Evolution and Study of Polymer-Supported Metal Catalysts for Oxygen Atom Transfer: Oxidation of Alkanes and Alkenes by Diamide Manganese Complexes

Miroslav Havranek, Arun Singh, and Dalibor Sames*
Department of Chemistry, Columbia University
New York, New York 10027
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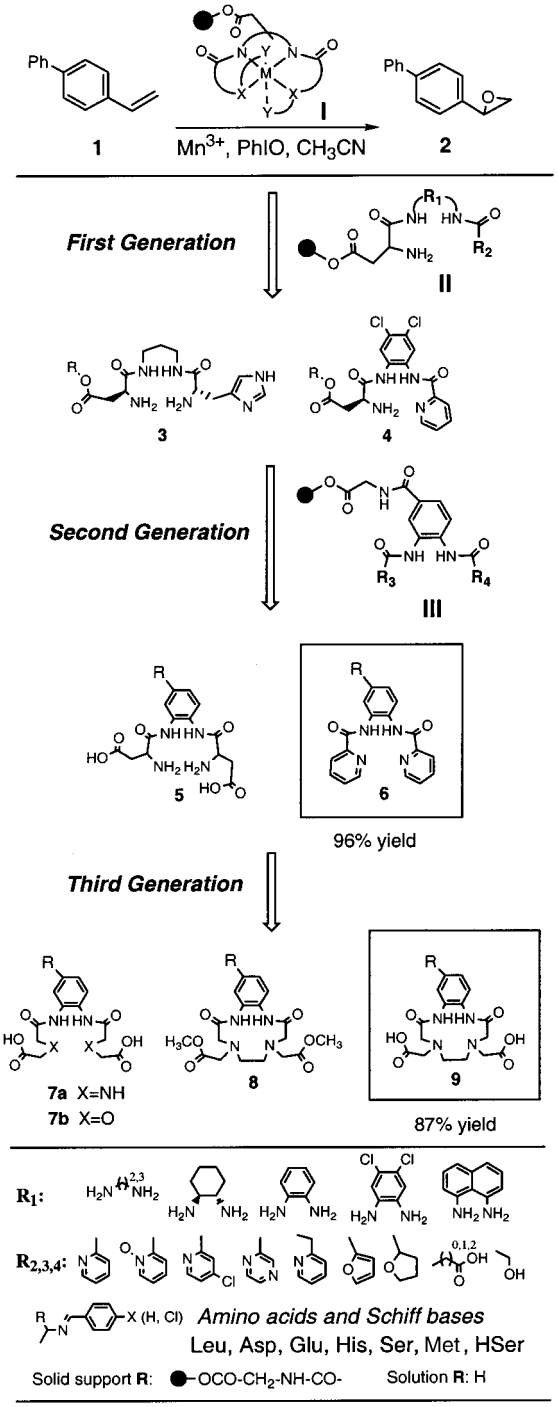
Catalytic oxygenation of alkenes, arenes, and alkanes is widely utilized by living systems. Cytochrome P450 oxygenase[1] has inspired many studies involving porphyrin[2] and salen[3] complexes as catalysts for catalytic oxygen transfer. The exploration of non-porphyrin systems[4] has also led to the development of interesting model catalysts (e.g., dimeric iron complexes,[5] bleomycin[6]). Herein we report that diamide complexes of manganese are efficient catalysts for oxygenation of C=C and C−H bonds. We have selected diamide systems of general design **I** as ligands due to their significant modular character, accessible through efficient amide assembly (Chart 1).[7] Furthermore, Collins,[8] and O'Halloran[9] characterized Mn(V)−oxo tetraamide cyclic complexes and acyclic Mn(V)−oxo diamide-dialkoxides, respectively, as stable compounds.

