"What I cannot create I do not understand."
Richard P. Feynman

Preface

It is now 18 years since the first antibody catalysts elicited against transition-state analogs were induced. At this age of maturation we found it appropriate to comprehensively cover the field of antibody catalysis in one volume. The catalytic antibody technology merges the combinatorial diversity of the immune system with a programmable design by the experimenter. In fact, no other area of bioorganic chemistry has taught us so much about the use of large libraries of molecules in the service of chemistry. We have learned from the immune system that natural evolution does not necessarily require billions of years; it may be completed on a laboratory timescale. This lesson of applying the three major components of evolution – diversity, selection and amplification – has inspired biologists and chemists alike on their quest to discover new functional biopolymers, new catalysts, new drugs, and even new solid-state materials with desired physical properties.

There are many conceptual steps on the way towards the realization of a new antibody catalyst, including mechanistic understanding of the specific reaction to be catalyzed, scholarly prediction of the transition state of highest energy, creative design of a chemically stable transition state analog (TSA), and the planning of synthetic schemes for haptens and substrates. Yet, as is appropriately expressed by the above-cited dictum of Feynman, antibody catalysis is primarily an experimental science where the keys to success reside in the details of the experimental procedures, including organic synthesis, immunization protocols, screening procedures, production of monoclonal antibodies, kinetic experiments, and crystallographic studies.

Many facets of biocatalysis are not yet fully understood, particularly those related to the dynamics of the protein catalyst along the reaction coordinate. Even when some of that can be envisaged, we do not yet know how to design the antibody active site in order to achieve the desired dynamic properties. Therefore, the use of a TSA, even an optimal one, which is often impossible to make, represents only a "snapshot" of a continuous, dynamic process and only a general guideline for the immune system to produce the appropriate catalyst. The resultant, broadly diverse population of relevant antibodies reflects the variety of ways by which the immune system can respond to the given TSA. The beauty of this approach is the element of serendipity, allowing us to find valuable items that were not looked for. Consequently, the importance of efficient screening strategies can never be overestimated.

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