Investigation of Electronic Effects on Enantioselective Catalysis with Hybrid Quantum Mechanics/Molecular Mechanics Calculations

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Introduction

Metal-organic frameworks (MOFs) show great promise for combining the best features of homogeneous and heterogeneous catalysis. MOFs are nanoporous materials formed from self-assembly of metal ion vertices and organic linkers into regular crystalline structures. An appealing strategy for developing MOF catalysts is to use a homogeneous asymmetric catalyst as the organic linker [1], but immobilization of the catalysts in the crystal presents a challenge for preserving high enantioselectivity. Modeling can provide insight into the effects of immobilizing the homogeneous catalyst on its ability for asymmetric induction. Recently, a MOF was synthesized from a (salen)Mn catalyst (**L**) (Figure 1), biphenyldicarboxylate, and zinc ions [1]. The MOF performed enantioselective epoxidation catalysis with ee values only slightly lower than the homogeneous catalyst (82% ee vs. 88% ee). It is well known that the electronic nature of the 5,5'-substituents on the salen ligand (see Figure 1a) strongly affects the enantioselectivity of the catalyst [2], and density functional theory (DFT) calculations have correlated the modified Hammett parameter σ^+ of the 5,5'-substituents to reactivity properties [3]. To study the electronic effect of coordination of the 5,5'-substituents to zinc ions in the MOF structure on the enantioselectivity of **L**, hybrid quantum mechanics/molecular mechanics (QM/MM) calculations were performed first to validate these methods for investigating electronic effects of salen ligands and second to determine the electronic effects of the ligand coordination in the MOF. This work lays the foundation for modeling epoxidation catalysis within the MOF cavity by determining an accurate and efficient computational method.
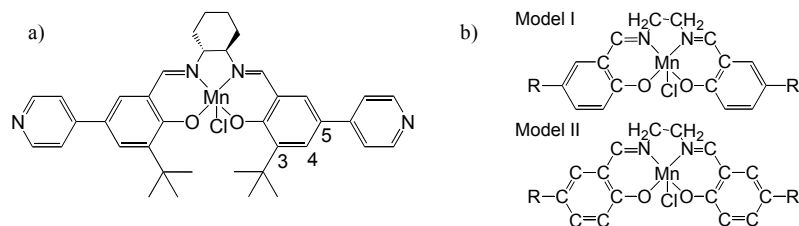

Figure 1. a) **L**; b) QM/MM partitioning schemes with QM atoms shown with atomic symbols and MM atoms shown with lines (R = H, NO$_2$, or OCH$_3$).

Materials and Methods

The QMMM program version 1.3.5 was used with Gaussian03 as the QM code and TINKER as the MM code. The partitioning schemes studied are shown in Figure 1b. The BP86 DFT functional with the TZVP basis set on Mn and SVP basis set on all other atoms was used for the QM method. The MM atoms were treated with the DREIDING-SALEN force field, a modified version of DREIDING that we developed to model the geometries of (salen)Mn accurately. Mechanical embedding (ME) was investigated as well as two electrostatic embedding techniques: Z3 and redistributed charge and dipole (RCD). The most accurate and efficient QM/MM method was validated to capture electronic correlations for the 5,5'-substituents using R = H, NO$_2$, and OCH$_3$ and was extended to the cases where R = CH$_3$, C(CH$_3$)$_3$, and Cl. Then it was applied to **L** with the 5,5'-substituents coordinated to the Zn paddlewheel clusters that form the MOF corners.

Results and Discussion

All QM/MM methods found optimized geometries in good agreement with full DFT results although the agreement was somewhat better when Model II was used. As expected, ME did not capture the electronic effects of the 5,5'-substituents on the salen ligand (Tables 1 and 2). The Z3 scheme produced opposing electronic correlations to full DFT results while results to date indicated qualitative agreement between RCD results and full DFT results (Tables 1 and 2). When the RCD scheme was used on Model II, spin state splittings and electronic correlations agreed quantitatively with full DFT results. A quantum description of the delocalization of the electrons over the phenyl rings and the electron distribution in response to the point charges on the MM atoms is necessary to describe the electronic correlations of 5,5'-substituents on (salen)Mn.

Table 1. Mulliken charges on oxo ligand correlated with σ^+ for various QM/MM methods

R	σ^+	Full DFT	ME Model I	Z3 Model I	RCD Model I	RCD Model II
OCH$_3$	-0.778	-0.323	-0.303	-0.299	-0.336	-0.314
H	0.000	-0.307	-0.303	-0.303	-0.324	N/A
NO$_2$	0.790	-0.291	-0.303	-0.317	-0.315	-0.287

Table 2. Oxidation energies in kJ/mol correlated with σ^+ for various QM/MM methods

R	σ^+	Full DFT	ME Model I	Z3 Model I	RCD Model I	RCD Model II
OCH$_3$	-0.778	-64.0	-368.8	-39.6	-87.0	-51.8
H	0.000	-47.3	-238.4	-45.7	-31.8	N/A
NO$_2$	0.790	-36.6	-578.6	-64.8	-55.6	-35.5

Significance

This work demonstrates the utility of appropriately chosen QM/MM methods to accurately capture electronic effects in large reacting systems. Extending this work to a (salen)Mn catalyst immobilized in a MOF should provide insight into electronic and steric effects of the MOF structure and aid in the design of more effective (salen)Mn MOF catalysts.

References

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