1990 PROGRAM

A.M.

9:00 **Registration and Coffee—Room 137, Chemistry-Physics Building**

9:30 **Welcome by Dr. Robert Hemenway, Chancellor, University of Kentucky, Room 139, Chemistry-Physics Building**

9:40 **Introductory Remarks**

9:45 **Dr. Andrew D. Hamilton, University of Pittsburgh**
New Artificial Receptors for Complexation and Catalysis

An important goal in modern bioorganic chemistry concerns the design of synthetic molecules that mimic various aspects of enzyme chemistry. Detailed study of such models can lead not only to insights into the nature of enzyme action but also to new chemical species with some of the specificity and speed normally associated only with enzymes. Our approach has been to focus on biologically significant substrates and to construct complementary receptors containing multiple binding interactions. In particular, we have incorporated several hydrogen bonding sites into a macrocyclic framework to provide a highly selective receptor for barbiturates. The approach has been extended to other substrates including urea, small peptides and the different nucleotide bases. Artificial receptors of this type may lead to the development of novel pharmaceutical strategies, drug delivery systems or chemical sensor designs.

10:45 **Discussion**

10:50 **Dr. William F. DeGrado, Central Research and Development Dept., E.I. du Pont de Nemours and Co.**
De Novo Design of Helical Proteins.

Our group has recently adopted a synthetic approach to understanding the structural basis for protein function. In order to test some of the rules and concepts which are believed to be important for protein folding and stability we are attempting to design some simple proteins which should fold into predetermined three-dimensional structures. Two types of helical proteins have been designed: the first is an idealized version of a four-helix bundle, a folding pattern found in the structures of a variety of natural water-soluble proteins including myohemerythrin, cytochrome C, and apoferittin, while the other class of designed proteins is meant to mimic the structures of proteins which form ion channels such as the acetylcholine receptor. The synthesis and characterization of these proteins are currently underway and will be the focus of the talk.

11:50 **Discussion**

P.M.

12:15 **Buffet Lunch, Faculty Club (Please return card by April 7, 1990 for reservations. Cost $6.00 to be paid at registration.)**

1:30 **Dr. Steven C. Zimmerman, University of Illinois**
Chemically Synthesized Mimics of Biological Receptors and Enzyme Catalysts.

Noncovalent interactions are of fundamental importance to all biological processes. The efficiency of enzymatic catalysis and the binding specificity of antibodies depends upon a large number of complementary intermolecular contacts. A promising approach to understanding the nature of these noncovalent interactions is through the study of chemical model systems. In this laboratory we have studied models for both biological "receptors" and for enzymic catalysis. The synthetic receptors have been designed to complex aromatic substrates using only aromatic π-stacking interactions, or a combination of π-stacking interactions and hydrogen bonding. These studies have shown that a very high degree of cooperativity can be obtained between multiple binding interactions. We have also developed a new model of the histidine-aspartate couple which contains a *syn* oriented carboxylate. Several enzymes, which have evolved independently, have been found to contain aspartic acid residues hydrogen bonded to catalytically active histidine residues. Previous small molecule mimics of the His-Asp couple have constrained the carboxylate to an anti orientation, while only the *syn* orientation is found in the enzymatic system.

2:40 **Discussion**

2:50 **Dr. Ronald Breslow, Columbia University**
Geometric Control of Binding and Catalysis

Multipoint binding interactions lead to increased affinity and multifunctional catalysis leads to increased rates. Both can produce increased selectivities for substrates and products. Examples from the first area include ditopic binders with antibody-like affinities, and ditopic functionalizing catalysts. Examples from the latter area include examples in which bifunctional catalysis is geometrically controlled in transaminase and ribonuclease mimics. Rigid binding can be useful for rate accelerations, but some freedom of motion must be left so the molecular complex can adapt to the changing geometric demands of the reaction path. We will describe an example of the rate improvement that this principle leads to.

3:50 **Discussion**

4:00 **Mixer.**

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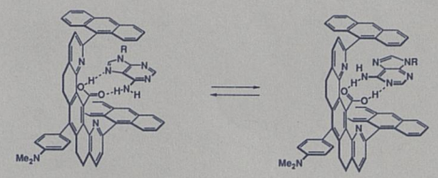
Sixteenth Annual
Symposium on

Chemistry & Molecular Biology



established in the memory of
Anna S. Naff

MOLECULAR RECOGNITION

SPEAKERS

Ronald Breslow
William F. DeGrado
Andrew D. Hamilton
Steven C. Zimmerman

Monday, April 16, 1990
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