Inorg. Chem. **1988**, *27*, 3740-3745

Contribution No. 3962 from the Central Research & Development Department,
Experimental Station, E. I. du Pont de Nemours & Company, Wilmington, Delaware 19898

Selectivity Control by Axial Ligand Modification in Manganese Porphyrin Catalyzed Oxidations

Mario J. Nappa* and Ronald J. McKinney

Received May 5, 1988

The addition of tin Lewis acids, $Ph_3SnO_2C_8F_{15}$ (**1a**) and $Ph_3SnO_3SC_6F_{13}$ (**1b**), increases the reactivity and reduces the radical character in hydrocarbon oxidation reactions using iodosylbenzene and manganese porphyrins, Mn(TPP)OAc and Mn(TpyP)OAc,[1] by substitution of $^-$OAc with the perfluoro anion to make Mn(porphyrin)$O_2C_8F_{15}$ or Mn(porphyrin)$O_3SC_6F_{13}$. This increase in reactivity and reduction of radical character are explained by using semiempirical molecular orbital calculations, which show the effects of anion exchange on the electronic structure of O=Mn^V(porphyrin)$^+$X$^-$. When $^-$OAc is replaced by a less coordinating axial ligand, the oxomanganese intermediate has less oxy radical character. Our cyclohexane, cyclohexene, norcarane, and *cis*-stilbene oxidation results as well as kinetic isotope effects are consistent with the oxygen atom insertion into C–H and C–C bonds becoming more concerted in nature. In addition to their role in anion substitution, these tin complexes function as radical inhibitors to further reduce the radical character of oxidation reactions using manganese porphyrins.

Introduction

Cytochromes P-450 are a class of heme enzymes that catalyze the monooxygenation of a variety of organic substrates using dioxygen and NADPH.[2] The observation that simple oxygen donors are functional replacements for O_2 and NADPH has led to a plethora of model studies using synthetic metalloporphyrin analogues.[3] Of all the metalloporphyrin systems studied, the most versatile and efficient are manganese porphyrins for the catalytic oxidation of organic substrates using a wide variety of oxygen atom transfer reagents such as iodosylbenzene,[4] peracids,[5] amine oxides,[6] alkyl hydroperoxides,[5a,7] persulfates,[8] hypochlorite,[9] periodate,[10] hydrogen peroxide,[11] oxaziridines,[12] as well as molecular oxygen.[13] Major advantages of manganese porphyrin systems over the more biologically relevant iron model systems are higher yields and long catalyst lifetimes. A major disadvantage, however, is that manganese porphyrin catalyzed oxidation reactions display considerable radical character, leading to radical byproducts and losses in selectivities due to formation of radicaloid intermediates.[14a,b] We have discovered that anion exchange in simple manganese porphyrin systems can lead to a concomitant reduction in radical character and an increase in overall reactivity in oxidation reactions using iodosylbenzene as the oxygen atom donor. In this study, the effects of anion exchange on the electronic structure of the putative oxomanganese porphyrin reactive intermediate are examined and rationalized by using semiempirical molecular orbital calculations, and the effects of these changes on the product distribution in oxidation reactions are discussed.

Experimental Section

Physical Measurements. UV/vis spectra were recorded at 25 °C on a Hewlett-Packard 3450A diode-array spectrometer. Gas chromatography was performed on a Hewlett-Packard 5880 with an FID detector and a Chrompak cross-linked Carbowax capillary column (25 m). Stilbene oxides were analyzed by HPLC on a Dupont Instruments 8800, using a Zorbax ODS column (250 mm × 4.6 mm i.d.) and a linear gradient elution (solvent A 10% CH_3OH/90% H_2O; solvent B 90% CH_3OH/10% H_2O; 0% B to 100% B in 20 min and 10-min hold at B). A UV detector at 254 nm was used to detect phenyl-containing compounds. GCMS was carried out with a Hewlett-Packard 5970B mass selective detector, coupled to a Hewlett-Packard 5880 GC.

Materials. Methylene chloride was distilled from P_2O_5, and cyclohexene and cyclohexane were distilled from a sodium dispersion. Iodosylbenzene was made by either chlorine oxidation[15] or peracetic acid oxidation[16] of iodobenzene followed by base hydrolysis. The product was dried under high vacuum for at least 12 h and stored in a drybox refrigerator (−35 °C). Norcarane,[17] norcaranols,[18] and 1-cyclohexene-3-methanol[19] were synthesized by literature methods. *cis*-Stilbene and *trans*-stilbene oxide were purchased from Aldrich and used as received. *cis*-Stilbene oxide was made as described in the literature.[20] Mn(TPP)Cl, Mn(TPP)OAc, and Mn(TpyP)OAc were purchased from Strem and used as received. $Ph_3SnO_2C_8F_{15}$ and $Ph_3SnO_3SC_6F_{13}$ were made from the reaction of Ph_3SnCN in acetonitrile with $C_8F_{15}O_2H$ and $C_6F_{13}SO_3H$, respectively, and crystallized from hexane. Mn(TPP)$O_2C_8F_{15}$ was made from the reaction of Mn(TPP)Cl and $AgO_2C_8F_{15}$ in toluene at 80 °C and crystallized with heptane.

