Chem 162/262 (2005) Assignment #6 Due Mon, Nov 28th

Structure-Based Drug Design

1. Development of HIV protease inhibitors is one of the most famous and widely publicized achievements of structure-based drug design. For example, your textbook provides a good example of the approach taken by the Abbot Laboratories that lead to the discovery of ritonavir. Discuss which steps in the rational process of HIV protease inhibitor development benefited most significantly from computer visualization and modeling. What specific approaches were used and why?

2. In less than 600 of your own words, explain what was done and achieved by Matthieu Schapira and co-workers in paper "Discovery of diverse thyroid hormone receptor antagonists by high-throughput docking" that is published in Proc. Natl. Acad. Sci., USA 100, 7354–7359 (2003). You do not need to explain the background of their techniques but make sure to tell why such techniques were used.

3. Compare advantages and disadvantages of free energy perturbation calculations over docking calculations in computer-aided drug discovery.