

BIOMIMETIC OXIDATION STUDIES, 6: SYNTHETIC AND MECHANISTIC ASPECTS OF MANGANESE CLUSTER MEDIATED ALKANE FUNCTIONALIZATION REACTIONS ¹

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ABSTRACT. — Manganese clusters, $[\text{Mn}_2\text{O}(\text{O}_2\text{CMe})(\text{tmima})_2](\text{ClO}_4)_3$ (tmima = tris[(1-methylimidazol-2-yl)methyl]amine), $\text{Mn}_3\text{O}(\text{O}_2\text{CMe})_6(\text{py})_3$, $[\text{Mn}_3\text{O}(\text{O}_2\text{CMe})_6(\text{py})_3](\text{ClO}_4)$, $\text{Mn}_4\text{O}_2(\text{O}_2\text{CPh})_7(\text{bipy})_2$, $[\text{Mn}_4\text{O}_2(\text{O}_2\text{CPh})_7(\text{bipy})_2](\text{ClO}_4)$, **1-5**, were found to functionalize ethane, propane, cyclohexane, adamantane, and toluene to their respective alcohols, aldehydes, and ketones with monooxygen transfer reagents, *t*-butyl hydroperoxide (TBHP) or iododisobenzene (IB), in the presence of O_2 . Factors such as solvent, oxidant, catalyst stability, substrate, and presence of O_2 affected the oxidation reactions. For example, in acetonitrile, the complexes showed no sign of decomposition or loss of activity upon repeated additions of TBHP. However, lower mmol of product/mmol of Mn complex and complex decomposition are seen if methylene chloride is substituted as the solvent or if IB was used as the monooxygen transfer reagent. Primary kinetic isotope effects (cyclohexane/cyclohexane- d_{12}) were determined to give values of approximately 8 and C-H selectivity studies with adamantane and toluene gave C_3/C_2 values of approximately 10 for the former, while the latter gave a benzaldehyde/benzyl alcohol ratio of 4 with no aromatic ring hydroxylation products, *o*, *m*, *p*-cresols, evident. In addition, the cyclohexane oxidation reactions were studied extensively and found to be quenched when oxygen gas was removed by an Argon gas purge, but not effected to any significant extent by the addition of a free radical inhibitor. There also is a direct Mn cluster catalyzed oxidation of alcohol to ketone or aldehyde, which is not affected by the absence of O_2 . The overall results imply that a putative Mn=O species is formed, via reaction of Mn complex with TBHP or IB, and homolytically abstracts hydrogen from C-H bonds of hydrocarbons to give a carbon radical and Mn-OH. The carbon radical, we speculate, is then trapped by O_2 to form a alkyl hydroperoxide, which decomposes via a alkyl peroxy-Mn complex intermediate to alcohol, ketone, aldehyde, and Mn=O complex; no alkyl *t*-butylperoxides were detected. Furthermore, the putative Mn=O complex can oxidize the alcohol product to provide the ketone or aldehyde in an O_2 independent reaction. The synthetic and mechanistic implications will be discussed.

Introduction

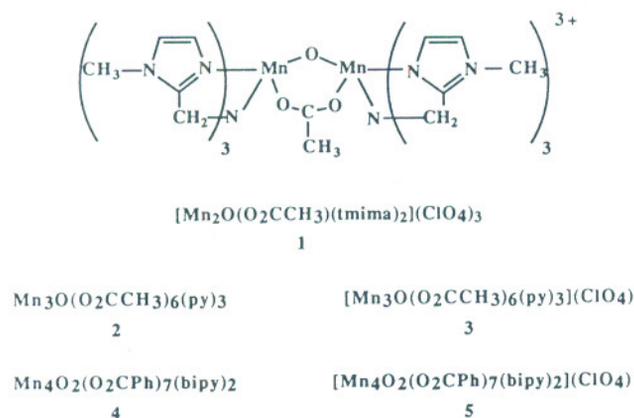
The study of biomimetic oxidation catalysts, structural mimics of the active sites of monooxygenase enzymes, that convert alkanes to alcohols in the presence of a monooxygen transfer reagent is a fascinating subject, which has garnered increasing research interest¹⁻⁴. The enzyme most responsible for the early success of the above-mentioned model studies has been cytochrome P-450, an Fe based porphyrin system, which catalyzes the monooxygenation of organic substrates with the use of oxygen gas and the co-factor NADPH⁵. Thus, considerable research effort has focused on synthetic metallo-porphyrin models as mimics of the P-450 enzyme active site and our current understanding of the oxidation mechanism with P-450 mimics is becoming more firmly established².

