Carbon–Hydrogen Activation Chemistry: Hydroxylation of C_2, C_3, and Cyclo-C_6 Hydrocarbons by Manganese Cluster Catalysts with a Mono-oxygen Transfer Reagent

Richard H. Fish,*[a] Raymond H. Fong,[a] John B. Vincent,[b] and George Christou*[b]

[a] *Lawrence Berkeley Laboratory, University of California, Berkeley CA 94720, U.S.A.*
[b] *Department of Chemistry, Indiana University, Bloomington IN 47405, U.S.A.*

Manganese clusters, $Mn_{3-4}O_{1-2}L_xL_y$ (L_x = RCO_2^-; L_y = pyridine or 2,2′-bipyridine), are novel catalysts that can convert C–H bonds to C–OH bonds in C_2, C_3, and cyclo-C_6 hydrocarbons in the presence of t-butyl hydroperoxide as the mono-oxygen transfer reagent.

The C–H bond activation of alkanes with homogeneous catalysts that mimic the active site of mono-oxygenase enzymes is currently an extremely important and intense area of research. While considerable effort has been focused on mimics of cytochrome P450,[1a–k] which has a metallo–porphyrin centre as the active site, few examples have been reported on non-porphyrin complexes.[2a–f] The interest in non-porphyrin complexes as C–H activation catalysts coincides with the recent reports on methane mono-oxygenase enzymes,[3a–c] which have tentatively been assigned, *via* EXAFS analysis, as having a μ-oxo di-iron non-porphyrin active site.[4a,b]

The metallo-non-porphyrin C–H activation catalysts that have been reported are predominantly mononuclear metal complexes,[2a–d] while two studies were directed towards metal clusters containing iron.[2f,g] We report that a series of manganese clusters, (**1**)—(**4**), originally synthesized as models for the photosynthetic water oxidation enzyme site in green plants,[5a–d] are novel C–H activation catalysts for the hydroxylation of C_2, C_3, and cyclo-C_6 hydrocarbons in the presence of a mono-oxygen transfer reagent. To our knowledge, this is the first reported attempt to evaluate the C–H bond reactivity of small hydrocarbons using non-porphyrin metal clusters as catalysts.

$Mn_3O(O_2CMe)_6(py)_3$ (**1**) $[Mn_3O(O_2CMe)_6(py)_3](ClO_4)$ (**2**)

$Mn_4O_2(O_2CPh)_7(bipy)_2$ (**3**) $[Mn_4O_2(O_2CPh)_7(bipy)_2](ClO_4)$ (**4**)

py = pyridine, bipy = 2,2′-bipyridine

Table 1 provides the results with manganese clusters (**1**)—(**4**) as catalysts, which we evaluated with C_2, C_3, and cyclo-C_6 hydrocarbons in the presence of t-butyl hydroperoxide (TBHP) using MeCN as the solvent. We observed with

Table 1. Comparison of the C–H bond reactivity of C_2, C_3, and cyclo-C_6 hydrocarbons with $Mn_{3-4}O_{1-2}L_xL_y$ catalysts (**1**)—(**4**) using t-butyl hydroperoxide as the mono-oxygen transfer reagent.[a]

Hydrocarbon	Catalyst	Products (%)[b]	Turnover no.[c]
Ethane	(**1**)	Ethanol (1)	2
	(**2**)	Ethanol (<1)	<1
	(**3**)	Ethanol (1)	2
	(**4**)	Ethanol (<1)	1
Propane	(**1**)	Propan-2-ol (2)[d]	3
	(**2**)	Propan-2-ol (<1)	<1
	(**3**)	Propan-2-ol (5)	9
	(**4**)	Propan-2-ol (3)	5
Cyclohexane	(**1**)	Cyclohexanol (60) Cyclohexanone(36)	121
	(**2**)	Cyclohexanol (50) Cyclohexanone (33)	114
	(**3**)	Cyclohexanol (41) Cyclohexanone (39)	126
	(**4**)	Cyclohexanol (44) Cyclohexanone (42)	127

[a] Reactions of ethane and propane 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 acetonitrile. The ratio of t-butyl hydroperoxide (TBHP) to catalyst was 150 : 1, while the catalyst concentration was 0.0025 M. The cyclohexane reactions were run in Schlenk flasks at room temperature for 1—3 h with a 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. [b] The analysis and quantitation was accomplished *via* capillary column g.c. and g.c.–m.s. 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. [c] Based on the mmol of oxidizing equivalents/mmoles catalyst. [d] Trace amounts of propan-1-ol ($\ll$1%) were also formed (g.c.). Trace amounts of acetone were also found; however, a control experiment verified its formation from the Mn cluster-catalysed decomposition of TBHP. Additionally, small amounts of propan-2-ol can also be oxidized to acetone under the reaction conditions.

catalysts (**1**) and (**2**) that TBHP is consumed after 2 h, while with catalysts (**3**) and (**4**), TBHP is consumed at a much faster rate (0.5 h). We found, not surprisingly, that the order of substrate reactivity is cyclohexane > propane > ethane, while methane (not reported in Table 1) did not provide any methanol.† This order reflects the differences in the C–H bond dissociation energies of cyclohexane (94 kcal mol^{-1}; cal = 4.184 J), propane (96), ethane (98), and methane (104).

