Strong Hydrogen Bonds to Weak Bases: An Orbital Overlap Perspective

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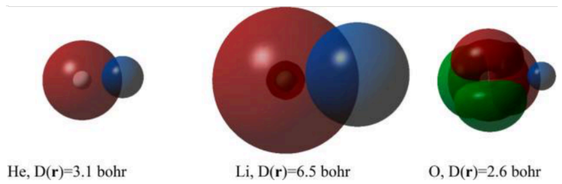
♦ Introduction

There are some compounds that are weak bases, but form strong hydrogen bonds. The orbitals of these compounds may explain this inconsistency. A large orbital overlap distance is commonly described as being Soft, according to the Hard-Soft Acid-Base Theory (HSAB). Soft describes an orbital that is big and puffy, versus hard describes an orbital that is small and compact. A soft orbital has more diffuse electrons and is therefore more polarizable. This polarizability is likely to be the reason why these weak bases form strong hydrogen bonds.

The ability to find general trends related to how a molecule will interact with other molecules will allow us to do basic calculations on an isolated molecule without having to explicitly simulate its interactions allowing us to determine qualitative information about any base.

♦ Orbital Overlap Distance D(r)

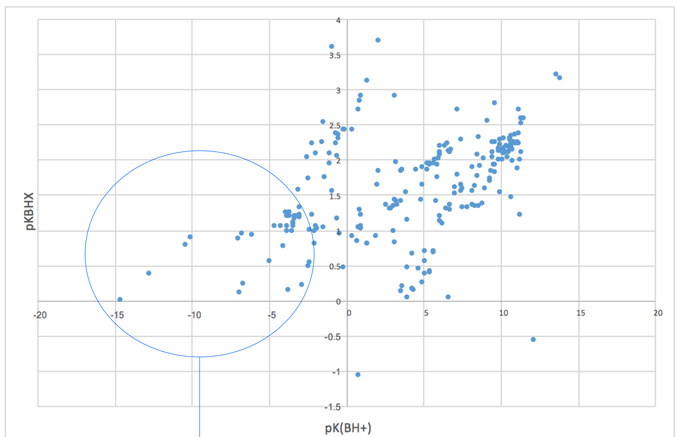


- Width of test function (blue) that best overlap Mos (red and green) at each point

♦ Calculations

- B3LYP Density functional theory (DFT) calculations of geometry, charge, overlap distance.
- Gaussian 09 and Multiwfn calculations
- Figure 1: Electrostatic potential and overlap distance at most negatively charged point on surface
- Figure 2: Overlap distance and electrostatic potential on entire surface
- Figure 3: Hirshfeld-averaged atomic partial charge and overlap distance

♦ Experiment



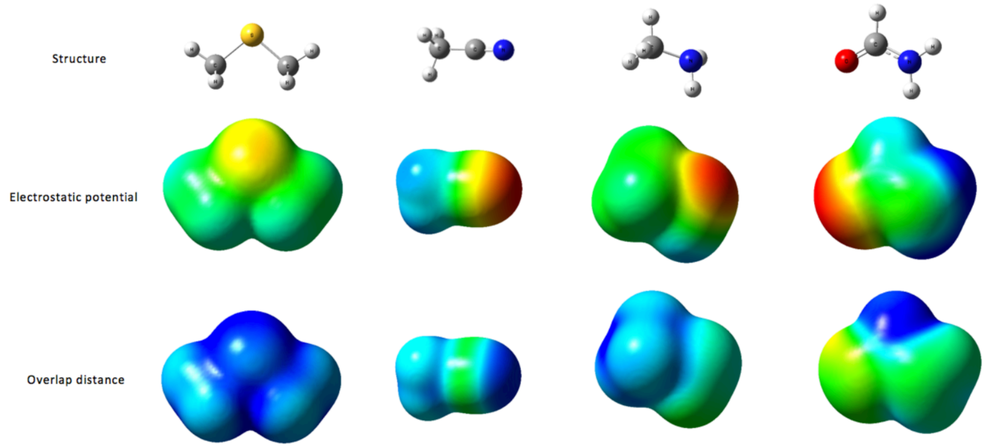
Experimental hydrogen-bond acceptor strength plotted vs. experimental proton affinity

Three very weak bases are good H-bond acceptors

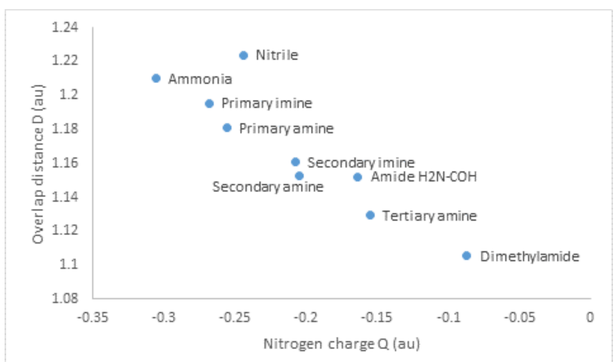
- Nitriles
- Sulfides
- Electron-rich phenyl groups

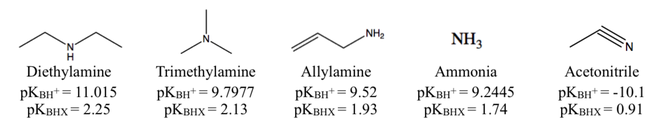
♦ What do these groups have in common?

- Large orbital overlap distance



♦ Systematic Analysis of Nitrogen Bases





- Overlap distance vs. partial atomic charge of nitrogen containing compounds
- More positively charged nitrogens have more compact orbitals, smaller overlap distance
- Ammonia, primary amines, secondary amines, tertiary amines lie on the same trend.
- Nitriles are experimentally weaker bases and computationally much more diffuse.
- Does chemical softness explain why nitriles form strong hydrogen bonds despite their weak basicity?

♦ References

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- Laurence, C.; Brameld, K. A.; Gratone, J.; Le Questel, J.; Renault, E. The pK_{BHX} Database: Toward a Better Understanding of Hydrogen-Bond Basicity for Medicinal Chemists. *J. Med. Chem.* **2009**, *52*, 4073-4086.