Oxidation Reactions. In a nitrogen-atmosphere drybox, 5 mL of cyclohexane/CH_2Cl_2 (3/7) was added to a 25-mL screw cap vial containing 0.0125 mmol of manganese porphyrin and a magnetic stir bar. At this point, tin complexes were added while the mixture was stirred. Immediately, while the mixture was stirred at ambient temperature, iodosylbenzene (0.25 mmol) was added all at once and the mixture stirred

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* To whom correspondence should be addressed at the Chemicals & Pigments Department, Jackson Laboratory, E. I. du Pont de Nemours & Co., Deepwater, NJ 08023.

(1) Abbreviations used in this paper: TPP, *meso*-tetraphenylporphyrin dianion; TpyP, *meso*-tetrakis(4-pyridylphenyl)porphyrin dianion; OAc, acetate; $O_2C_8F_{15}$, perfluoro-*n*-octanoate; $O_3SC_6F_{13}$, perfluoro-*n*-hexanesulfonate; Ph, phenyl; $T_{4\text{-MeO}}PP$, *meso*-tetrakis(4-methoxyphenyl)porphyrin dianion; py, pyridine; salen, *N,N'*-ethylenebis(salicylideneaminato).

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Table I. Cyclohexane Oxidation

entry no.	manganese porphyrin	additive	equiv no. of	yield, % cyclohexanol[a]	cyclohexanone[a]	cyclohexyl chloride[a]	cyclohexene oxide[b]
1	Mn(TpyPP)OAc	**1a**		34.3	1.5	14.3	0.9
2	Mn(TpyPP)OAc	**1a**	0.39	42.8	1.3	9.0	2.1
3	Mn(TpyPP)OAc	**1a**	0.94	51.1	1.8	4.9	3.3
4	Mn(TpyPP)OAc	**1a**	1.36	49.3	1.8	3.1	4.0
5	Mn(TpyPP)OAc	**1a**	1.96	44.9	2.5	1.4	4.4
6	Mn(TpyPP)OAc	**1a**	2.97	40.9	3.1	0.5	4.6
7	Mn(TpyPP)OAc	**1a**	4.46	36.3	3.4	0.3	4.7
8	Mn(TpyPP)OAc	**1b**	1.09	38.1	10.8	1.7	3.9
9	Mn(TpyPP)OAc	**1b**	2.85	49.2	7.8	0.2	2.7
10	Mn(TpyPP)OAc	**2a**	0.58	40.6	1.2	10.6	2.2
11	Mn(TpyPP)OAc	**2a**	1.20	42.7	1.9	5.6	4.9
12	Mn(TpyPP)OAc	**2a**	1.93	41.2	1.5	4.8	4.8
13	Mn(TpyPP)OAc	**2a**	3.47	35.6	1.9	4.5	1.3
14	Mn(TpyPP)OAc	**2a**	4.96	36.4	3.0	4.7	3.0
15	Mn(TPP)OAc	**1a**		22.4	2.8	13.3	0.6
11	Mn(TPP)OAc	**1a**	0.49	28.5	2.3	11.9	0.7
17	Mn(TPP)OAc	**1a**	0.86	32.2	2.6	10.5	1.1
18	Mn(TPP)OAc	**1a**	1.35	29.9	2.6	6.7	1.4
19	Mn(TPP)OAc	**1a**	1.85	28.0	3.0	4.5	2.3
20	Mn(TPP)OAc	**1a**	3.00	26.2	2.6	1.8	2.1
21	Mn(TPP)OAc	**1a**	4.84	18.6	1.9	0.7	1.6
22	$Mn(TPP)O_2C_8F_{15}$	**1a**		31.8	1.9	8.4	0.9
23	$Mn(TPP)O_2C_8F_{15}$	**1a**	1.64	28.6	1.5	2.9	2.0
24	$Mn(TPP)O_2C_8F_{15}$	**1a**	2.81	22.2	2.6	1.4	1.6

[a] Yields are based on iodosylbenzene and are the average of at least two runs; all yields are ±0.5%. [b] We have observed that under the reaction conditions an excess of **2a** catalyzes epoxide ring opening.

vigorously for 2 h. The vial was then removed from the drybox, a 10% solution (1 mL) of sodium bisulfite added to quench unused iodosylbenzene or formed iodoxybenzene, and the mixture shaken vigorously. Sodium bisulfite solution was not used in olefin oxidations. Chlorobenzene or *m*-chlorofluorobenzene (5 μL) was added as an internal standard, the mixture was shaken vigorously and allowed to separate for 15 min, and the organic products were analyzed by GPLC. All yields reported are based on iodosylbenzene charged. All reactions were run in at least duplicate and did not always use the same batch of iodosylbenzene. In cyclohexane oxidations, a 5% yield of cyclohexanol corresponds to one catalyst turnover and 0.05% cyclohexane conversion. In cyclohexene oxidation, 100 μL of cyclohexene (0.99 mmol) and 5 mL of CH_2Cl_2 were used. In *cis*-stilbene oxidation, 180 mg (1.0 mmol) of *cis*-stilbene and 5 mL of CH_2Cl_2 were used. Control reactions without manganese porphyrins showed no oxidation products.

