COMPUTING ^{1}H NMR CHEMICAL SHIFTS

Computed NMR spectra have been a major theme of the blog. General consensus is that they can be enormously helpful in characterizing structures and stereochemistry, but there has been a nagging sense that one needs to use very large basis sets to get reasonable accuracies.

Bally and Rablen[1] now confront that claim and suggest instead that quite modest basis sets along with a number of flavors of DFT can provide very good ^{1}H NMR shifts. They examined 80 organic molecules spanning a variety of functional groups. A key feature is that these molecules exist as a single conformation or their conformational distribution is dominated by one conformer. This avoids the need of computing a large number of conformers and taking a Boltzman average of their shifts – a task that would likely require a much larger basis set than what they hope to get away with.

The most important conclusion: the WP04 functional,[2] developed by Cramer to predict proton spectra, with the very small 6-31G(d,p) basis set and incorporation of the solvent through PCM provides excellent cost/benefit performance. The rms error of the proton chemical shifts is 0.198 ppm, and this can be reduced to 0.140 ppm with scaling. The 6-31G(d) basis set is even better if one uses a linear scaling; its error is only 0.120 ppm. B3LYP/6-31G(d,p) has an rms only somewhat worse. Use of aug-cc-pVTZ basis sets, while substantially more time consuming, provides *inferior* predictions.

The authors contend that this sort of simple DFT computation, affordable for many organic systems on standard desktop PCs, should be routinely done, especially in preference to increment schemes that are components of some drawing programs. And if a synthesis group does not have the tools to do this sort of work, I'm sure there are many computational chemists that would be happy to collaborate!

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