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Computational Studies of Artificial Metalloenzymes: From Methods and Models to Design and Optimization

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4.1 Introduction

This chapter is aimed to present how molecular modeling, understood as a series of computational methods based on physical models with different degrees of accuracy and computational needs, is involved in the design and optimization of artificial metalloenzymes (ArMs) devised to catalyze organic reactions. The chapter is intended to be didactic and oriented toward an audience of organometallic chemists interested in widening their research scope with the use of ArMs in catalysis. The focus is primarily practical: to give a brief overview of methods and to demonstrate with examples of practical applications that in the area of ArMs, molecular modeling can be an invaluable tool for catalysts' design, just as it is in the organometallic field. We will not delve into the details of technicalities of the computational approaches employed. The starting point of this chapter is the wide knowledge and the significant experience in the use of computational techniques to compute reaction mechanisms that the organometallic community has acquired in recent years. In this line, in the first section we make a comparison with homogeneous transition metal catalysis, highlighting the differences and the complexity that entails the computational study of processes catalyzed by ArMs. In the next section we summarize the most important concepts of the methodologies that molecular modeling encompasses. Then we illustrate, with selected examples, how the computational tools described before have been used for constructing ArMs with novel or improved activities and specificities, aimed to participate in catalytic transformations. Finally, we conclude summarizing where we are and what are the perspectives for molecular modeling in the field of artificial enzymes in catalysis. Directed evolution techniques, a complementary approach for optimizing ArM, is the subject of Chapter 5 and will not be overviewed here. A number of excellent reviews have been published recently dealing with computational design of enzymes [1–4] as well as the general subject of ArMs in catalysis [5–11]. Catalytic antibodies (abzymes) are not covered in this chapter because few of those rely on metal cofactors. Moreover, they have been less frequently used

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