

# APPLICATION OF QUANTUM MECHANICS/MOLECULAR MECHANICS METHODS TO FAST (SALEN)Mn LIGAND SCREENING

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## Summary

Hybrid quantum mechanics/molecular mechanics (QM/MM) methods were employed to study electronic effects of 5,5'-substituents on the enantioselectivity of (salen)Mn catalysts. Correlations obtained from the QM/MM calculations elucidated electronic framework effects on enantioselectivity for (salen)Mn heterogenized in a metal-organic framework (MOF). The correlations also enabled fast ligand screening for the prediction of highly enantioselective (salen)Mn that could be used in MOFs.

## Keywords

Computational catalysis, Rational design of catalysts.

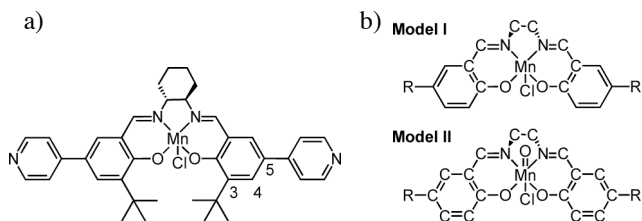
## Introduction

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,<sup>1</sup> 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 1a), biphenyldicarboxylate, and zinc ions.<sup>1</sup> 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 reactivity and thus the enantioselectivity of the catalyst,<sup>2</sup> and density functional theory (DFT) calculations

have correlated the modified Hammett parameter  $\sigma^+$  of the 5,5'-substituents to reactivity properties of (salen)Mn=O.<sup>3</sup> To study electronic effects of the MOF on **L**, hybrid quantum mechanics/molecular mechanics (QM/MM) calculations were performed first to validate these methods for investigating electronic effects of salen ligands and then to determine the electronic effects of coordination of the 5,5'-substituents to zinc ions in the MOF.

## Methods

The QMMM program version 1.3.5<sup>4</sup> was used with Gaussian03 as the QM code and TINKER as the MM code. The partitioning schemes investigated 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 was studied as well as three electrostatic embedding techniques: SEE, Z3, and redistributed charge and dipole (RCD). The most accurate and efficient QM/MM method was validated by assessing its ability to capture electronic correlations for the 5,5'-substituents using R = OCH<sub>3</sub>, H, and NO<sub>2</sub> and was extended to R = CH<sub>3</sub>, C<sub>6</sub>H<sub>5</sub>, CO<sub>2</sub>CH<sub>3</sub>, and CN.



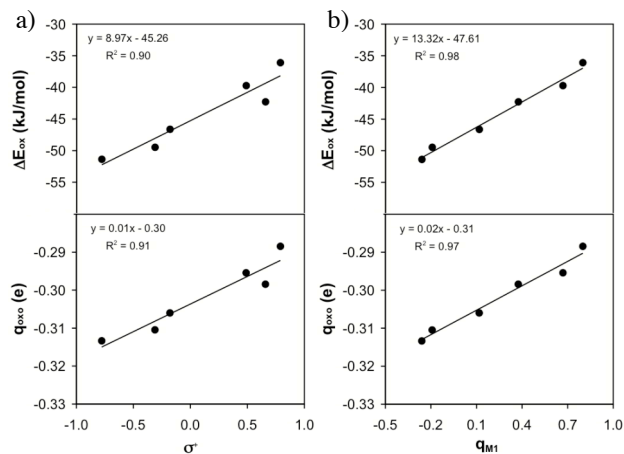
**Figure 1.** a) **L**; b) QM/MM partitioning schemes with QM atoms shown with atomic symbols and MM atoms shown with lines (R = OCH<sub>3</sub>, H, or NO<sub>2</sub>)

## Results and Discussion

While mechanical embedding was unable to capture electronic effects of the 5,5'-substituents on the reactivity