Computational Details. Molecular orbital calculations were carried out with the use of a semiempirical theory derived by Anderson.[21] The theory is related to extended Hückel theory (EHT)[22] but contains a correction for two-body repulsions. EHT calculations have been used successfully to describe oxoiron porphyrin systems.[23] The parameter set and optimization routines have been described previously.[24]

Results

Hoping to see effects due to Lewis acid coordination to pyridyl groups, we added triphenyltin perfluoro-*n*-octanoate [$Ph_3SnO_2C_8F_{15}$ (**1a**)] to Mn(TpyP)OAc-catalyzed cyclohexane oxidations using iodosylbenzene. The results are shown in Figure 1 and Table I. With the addition of **1a**, the cyclohexanol/cyclohexyl chloride ratio increases from 1.6 to ~120 (at 4.5 equiv of **1a**/equiv of Mn). After the addition of 1 equiv of **1a**, the yield of cyclohexyl chloride falls below that of cyclohexene oxide. Similar results are obtained with Mn(TPP)OAc (see Table I), indicating that pyridyl groups on the porphyrin are not required for this effect. The addition of triphenyltin perfluoro-*n*-hexanesulfonate [$Ph_3SnO_3SC_6F_{13}$ (**1b**)] to reactions using Mn(TpyP)OAc also result in changes in the product ratios in cyclohexane oxidation. There is considerable overoxidation to cyclohexanone when **1b** is used (Table I), suggesting that $^-O_3SC_6F_{13}$ generates a stronger oxidant than $^-O_2C_8F_{15}$. A comparison of entries 3 and 8 shows a marked difference in product distribution. With **1b** added (entry 8), the alcohol/ketone ratio is 3.5 compared to 28.3 when **1a** is added (entry 3). There is also more cyclohexene oxide and considerably less cyclohexyl chloride (cyclohexanol/cyclohexyl chloride = 22.4 when **1b** is added versus 10.4 when **1a** is added). **1b** also appears to result in better radical inhibition than **1a**, as indicated by a lower yield of cyclohexyl chloride (compare entries 6 and 9).

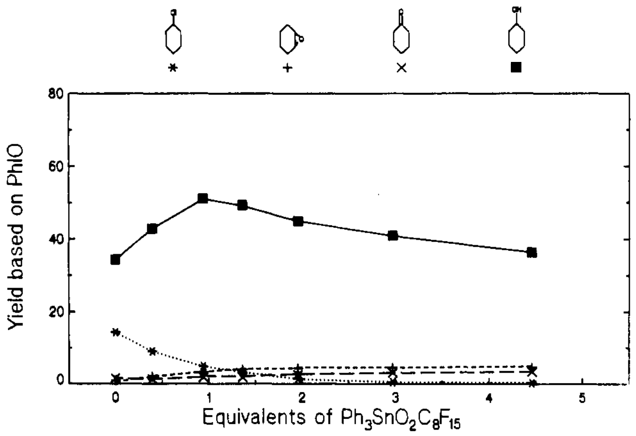

Figure 1. Yields of cyclohexanol (■), cyclohexyl chloride (*), cyclohexene oxide (+), and cyclohexanone (×) as a function of **1a** added to cyclohexane oxidations using Mn(TpyP)OAc. $[PhIO]_0 = 0.05$ M, and $[Mn(TpyP)OAc]_0 = 2.5 \times 10^{-3}$ M in CH_2Cl_2. Yields are based on PhIO.

The UV/vis spectral changes for the addition of **1a** to Mn(TPP)OAc are shown in Figure 2 and are consistent with a stoichiometric substitution of ^-OAc for $^-O_2C_8F_{15}$. The hypsochromic shifts of the α and β bands upon the addition of **1a** to Mn(TPP)OAc are consistent with observations made by Boucher et al. in a study of the axial interactions in manganese porphyrins.[25]

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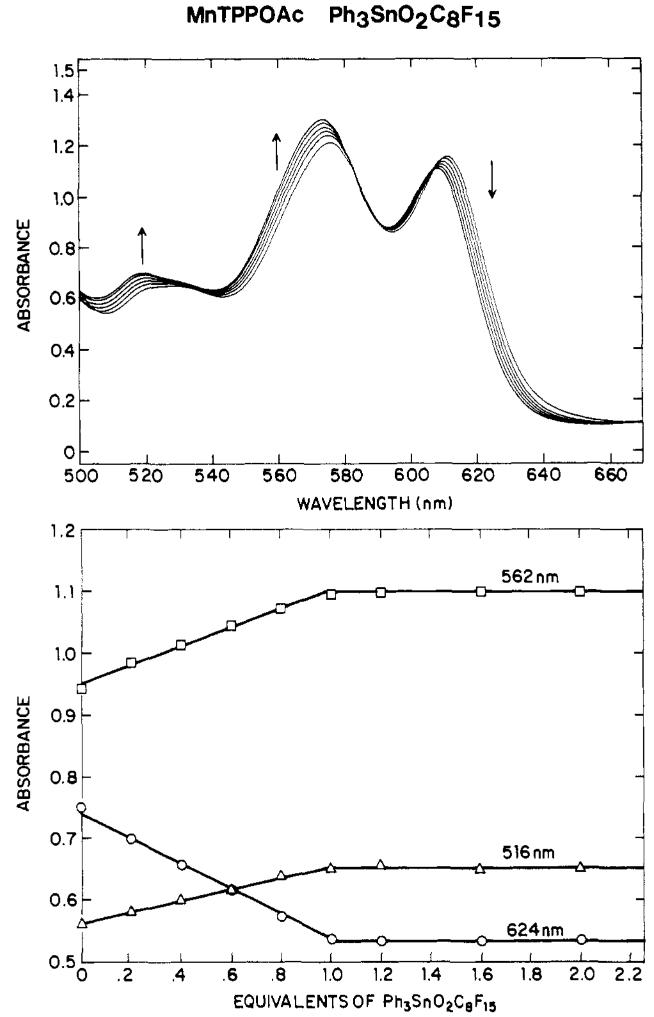


