Probing chiral properties of medium-to-large organic molecules: The VPT2 approach

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The biological activity of molecules is strongly dependent on their chirality. Understanding this property is thus of critical importance in pharmaceutical industries, but has gained growing interest in other technological applications. Chiral spectroscopies, in particular Vibrational Circular Dichroism (VCD) and Raman Optical Activity (ROA), are the methods of choice to probe and analyze the dynamic and structural characteristic of such molecules.[1] The wealth of information contained in experimental spectra cannot be fully exploited through phenomenological studies, and quantum mechanical simulations are now systematically used to support and complement observations. While the harmonic approximation is often sufficient to assign absolute configurations, it has inherent limitations, which can hinder a detailed analysis of the vibrational properties of a system, like the overestimation of transition energies or the impossibility to reproduce non-fundamental bands. Such issues are often exacerbated by the sensitivity of chiroptical spectroscopies. Significant improvements are obtained by proper inclusion of anharmonic effects. However, the computational cost of such methods has confined them to small molecular systems.
Thanks to hardware improvements and its good cost-accuracy ratio, vibrational second-order perturbation theory (VPT2)[2] can now be applied to the anharmonic simulation of medium-to-large systems.[3,4] Nonetheless, the increase in problem size and structural complexity also worsens the well-known issue of resonances, which can seriously affect the accuracy and reliability of VPT2 results. As a "visual" identification of resonances becomes unpractical, robust automatic procedures are necessary,[5] and their validation requires extensive studies on small- to medium-sized molecules. In this contribution, the importance of a correct identification and treatment of resonances will be illustrated. The impact of the quality of the harmonic approximation, and the underlying electronic structure calculation method will also be considered. The design of a reliable protocol will build the path to systematic application of VPT2 to larger systems, here represented by pinene and artemisinin.

References

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