However, the mechanisms for non-porphyrin biomimetic systems are less understood with fewer examples of C-H functionalization reactions being reported^{1,3,4}. The interest in non-porphyrin complexes as C-H functionalization catalysts coincides with the recent reports on methane monooxygenase enzymes (MMO)⁶, which has been assigned, via EXAFS analysis, a μ -oxo (or μ -hydroxo)-diiron non-porphyrin active site $[\text{Fe}_2\text{O}(\text{Fe}_2\text{OH})]$ ⁷. MMO catalyzes the oxidation of methane and a variety of other hydrocarbons with oxygen gas to provide methanol and higher homologous alcohols⁶.

We recently communicated on the use of μ -oxo-manganese complexes for C-H functionalization of hydrocarbons^{1a, b} and, in this paper, we report our complete studies on manganese clusters, **1-5**, for C-H functionalization of ethane, propane, cyclohexane, adamantane and toluene in the presence of mono-

oxygen transfer reagents, *t*-butyl hydroperoxide (TBHP) and iodobenzene (IB) as well as oxygen gas. Crabtree *et al.* have also recently verified the use of similar Mn clusters for the C–H functionalization of hydrocarbons^{4a}.

It is interesting to note that these manganese complexes, **1-5**, were originally synthesized as plausible models for the photo-synthetic water oxidation enzyme site in green plants, Photo System II, as well as Mn containing pseudocatalases^{8, 9, 1f}. This study then enhances the versatility of these manganese clusters as biomimetic enzyme analogues for C–H functionalization and plausible synthetic reagents for conversion of hydrocarbons to alcohols, ketones and aldehydes.



Results

ALKANE FUNCTIONALIZATION AND SYNTHETIC STUDIES

Cyclohexane oxidation

Manganese clusters, **1-5**, were found to initiate the oxidation of cyclohexane with TBHP or IB under mild conditions in the presence of O_2 gas to give cyclohexanol and cyclohexanone as the major products. In all cases, the reactions were conducted at ambient temperature with a cyclohexane/catalyst ratio of 1100/1. The TBHP reactions had oxidant/catalyst ratios of 150/1, while with IB the ratio was 20/1. The material balance of products formed was > 98% for all oxidation reactions studied.

The initial oxidation experiments utilized methylene chloride (CH_2Cl_2) as the solvent in which all catalysts were soluble except complex **1**. The TBHP mediated reactions gave cyclohexanol (CyOH) and cyclohexanone (CyONE) as the major products with only trace amounts of cyclohexyl chloride (CyCl). The mmol of product/mmol of Mn complex with TBHP was 12-15 for all catalysts except **3**, which gave 7. As well, oxidation with IB in CH_2Cl_2 provided a lower mmol of product/mmol of Mn complex (< 5) with CyOH and CyONE as the major oxidation products, along with formation of cyclohexyl chloride. The formation of CyCl indicates solvent participation in the oxidation process. The addition of either TBHP or IB to the Mn complexes in CH_2Cl_2 initially gave red solutions, which turned slightly darker and then slowly turned to a light red color. As well, Mn complex decomposition and less activity occurred upon further addition of either oxidant in CH_2Cl_2 .

When we replaced CH_2Cl_2 with acetonitrile (CH_3CN) as the solvent, dramatic differences were observed in the hydrocarbon oxidation reactions. Upon addition of TBHP to CH_3CN solutions containing the Mn complexes, **1-5**, respectively, the initial red or light brown solutions turned slightly darker with cyclohexane oxidations providing approximately 50-55 mmol of pro-

duct/mmol of Mn complex with no sign of any catalyst decomposition (Table I). The dinuclear cluster, **1**, provided an alcohol/ketone ratio (CyOH/CyONE) of 0.8, while rapidly consuming the TBHP in 0.5 h. The trinuclear clusters, **2** and **3**, were observed to give about twice as much ketone as alcohol (CyOH/CyONE=0.42 and 0.38) and complete consumption of TBHP after 2 h, while tetranuclear clusters, **4** and **5**, gave almost four times more ketone than alcohol (CyOH/CyONE = 0.25 and 0.27) and consumed TBHP at a rate similar to **1** (0.5 h).