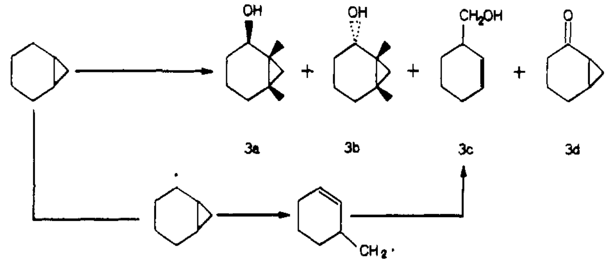
Figure 2. Visible spectral changes of Mn(TPP)OAc upon the addition of **1a**. $[Mn(TPP)OAc]_0 = 1.25 \times 10^{-4}$ M.

Table II. Deuterium Isotope Effects for Cyclohexane Oxidation

catalyst system	k_H/k_D
Mn(TPpyPP)OAc	11.8
Mn(TPpyPP)OAc + 1 equiv of $Ph_3SnO_2C_8F_{15}$ (**1a**)	5.7
Mn(TPpyPP)OAc + 2 equiv of $Ph_3SnO_2C_8F_{15}$ (**1a**)	5.7
Mn(TPpyPP)OAc + 1 equiv of $Ph_3SnO_3SC_6F_{13}$ (**1b**)	3.7
Fe(TTP)Cl	12.9[a]

[a] TTP = *meso*-tetrakis(2-methylphenyl)porphyrin dianion; ref 32.

Table III. Norcarane Oxidation



Relative Yields[a]

	3a	3b	3c	3d
MnTpyPPOAc	1.00	.27	.14	.16
MnTpyPPOAc + 1 eq. $Ph_3SnO_2C_8F_{15}$	1.77	.42	.01	.18

[a] Yields are based on iodosobenzene; for absolute yields multiply the relative yields by a factor of 11.3.

In general, removing electron-donating axial ligands is known to cause hypsochromic shifts of metalloporphyrin visible absorption bands.[26] Whether the tin scavenges free $^-$OAc or actively removes it from the manganese is unclear; the preference for 5-coordination by trialkyltin species would not rule out the latter.[27] Nevertheless, there appears to be a thermodynamic preference for the more basic $^-$OAc to coordinate to tin. Addition of **1a** to Mn(TPP)Cl results in incomplete conversion to $Mn(TPP)O_2C_8F_{15}$, determined by vis/UV spectroscopy, indicating that the equilibrium constant for this reaction is not large, perhaps due to a stronger Mn–X bond in Mn(TPP)Cl. Therefore, we subsequently used manganese porphyrins with acetate as the axial ligand.

Addition of the corresponding Brønsted acid, $C_8F_{15}O_2H$ (**2a**), to Mn(TpyP)OAc results in a similar effect on the product distribution, as shown in Table I. The amount of cyclohexyl chloride formed reaches a minimum (~4.8%) when 1–2 equiv of **2a** is added (entry 12) and remains constant; this is equal to the yield of cyclohexyl chloride obtained when 1 equiv of **1a** is added (Table I, entry 3). This suggests that the addition of more than 1 equiv of **1a** reduces the amount of cyclohexyl chloride by some other mechanism, probably as a radical inhibitor.[28] Although Brønsted and Lewis acids (up to 1 equiv) appear to have the same effect on the yields of cyclohexyl chloride, yields of cyclohexanol are consistently lower with the Brønsted acid.

We confirmed that anion substitution is occurring with the tin Lewis acids by preparing authentic $Mn(TPP)O_2C_8F_{15}$ from Mn(TPP)Cl and $AgO_2C_8F_{15}$. The results for cyclohexane oxidation are the same as with the $Mn(TPP)OAc/Ph_3SnO_2C_8F_{15}$ system (see Table I, entry 22 versus entries 17 and 18). The residual 1 equiv of Ph_3SnOAc, formed from the reaction between Mn(TPP)OAc and $Ph_3SnO_2C_8F_{15}$, does not appear to have any effect on the product distribution. However, the addition of **1a** to reactions using $Mn(TPP)O_2C_8F_{15}$ does continue to reduce the amount of cyclohexyl chloride formed, having the same effect of excess **1a** added to reactions using Mn(TPP)OAc (Table I, entries 22 and 23 versus 17 and 19).

To probe the nature of the change in product distribution with anion substitution, we compared the deuterium isotope effect for cyclohexane oxidation using Mn(TpyP)OAc with tin Lewis acid treated reactions (Table II).[29] There is a reduction in k_H/k_D when 1 equiv of **1a** is added (anion substitution is complete), and the second equivalent of added **1a** has no effect on k_H/k_D, indicating that, although the product distribution changes when more than 1 equiv of **1a** is added (see Table II), it is not due to altering the mechanism. When 1 equiv of **1b** is used, thereby replacing the acetate by an even weaker anion, k_H/k_D is 3.7, an indication that the mechanism changes as the Mn–X bond in Mn(TPP)X weakens.

