Nuclear quantum effects in an HIV/cancer inhibitor: The case of ellipticine.

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Abstract:

Ellipticine is a natural product that is currently being actively investigated for its inhibitory cancer and HIV properties. Here we use path-integral molecular dynamics coupled with excited state calculations to characterize the role of nuclear quantum effects on the structural and electronic properties of ellipticine in protic solvents (such as water, methanol, and ethylene glycol). Quantum effects collectively enhance the fluctuations of both light and heavy nuclei of the covalent and hydrogen bonds in ellipticine. In particular, for the ellipticine-water system, where the proton donor and acceptor have different proton affinities, we find that nuclear quantum effects (NQEs) strengthen both the strong and the weak H bonds. This is in contrast to what is observed in the cases where the proton affinity of the donors and acceptors is same. However, ellipticine-methanol (and ethylene glycol) behave distinctly from the ellipticine-water system. These structural fluctuations cause a significant red-shift in the absorption spectra and an increase in the broadening, bringing it into closer agreement with the experiments. Our work shows that nuclear quantum effects alter both qualitatively and quantitatively the optical properties of this biologically relevant system and highlights the importance of the inclusion of these effects in the microscopic understanding of their optical properties.