The Structure and Reactivity of Metallohydroporphyrins

Warren A. Kaplan Final Seminar December 5, 1989

Metallohydroporphyrins are metal containing porphyrins that have been reduced at one or more of the porphyrin macrocycle positions. Such complexes have been identified as being essential in a variety of biological systems including nitrite and sulfite reductases [1,2] and S-methyl coenzyme M reductase [3]. Of particular interest is the highly reduced nickel-containing macrocyclic tetrapyrrole F_{430} [4], found in the S-methyl coenzyme M reductase of methanogenic bacteria [5]. This cofactor possesses the most highly reduced porphyrin macrocycle yet encountered in nature. In addition, S-methyl coenzyme M reductase is one of only four enzymes known to contain or specifically require nickel for their activity [6].

An important research emphasis has been to develop an understanding of why metallohydroporphyrins are essential in certain enzymatic systems. The relative rigidity of the macrocycle is expected to be important in metallohydroporphyrin enzymes containing metal ions which undergo changes in either spin state or oxidation state during the course of catalytic activity. Such reactions can induce metal ion size changes of up to 0.2 Å (as in the case of nickel). The reduction of the macrocycle is generally thought to be responsible for the enhanced reactivity in these systems. It has been argued that ring reduction gives the macrocycle greater flexibility: the expected reduction in aromaticity [7] and observed S_4-ruffling both in the solid state [8] and in solution [9] lend support to this argument. Through ligand binding experiments with a series of tetraphenyl- and octaethyl-substituted metallo(hydro)porphyrins (see Figure 1), we have determined how reactivity varies as a function of macrocycle reduction level. In addition, through the binding of sterically hindered imidazoles and pyrrolidines which perturb the macrocycle plane, we have determined that macrocycle flexibility does not increase when the metalloporphyrin is reduced at β-pyrrole positions [10].

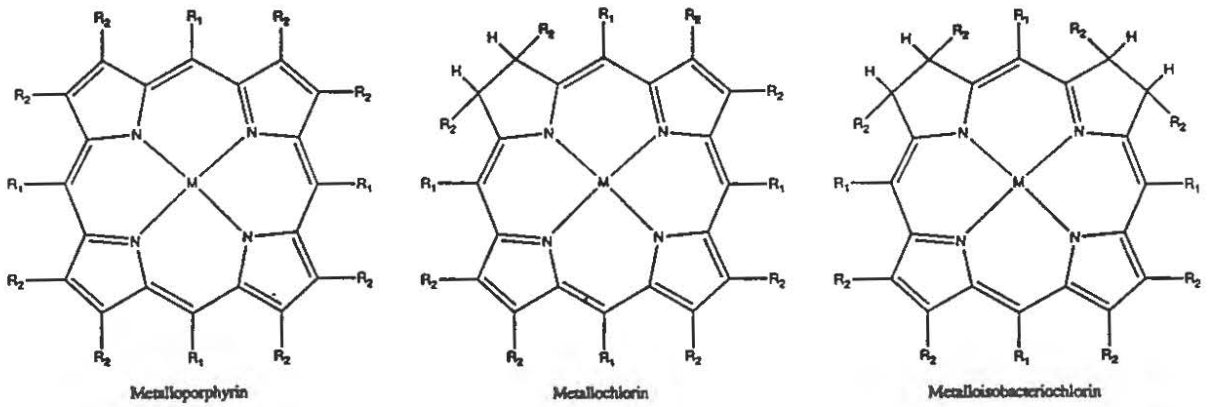

Figure 1: Tetraphenyl (R_1 = Phenyl, R_2 = H) and octaethyl (R_1 = H, R_2 = Ethyl) metallo(hydro)porphyrins.

Molecular mechanics [11] calculations have been performed on a variety of metallo(hydro)porphyrins in order to further examine the thermodynamic

and structural properties of these molecules. A modified version of the MMP2 force field has been developed, and its ability to reproduce energetic and geometric characteristics of metallo(hydro)porphyrins has been demonstrated. It is shown that molecular mechanics accurately predicts the properties of metallo(hydro)porphyrins and metallo(hydro)porphyrin-ligand complexes provided that the bonded axial ligand is not sterically bulky. The molecular mechanics technique is used to determine how cavity size and flexibility vary as a function of tetrapyrrole reduction level and position. It is shown that macrocycle hole sizes change significantly upon reduction. In addition, molecular mechanics predicts that while reduction of a tetrapyrrole at β-pyrrole positions does not increase the macrocycle's flexibility, reduction at meso-positions does. Finally, the molecular mechanics technique has been extended to study the epimers of F_{430}. The technique has accounted for experimentally determined F_{430} reactivity properties [12] and has identified important structural features of the molecule. The consequences of both specific peripheral substituents and the highly reduced nature of the macrocycle will be discussed to demonstrate why this cofactor is well-suited for catalytic activity.

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