The suppression of the radical character in the cyclohexane oxidation reaction when using manganese porphyrins with weakly coordinating axial ligands prompted us to use different substrates to determine the origin of these changes in the product distribution. Oxidation of norcarane was used by Groves et al. in manganese porphyrin catalyzed oxidations to probe the radical character of the oxidation reaction;[14b] our results for reactions using this substrate are shown in Table III. There is an overall increase in the yield of alcohols produced, as well as an increase in the norcaranols/1-cyclohexene-3-methanol ratio from 9.1 to 220.[14c] The suppression of the radical rearrangement pathway is consistent with our cyclohexane results.

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(29) The method used was described previously. See: Hamilton, G. A.; Ribner, B. S.; Hellman, T. M. *Adv. Chem. Ser.* **1968**, *No. 77*, 15.

Table IV. Cyclohexene Oxidation

entry no.	manganese porphyrin	additive	no. of equiv	yield,[a] cyclohexene oxide	yield,[a] 1-cyclohexene-3-ol	yield,[a] 1-cyclohexen-3-one	epoxide/allylic oxidn
1	Mn(TPP)OAc			44.0	20.9	2.4	1.9
2	Mn(TPP)OAc	**1a**	0.94	58.1	23.2	2.8	2.2
3	Mn(TPP)OAc	**1a**	2.72	66.4	18.0	2.1	3.3
4	Mn(TPP)OAc	**1b**	1.02	77.6	5.8	2.2	9.7
5	Mn(TPP)OAc	**1b**	3.03	48.9	7.0	0.4	6.6
6	Mn(TPP)O$_2$C$_8$F$_{15}$			57.6	23.0	3.2	2.2
7	Mn(TPP)O$_2$C$_8$F$_{15}$	**1a**	2.14	64.9	16.7	2.0	3.5

[a] Yields are based on iodosylbenzene and are the average of at least two runs; all yields are ±0.5%.

Table V. *cis*-Stilbene Oxidation Using Mn(TPP)OAc

entry no.	additive	no. of equiv	yield,[a] % *cis*-stilbene oxide	yield,[a] % *trans*-stilbene oxide	yield,[a] % deoxybenzoin
1			33	66	3
2	**1a**	0.94	45	45	10

[a] Yields are based on iodosylbenzene and are the average of at least two runs; all yields are ±3%.

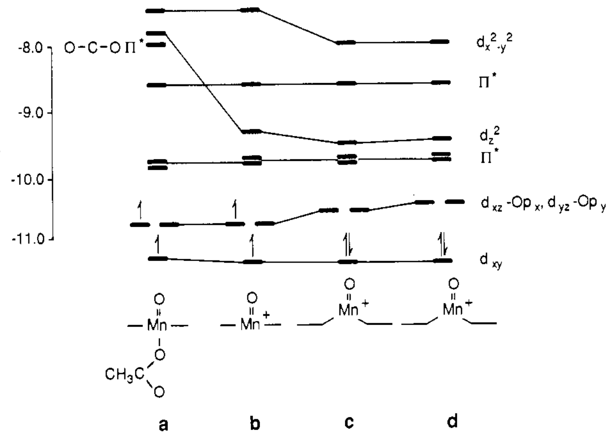
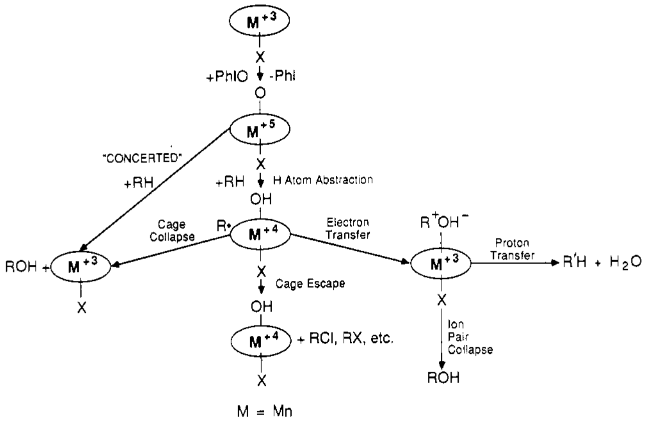


Figure 3. Correlation diagram mapping d-orbital energies for four geometries of a proposed monomeric oxomanganese intermediate: (a) Mn–O(oxo) = 1.59 Å and Mn–O($^-$OAc) = 2.201 Å, with Mn in the porphyrin plane; (b) Mn–O(oxo) = 1.59 Å; (c) Mn–O(oxo) = 1.59 Å, with Mn 0.3 Å out of the plane; (d) Mn–O(oxo) = 1.55 Å, with Mn 0.3 Å out of the plane.

Scheme I



The effect of anion exchange on cyclohexene oxidation is shown in Table IV. With the addition of approximately 1 equiv of **1a** to oxidations using Mn(TPP)OAc, the epoxide/allylic oxidation ratio increases slightly. This ratio is the same as when Mn(TPP)O$_2$C$_8$F$_{15}$ is used. Additional equivalents of **1a** (entry 3) result in an increase in the ratio of epoxide formed. A comparison of entries 2 and 4 show that the addition of **1b** generates a more active and chemiselective catalyst.

