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and Cyclo $C_6$  Hydrocarbons by Manganese Porphyrin  
and Non-Porphyrin Catalysts in the Presence of  
Monooxygen Transfer Reagents**

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**MASTER**

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# **Biomimetic Catalysis: Hydroxylation of C<sub>2</sub>, C<sub>3</sub>, and CycloC<sub>6</sub> Hydrocarbons by Manganese Porphyrin and Non-Porphyrin Catalysts in The Presence of Monooxygen Transfer Reagents**

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## **ABSTRACT**

Metal complexes that mimic the active site of monooxygenase enzymes and convert carbon-hydrogen bonds to carbon-hydroxyl in the presence of a monooxygen transfer reagent are called biomimetic catalysts. Studies concerning the activation of methane, ethane, propane, and cyclohexane to their respective alcohols with biomimetic catalysts that encompass manganese supramolecule porphyrins and open-faced porphyrins, manganese non-porphyrin tri and tetranuclear clusters and a mononuclear manganese-substituted Keggin ion in the presence of monooxygen transfer reagents such as iodosylbenzene and t-butyl hydroperoxide will be discussed.

## **INTRODUCTION**

The use of biomimetic catalysts, that mimic monooxygenase enzymes such as cytochrome P-450 and methane monooxygenase by convert C-H to C-OH bonds in the presence of a monooxygen transfer reagent, is an area of intense research interest.<sup>1</sup> The monooxygenase enzyme, cytochrome P-450, has a metallo-porphyrin active site,<sup>2</sup> while methane monooxygenase has a metallo-non-porphyrin active site.<sup>3</sup> These two diverse monooxygenases also have different selectivities for hydrocarbon activation. For example, cytochrome P-450 will activate hydrocarbons greater than C<sub>3</sub>, while methane monooxygenase will activate C<sub>1</sub>-C<sub>6</sub> and possibly higher homologues.

While the focus of our research is to ultimately activate methane to methanol, as is readily done by methane monooxygenase, we also want to understand what types of biomimics will activate higher homologues as well (C<sub>2</sub>, C<sub>3</sub>, and cycloC<sub>6</sub>). In addition, the bond dissociation energies may play an important role in our ability to activate methane at ambient temperature, since methane has the highest C-H bond dissociation energy (kcal) of all alkanes, i.e., methane (104); ethane (98); propane(96); and cyclohexane (94).

Thus, we have evaluated several biomimetic catalysts, which encompass manganese supramolecule and open-faced porphyrins, manganese tri and tetranuclear clusters, and a mononuclear metal active site in a totally inorganic matrix, a manganese-substituted Keggin ion, with C<sub>1</sub>-C<sub>3</sub> and cycloC<sub>6</sub> hydrocarbons in the presence of monooxygen transfer agents, iodosylbenzene and t-butyl hydroperoxide. We will also discuss solvent, catalyst lifetimes, and monooxygen transfer reagent as they effect the C-H activation reaction.

## RESULTS AND DISCUSSION

### MANGANESE SUPRAMOLECULE AND OPEN-FACED PORPHYRIN CATALYSTS, 1 AND 2.

Table 1 shows our results with C<sub>1</sub>-C<sub>3</sub> and cycloC<sub>6</sub> hydrocarbons and manganese porphyrin catalysts 1 and 2 (Figure 1), with iodosylbenzene as the monooxygen transfer reagent, at room temperature in methylene chloride. It is evident that the supramolecule and open-faced porphyrin catalysts have similar reactivities with the hydrocarbons studied. Also, it is unfortunate that methane is not activated to methanol; however, ethane, propane, and cyclohexane are converted to their respective alcohols. Hence, we did not see any special reactivity with the supramolecule catalyst, 1, and rationalize that too much flexibility in the "basket handles" does not provide the shape selectivity that we hoped for to gain a kinetic advantage with the difficult to react methane gas.

It is interesting to note that the corresponding iron complexes were less reactive than their manganese analogues, while catalyst lifetimes for 1 and 2 were on the order of 1-2 hr. Thus, both catalyst appear to undergo oxidative degradation and this reaction competes with the conversion of C-H to C-OH bonds. As well, the C-H activation results clearly show a trend of C<sub>6</sub> > C<sub>3</sub> > C<sub>2</sub> and follows the order of the bond dissociation energies.<sup>4</sup>

