

BENCHMARKING AB INITIO BINDING ENERGIES OF HYDROGEN- BONDED MOLECULAR CLUSTERS BASED ON FTIR SPECTROSCOPY

One of the holy grails of computational chemistry is a method that consistently can compute standard binding free energies in bulk solvent to within 1 kcal/mol. When using electronic structure theory one of the (many) potential problems is the use of the harmonic approximation because low-frequency modes can make a sizable contribution to the vibrational entropy. This paper provides some valuable benchmarking data.

Kjærsgaard and co-workers measure the gas phase binding free energy at 295 K of acetonitrile-HCl to be between 1.2 and 1.9 kcal/mol. CCSD(T)/aug-cc-pV(T+d) predicts 2.3 kcal/mol using the harmonic frequencies and 1.9 kcal/mol using the anharmonic scaling factors suggested by Shields and co-workers. So, at least in this case, the harmonic approximation works quite well, but can be improved quite easily using anharmonic scaling factors. If this effect is additive and transferable, then making such a correction will be important for systems that bind using several hydrogen bonds of the 1 kcal/mol accuracy-target is to be met.

The authors write "We find that this energy lowering originates almost entirely from the scaling of the two lowest frequency modes (between 28 and 35 cm^{-1} , depending on method), emphasizing the importance of calculating the low frequency modes accurately."

Indeed, such low frequency modes are susceptible to numerical noise (e.g. from coarse DFT grids or sloppy optimization convergence criteria) which can even lead to them turning up as imaginary frequencies in the vibrational analysis. Because imaginary frequencies are not included in the vibrational free energy, this can lead to sizable errors in the binding free energy. For example, a 28 cm^{-1} frequency contributes 1.8 kcal/mol to the free energy at 295 K.

B3LYP-D3, MP2 and PW91/aug-cc-pV(T+d) calculations also yield binding free energies within the experimentally measured range, but in the last two cases this is due for fortunate cancellation of errors in the electronic and free energy components based on comparison to the CCSD(T) calculations. Having said that, with the exception of B3LYP, all functionals tested in this study are able to predict the binding energy to within 1 kcal/mol using the aug-cc-pV(T+d) basis set.

It is worth noting that the approach by Shields and co-workers find scaling factors by fitting to *harmonic* vibrational energy and entropy-expressions evaluated using anharmonic fundamental frequencies. It is not at all obvious (at least to me) that this approach will result in good agreement with experimental binding free energies involving 28 cm⁻¹ frequencies, so this (and a previous) study provides very valuable validation of this general approach.

Source: <http://www.compchemhighlights.org/2014/12/benchmarking-ab-initio-binding-energies.html>