We also used *cis*-stilbene as a substrate to measure the anion effects on the stereospecificity of oxidation to stilbene oxides; the results are shown in Table V. The oxidation reaction becomes more stereospecific (*cis*-stilbene oxide/*trans*-stilbene oxide increases from 0.5 to 1.1) as acetate is replaced by the more weakly coordinating $^-O_2C_8F_{15}$. There is an increase in the amount of deoxybenzoin formed, indicating that Ph$_3$SnOAc catalyzes epoxide rearrangement. All of our results demonstrate that decreasing the donor ability of the manganese porphyrin axial ligand reduces the radical character of the oxidation products, and this is consistent with a change in the electronic structure of the oxomanganese intermediate.

Theoretical Results. An extreme case for the decreasing donor strength indicated by the perfluoro anions is the removal of the axial ligand altogether. Four hypothetical geometries for the high-valent oxomanganese porphyrin were considered by using semiempirical molecular orbital calculations: (a) oxomanganese porphyrin acetate, Mn-O(oxo) = 1.59 Å, Mn–O(acetate) = 2.201 Å,[30a] Mn in the plane of the four nitrogen atoms; (b) oxomanganese porphyrin, same as (a) with the acetate ligand removed; (c) same as (b) with the manganese atom 0.3 Å out of the plane of the four nitrogen atoms toward the oxo ligand retaining a Mn–O(oxo) bond distance of 1.59 Å; (d) same as (c) with the Mn–O(oxo) bond distance shortened to 1.55 Å. The atom coordinates for the porphine nucleus were obtained from the literature.[30b] Figure 3 is a correlation diagram mapping the d-orbital energies calculated for these four geometries. High-valent oxomanganese porphyrin reactive intermediates are proposed to be formally Mn^V, with a d^2 electron configuration. For a spin-paired configuration this would make orbital d_{xy} the HOMO and Mn$_{yx}$–O p$_y$ the LUMO. Because the HOMO–LUMO gap is relatively small (0.59 eV) for geometry a, we may expect a considerable contribution from spin-unpaired configurations, thereby giving the oxomanganese intermediate oxy radical character, consistent with experimental observations. As the acetate ligand is removed, there is no significant change in the HOMO–LUMO gap (0.57 eV). However, removal of the axial ligand leaves the molecule in an unhappy geometrical state, and it relaxes by moving the oxomanganese moiety 0.3 Å out of the plane of the porphyrin, geometry c, thereby lowering the energy 0.25 eV from that of geometry b and increasing the HOMO–LUMO gap (0.79 eV). The oxomanganese intermediate can relax further by shortening the Mn–O(oxo) bond distance, and a shortening of 0.04 Å (geometry d) further increases the HOMO–LUMO gap (0.89 eV) while lowering the energy 0.34 eV from that of geometry c. The substantial increase in the HOMO–LUMO gap in going from geometry a to geometry d (0.59 to 0.89 eV) would be expected to reduce the contribution from spin-unpaired configurations and thereby significantly reduce the oxy radical character of the oxomanganese intermediate.

It should be noted that whereas the complete removal of the acetate ligand may reflect the situation for the perfluorosulfonate ligand (from **1b**), the deuterium isotope results clearly show that the perfluoro carboxylate ligand (from **1a**) does interact with the

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manganese and is therefore a case intermediate between geometries a and d.

Discussion

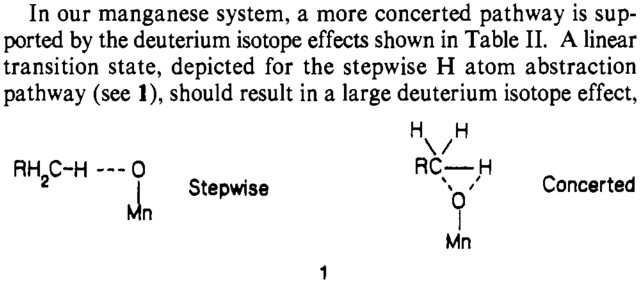
The effects of changing the axial ligands on the product distribution in cyclohexane oxidation are best discussed with respect to the mechanism proposed in Scheme I, which is similar to that proposed by Hill et al.[31] Our mechanism invokes both a concerted pathway to explain the reduction in radical character of the oxidation reaction and a proton-transfer pathway to explain the formation of cyclohexene oxide. The initial step in this mechanism is the oxygen atom transfer from iodosylbenzene to Mn$^{\mathrm{III}}$(porphyrin)X to generate a high-valent oxomanganese porphyrin complex, Mn$^{\mathrm{V}}$=O(porphyrin)X. A formulation having a Mn$^{\mathrm{IV}}$ ground electronic state and an oxygen-centered radical Mn$^{\mathrm{IV}}$—O$^{\bullet}$ is another canonical form of Mn$^{\mathrm{V}}$=O. It has been proposed for both manganese[31] and iron porphyrins[32] that this high-valent oxometal intermediate reacts with a hydrocarbon substrate to generate Mn$^{\mathrm{IV}}$–OH(porphyrin)X and a carbon-centered organic free radical. The high degree of free-radical character in manganese porphyrin catalyzed oxidations compared to that for iron reactions has been attributed to the relative stability of Mn$^{\mathrm{IV}}$–OH(porphyrin)X compared to that of Fe$^{\mathrm{IV}}$–OH(porphyrin)X. As a result, cage escape and electron transfer effectively compete with cage collapse. By removing the trans axial ligand, we would expect to strengthen the Mn$^{\mathrm{IV}}$–OH bond, thereby resulting in more free-radical character in the oxidation reactions; however, we observe the opposite: as X is removed or its coordinating ability reduced, the radical character of the oxidation reaction is reduced; we form less cyclohexyl chloride as we titrate off the acetate (Table I). This would indicate either that more of the (R$^{\bullet}$)Mn$^{\mathrm{IV}}$–OH(porphyrin)X intermediate is partitioning through the electron-transfer pathway or that we have an earlier transition state for this intermediate or, in essence, a more concerted oxygen atom insertion into the C–H bond, which is consistent with our calculations.

