# Prediction of Vibrational Circular Dichroism Spectra Using Density Functional Theory: Camphor and Fenchone

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Density functional theory (DFT) is increasingly the method of choice in the *ab initio* prediction of molecular properties.[1] Here, we document a new application of DFT: the prediction of vibrational circular dichroism (VCD) spectra. VCD is exhibited by chiral molecules[2] and can be used as a structural tool for the investigation of this important class of molecules. Until now reliable calculations of VCD spectra have only been practicable for a limited range of molecular size. The development we report here greatly expands this range and, hence, the utility of the VCD technique.

The prediction of a VCD spectrum within the harmonic approximation requires the harmonic force field (HFF), atomic polar tensors (APTs), and atomic axial tensors (AATs).[3] Efficient implementations of DFT algorithms for calculating HFFs and APTs[4]—and, hence, vibrational frequencies and dipole strengths and unpolarized vibrational absorption spectra—are already in widespread use.[5] Here, we report the application of DFT to the calculation of AATs and, thence, vibrational rotational strengths and VCD spectra. The details of the theoretical methodology are presented elsewhere.[6] Magnetic field-dependent basis functions, specifically gauge-invariant (including) atomic orbitals (GIAOs), are used. These functions are well-known in the calculation of magnetic properties[7] and have recently been incorporated in DFT calculations of nuclear magnetic shielding tensors.[8] They have previously been used in calculating AATs at the SCF and MCSCF levels of approximation.[9] As a result of the use of GIAOs, calculated vibrational strengths are origin independent. Direct, analytical derivative techniques are used, optimizing efficiency. The implementation is general, permitting the use of any density functional including the recently introduced “hybrid” functionals[10] in which exact (Hartree−Fock) exchange is admixed with exchange and correlation functionals. The methodology is implemented within the GAUSSIAN program suite.[11]

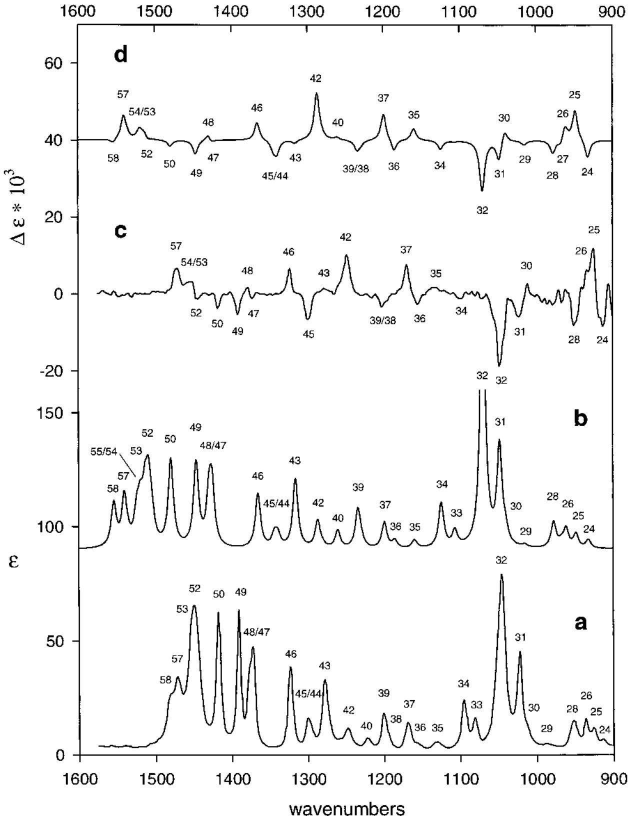

**Figure 1.** Unpolarized absorption spectra (a, b) and VCD spectra (c, d) of camphor (**1**). Experimental spectra (a, c)[12] are for a 0.6 M $CCl_4$ solution and at 4 $cm^{-1}$ resolution. Calculated spectra (b, d) use Lorentzian band shapes[16] with $\gamma = 4$ $cm^{-1}$. Fundamentals are numbered. VCD spectra are for (1*R*,4*R*)-(+)-**1**.

The new methodology has been used to predict the VCD spectra of two monoterpene natural products: 1,7,7-trimethyl-2-norbornanone, camphor (**1**), and 1,3,3-trimethyl-2-norbornanone, fenchone (**2**). Experimental mid-infrared VCD spectra of **1**[12] and **2**[13] are reproduced in Figures 1 and 2. Corresponding unpolarized absorption spectra are also shown. Our calculations use the hybrid functional B3PW91[14] and the 6-31G* basis set. VCD spectra predicted from calculated vibrational frequencies and rotational strengths using Lorentzian band shapes of constant width are shown in Figures 1 and 2; corresponding absorption spectra obtained from calculated frequencies and dipole strengths are also shown.