Table I. – Comparison of the C–H bond functionalization of cyclo C_6 , C_3 and C_2 hydrocarbons with $\text{Mn}_{2,4}\text{O}_{1,2}\text{L}_x$ catalysts, **1-5**, using *t*-butyl hydroperoxide as the monooxygen transfer reagent^a.

Hydrocarbon	Catalyst	Products (%) ^b	mmol product/mmol of Mn complex
Cyclo C_6H_{12}	1	cyclohexanol (15)	50
	2	cyclohexanone (37)	53
	3	cyclohexanol (11)	50
	4	cyclohexanone (26)	55
	5	cyclohexanone (24)	56
$\text{CH}_3\text{CH}_2\text{CH}_3$ ^c	1	cyclohexanol (7)	3
	2	cyclohexanone (28)	3
	3	cyclohexanol (9)	< 1
	4	cyclohexanone (24)	9
	5	cyclohexanone (30)	5
CH_3CH_3	1	cyclohexanol (8)	2
	2	cyclohexanone (28)	2
	3	cyclohexanol (9)	< 1
	4	cyclohexanone (24)	2
	5	cyclohexanone (30)	1

^a The cyclohexane reactions were run in Schlenk flasks at room temperature for 1-3 h with substrate: oxidant: catalyst ratio of 1100:150:1 and a catalyst concentration of 0.001 M in acetonitrile. TBHP was added as a benzene solution. 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 1-3 h in acetonitrile. The ratio of *t*-butyl hydroperoxide (TBHP) to catalyst was 150:1, while the catalyst concentration was 0.0025 M.

^b The analysis and quantitation was accomplished via capillary column GC and GC-MS. 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.

^c Trace amounts of *n*-propanol (<< 1%) were also formed in all Mn cluster-catalyzed reactions (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.

In addition to increased product yield, complexes **1-5** were also found to have increased lifetimes in CH_3CN . Complex **5**, for example, was still active after 750 mM of TBHP (*ca.* 275 mmol of product/mmol of Mn complex) had been added with no apparent sign of complex decomposition. We found that with repeated additions of TBHP, the ratio of CyOH/CyONE decreased. Moreover, the recent reports by Sawyer and Barton and co-workers^{4c, g} on the direct formation of CyONE from cyclohexane, but not the alcohol, prompted us to use CyOH as the substrate. In fact, CyOH (900 mM) could be used as a substrate and was oxidized with complex **1** to CyONE giving 120 mmol of product/mmol of Mn complex in 4 h, while complex **5** gave 112 mmol of product/mmol of Mn complex.

The fate of the complexes **1-5** during the oxidation reactions were studied with the following control experiments. For example, with **5** and TBHP (1:20) in CH₃CN, the complex (IR analysis) was recovered almost quantitatively (94%), while TBHP was converted to *t*-butyl alcohol (GC) with the added observation of oxygen gas being evolved from the reaction mixture. Similar observations with **1-4** were also found.

In corresponding studies with Fe clusters and H₂O₂, we found that oxidation of cyclohexane proceeded to give cyclohexyl hydroperoxide as the intermediate oxidation product, via trapping of cyclohexyl radical with O₂, that then catalytically decomposed to CyOH and CyONE^{1e}. Indeed, we found that O₂ was a critical component of the Mn catalyzed cyclohexane oxidation chemistry with TBHP or IB and that removal of O₂ by purging the reaction with Argon gas quenched catalysis (100%). Thus, it appeared that alkyl hydroperoxides might be one pathway to both CyOH and CyONE, while CyONE could also be formed by the direct oxidation of CyOH and occurs independent of the presence of O₂.

We attempted to determine the intermediacy of cyclohexyl hydroperoxide, for possible isolation and further ¹³C NMR characterization, by addition of iodide (I⁻) to the reaction solutions. In the Fe cluster/H₂O₂ reactions^{1e}, we found that the I⁻ reaction would dramatically change the CyOH/CyONE ratio: this being consistent with the reaction of CyOOH and I⁻ giving predominantly CyOH. Addition of I⁻ to the Mn cluster catalyzed oxidation reactions of cyclohexane did not show a change in the CyOH/CyONE ratios; therefore, it would appear that the Mn complexes were decomposing any formed CyOOH to product very rapidly, precluding their isolation.