Using cyclohexane as a substrate, we are unable to determine the extent of partitioning through the electron-transfer pathway; however, we do observe a considerable amount of cyclohexene oxide as a product. This is consistent with Mn$^{\mathrm{IV}}$–OH(porphyrin)$^{+}$ being a better oxidizing agent, having removed the coordinating axial ligand and reducing the electron density on manganese, making it more electrophilic. Thus, **1b** can generate more R$^{+}\cdot$ $\cdot$Mn$^{\mathrm{III}}$–OH(porphyrin) by electron transfer than **1a**; this in turn can undergo proton transfer to generate cyclohexene (R′H in the scheme), which readily reacts to form cyclohexene oxide. It is conceivable that a large fraction of Mn$^{\mathrm{IV}}$–OH(porphyrin)$^{+}$ is partitioning through the electron-transfer pathway and that R$^{+}\cdot\cdot$Mn$^{\mathrm{III}}$–OH(porphyrin) decomposes predominantly by ion-pair collapse. The fact that we still observe some cyclohexyl chloride when X is removed, however, indicates that cage escape and, therefore, cage collapse are operating to some extent.

The formation of cyclohexene oxide is consistent with our observations in iron porphyrin catalyzed oxidations, in which case more cyclohexene oxide was formed with fluorine atom substituted tetraphenylporphyrins.[33] It is unlikely that cyclohexene oxide is derived from a radical pathway (the epoxidation of cyclohexene made from the disproportionation of cyclohexyl radicals) because the addition of excess tin Lewis acid, which acts as a radical inhibitor, results in an increase in the amount of cyclohexene oxide produced. This is the case for the addition of excess **1a** or **1b** to Mn(TPP)OAc or the addition of **1a** to Mn(TPP)O$_2$C$_8$F$_{15}$.

Our norcarane results are also consistent with a shift to a more concerted oxygen atom insertion. With X removed, we observe less ring opening. On the basis of the argument used in cyclohexane oxidation, removal of X should strengthen the Mn$^{\mathrm{IV}}$–OH bond in Mn$^{\mathrm{IV}}$–OH(porphyrin)$^{+}$, and we should see more rearrangement products, but again we see less evidence for long-lived radical intermediates. A possible explanation for this reduction in free-radical character is that, by removing the axial ligand, we alter the electronic structure of the Mn$^{\mathrm{V}}$=O intermediate, thus favoring a more concerted oxygen atom insertion into C—H bonds. It should be noted, however, that in iron porphyrin systems, which are known to involve H atom abstraction, ring opening of norcarane was not observed.[34] H atom abstraction may be operating, but compared to Mn$^{\mathrm{IV}}$–OH(porphyrin)X, Fe$^{\mathrm{IV}}$–OH(porphyrin)X is very reactive and norcaranyl radicals are short-lived.

In our manganese system, a more concerted pathway is supported by the deuterium isotope effects shown in Table II. A linear transition state, depicted for the stepwise H atom abstraction pathway (see **1**), should result in a large deuterium isotope effect, since there is considerable C–H bond breaking in the transition state. On the other hand, a more concerted oxygen atom insertion into C–H bonds should have a small or possibly an inverse isotope effect. A change from 12 to 1 in $k_{\mathrm{H}}/k_{\mathrm{D}}$ would require only a difference in ΔG of 1.5 kcal/mol. A continuum of transition-state geometries differing little in energy may be visualized between the extremes pictured in **1**, and the reduction of $k_{\mathrm{H}}/k_{\mathrm{D}}$ to 3.7, by removing the axial ligand, suggests that we are moving along this continuum where the transition state now looks more triangular than linear, thus explaining our cyclohexane, norcarane, and deuterium isotope results. *If the decrease in radical character we observe is merely due to the partitioning of the Mn$^{\mathrm{IV}}$–OH(porphyrin)$^{+}$ intermediate, the deuterium isotope effect should not change.* A $k_{\mathrm{H}}/k_{\mathrm{D}}$ value of 11.8 for Mn(TPP)OAc is consistent with the stepwise process and is in agreement with the value measured by Groves et al. for an iron porphyrin system (Table II).[32]



1

The reactivity of Mn$^{\mathrm{V}}$=O(porphyrin)$^{+}$ having the axial ligand removed closely resembles the reactivity of ozone.[29] As with Mn$^{\mathrm{V}}$=O(porphyrin)$^{+}$, oxygenation of norcarane by ozone adsorbed onto silica gel has been shown to give unrearranged alcohols.[35] $k_{\mathrm{H}}/k_{\mathrm{D}}$ for the ozonation of cyclohexane was found to be 4.5, and a mechanism was proposed, involving an insertion reaction, whose transition state has considerable radical character. It was suggested that the ozonation did not proceed through free-radical intermediates and that the alcohol was formed in a direct reaction of ozone with the hydrocarbon.[27]