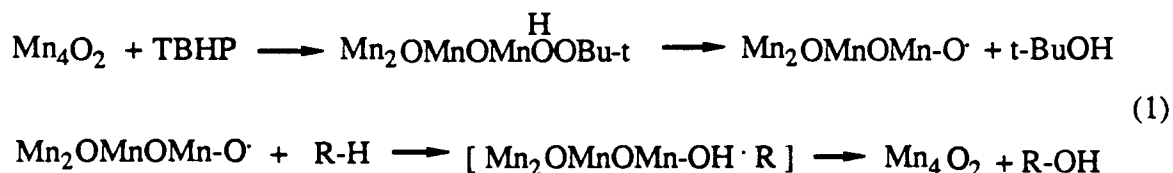
### MANGANESE NON-PORPHYRIN CLUSTERS, 1-4

Table 2 shows the results with C<sub>2</sub>, C<sub>3</sub>, and cycloC<sub>6</sub> and manganese clusters 1-4 (Figure 1) with t-butyl hydroperoxide at room temperature in acetonitrile (methane did not react under the reaction conditions). The important observation of no catalyst decomposition upon continual addition of t-butyl hydroperoxide to again provide the initial turnover number is an extremely important characteristic of any biomimetic catalyst. It is interesting to note that this increase in catalyst lifetimes occurred in acetonitrile and not methylene chloride and shows the dramatic effect of a coordinating solvent.

The Mn<sub>4</sub>O<sub>2</sub> clusters were more active than the Mn<sub>3</sub>O clusters and the Mn clusters also catalyzed t-butyl hydroperoxide decomposition (@ 1%) to acetone and methanol, which

prevented reliable analysis of methane activation results. We could not compare the dinuclear manganese complexes to their tri and tetra analogues because of relative solubility differences; however, we were able to do this with several iron di and tetra clusters and found that the  $\text{Fe}_4\text{O}_2$  clusters were more active with the hydrocarbons studied. Therefore, higher nuclearity or a variety of ligands may provide the shape selectivity we seek for ultimate methane activation with Mn and Fe clusters.

We also have attempted to inhibit these free radical reactions with 2,6-di-*t*-butyl-4-methylphenol and found no effect on the formation of cyclohexanol or cyclohexanone using catalyst 4. This latter result strongly suggests that peroxy, alkoxy, or hydroxyl radicals are not intermediates in these reactions. The intermediacy of a putative oxo-manganese complex is further strengthened by the reaction of 1-4 with cyclohexene in the presence of TBHP or iodosylbenzene to provide cyclohexene epoxide and our proposed mechanism is shown in Eq 1.<sup>5</sup>



### MANGANESE SUBSTITUTED KEGGIN IONS, $\text{MnPW}_{11}\text{O}_{39}^{5-}$

Preliminary results with a manganese-substituted Keggin ion catalyst that has an extremely stable  $\text{PW}_{11}\text{O}_{39}^{5-}$  backbone, shows some promise with small hydrocarbons.<sup>4</sup> This catalyst can be heated to 65 °C for long periods without decomposition.<sup>6</sup> An initial experiment with ethane and *t*-butyl hydroperoxide in benzene gave 2 turnovers of ethane to ethanol in three hr at 65 °C, while with propane the turnover number was 24 and provided isopropanol and *n*-propanol in a 5:1 ratio (Table 3).

Unfortunately, methane did not provide methanol under these conditions. We are presently evaluating other metal-substituted Keggin ions as C-H activation catalysts for  $\text{C}_1\text{-C}_3$  hydrocarbons.

### CONCLUSIONS

Although we have not as yet succeeded in our main goal of activating methane, we have learned how to activate ethane and propane with several manganese mono, tri, and tetranuclear complexes. We hope to use these results as a foundation for the future utilization of oxygen gas

as the monooxygen transfer reagent with iron cluster catalysts to give a system that mimics methane monooxygenase enzyme.

## ACKNOWLEDGMENTS

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Table 1

| Carbon-Hydrogen Activation of Hydrocarbons<br>Using Compounds 1 and 2 as Catalysts and<br>Iodosylbenzene as the Monooxygen Transfer Agent <sup>a</sup> |  |  |              |      |
|--|--|--|--------------|------|
| Hydrocarbon  | Product (%) <sup>b</sup>                                 |  | Turnover no. |      |
|  | 1  | 2  | 1            | 2    |
| CH <sub>4</sub>  | NPD <sup>c</sup>   | NPD  | —            | —    |
| CH <sub>3</sub> CH <sub>3</sub>  | CH <sub>3</sub> CH <sub>2</sub> OH (1)                   | CH <sub>3</sub> CH <sub>2</sub> OH ( 2.7 )               | 0.23         | 0.54 |
| CH <sub>3</sub> CH <sub>2</sub> CH <sub>3</sub>  | (CH <sub>3</sub> ) <sub>2</sub> CHOH (9.6) <sup>d</sup>  | (CH <sub>3</sub> ) <sub>2</sub> CHOH (13.5) <sup>e</sup> | 2.1          | 2.8  |
|  | CH <sub>3</sub> CH <sub>2</sub> CH <sub>2</sub> OH (0.6) | CH <sub>3</sub> CH <sub>2</sub> CH <sub>2</sub> OH (1)   |              |      |
| CycloC <sub>6</sub> H <sub>12</sub>  | C <sub>6</sub> H <sub>11</sub> OH (72)                   | C <sub>6</sub> H <sub>11</sub> OH (69.4)                 | 16.7         | 14   |
|  | C <sub>6</sub> H <sub>10</sub> O (5.2)                   | C <sub>6</sub> H <sub>10</sub> O (1)                     |              |      |
|  | C <sub>6</sub> H <sub>11</sub> Cl (4.5)                  | NPD  |              |      |

