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Gas-Phase Stereoselective Binding to Mn/Salen Catalysts

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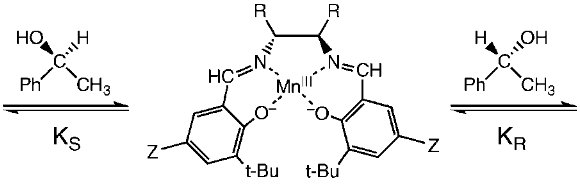
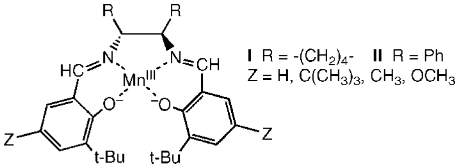
ABSTRACT



Gas-phase equilibrium measurements have been used to determine the stereoselectivity of binding the enantiomers of 1-phenylethanol to manganese/salen asymmetric epoxidation catalysts. There is significant selectivity in the gas-phase binding, and the results are compared to data from condensed-phase epoxidations. The study demonstrates the utility of a novel internal standard approach that allows for rapid, accurate measures of the stereoselectivity of gas-phase ligand binding. Moreover, the data suggest that gas-phase binding stereoselectivity could be a potential predictor of condensed-phase enantioselectivity.

Scheme 1. Metal Salen Complexes



Since their discovery in the mid-1990s by Jacobsen[1] and Katsuki,[2] chiral manganese salen complexes, such as **I** and **II** (Scheme 1), have proven to be exceptionally useful catalysts for asymmetric epoxidations.[3] Multiple mechanisms have been suggested, and it is possible that some compete under various reaction conditions.[4–12] A commonly invoked mechanism involving a radical intermediate, **A**, is presented in Scheme 2. Although intermediates in metal/salen epoxidations have been probed in the past by mass spectrometry,[13–20] here we provide the first report of the gas-phase stereoselectivity of binding manganese/salen catalysts to chiral ligands.

Previous gas-phase work with these catalysts has focused on the reactivity of intermediates in the catalytic cycle. Plattner and co-workers[13–17] have shown that a variety of ligated and oxidized Mn(salen)$^+$ species can be formed by

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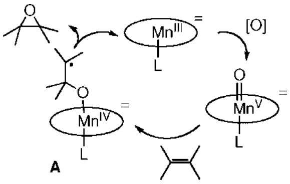
Scheme 2. Epoxidation Catalytic Cycle



electrospray ionization. The bare metal complexes, Mn(salen)$^+$, can capture ligands in gas-phase reactions, and there is evidence that the oxo species can transfer oxygen to electron-rich alkenes and sulfides. Vairamani and co-workers[20] have observed related behavior with chromium salen species. Finally, Chen and Chisholm[18,19] have examined the gas-phase reactivity of propylene oxide/M(salen)$^+$ complexes.

Intermediate **A** is not a practical target for gas-phase experiments, so instead, we have focused on a very simple model system to explore the asymmetric environment created by the catalyst, namely the binding of a chiral alcohol to the catalyst. Although the nature of the Mn−O bond is very different and the axial ligand is missing in this model, it can probe the overall steric interactions involved in binding to an asymmetric salen complex. Support for this choice comes from DFT calculations on the parent Mn(salen)$^+$ species.[21] Comparison of the geometries of complexes with $^{\bullet}CH_2CH_2O^{\bullet}$ and CH_3CH_2OH as ligands (Figure 1) shows that there are general similarities in the structures, with the major difference being a longer Mn−O distance with the alcohol. This suggests that alcohol models can provide a rough measure of the asymmetric environment created by the salen ligand but will exhibit weaker steric interactions. Support for the model also comes from experimental work by Xia,[22,23] who has shown that these catalysts give stereoselective alcohol oxidations. It should be emphasized that we are not attempting to model the epoxidation process itself (which is mechanistically complex), but rather the general chiral recognition features of the salen catalysts.

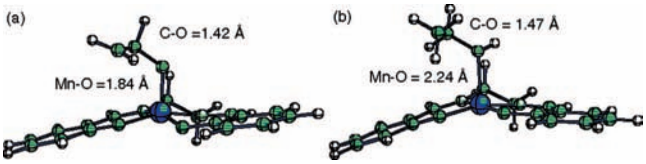


Figure 1. Optimized geometries of Mn(salen)$^+$ complexed to (a) $^{\bullet}CH_2CH_2O^{\bullet}$ and (b) CH_3CH_2OH at the BP86 level in the quintet state.