Therefore, we decided to prepare CyOOH and study its decomposition directly with complexes **1** and **4**. In fact, with complex **1** and CyOOH (1:20 mmol ratio) in the absence of TBHP the ratio of CyOH/CyONE was 1.2, while in the presence of TBHP (150 mM), the ratio of CyOH/CyONE was 0.5. Similar experiments with complex **4** in the presence of TBHP gave a CyOH/CyONE ratio of 0.31. The direct oxidation of cyclohexane with **1** gave a ratio of 0.8, while with **4** the ratio was 0.41. In other studies in our laboratory with [Fe₂O(O₂CMe)(tmima)₂](ClO₄)₃ and TBHP, we found that the Fe analogue of complex **1** reacted very slowly with CyOOH^{1f}. Thus, the presence of CyOOH might be detected with the Fe system using the I⁻ reaction. If the [Fe₂O(O₂CMe)(tmima)₂](ClO₄)₃/TBHP/cyclohexane reaction was analyzed after 2 h with I⁻, a 20% increase in the CyOH/CyONE ratio was observed (1.2 to 1.5)^{1f}. These latter results imply that CyOOH could be an intermediate to both CyOH and CyONE, but the concentrations of TBHP appear to cause its decomposition to occur more rapidly as shown above. Furthermore, the formation of *t*-butyl cyclohexyl peroxide (CyOOBu-*t*) as a precursor to CyOH and CyONE was not observed by GC or GC-MS analysis of the reaction mixtures.

Propane oxidation

Although oxidation of propane with IB (20 mM) gave mostly acetone (1-2 turnovers) with complexes **1-5**, extensive study of IB as an oxidant was not conducted, due to its low solubility in the reaction medium. Oxidation of propane with TBHP was carried out with manganese clusters, **1-5**, at concentrations of 0.0025 M in CH₃CN (Table I). The TBHP to catalyst ratio was 150/1 and all reactions were carried out at 90 psi of propane in a Parr Kinetic Apparatus at room temperature. In all cases, isopropanol was the major alcohol formed with only trace amounts of *n*-propanol (< 1%). The tetranuclear clusters **4** and **5** gave slightly more alcohol (5-10 turnovers) than clusters **1-3**.

Acetone was also observed in each case, but TBHP is known to decompose to small amounts of acetone and methanol in the presence of metals¹⁰. In fact, control experiments in the absence of propane indicated that the manganese clusters also decomposed TBHP to small amounts of acetone and methanol (< 1%).

Ethane oxidation

Oxidation of ethane in the presence of 150 mmol of TBHP was conducted under the same reactions as propane except at a pressure of 250 psi (Table I). With all clusters, 1-2 mmol of product/mmol of Mn complex of ethanol were observed along with small amounts of acetaldehyde.

Cyclohexane oxidation in the presence of TBHP

In the TBHP reactions with methylene chloride as the solvent, small amounts of cyclohexyl chloride were obtained indicating that a radical process is involved. However, attempts to inhibit the formation of cyclohexanol and cyclohexanone with a free radical trap, 2,4,6-tri-*t*-butylphenol (TBP), using the Mn complexes in CH₃CN were not successful. We observed no inhibition of the rate of formation of the products in the presence of 10 mM of TBP, nor a change in the ratio of products. However, at 20 mM of TBP there was a slight reduction of the mmol of product/mmol of Mn complex of 26%.

Cyclohexene reaction with TBHP and IB

While the above-mentioned cyclohexane reactions with TBHP were slightly affected by a free radical inhibitor, we thought comparison of a Mn cluster catalyzed oxidation of cyclohexene with both TBHP and IB in CH₃CN might be informative (substrate/catalyst ratio = 1,100). This type of experiment could help decide about the involvement of oxygen centered radicals in these reactions, since IB is a monooxygen transfer reagent that should not participate in long chain free radical chemistry².

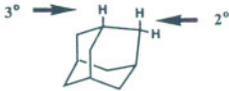
The conversion of cyclohexene to cyclohexane epoxide, cyclohex-2-en-1-ol, and cyclohex-2-en-1-one with both TBHP and IB using catalysts **2** and **4**, respectively, gave a similar ratio of products. Thus, with TBHP the ratio of epoxide: enol: enone was 1:2.5:2.6, while with IB the ratio was 1:2.3:2.8. It appears that both oxidants may provide the same initial Mn oxidation intermediate, since the product ratios are similar within the experimental errors of the analytical method^{3g}.

