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

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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 water, a common biological solvent and as well as protic solvents such as 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, a contrast to what is observed for the cases where the proton affinity of the donors and acceptors is same. 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. We propose that isotopic substitution will produce a blue shift and a reduction in the broadening of the absorption peak.