*, 410−414.

(15) Grigoleit, S.; Buhl, M. *Chem.*−*Eur. J.* **2004**, *10*, 5541−5552.

(16) Ruden, T. A.; Lutnæs, O. B.; Helgaker, T.; Ruud, K. *J. Chem. Phys.* **2003**, *118*, 9572−9581.

(17) Ruden, T.; Helgaker, T.; Jaszunski, M. *Chem. Phys.* **2004**, *296*, 53−62.

(18) Ruud, K.; Taylor, P. R.; Åstrand, P.-O. *Chem. Phys. Lett.* **2001**, *337*, 217−223.

(19) Ruud, K.; Zanasi, R. *Angew. Chem., Int. Ed.* **2005**, *44*, 3594−3596.

(20) Herschbach, D. R.; Laurie, V. W. *J. Chem. Phys.* **1962**, *37*, 1668−1686.

(21) Toyama, M.; Oka, T.; Morino, Y. *J. Mol. Spectrosc.* **1964**, *13*, 193−213.

(22) Kern, C. W.; Matcha, R. L. *J. Chem. Phys.* **1968**, *49*, 2081−2091.

(23) Krohn, B. J.; Ermler, W. C.; Kern, C. W. *J. Chem. Phys.* **1974**, *60*, 22−33.

(24) Riley, G.; Raynes, W. T.; Fowler, P. W. *Mol. Phys.* **1979**, *38*, 877−892.

(25) Fowler, P. W. *Mol. Phys.* **1981**, *43*, 591−600.

(26) Fowler, P. W. *Mol. Phys.* **1984**, *51*, 1423−1428.

(27) Åstrand, P.-O.; Ruud, K.; Taylor, P. R. *J. Chem. Phys.* **2000**, *112*, 2655−2667.

(28) Ruud, K.; Åstrand, P.-O.; Taylor, P. R. *J. Chem. Phys.* **2000**, *112*, 2668−2683.

(29) Wiberg, K. B.; Vaccaro, P. H.; Cheeseman, J. R. *J. Am. Chem. Soc.* **2003**, *125*, 1888−1896.

(30) Wiberg, K. B.; Wang, Y.; Vaccaro, P. H.; Cheeseman, J. R.; Trucks, G.; Frisch, M. J. *J. Phys. Chem. A* **2004**, *108*, 32−38.

(31) Polavarapu, P. L. *Chirality* **2002**, *14*, 768−781.

(32) Giorgio, E.; Rosini, C.; Viglione, R. G.; Zanasi, R. *Chem. Phys. Lett.* **2003**, *376*, 452−456.

(33) Giorgio, E.; Viglione, R. G.; Zanasi, R.; Rosini, C. *J. Am. Chem. Soc.* **2004**, *126*, 12968−12976.

(34) McCann, D. M.; Stephens, P. J. *J. Org. Chem.* **2004**, *69*, 8709−8717.

(35) Marchesan, D.; Coriani, S.; Forzato, C.; Nitti, P.; Pitacco, G.; Ruud, K. *J. Phys. Chem. A* **2005**, *109*, 1449−1453.

(36) Kongsted, J.; Pedersen, T. B.; Strange, M.; Osted, A.; Hansen, A. E.; Mikkelsen, K. V.; Pawlowski, F.; Jorgensen, P.; Hattig, C. *Chem. Phys. Lett.* **2005**, *401*, 385−392.

(37) Cheeseman, J. R.; Frisch, M. J.; Devlin, F. J.; Stephens, P. J. *J. Phys. Chem. A* **2000**, *104*, 1039−1046.

(38) Tam, M. C.; Russ, N. J.; Crawford, T. D. *J. Chem. Phys.* **2004**, *121*, 3550−3557.

(39) Rosenfeld, L. *Z. Phys.* **1928**, *52*, 161−168.

(40) Kauzmann, W. *Quantum Chemistry*; Academic Press: New York, 1957.

(41) Buckingham, A. D. *Adv. Chem. Phys.* **1967**, *12*, 107−142.

(42) Stephens, P. J.; Devlin, F. J.; Cheeseman, J. R.; Frisch, M. J. *J. Phys. Chem. A* **2001**, *105*, 5356−5371.

(43) Grimme, S. *Chem. Phys. Lett.* **2001**, *339*, 380−388.

(44) Ruud, K.; Helgaker, T. *Chem. Phys. Lett.* **2002**, *352*, 533−539.

(45) Autschbach, J.; Ziegler, T. *J. Chem. Phys.* **2002**, *116*, 891−896.