Adamantane selectivity

Oxidation of adamantane was conducted to determine C₃/C₂ selectivity values (Table II) and to compare the results with other metallo-porphyrin and non-porphyrin oxidation systems. Interestingly, **1-5** gave a similar range of values from 9 to 11 (normalized) when using TBHP. Oxidation using IB also gave similar values of 10-12 for both the tetranuclear and the trinuclear clusters. Other biomimetic studies with cytochrome P450 models (oxo-metallo-porphyrins) have provided C₃/C₂ selectivities values ranging from 3 to 48^{3a-f}, while non-porphyrin systems have been found to give C₃/C₂ selectivity values ranging from 1-13^{3b-e}.

Toluene selectivity

The toluene selectivity was only studied with complex **1** and provided benzaldehyde (13 mmol of product/mmol of Mn complex) and benzyl alcohol (3 mmol of product/mmol of Mn

Table II. – Adamantane C₃/C₂ selectivities with Mn complexes, 1–5^a.


Catalyst	Ox	C ₃ /C ₂ selectivity
1	TBHP	10.8
2	TBHP	11.0
3	TBHP	10.7
4	TBHP	9.1
5	TBHP	9.4
2	IB	10.0
3	IB	12.5
4	IB	10.0
5	IB	11.1

^a See experimental section for details.

complex). Furthermore, benzyl alcohol (900 mM) could be oxidized to benzaldehyde with 137 mmol of product/mmol of Mn complex in a slow process (10 days). Since no aromatic C–H activation products, *o*, *m*, or *p*-cresols, were detected by GC-MS analysis, then this result implies that hydroxyl radicals are not involved in these oxidation reactions.

Primary kinetic isotope effect

The primary kinetic isotope effects for the hydroxylation of cyclohexane (C₆H₁₂/C₆D₁₂) were determined with the clusters 1, 2 and 4 (Table III). TBHP gave a k_H/k_D values of 9 for the dinuclear cluster, 1, 7 with the tetranuclear cluster, 4, while the trinuclear cluster, 2, gave a value of 8 (ketone formation included in the calculation). Values of 10 and 6 were observed for the tetra- and trinuclear clusters, 4 and 2, respectively, when IB was substituted for TBHP. These k_H/k_D values are well within the range of those found in metallo-porphyrin systems (4–13)^{3a-f}, and also for those values found in non-porphyrin systems (1–10)^{4a-e}.

Table III. – Cyclohexane k_H/k_D Values with Mn complexes 1, 2 and 4^a.


Catalyst	Ox	k_H/k_D
1	TBHP	9.0
2	TBHP	7.7
4	TBHP	7.4
2	IB	6.2
4	IB	9.5

^a See experimental section for details.

Discussion

The functionalization of small hydrocarbons by these manganese clusters has allowed a better understanding of the critical factors associated with these oxidation reactions. We found that solvent, monooxygen transfer reagent, presence of O₂, hydrocarbon, and Mn complex lifetimes were important parameters. Thus, CH₃CN was the superior solvent, providing a four-fold increase in the mmol of product/mmol of Mn complex relative

to those reactions in CH₂Cl₂. Additionally, TBHP was the monooxygen transfer reagent of choice, since IB had such limited solubility in CH₃CN or CH₂Cl₂.

It is interesting to note that we also tried to use H₂O₂ as a monooxygen transfer reagent; however, the Mn complexes decomposed, concomitant with O₂ evolution, and did not provide any C–H functionalization products. The above-mentioned decomposed complexes that formed in the presence of H₂O₂ were transparent in the visible region indicating that the Mn³⁺ ions had been reduced to Mn²⁺ ions. Since there are no known examples of μ -oxo bridged Mn²⁺ ions, the need for high-valent μ -oxo bridged Mn species may be necessary for C–H functionalization¹¹.

We noted earlier, in the cyclohexane oxidation studies, that the normal reddish-brown solutions turned red upon the addition of TBHP and slowly turned lighter as the oxidation reactions progressed. We attempted to follow these changes by UV-vis spectroscopy, as well, but saw only minor shifts in the ligand field bands with no attenuation in their relative intensities.

The cyclohexane reaction with neutral and cationic di, tri and tetranuclear Mn clusters did show significant differences in the CyOH/CyONE ratios with lower ratios occurring as we went from the di to tetranuclear complexes, while with ethane and propane there was some variation in reactivity as a function of catalyst structure and charge. For example, the neutral Mn clusters, 2 and 4, were more reactive with ethane than their cationic analogues, 3 and 5. Alternatively, Mn clusters 4 and 5 were more reactive toward propane than 2 and 3. It is not clear what these latter results mean with regard to the mechanism of oxidation, but could be related to the redox chemistry associated with electron transfer between Mn centers to provide higher Mn oxidation states.