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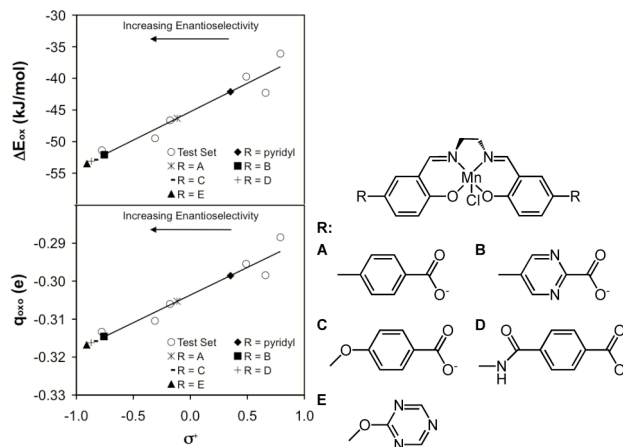
properties of (salen)Mn=O, namely the oxidation energy  $\Delta E_{\text{ox}}$  and the charge on the oxo ligand  $q_{\text{oxo}}$ , all electrostatic embedding techniques captured the dependence of catalyst reactivity on the electronic nature of the substituents. The most accurate electrostatic embedding technique was determined by comparing QM/MM geometries, spin state splittings, and electronic properties to those obtained from full DFT calculations. The RCD scheme applied to Model II gave results in best agreement with full DFT results and was therefore used to obtain the electronic correlations shown in Figure 2.



**Figure 2.** Oxidation energy and charge on the oxo ligand of (salen)Mn=O correlated to a)  $\sigma^+$  of the 5,5'-substituents and b) point charge at the QM/MM boundary  $q_{\text{M1}}$

It was observed that the calculated reactivity parameters of (salen)Mn=O depended on the point charge at the QM/MM boundary ( $q_{\text{M1}}$ ) (Figure 2b). These correlations eliminate the need to perform time-consuming QM/MM optimizations to obtain the reactivity properties of homogeneous (salen)Mn catalysts and clusters representing (salen)Mn in the MOF environment. Instead, DREIDING-SALEN can be used to classically optimize (salen)Mn. Then the value of  $q_{\text{M1}}$  can be obtained from single-point DFT calculations and used in the correlations in Figure 2 to calculate the relative reactivity of different (salen)Mn catalysts.

Using this methodology, new (salen)Mn ligands were quickly screened for use in MOFs. The catalyst used in the MOF (**L**, Figure 1a) was predicted to have poor enantioselectivity compared to the designed ligands in Figure 3. Substituents with ether (C or E, Figure 3) or amide (D, Figure 3) linkages at the QM/MM boundary were predicted to be the most enantioselective catalysts. Coordinating the 5,5'-substituents to Zn paddlewheel clusters to represent the MOF catalyst resulted in slight increases in the calculated reactivity parameter values and in  $\sigma^+$ . These results indicate that the decrease in enantioselectivity upon heterogenization of (salen)Mn in the MOF may be due to increasing catalyst reactivity caused by the electronic structure of the MOF.



**Figure 3.** Oxidation energy and charge on the oxo ligand of (salen)Mn=O vs.  $\sigma^+$  for the 5,5'-substituents shown

## Conclusions

QM/MM methods offer an efficient means of studying heterogeneous catalysts and have been shown to be able to capture electronic effects of the (salen)Mn ligand on its reactivity and thus its enantioselectivity. The calculated reactivity of the catalyst is highly dependent on the point charge  $q_{\text{M1}}$  at the QM/MM boundary. Because of this dependence, fast ligand screening can be performed using a combination of classical optimizations, single point DFT calculations, and simple correlations. This methodology has been applied to the design of new (salen)Mn ligands for use in MOFs. While further study of representative (salen)Mn MOF catalysts has demonstrated a slightly negative impact of the MOF electronic structure on the enantioselectivity, the ligands designed in this work represent a significant potential for increasing the enantioselectivity of (salen)Mn MOF catalysts.

## References

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