It is interesting to note that catalysts (**1**)—(**4**) provided similar turnover numbers with cyclohexane. In contrast, catalysts (**3**) and (**4**), the tetranuclear Mn clusters, are more active with propane than the corresponding trinuclear clusters, (**1**) and (**2**). Also, catalysts (**1**) and (**3**), the neutral complexes, are slightly more active with ethane than their cationic analogues, (**2**) and (**4**). Although we do not completely understand these results yet, it is possible that the lower oxidation states of the Mn atoms in the neutral cluster complexes assists the formation of the putative 'oxo' manganese intermediate, *via* possible internal electron transfer.

Other important factors such as solvent, catalyst lifetime, and mono-oxygen transfer reagent have been found to have a profound effect on the mono-oxygen transfer reaction. For instance, if we substituted CH_2Cl_2 for MeCN as the solvent, we found lower turnover numbers for the three hydrocarbons: *e.g.*, in CH_2Cl_2, the turnover numbers for cyclohexane are *ca.* 20—50 with catalysts (**1**)—(**4**). Also, small amounts of chlorocyclohexane were obtained indicating that a radical process is involved in the reaction. Attempts to inhibit the formation of cyclohexanol and cyclohexanone with a free radical trap, 2,6-di-t-butyl-4-methylphenol (10 equiv.), were not successful. This result strongly implies that free alkoxyl or peroxyl radicals are not involved in these mono-oxygen transfer reactions.‡ In addition, catalyst lifetimes are dramatically prolonged in MeCN compared with CH_2Cl_2. For example, catalyst (**4**) has a lifetime of *ca.* 20 min in CH_2Cl_2 in the presence of cyclohexane and 85 equiv. of TBHP, while in MeCN (**4**) is still active after 750 equiv. of TBHP (*ca.* 600 turnovers) have been added portionwise (150 equiv. every hour) with no apparent sign of catalyst decomposition. However, we noticed that with repeated additions of TBHP the ratio of cyclohexanol/cyclohexanone decreased. Thus, for all the hydrocarbons studied in MeCN, initial turnover numbers of substrate to product can be repeated with continual TBHP addition. We also found that if we substituted the insoluble iodosylbenzene for TBHP, as the mono-oxygen transfer reagent, yields of product and turnover numbers were markedly reduced.

Another important factor for small hydrocarbon activation (C_1—C_3) might be shape selectivity of the catalyst. It appears from the crystal structures of (**1**) and (**4**)[5a,d] that it may be possible that either changes in ligand environment or higher nuclearity Mn clusters (>4) could provide the shape selectivity to trap methane and provide the kinetic advantage for C–H activation in order to overcome the high C–H bond dissociation energy (CH_4 *ca.* 104 kcal mol^{-1}). While the Mn_4O_2 clusters appear slightly more reactive than the Mn_3O clusters, we could not test the available Mn_2O complexes as C–H activation catalysts owing to their relative insolubility. However, we have prepared Fe_2O and Fe_4O_2 substituted complexes and found the latter to be a much more active oxidation catalyst with cyclohexane.[6] The critical point might be that the higher the nuclearity of the cluster, the more active the catalyst in conversion of C–H bonds to C–OH bonds.

We also attempted to ascertain the fate of (**4**) in the presence of TBHP and in the absence of substrate. We found at a TBHP/(**4**) ratio of 20 : 1 (MeCN) that (**4**) was recovered almost quantitatively (94%) and that TBHP was converted predominantly to t-butyl alcohol with evolution of oxygen gas. Catalysts (**1**)—(**3**) were also found to decompose TBHP in a similar manner. We are in the process of trying to identify the putative 'oxo'-Mn intermediate from reaction of TBHP with (**1**)—(**4**) *via* low temperature isolation techniques.[2d]‡

Finally, the mechanism we propose for the C–H activation might involve formation of an intermediate Mn–OOBu^t complex followed by homolytic cleavage to provide an Mn–O•; complex and t-butyl alcohol.[7] This Mn–O• complex could then homolytically remove hydrogen from carbon, followed by rapid OH rebound to the carbon radical to give product (Scheme 1).

† Although methanol was detected in all the reactions studied, control experiments clearly showed that, in the absence of substrate, the catalysts (**1**)—(**4**) decompose very small amounts of TBHP to acetone and methanol.

