Guest Speaker:
Professor John P. Richard
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ORGANIC SEMINAR
Friday,
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9:00 a.m.

Hutchison Hall 473
University of Rochester
Department of Chemistry

"The Architecture of Enzyme Dianion Activation Sites"

Abstract: Enzymes are distinguished from small molecule catalysts by highly-evolved mechanisms, which enable the utilization of binding interactions with non-reacting portions of the substrate for transition state stabilization. Specificity in transition state binding is obtained by the utilization of the binding energy of substrate fragments, such as a phosphodianion, to stabilize high-energy and catalytically active, caged Michaelis complexes with substrate. For example, triosephosphate isomerase (TIM), orotidine monophosphate decarboxylase (OMPDC), and glycerol 3-phosphate dehydrogenase (GPDH) are activated for catalysis of reactions of their respective phosphodianion truncated substrates by a variety oxydianions, which bind weakly to these enzymes; and, tightly to the transition state complex, with intrinsic binding free energies of as large as -8.4 kcal/mol for activation of GPDH-catalyzed reduction of glycolaldehyde by fluorophosphate. These results are consistent with a cryptic function for the similarly structured oxydianion binding domains of TIM, OMPDC and GPDH. Each enzyme utilizes the interactions with tetrahedral inorganic oxydianions to drive a conformational change that locks the substrate in a caged Michaelis complex, which provides optimal stabilization of the different enzymatic transition states. Similarities and differences in the architecture of the dianion activation sites for TIM, OMPDC and GPDH will be presented, with an emphasis on the extraordinarily large transition state stabilization obtained for each enzyme from strong cation-phosphdianion pairs.

Host: Professor Joseph Dinnocenzo, email: jpd@chem.rochester.edu