We have developed a stepwise evolutionary process combining design and parallel screening of solid-bound manganese complexes (Chart 1).[10] The search was divided into several cycles (generations) of variation sets.[11] In cases of focused systems of limited structural diversity, and limited screening capacity, the designer's judgment must be exercised as to which species possess the potential for further improvement (evolutionary potential). These are *not necessarily the best performing species* of the particular cycle, but can typically be identified among above-average-performing catalysts with the *possibility for further synthetically accessible structural variations*.

The entire protocol, including ligand assembly and deprotection, complex preparation, and catalyst evaluation, was performed on solid support (Tentagel, Macroporous PS).[12] A choice of vinylbiphenyl **1** as a substrate allowed both TLC and GC detection of the product mixture. PhIO was selected as an oxidant to avoid the formation of diffusible radicals.[13]

Chart 1. Evolution of Diamide Ligands for Mn(III)-Catalyzed Oxygenation on Solid Support



The first generation library of type **II** quickly showed that a number of structural variants led to respectable yields of epoxide **2** (system **3**, **4**, 70−74%, Chart 1) without revealing any obvious

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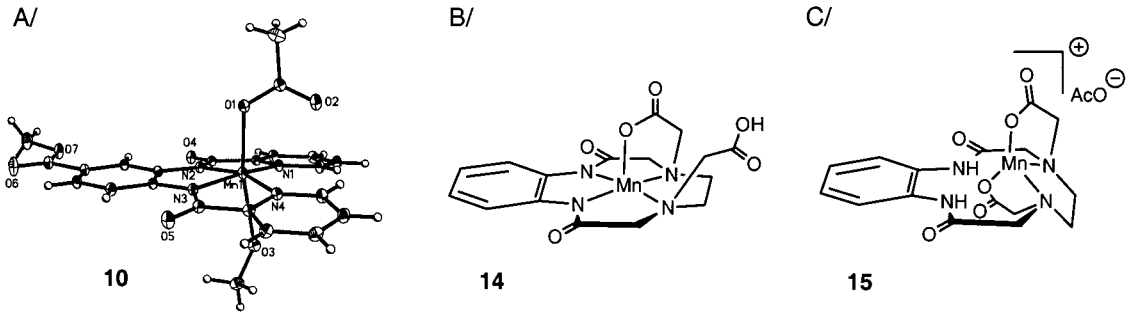
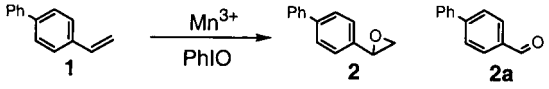


Figure 1. (A) ORTEP representation of complex **10**. (B) Proposed coordination mode of complex **14**. (C) Proposed coordination mode of **15**.

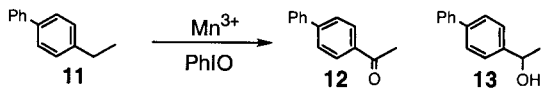
Table 1. Epoxidation Kinetics with Selected Complexes in Solution



entry	catalyst	2 min	10 min	30 min	2 h	4 h
1	**6**[a]	9%	47%	69%	82%	98%
2	**7a**[b]			6%	14%	22%
3	**8**[b]			5%	12%	20%
4	**9**[b,c]	91%	92%	92%	91%	92%
5	**9**[b,d]	96%	96%	96%	97%	96%

[a] 0.05 M **11** in CH_3CN, 5 mol % of catalyst, 2 equiv of PhIO. [b] CH_3CN-H_2O (4:1). [c] Complex **14**. [d] Complex **15**. Percent yield was determined by GC. Aldehyde **2a** <2% in all entries.