The calculated absorption and VCD spectra of **1** and **2** are in obvious correspondence with the experimental spectra, allowing

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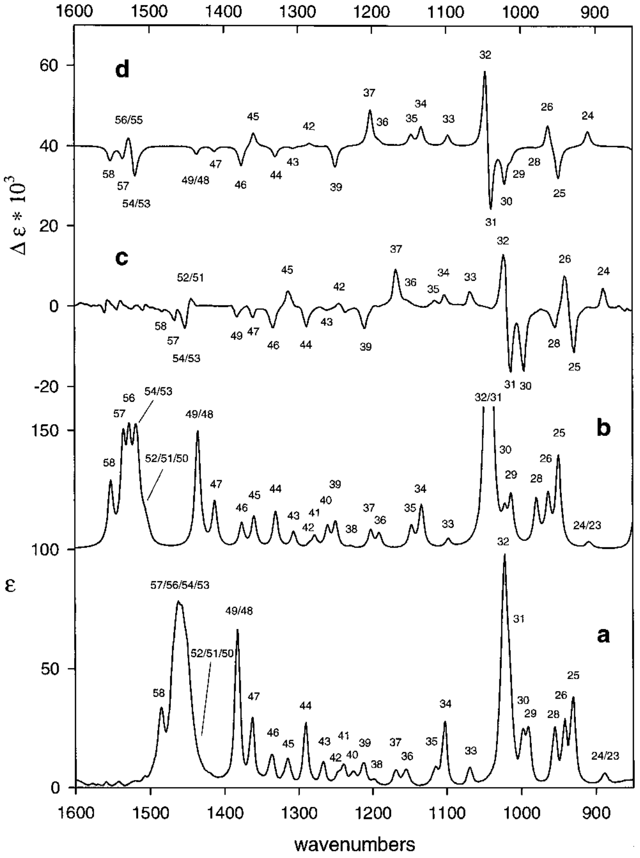

**Figure 2.** Unpolarized absorption spectra (a, b) and VCD spectra (c, d) of fenchone (**2**). Experimental spectra (a, c)[13] are for a 1 M $CCl_4$ solution and at 5 $cm^{-1}$ resolution. Reported $A$ and $\Delta A$ values were converted to $\epsilon$ and $\Delta\epsilon$ values using a path length of 84 $\mu$m. estimated by comparison of the reported absorption spectrum to a spectrum measured in our laboratory. Calculated spectra (b, d) use Lorentzian band shapes[16] with $\gamma = 4$ $cm^{-1}$. Fundamentals are numbered. VCD spectra are for (1*S*,4*S*)-(+)-**2**.

for the expected overall shift to higher frequencies,[15] permitting straightforward assignment of almost all fundamental bands, as indicated in Figures 1 and 2. The experimental rotational strengths of those bands assigned as fundamentals, obtained by Lorentzian fitting of the experimental VCD spectra,[16] are compared to the calculated values in Figure 3. The agreement is excellent. Residual errors can be attributed predominantly to basis set incompleteness, anharmonicity, solvent effects, and experimental error.

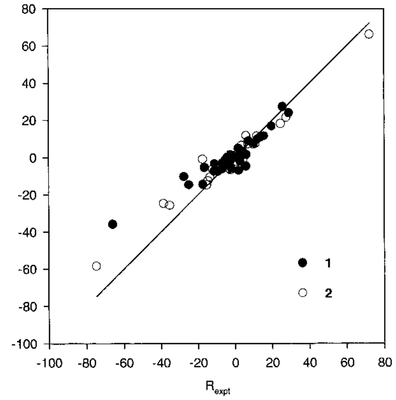

**Figure 3.** Comparison of calculated and experimental rotational strengths of **1** (●) and **2** (○). Experimental rotational strengths were obtained by Lorentzian fitting of the VCD spectra (Figures 1 and 2). The line is of unit slope. Rotational strengths, *R*, are in $10^{-44}$ $esu^2$ $cm^2$.

DFT combines the computational simplicity of the Hartree–Fock method with the accuracy of correlated methods such as MP2. DFT predictions of VCD spectra are now practicable. The results presented here demonstrate that, when a hybrid functional and an adequate basis set are used, predicted VCD spectra are of excellent accuracy. The calculations on **1** and **2** were carried out on a desktop workstation. As a result of the use of direct methods, calculations on much larger molecules are now feasible, as will be documented in forthcoming publications. This new capability should substantially enhance the utility of VCD spectroscopy in the elucidation of the stereochemistry of chiral molecules.

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