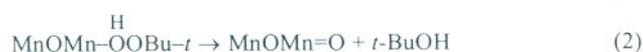
The thermodynamic parameter most important in these hydrocarbon C–H functionalization reactions appears to be the bond dissociation energies. Thus, the sequence of hydrocarbon activity with the Mn cluster complexes, not too surprisingly, follows those bond dissociation energies (kcal/mol): cyclohexane (94) >>> propane (96) >> ethane (98).

The factors concerning the C–H functionalization step were addressed with a variety of mechanistic probes. A free radical trap, TBP, did not effect the rate of product formation (cyclohexanol/cyclohexanone) nor the product ratios. This fact together with the experiment with cyclohexene and TBHP or IB appears to rule out long chain free radical reactions. However, the free radical nature of these reactions was consistent with the finding that CyCl was a minor product in both the TBHP and IB reactions with cyclohexane in CH₂Cl₂. Also consistent with the radical nature of these reactions was the fact that the reactions were dependent upon oxygen with no catalysis observed when Argon gas was used as a purge. Oxygen is well known to react with alkyl radicals at rates near 1×10^9 ¹².

The adamantane selectivity results favor tertiary hydrogen over secondary hydrogen reactivity. The significance of this result is that radical stability is important in the C–H functionalization step^{3,4}. The k_H/k_D results imply considerable bond breaking in the transition step of the C–H functionalization reaction with values reminiscent of those obtained for P-450 biomimics (~4–13)^{2a,i} where it has been firmly established that oxo-metallo-porphyrins are the intermediate oxidants formed. As well, several non-porphyrin systems with IB as the monooxygen transfer reagent have also implicated oxo-metallo intermediates^{3b,f,g}, but recent reports by Valentine *et al.* indicate that complexed iodosyl species and not M=O species are the active oxidants¹³. However, it is important to note that it is difficult to place more meaning in these k_H/k_D values given the complica-

tions involved in knowing that these values encompass several C-H functionalization reactions.

Since our oxidation results with TBHP and IB are somewhat similar, this then leads us to speculate that the oxygen transfer reaction, illustrated with TBHP, provides a putative Mn=O intermediate with concomitant formation of *t*-butyl alcohol (Eqs. 1 and 2) and initiates the following sequence of reactions in the presence of an excess of hydrocarbon. The Mn=O complex homolytically reacts with C-H bonds to form a carbon radical (Eq. 3) followed by rapid trapping with O₂ to provide an alkyl hydroperoxide, which decomposes to alcohol and ketone via an alkyl peroxy-Mn complex (Eqs. 4, 5 and 6). The formed alcohol, from the decomposition of the alkyl peroxy-Mn complex, can then be further oxidized to the ketone without O₂ involvement (Eq. 7).



Equations 1 and 2 have been postulated to occur with other metal complexes^{3e, 14-16} and the O-O bond cleavage reaction, to form in this case the Mn=O species, is postulated to occur either by homolysis¹⁴ or by a heterolytic mechanism¹⁶. Equation 3 is well known from metallo-porphyrin catalyzed oxidation chemistry^{2, 3}. The critical role of O₂, in the air and from TBHP decomposition, is involved in trapping the carbon radical to form an alkyl hydroperoxide (Eq. 4); an autoxidation reaction¹⁷. The decomposition of the alkyl hydroperoxide, via an alkylperoxy Mn complex, to alcohol, aldehyde, or ketone (Eq. 5 and 6) is somewhat similar to Equation 1^{14, 15} and to the decomposition of a Fe porphyrin-OOBu-*t*-complex; the difference being the hydrogen α to the OOH functionality¹⁸. Equation 7 also has been postulated to occur, for example, in metallo-porphyrin^{2p} and non-porphyrin chemistry^{3s}.

Conclusions

The results indicate that Mn clusters are long-lived C-H functionalization complexes for small hydrocarbons and that monooxygen transfer reagents, TBHP and IB, predominantly form a putative Mn=O intermediate with the clusters that homolytically removes tertiary over secondary hydrogens to provide carbon radicals. These carbon radicals are thought to be initially trapped by O₂ to form an alkyl hydroperoxide that rapidly decomposes to alcohol, aldehyde, or ketone via an alkyl peroxy-Mn complex. The alcohol product can then be further oxidized to ketone; a process that is independent of O₂ involvement.

