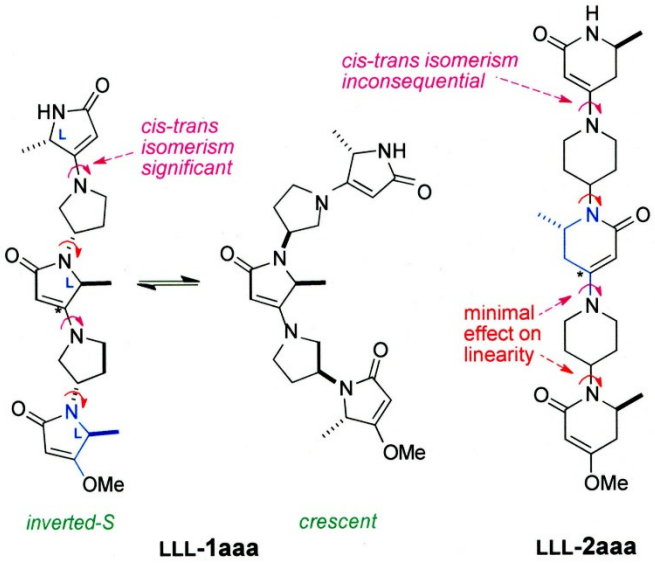
Materials Seminar

Monday, November 10, 2014
3:30 p.m. in Room 1315 Chemistry

EKO and EKOS: A New Perspective On Discovery Of Small Molecules To Perturb Protein-protein Interactions

Small molecules that perturb protein-protein interactions (PPIs) have enormous potential in the treatment of diseases, but they are difficult to discover or design. For instance, high throughput screening, and the various fragment-based approaches have limitations that are so severe that in some cases the data obtained does not justify the cost and time invested in these methods.

We devised a new approach to the problem of finding molecules that perturb specific PPIs; we call this *Exploring Key Orientations*. It involves defining chemotypes ideally suited to this function (*eg* **1** and **2**), then matching their preferred conformations with structural features of PPI-interfaces on a massive scale. EKO can be used in a *chemistry-centered* approach wherein small molecule design precedes selection of the PPI target. Alternatively, *biology-centered* applications of EKO screen a range of suitable chemotypes for compatibility with a specific PPI target. It also may be useful to augment these analyses with a related technique we call EKOS (*Exploring Key Orientations on Secondary structures*) which matches chemotypes to secondary structures seen at PPI interfaces; this will be discussed as a prelude to understanding EKO.



Kevin Burgess

Texas A&M University
Dept. of Chemistry