‡ Other evidence against hydroxyl, alkoxyl, or peroxyl radical involvement in these oxidation reactions, and in favour of an intermediate 'oxo' manganese species, is the fact that the manganese clusters (**1**)—(**4**) catalysed the mono-oxygen transfer from TBHP or iodosylbenzene to cyclohexene to provide cyclohexene epoxide.

$$Mn_4O_2 + TBHP \longrightarrow Mn_2OMnOMnO\overset{H}{O}Bu^t \longrightarrow Mn_2OMnOMn\text{–}O^{\cdot} + Bu^tOH$$

$$Mn_2OMnOMn\text{–}O^{\cdot} + R\text{–}H \longrightarrow [Mn_2OMnOMn\text{–}OH \cdot R] \longrightarrow Mn_4O_2 + R\text{–}OH$$

Scheme 1. Bridging carboxylate and terminal nitrogen ligands are omitted.

We are in the process of evaluating various nuclearity Mn and Fe complexes for C–H activation of small hydrocarbons such as methane.

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References

1 (a) J. T. Groves, T. E. Nemo, and R. S. Myers, *J. Am. Chem. Soc.*, 1979, **101**, 1032; (b) C. K. Chang and F. J. Ebina, *J. Chem. Soc., Chem. Commun.*, 1981, 778; (c) C. L. Hill and B. C. Schardt, *J. Am. Chem. Soc.*, 1980, **102**, 6375; (d) J. T. Groves and T. E. Nemo, *ibid.*, 1983, **105**, 6243; (e) M. Fontacave and D. Mansuy, *Tetrahedron*, 1984, **21**, 4297; (f) K. Suslick, B. Cook, and M. Fox, *J. Chem. Soc., Chem. Commun.*, 1985, 580; (g) J. A. Smegal, B. C. Schardt, and C. L. Hill, *J. Am. Chem. Soc.*, 1983, **105**, 3510; (h) B. DePoorter, M. Ricci, and B. Meunier, *Tetrahedron Lett.*, 1985, **26**, 4459; (i) M. J. Nappa and C. A. Tolman, *Inorg. Chem.*, 1985, **24**, 4711; (j) B. R. Cook, T. J. Reinert, and K. S. Suslick, *J. Am. Chem. Soc.*, 1986, **108**, 7281; (k) J. Smegal and C. L. Hill, *ibid.*, 1983, **105**, 3515.

2 (a) M. Farji and C. L. Hill, *J. Chem. Soc., Chem. Commun.*, 1987, 1487; (b) J. D. Koola and J. K. Kochi, *Inorg. Chem.*, 1987, **26**, 908; (c) K. Srinivasan, P. Michaud, and J. K. Kochi, *J. Am. Chem. Soc.*, 1986, **108**, 2309; (d) L. Saussine, E. Brazil, A. Robine, H. Mimoun, J. Fisher, and R. Weiss, *ibid.*, 1985, **107**, 3534; (e) H. Mimoun and I. Seree De Roch, *Tetrahedron*, 1975, **31**, 777; (f) S. Ito, K. Inoue, and M. Mastumoto, *J. Am. Chem. Soc.*, 1982, **104**, 6450; (g) D. H. R. Barton, M. J. Gastiger, and W. B. Motherwell, *J. Chem. Soc., Chem. Commun.*, 1983, 731.

3 (a) I. J. Higgins, D. J. Best, and R. J. Hammond, *Nature*, 1980, **286**, 561; (b) H. Dalton, *Adv. Appl. Microbiol.*, 1980, **26**, 71; (c) D. L. Leak and H. Dalton, *Biocatalysis*, 1987, **1**, 23.

4 (a) R. C. Prince, G. N. George, J. C. Savas, S. P. Cramer, and R. N. Patel, *Biochim. Biophys. Acta*, 1988, **952**, 220; (b) A. Ericson, B. Hedman, K. O. Hodgson, J. Green, H. Dalton, J. G. Bentsen, R. H. Beer, and S. J. Lippard, *J. Am. Chem. Soc.*, 1988, **110**, 2330.

5 (a) J. B. Vincent, C. Christmas, J. C. Huffman, G. Christou, H.-R. Chang, and D. N. Hendrickson, *J. Chem. Soc., Chem. Commun.*, 1987, 236; (b) C. Christmas, J. B. Vincent, J. C. Huffman, G. Christou, H.-R. Chang, and D. N. Hendrickson, *ibid.*, 1987, 1303; (c) J. S. Bashkin, H.-R. Chang, W. E. Streib, J. C. Huffman, D. N. Hendrickson, and G. Christou, *J. Am. Chem. Soc.*, 1987, **109**, 6502; (d) J. B. Vincent, H.-R. Chang, K. Folting, J. C. Huffman, G. Christou, and D. N. Hendrickson, *ibid.*, 1987, **109**, 5703.

6 J. B. Vincent, J. C. Huffman, G. Christou, Q. Li, M. A. Nanny, D. N. Hendrickson, R. H. Fong, and R. H. Fish, *J. Am. Chem. Soc.*, 1988, **110**, 6898.

7 L.-C. Yuan and T. C. Bruice, *J. Am. Chem. Soc.*, 1985, **107**, 512.