a) Reactions of methane, ethane, and propane were run in a Parr kinetic apparatus at room temperature for 24 h at 100-500 psi with a iodossylbenzene to catalyst ratio of 20:1. Catalyst concentration was .0025 molar in methylene chloride. The cyclohexane reactions were run at room temperature in Schlenk tubes with substrate : iodossylbenzene: catalyst ratios of 1100:20:1 in methylene chloride. Analysis and quantitation of products was obtained via capillary column GC analysis with a 15m · .035 mm DB5 column.

b) Based on the mmoles of iodossylbenzene

c) No product detected

d) Ratio of 2<sup>0</sup> to 1<sup>0</sup> C-H bond reactivity on a per H basis is 45:1

e) Ratio is 42:1



Table 2

**Comparison of the C-H Bond Reactivity of C2, C3, and Cyclo C6  
Hydrocarbons with Mn<sub>3</sub>-4O<sub>1-2</sub>L<sub>x</sub>L<sub>y</sub> Catalysts, 1-4, Using  
t-Butyl Hydroperoxide as the Monooxygen Transfer Reagent <sup>a</sup>**

| Hydrocarbon                                       | Catalyst | Products(%) <sup>b</sup>                      | Turnover No. <sup>c</sup> |
|---|----------|---|---------------------------|
| <b>CH<sub>3</sub>CH<sub>3</sub></b>               | <b>1</b> | <b>ethanol(1)</b>                             | <b>2</b>                  |
|   | <b>2</b> | <b>ethanol(&lt;1)</b>                         | <b>&lt;1</b>              |
|   | <b>3</b> | <b>ethanol(1)</b>                             | <b>2</b>                  |
|   | <b>4</b> | <b>ethanol(&lt;1)</b>                         | <b>1</b>                  |
| <b>CH<sub>3</sub>CH<sub>2</sub>CH<sub>3</sub></b> | <b>1</b> | <b>isopropanol(2)<sup>d</sup></b>             | <b>3</b>                  |
|   | <b>2</b> | <b>isopropanol(&lt;1)</b>                     | <b>&lt;1</b>              |
|   | <b>3</b> | <b>isopropanol(5)</b>                         | <b>9</b>                  |
|   | <b>4</b> | <b>isopropanol(3)</b>                         | <b>5</b>                  |
| <b>CycloC<sub>6</sub>H<sub>12</sub></b>           | <b>1</b> | <b>cyclohexanol(60)<br/>cyclohexanone(36)</b> | <b>121</b>                |
|   | <b>2</b> | <b>cyclohexanol(50)<br/>cyclohexanone(33)</b> | <b>114</b>                |
|   | <b>3</b> | <b>cyclohexanol(41)<br/>cyclohexanone(39)</b> | <b>126</b>                |
|   | <b>4</b> | <b>cyclohexanol(44)<br/>cyclohexanone(42)</b> | <b>127</b>                |

**<sup>a</sup> Reactions of ethane and propane were reacted in a Parr Kinetic Apparatus at partial pressures of 250 and 90 psi, respectively, at room temperature for 1-3h in acetonitrile. The ratio of t-butyl hydroperoxide (TBHP) to catalyst was 150:1, while the catalyst concentration was .0025M. The cyclohexane reactions were run in Schlenk flasks at room temperature for 1-3h with**

**substrate : oxidant: catalyst ratio of 1100 : 150 : 1 and a catalyst concentration of .001M in acetonitrile. TBHP was added as a benzene solution.**

**<sup>b</sup> The analysis and quantitation was accomplished via capillary column GC and GC-MS analysis. Yields of alcohol and ketone were based on TBHP consumed (iodometric titration). The ketone yields are molar yields multiplied by 2, since two equivalents of TBHP are required to make one equivalent of ketone.**