The experiments were completed on a modified Finnigan LCQ quadrupole ion trap,[24] and nanospray ionization was used to generate Mn(salen)$^+$ ions from Mn(salen)$^+$Cl$^-$ precursors. The Mn(salen)$^+$ ions were isolated in the ion trap and then allowed to react with alcohol vapor mixtures (partial pressure $\sim 10^{-6}$ torr) in the helium buffer gas. Cations **I** and **II** readily add one alcohol ligand to give a five-coordinate species. Addition of a second alcohol ligand is not observed to a significant extent. After 200−500 ms, increasing the reaction time did not alter the spectra, an indication that equilibrium had been attained (Figure 2). Data are given in Table 1. For simple alcohols, it appears that polarizability drives the equilibrium and larger alcohols are favored. Little stereoselectivity is seen with the enantiomers of 2-butanol, but this is not surprising given its small size.

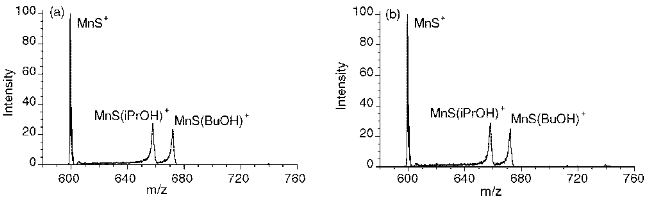


Figure 2. (a) Reaction of (RR) **I** (Z = C(CH$_3$)$_3$) with a 2:1 2-propanol/1-butanol mixture, 200 ms reaction time. (b) Reaction of (RR) **I** (Z = C(CH$_3$)$_3$) with a 2:1 2-propanol/1-butanol mixture, 500 ms reaction time. MnS$^+$ is the reactant ion.

Table 1. Gas-Phase Equilibrium Constants for Binding Ligands to Manganese Salen Catalysts (Scheme 1):[a]

$$MnS(L_1)^+ + L_2 \rightarrow MnS(L_2)^+ + L_1$$

L_1	L_2	catalyst	K
i-PrOH	BuOH	**I** (Z = C(CH$_3$)$_3$)	1.7[b]
BuOH	PentOH	**I** (Z = C(CH$_3$)$_3$)	1.8[b]
i-PrOH	(*R*)-2-BuOH	**I** (Z = C(CH$_3$)$_3$)	2.1[b]
i-PrOH	(*S*)-2-BuOH	**I** (Z = C(CH$_3$)$_3$)	2.0[b]
(*R*)-1-PhEtOH	(*S*)-1-PhEtOH	**I** (Z = C(CH$_3$)$_3$)	1.3[c]
(*R*)-1-PhEtOH	(*S*)-1-PhEtOH	**I** (Z = CH$_3$)	1.3[c]
(*R*)-1-PhEtOH	(*S*)-1-PhEtOH	**II** (Z = H)	1.4[c,d]
(*R*)-1-PhEtOH	(*S*)-1-PhEtOH	**II** (Z = OCH$_3$)	1.5[c]

[a] (*R*,*R*) enantiomer of catalyst. Averages of at least six measurements on three different days. [b] Direct equilibrium measurements with expected uncertainties of ±10%. [c] From experiments employing internal standard and corrected for isotope effects (Scheme 3, eqs 1−4). Expected uncertainties are ± 4%. [d] SS salen was used. 1/*K* is listed for consistency.

To gain more insight into the stereoselectivity of the binding, we turned to 1-phenylethanol (1-PhEtOH) as a probe

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alcohol.[25] For greater accuracy in the measurements, an internal standard approach was adopted (Scheme 3). The catalyst ion was allowed to react with a 50/50 mixture of enantiomerically pure $C_6H_5CHOHCH_3$ (R or S) and racemic $C_6D_5CHOHCH_3$. This approach eliminates the need for absolute pressure measurements and cancels out any mass discrimination in ion detection. Assuming that all the diastereomeric complexes have similar isotope effects, the stereochemical preference, $K_{S/R}$, and generic isotope effect, K_H/K_D, can be extracted from the data. The method is general and greatly reduces experimental uncertainties.