As shown in Table I, there is also an overall increase in the yield of products derived from cyclohexane as the coordinating ability of the axial ligand is reduced. The active intermediate in the catalytic cycle for the enzyme cytochrome P-450 is proposed to be RS^{-}—Fe$^{\mathrm{IV}}$=O(porphyrin$^{\bullet+}$). The actual electron configuration could be RS$^{\bullet}$—Fe$^{\mathrm{IV}}$=O(porphyrin), with the thiolate axial ligand having transferred an electron to the oxidized porphyrin ring. If one thinks of the active intermediate in cytochrome P-450 as RS$^{\bullet}$—Fe$^{\mathrm{IV}}$=O(porphyrin) and *not* RS^{-}—Fe$^{\mathrm{IV}}$=O(porphyrin$^{\bullet+}$), then it differs from closely related model compounds studied by Balch et al. (B—Fe$^{\mathrm{IV}}$=O(porphyrin), B = pyridine or *N*-methylimidazole) only in the axial ligands;[36] in the cytochrome P-450 case, the thiolate has been oxidized to thiyl and would be a poor donor ligand, whereas in the Balch model compounds the axial ligand is a good nitrogen donor ligand. The Balch model complexes are not reactive enough to oxidize olefins, but *completely* removing the axial ligand should activate the oxoiron group

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toward less reactive substrates.

In Figure 3, we show four geometries used in the molecular orbital calculations. Recently, Kochi et al.[40] have reported that, upon coordination of pyridine *N*-oxide to $O{=}Cr^V$(salen), the Cr—O bond increases by 0.01 Å and the chromium atom is pulled back by 0.27 Å, being only 0.259 Å above the ligand plane in the pyridine *N*-oxide adduct; our changes in geometries used for the calculations are consistent with these changes. We propose that, upon removal of the axial ligand, the manganese moves out of the plane to form square-pyramidal $O{=}Mn^V(porphyrin)^+$. In the reported crystal structure for diamagnetic $N{\equiv}Mn(T_{4\text{-MeO}}PP)$, which is isoelectronic with $O{=}Mn^V(porphyrin)^+$, the manganese is out of the plane by 0.39 Å.[30b] Our calculations show that one of the most important factors governing the HOMO–LUMO energy gap is the extent that the manganese is out of the porphyrin plane; thus, it is not surprising that $N{\equiv}Mn(T_{4\text{-MeO}}PP)$ is diamagnetic. Similar observations have been observed by Hoffmann in an extended Hückel study of oxoiron porphyrin complexes.[23a] As they removed a σ-donor axial ligand trans to the oxo ligand, the dz^2 orbital stabilized and the Fe d_{yz}–O p_z and Fe d_{xz}–O p_x destabilized. This was confirmed by a calculation on $O{=}Fe(porphyrin)^+$, where the iron moved out of the plane by 0.5 Å. Ab initio calculations by Strich and Veillard on O=Fe(porphyrin) show that the most stable geometry places the iron out of the plane by 0.25 Å (versus 0.4 Å and in the plane).[37] In this case, the Fe–O(oxo) bond distance was estimated to be 1.7 Å, which may be a little long in light of EXAFS studies on model compounds.[38] We also show that, by shortening the Mn–O(oxo) bond distance, we stabilize the complex and further destabilize Mn d_{yz}–O p_z and Mn d_{xz}–O p_x.

The active intermediate in iron porphyrin catalyzed oxidations, presumably $Fe^{IV}{=}O(porphyrin^{\bullet +})X$, was shown to be electrophilic in reactions with olefins.[39] Hoffmann's calculations for iron showed that as the axial ligand is removed, the net negative charge due to unpaired spin on the oxo oxygen atom is reduced,[23a] consistent with increased reactivity we see under these conditions using manganese porphyrins. That the oxomanganese porphyrin intermediate is more diamagnetic when the donor ability of X is reduced is also in agreement with the reduced radical character we observe in oxidation reactions.

In stilbene epoxidation with manganese porphyrins systems, the stereospecificity is often used as a measure of the radical character of the epoxidation reaction.[3,7a,9b,12] We have observed that as donor ability of the axial ligand is reduced, the epoxidation becomes more stereospecific, indicating that the oxomanganese intermediate has less oxy radical character.

Conclusions

Varying the axial ligands of manganese porphyrin catalysts in hydrocarbon oxidation reactions results in marked changes on product distributions. Reducing the donor ability of the axial ligand on manganese reduces the oxy radical character of the oxomanganese intermediate, which results in a shift from stepwise to more concerted processes for oxygen atom transfer. Reducing the donor ability of the axial ligand also increases the oxidizing power of the catalyst, and both of these factors are important for designing more selective and active hydrocarbon oxidation catalysts.

Acknowledgment. We thank V. C. Cannelongo for expert technical assistance and Dr. D. L. Thorn for many stimulating discussions. We also thank Dr. A. Vatvars for HPLC analyses.

Registry No. **1a**, 116211-34-8; **1b**, 116211-35-9; Mn(TPP)OAc, 58356-65-3; Mn(TpyP)OAc, 116211-36-0; D_2, 7782-39-0; cyclohexane, 110-82-7; cyclohexene, 110-83-8; norcarane, 286-08-8; *cis*-stilbene, 645-49-8; iodosylbenzene, 536-80-1.

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