Table 2. C−H Oxidation Kinetics with Selected Complexes in Solution



entry	catalyst	10 min	30 min	2 h	4 h
1	**6**[a]	5%	15%	52%	60%
2	**7a**[b]		0%	1%	1%
3	**8**[b]		0%	0%	1%
4	**9**[b,c]	8%	12%	12%	12%
5	**9**[b,d]	16%	17%	18%	17%

[a] 0.05 M **11** in CH_3CN, 10 mol % of catalyst, 2 equiv of PhIO. [b] CH_3CN-H_2O (4:1). [c] Complex **14**. [d] Complex **15**. Percent yield was determined by GC. Alcohol **13** <2% in all entries.

trends. Aromatic diamide **4**, founded on 4,5-dichloro-1,2-diaminobenzene, showed high conversion of the substrate and therefore served as the template for the second generation of type **III**. The second round identified system **6**, which led to nearly complete consumption of vinylbiphenyl in 12 h (96% yield). Thus, further improvements could be accomplished only in turnover rate and selectivity. The bis-aspartate construct **5** demonstrated good yield (75% yield of epoxide **2**, Chart 1) and was judged a promising candidate for the next round of variations, which proved to be a fruitful direction.

The third generation cycle stemming from different arrangements of the carboxyl residues provided cyclic system **9**, which exhibited the highest turnover rate of the entire enterprise. The kinetics of product formation catalyzed by selected complexes was investigated in solution, and thus the results from solid-support experiments were confirmed with re-synthesized complexes (Table 1). *Remarkably, 5 mol % of catalyst **9** yielded 98% of epoxide **2** in 2 min while catalyst **6** required 4 h to reach the same conversion (2 orders of magnitude rate enhancement).*

We then turned to study the diamide complexes as catalysts for C−H bond oxidation, and as such, the much less reactive ethylbiphenyl substrate **11** was examined (Table 2). The diamide manganese complexes were capable of C−H oxidation yielding ketone **12** and alcohol **13** as products. In the C−H bond oxygen transfer, the Mn(III) complex of **9** also demonstrated the highest turnover rate (approximately 10 min), whereupon the catalytic activity vanished (16% yield of ketone with **9,** and 5% yield of ketone with **6**, Table 2). In contrast, the complex of **6** led to 60% yield of methylbiphenyl ketone **12** after 4 h.

From these results, the decisive role of the properly positioned carboxyl unit on the rate of oxygen transfer became evident (**9** vs **5**, **7**, and **8**). However, we demonstrated that the manganese complex of **9** and other amino-group-containing complexes undergo degradation of the ligand itself, thus explaining the brevity of their catalytic existence.[14] In contrast, ligand **6** proved more resistant to oxidative degradation as less than 5% of the ligand was degraded by the addition of PhIO to the complex **10** in the absence of the substrate.

The structure of Mn(III)−**6** has not been rigorously established.[15] To do so we obtained an X-ray crystal structure **10** (Figure 1A). As postulated at the onset of our study, **6** forms a monomeric octahedral complex with the deprotonated amide nitrogens coordinated to manganese. To the best of our knowledge, manganese complexes of **9** are without precedent. We propose the coordination mode (metal−ligand bond connectivity) of complexes **14** and **15** shown in Figure 1 based on IR and MS studies (**14**, absence of ν_{N-H} 3250 cm^{-1}, ES-MS 415 (M − H); **15**, ν_{N-H} 3340 cm^{-1}, ES-MS 416 (M − AcOH)). Interestingly, complexes **14** and **15** exhibit similar catalytic profile (Tables 1 and 2).

The fundamental characteristics of any catalyst, namely selectivity, turnover rates, and catalyst stability, can be assessed, and improved, by subjecting evolvable systems to proper screening conditions. Pinpointing some essential structural features eliciting such characteristics has provided guidelines for the further development of more efficient and robust catalytic species. (1) The most striking feature is the aforementioned sensitivity of the catalysts to the carboxyl group arrangement around the metal center. (2) The presence of free amines compromises oxidative stability of the ligands. (3) We found that Schiff base ligands did not provide any improvement over the free amino-group-containing ligands. (4) Any perturbation of the best systems **6** and **9** led to a decrease of the catalytic performance.

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Supporting Information Available: Experimental protocol for preparation of solid-bound ligands and complexes, results of all tested libraries (Library 1−4), and crystallography data for **10** (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

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