Scheme 3. Gas-Phase Reaction System

$$\mathrm{MnS(L_{Rac})^+} + \mathrm{L_S} \underset{}{\overset{K_S}{\rightleftharpoons}} \mathrm{MnS(L_S)^+} + \mathrm{L_{Rac}} \qquad (1)$$

$$\mathrm{MnS(L_{Rac})^+} + \mathrm{L_R} \underset{}{\overset{K_R}{\rightleftharpoons}} \mathrm{MnS(L_R)^+} + \mathrm{L_{Rac}} \qquad (2)$$

$$K_{S/R} = K_S/K_R \quad (3) \qquad\qquad K_H/K_D = \frac{K_S + K_R}{2} \quad (4)$$

L_S is (S) enantiomer, L_R is (R) enantiomer
L_{Rac} is deuterated racemic mixture

Sample spectra are shown in Figure 3 for the *R*,*R* enantiomer of **I** (Z = $C(CH_3)_3$). The data indicate an absolute binding free energy of about −12.5 kcal/mol for the alcohols. Applying the equations in Scheme 3 to this data, one obtains an S preference of 1.29, which is equivalent to a de of 12% in the complexation process. Although small in comparison to the ee's typically seen in epoxidations, the value is significant for a room temperature gas-phase process, particularly given the weak binding in the alcohol complex. The data also indicate a modest isotope effect correction, $K_H/K_D = 0.97$. It is interesting to note that a preference for reaction with the *S* enantiomer of the alcohol previously was seen in the condensed-phase oxidation of 1-phenylethanol with diacetoxyiodobenzene and the *R*,*R* enantiomer of **I** (Z = $C(CH_3)_3$).[22] However, the mechanism of that reaction is complicated by the need for KBr as a cocatalyst.

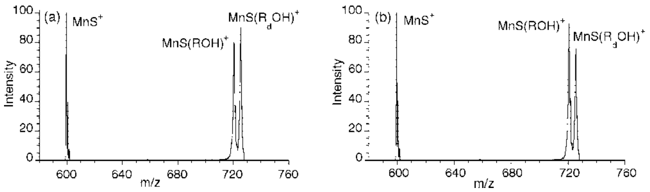

Figure 3. (a) Reaction of (*R*,*R*)-**I** (Z = $C(CH_3)_3$) with a 1:1 mix of (*R*)-$C_6H_5CH(OH)CH_3$ and racemic $C_6D_5CH(OH)CH_3$. (b) Reaction of (*R*,*R*)-**I** (Z = $C(CH_3)_3$) with a 1:1 mix of (*S*)-$C_6H_5CH(OH)CH_3$ and racemic $C_6D_5CH(OH)CH_3$. MnS^+ is the reactant ion.

Experiments using the (R,R) enantiomer of catalyst **I** (Z = CH_3) give nearly the same preference and have a $K_{S/R}$ value of 1.29. However, changing the overall structure of the catalyst has a significant effect on the stereoselectivity of the ligand binding. Similar experiments with catalysts **II** (Z = H) and **II** (Z = OCH_3) lead to considerably larger $K_{S/R}$ values, 1.45 and 1.48, respectively. These values correspond to de's of approximately 20%. The effect of catalyst structure on binding stereoselectivity is noteworthy because condensed-phase epoxidations of styrene[26] give higher ee's for catalysts of structure **II** than **I**.[27] These outcomes suggest that the gas-phase binding experiments might offer insight into the inherent stereoselectivity of the epoxidation catalyst.

In summary, we have reported a sensitive, gas-phase technique for assessing the stereoselectivity of model ligand binding to manganese/salen catalysts and observed systematic trends in binding selectivity. In addition, there are some intriguing correlations with condensed-phase enantioselectivities. The approach can be generalized to other systems and potentially provide crude, but rapid measures of catalysts' asymmetric induction capabilities. Moreover, the data provide excellent target values for calibrating the accuracy of computational models of binding stereoselectivity in these model systems.

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Supporting Information Available: Tables containing the computed geometries and the measured isotope effects. This material is available free of charge via the Internet at http://pubs.acs.org.

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