(46) Autschbach, J.; Ziegler, T.; Patchkovskii, S.; van Gisbergen, S. J. A.; Baerends, E. J. *J. Chem. Phys.* **2002**, *117*, 581−592.

(47) Grimme, S.; Furche, F.; Ahlrichs, R. *Chem. Phys. Lett.* **2002**, *361*, 321−328.

(48) Quantum Chemistry Group *Turbomole*, version 5.7; Universitaet Karlsruhe.

(49) Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Montgomery, J. A., Jr.; Vreven, T.; Kudin, K. N.; Burant, J. C.; Millam, J. M.; Iyengar, S. S.; Tomasi, J.; Barone, V.; Mennucci, B.; Cossi, M.; Scalmani, G.; Rega, N.; Petersson, G. A.; Nakatsuji, H.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Klene, M.; Li, X.; Knox, J. E.; Hratchian, H. P.; Cross, J. B.; Bakken, V.; Adamo, C.; Jaramillo, J.; Gomperts, R.; Stratmann, R. E.; Yazyev, O.; Austin, A. J.; Cammi, R.; Pomelli, C.; Ochterski, J. W.; Ayala, P. Y.; Morokuma, K.; Voth, G. A.; Salvador, P.; Dannenberg, J. J.; Zakrzewski, V. G.; Dapprich, S.; Daniels, A. D.; Strain, M. C.; Farkas, O.; Malick, D. K.; Rabuck, A. D.; Raghavachari, K.; Foresman, J. B.; Ortiz, J. V.; Cui, Q.; Baboul, A. G.; Clifford, S.; Cioslowski, J.; Stefanov, B. B.; Liu, G.; Liashenko, A.; Piskorz, P.; Komaromi, I.; Martin, R. L.; Fox, D. J.; Keith, T.; Al-Laham, M. A.; Peng, C. Y.; Nanayakkara, A.; Challacombe, M.; Gill, P. M. W.; Johnson, B.; Chen, W.; Wong, M. W.; Gonzalez, C.; Pople, J. A. *Gaussian 03*, revision B.05; Gaussian, Inc.: Wallingford, CT, 2003.

(50) Ermler, W. C.; Kern, C. W. *J. Chem. Phys.* **1971**, *55*, 4851−4860.

(51) Schneider, W.; Thiel, W. *Chem. Phys. Lett.* **1989**, *157*, 367−373.

(52) Dressler, S.; Thiel, W. *Chem. Phys. Lett.* **1997**, *273*, 71−78.

(53) Barone, V. *J. Chem. Phys.* **2005**, *122*, 014108−10.

(54) Dunning, T. H., Jr. *J. Chem. Phys.* **1989**, *90*, 1007−1023.

(55) Woon, D. E.; Dunning, T. H., Jr. *J. Chem. Phys.* **1993**, 1358−1371.

(56) Woon, D. E.; H., D. J. T. *J. Chem. Phys.* **1994**, *100*, 2975−2988.

(57) Becke, A. D. *J. Chem. Phys.* **1993**, *98*, 5648−5652.

(58) Stephens, P. J.; Devlin, F. J.; Chabalowski, C. F.; Frisch, M. J. *J. Phys. Chem.* **1994**, *98*, 11623−11627.

(59) Ditchfield, R. *Mol. Phys.* **1974**, *27*, 789−807.

(60) Pedersen, T. B.; Koch, H.; Boman, L.; Sanchez de Meras, A. M. J. *Chem. Phys. Lett.* **2004**, *393*, 319−326.

(61) Autschbach, J.; Ziegler, T.; van Gisbergen, S. J. A.; Baerends, E. J. *J. Chem. Phys.* **2002**, *116*, 6930−6940.

(62) Åstrand, P.-O.; Ruud, K.; Sundholm, D. *Theor. Chem. Acc.* **2000**, *103*, 365−373.

(63) Wiberg, K. B.; Wang, Y.; Murphy, M. J.; Vaccaro, P. H. *J. Phys. Chem. A* **2004**, *108*, 5559−5563.

(64) Muller, T.; Wiberg, K. B.; Vaccaro, P. H. *J. Phys. Chem. A* **2000**, *104*, 5959−5968.

(65) Kumata, Y.; Furukawa, J.; Fueno, T. *Bull. Chem. Soc. Jpn.* **1970**, *43*, 3920.

(66) Crawford, D. T.; Owens, L. S.; Tam, M. C.; Schreiner, P. R.; Koch, H. *J. Am. Chem. Soc.* **2005**, *127*, 1368−1369.

(67) Rinderspacher, B. C.; Schreiner, P. R. *J. Phys. Chem. A* **2004**, *108*, 2867−2870.