It is also evident that these manganese clusters can be useful as synthetic reagents for alcohol and especially ketone or alde-

hyde synthesis. Future studies will address structure/reactivity relationships and how redox chemistry affects this relationship as well as modification of these complexes for incorporation into host-guest polymers and inorganic supports.

Acknowledgments

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Experimental

INSTRUMENTATION

Gas chromatography was done on a Hewlett-Packard 5880 instrument with an FID detector and a J&W DB5 Carbowas capillary column, while GC/MS analyses were performed on a Hewlett-Packard MSD 5971A Instrument in the EI mode. The Parr Kinetic Apparatus was described elsewhere¹⁹.

MATERIALS

Cyclohexane, adamantane, methylene chloride, acetonitrile, and benzene were purchased from Aldrich. Cyclohexane was washed with acid²⁰ and distilled from calcium hydride before use. Methylene chloride was also washed with acid and distilled from P₂O₅. Acetonitrile was dried over 4 Å sieves before using. Benzene was distilled from sodium/benzophenone. TBHP was purchased as a 90% solution from Aldrich. An anhydrous solution of TBHP in benzene was prepared following the procedure by Sharpless et al.²¹. IB was prepared by peracetic acid oxidation of iodobenzene, followed by base hydrolysis²². Propane and ethane were purchased from Matheson at purities of 99.97% and 99.99% respectively.

[Mn₂O(O₂CMe)(tmima)₂](ClO₄)₃, Mn₃O(OCMe)₆(py)₃, [Mn₃O(O₂CMe)₆(py)₃](ClO₄), Mn₄O₂(O₂CPh)₇(bipy)₂, and [Mn₄O₂(O₂CPh)₇(bipy)₂](ClO₄)₁₋₅, were prepared by published procedures^{8, 23}.

CYCLOHEXANE, CYCLOHEXANOL AND CYCLOHEXENE OXIDATIONS

Oxidation reaction procedures with TBHP were as follows: all reactions were performed at room temperature. The Mn complexes (0.0025 mmol) were dissolved in CH₃CN and 2.75 mmol of cyclohexane (substrate/Mn complex = 1,100) was added. After stirring for 15 min, 150 mM of TBHP (benzene solution) was then added and the reaction mixture stirred for 1-3 h. 5 μ L of cyclopentanone was then added as an internal standard and the organic products quantified by GC and verified by GC/MS. In all cases, TBHP was completely consumed (iodometric titration). The cyclohexanol reactions were performed in a similar manner with 900 equivalents, while those with cyclohexene were done with 1,100 equivalents.

OXIDATION WITH IODOSYLBENZENE

The same procedure as with the TBHP oxidation reactions was followed except that 20 mmol of IB was added. Analysis and workup were conducted in the same manner.

PROPANE AND ETHANE OXIDATION

The reactions of propane and ethane were carried out in a Parr kinetic apparatus at partial pressures of 250 and 90 psi, respectively, at room temperature for 1-3 h in CH₃CN. The apparatus was charged with a CH₃CN solution of the Mn complex, all accomplished inside an argon-atmosphere drybox. The set-up was then taken out of the drybox

and flushed twice with the appropriate gas. TBHP was then syringed into the Parr kinetic apparatus and the system pressurized with the desired gas. After the reaction, the solution was transferred to a vial; pyridine and benzoyl chloride were used to derivatize any ethanol or propanols to their respective benzoate esters. The resulting products were then analyzed and quantified by GC and GC/MS.

ADAMANTANE OXIDATION

20 mM of adamantane was added to a 0.0025 M solution of the Mn complexes **1-5** in 20 mL of CH₃CN and the reaction stirred for 15 min. The 100 mM of TBHP (benzene solution) was added and the reaction stirred for 3 h. The resulting products, adamantan-1-ol, adamantan-2-ol, and adamantan-2-one, were quantified by GC and verified by GC/MS. Oxidation with IB was performed in the same manner, but with approximately 15 mM of IB and 15 mM of adamantane (see Table II for the results).

TOLUENE OXIDATION

A similar procedure as described above for adamantane was utilized with a substrate/catalyst/oxidant mmol ratio of 900/1/150. We observed no further oxidation of benzaldehyde to benzoic acid under our standard reaction conditions.