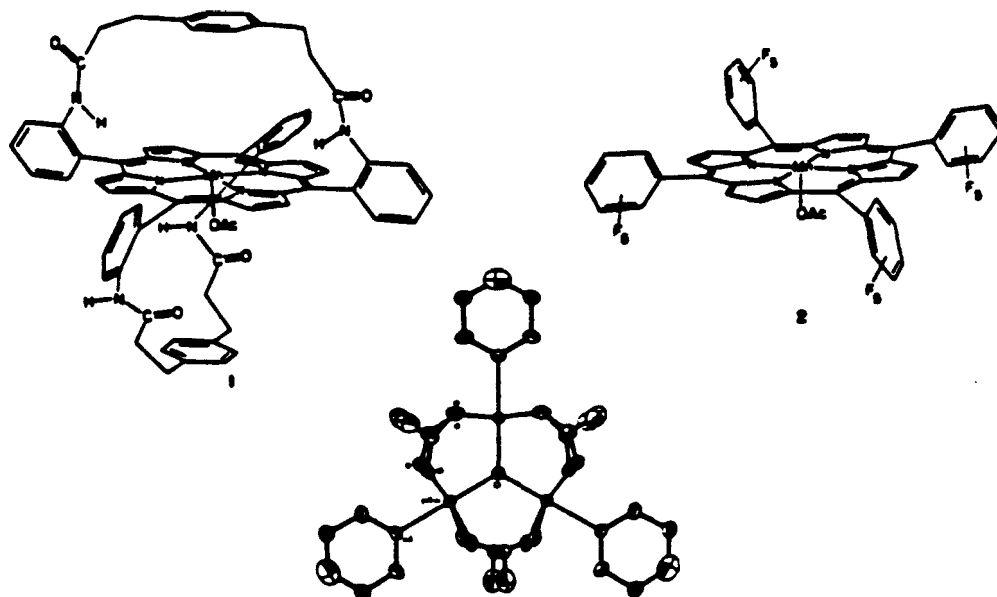
**<sup>c</sup> Based on the mmoles of oxidizing equivalents/mmoles catalyst.**

**<sup>d</sup>Trace amounts of n-propanol (<<1%) were also formed(GC). As well, trace amounts of acetone were also found; however, a control experiment verified its formation from the Mn cluster-catalyzed decomposition of TBHP. Additionally, small amounts of isopropanol can also be oxidized to acetone under the reaction conditions.**

**Table 3**

| Carbon-Hydrogen Activation of C <sub>1</sub> -C <sub>3</sub> Hydrocarbons with a Manganese-Substituted Keggin Ion Catalyst Using t-Butyl Hydroperoxide as the Monooxygen Transfer Reagent in Benzene <sup>a</sup> |                                    |                 |
|---|------------------------------------|-----------------|
| Hydrocarbon   | Product (%)                        | Turnover Number |
| CH <sub>4</sub>   | -                                  | -               |
| CH <sub>3</sub> CH <sub>3</sub>   | ethanol (2)                        | 2               |
| CH <sub>3</sub> CH <sub>2</sub> CH <sub>3</sub>   | isopropanol (30)<br>n-propanol (6) | 24              |

<sup>a</sup> Reactions of methane, ethane, and propane were reacted in a Parr Kinetic Apparatus at pressures of 500, 250, and 90 psi, respectively, at 65 °C in benzene. The t-butyl hydroperoxide(TBHP) / catalyst ratio was 177:1 with a catalyst concentration of  $2.0 \times 10^{-4}$  M. TBHP was added as a benzene solution. Yields were based on TBHP consumed(iodometric titration); ~ 75% in each case.



**Mn<sub>3</sub>O(O<sub>2</sub>CCH<sub>3</sub>)<sub>6</sub>(py)<sub>3</sub> [Mn<sub>3</sub>O(O<sub>2</sub>CCH<sub>3</sub>)<sub>6</sub>(py)<sub>3</sub>](ClO<sub>4</sub>)**

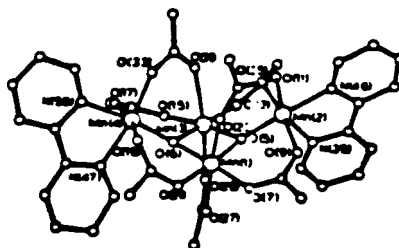
**1**

**2**

**Mn<sub>4</sub>O<sub>2</sub>(O<sub>2</sub>CPh)<sub>7</sub>(bipy)<sub>2</sub> [Mn<sub>4</sub>O<sub>2</sub>(O<sub>2</sub>CPh)<sub>7</sub>(bipy)<sub>2</sub>](ClO<sub>4</sub>)**

**3**

**4**



**Figure 1. Structures of manganese porphyrin and non-porphyrin catalysts.**