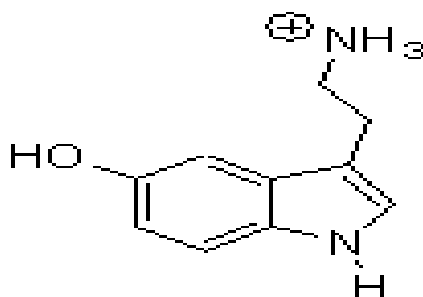


STRUCTURE OF PROTONATED SEROTONIN

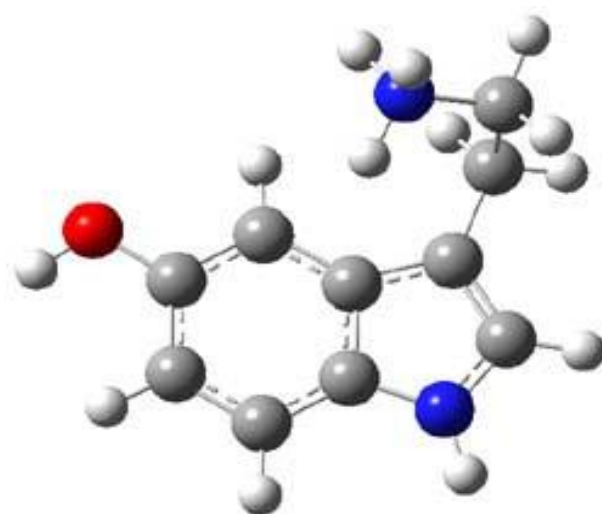
The structure of organic molecules of biochemical significance remains an important pursuit, one that I have discussed in a number of blog posts. Highlighted particularly in this blog (and in my book) has been the interplay of experiment and computation in structure determination. Dopfer and co-workers combine IR multiple photon dissociation (IRMPD) with DFT and MP2 computations to determine the structure of protonated serotonin **1H⁺**.¹



1H⁺

B3LYP/cc-pVDZ and MP2/cc-pVDZ computations of the conformations of **1H⁺** give nearly identical results. The lowest energy conformer (see Figure 1) has the ethylamine group in a *gauche* arrangement so that the protonated amine can interact with the π -system of the ring. The hydroxyl group is orientated *trans* relative to the ethylamine group.

Conformer generated by rotation about the C-O bond or the C-C and C-N bond of the ethylamine group are higher in energy, anywhere from 0.5 to about 5 kcal mol⁻¹ above the lowest conformer. Protonation at the ring nitrogen or the oxygen are more than 20 kcal mol⁻¹ higher in energy than the lowest conformer.



1H+

Figure 1. B3LYP/6-31G(d) optimized geometry of **1H+**. Note that the authors did not supply sufficient information in their supporting materials to generate the full 3-D coordinates of the molecule, and I did not want to reoptimize at cc-pVDZ. *Referees – please insist on complete supporting information!*

Comparison of the experimental IR spectrum of **1H**+ with the computed IR frequencies (either B3LYP or MP2 – they are very similar) reveals a remarkable agreement with the computed spectra of just the lowest energy conformer.

While the lowest energy conformer is predicted to be nearly 70% of the population, there is little spectroscopic evidence of the participation of any other conformer. In fact, the next three lowest energy conformers have a distinctive peak (in their computed IR spectrum) at about 1400 cm^{-1} , a region that has virtually no absorption in the experimental IR.

Source: <http://comporgchem.com/blog/?p=1380>