PRIMARY KINETIC ISOTOPE EFFECT

A 0.0025 M solution of the Mn complexes **1, 2** and **4** in CH₃CN was stirred at room temperature with approximately 500 mM each of cyclohexane and cyclohexane-d₁₂. After stirring for 15 min, 150 mM of TBHP was added and the reaction stirred for 1-3 h. The products were then quantified by GC and verified by GC/MS. The same procedure was done using IB as the oxidant; however, only 15 mM was used (see Table III for the results). Calculations were done by simply dividing the concentrations of: CyOH and CyONE/CyOH-d₁₁ and CyONE-d₁₀.

CONTROL EXPERIMENTS FOR Mn COMPLEX FATE IN THE PRESENCE OF TBHP

Several control experiments were conducted to verify that the Mn catalysts remain intact after the oxidation reactions. The following is example of a procedure performed to determine the fate of a Mn catalyst: 750 mg (0.5 mmol) of complex **5** was dissolved in 20 mL of either CH₂Cl₂ or CH₃CN along with an excess of TBHP (3 mL of a 3M solution in toluene). Gas evolution was evident immediately and, after it ceased, the solution was filtered and the solvent removed. Infrared analysis of the isolated material showed no differences between it and the starting complex.

REACTION OF COMPLEX **4** WITH CYCLOHEXANE AND TBHP IN THE PRESENCE OF 2,4,6-TRI-*t*-BUTYLPHENOL (TBP)

Complex **4** 3.7 mg (0.0025 mmol) was dissolved in CH₃CN (2.2 mL). Cyclohexane (0.19 g, 2.2 mmol, 900 equivalents), TBP (13.1 mg, 0.050 mmol, 20 equivalents) and then TBHP (70 μ L @ 3.4 M, 0.24 mmol, 95 equivalents) were added and the solution was stirred for 2 h. Cyclopentanone (2.0 μ L, 0.0026 mmol) was added as an internal standard and the amount of products was determined. CyOH, 4.8 mmol of product/mmol of Mn complex, CyONE, 12.8 mmol of product/mmol of Mn complex. In a control experiment (no TBP) the mmol of product/mmol of Mn complex were CyOH, 7.3, CyONE, 16.9. The mmol of product/mmol of Mn complex were 73% of normal in the presence of TBP and indicate that a free radical chain process is involved. At 10 equivalents of TBP/Mn complex no change of mmol of product/mmol of Mn complex was observed.

REACTION OF COMPLEX **4** AND TBHP AND THAT OF COMPLEX **1** AND IB WITH CYCLOHEXANE IN THE PRESENCE OF AN ARGON GAS PURGE

Complex **4** (14.8 mg, 0.010 mmol) was dissolved in CH₃CN (28.7 mL). Cyclohexane (0.78 g, 9.0 mmol, 900 equivalents) was ad-

ded and argon was bubbled through the solution with vigorous stirring for 20 min. TBHP (280 μ L @ 3.4 M, 0.95 mmol, 95 Eq) which had been purged with Argon gas for 20 min was added and the solution was stirred vigorously under an Argon purge for 4 h. The final volume of solution was ~ 22 mL. Cyclopentanone (5 μ L, 0.0565 mmol) was added as an internal standard and the products were analyzed by GC. Products yields were CyOH, 0.24 mmol of product/mmol of Mn complex, CyONE, 0.53 mmol of product/mmol of Mn complex and were 3.4% and 3.7% respectively, of a control reaction (7.0 CyOH and 14.5 CyONE mmol of product/mmol of Mn complex). In a similar experiment, complex **1** (1 mM), Iodosylbenzene (20 mM) and cyclohexane (900 mM) in 5 mL of CH₃CN were reacted for 3 h under an argon purge to provide no CyOH and only traces of CyONE.

DECOMPOSITION OF CYCLOHEXYL HYDROPEROXIDE (CyOOH) BY COMPLEX **4** AND TBHP

Complex **4** (3.7 mg, 0.0025 mmol) was dissolved in CH₃CN (2.4 mL). CyOOH (5.8 mg, 5.7 μ L, 0.050 mmol, 20 equivalents) and TBHP (110 μ L @ 3.4 M, 0.38 mmol, 150 equivalents) were added and the solution was stirred for 4 h. Cyclopentanone (2.0 μ L, 0.0226 mmol) was added as an internal standard and the products were analyzed by GC to give a CyOH/CyONE ratio of 0.31 (the ratio was not changed by the addition of iodide and is an average of 2 runs). This compares to a CyOH/CyONE ratio of 0.41 obtained in the actual catalytic reactions (average of 3 experiments).

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