Pergamon

Tetrahedron 54 (1998) 3367–3378

TETRAHEDRON

Evidence for a Higher Oxidation State of Manganese in the Reaction of Dinuclear Manganese Complexes with Oxidants. Comparison with Iron Based Gif Chemistry.

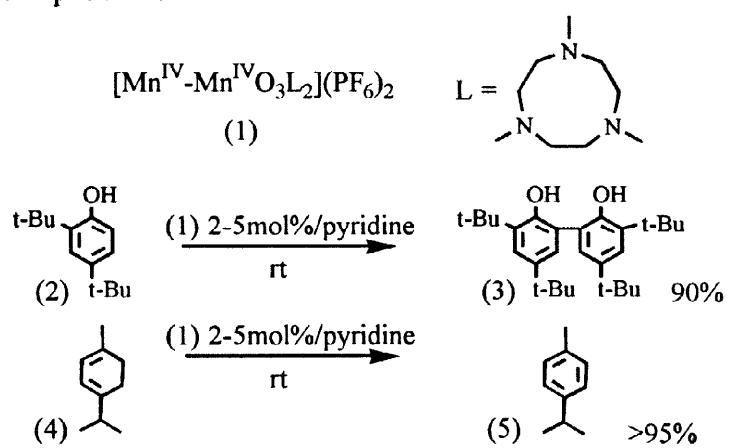
Derek H.R. Barton*, Seung-Yong Choi, Bin Hu and Jason A. Smith*

Department of Chemistry, Texas A&M University, College Station, TX, 77843-3255, USA.

Received 3 November 1997; revised 14 January 1998; accepted 15 January 1998

Abstract: Binuclear manganese complexes mimic the catalase enzyme by converting hydrogen peroxide rapidly and efficiently to oxygen and water. The complex (1) may be activated by either periodic acid or Oxone® and can oxidize selected organic substrates. Potassium manganate gave similar oxidation products suggesting that the manganese is transformed to a higher oxidation state. Kinetic studies with the Mn^{IV}-Mn^{IV} complex show an induction period indicating that it is not the active catalyst. Further studies suggested that the actual catalytic species is a Mn^{III}-Mn^{IV} complex. These complexes show similar properties to the activation of $FeCl_3$ with hydrogen peroxide. This is particularly evident by the formation of a new and unusual peroxide from ergosterol acetate.

Binuclear manganese complexes have received increasing interest over recent years due to the role that they play in biological redox systems.[1] As a result, there has been a considerable effort to synthesize and characterize model complexes, although the chemistry of these complexes was not studied until recently. Binuclear manganese complexes have recently been reported to catalyze many oxidation reactions including bleaching[2], epoxidation[2] and the oxidation of hydrocarbons[3] and alcohols.[4] Hage *et al.* have studied the epoxidation of water-soluble alkenes with complex **1** and hydrogen peroxide at pH~10 in an attempt to understand the mechanism of the bleaching process.[2] A large excess of hydrogen peroxide was required as oxygen was also generated. We proposed that complex **1** could be activated by oxidants other than hydrogen peroxide that would not produce oxygen. This could oxidize organic substrates more efficiently. We now report the results of this work and the comparison with $FeCl_3$/hydrogen peroxide chemistry. We also discuss the mechanistic implications.



Scheme 1

0040-4020/98/$19.00
PII: S0040-4020(98)00096-9

Periodic acid was chosen as a suitable co-oxidant as no oxygen formation was observed on addition to a solution of **1** in either water (pH=10) or pyridine. The oxidation of 2,4-di-*t*-butylphenol (**2**) in pyridine with **1** (~2-5mol%) and periodic acid gave the biphenyl compound **3** in 90% yield. When α-terpinene (**4**) was reacted under the same conditions only *p*-cymene (**5**) was formed in > 95% yield. Both reactions were complete in 60min. The reaction of **2** with periodic acid in the absence of **1** showed a very slow formation of 4,6-di-*t*-butyl-*o*-quinone and for α-terpinene only 40% of *p*-cymene was formed after 4h. These substrates did not react with equimolar quantities of complex **1**. Clearly it appears that we are forming a new species which is responsible for the oxidation. This is evident from the fact that with the phenol **2**, we obtain two different products depending upon whether **1** is present or not. The use of other solvents gave a mixture of products as it appears that periodic acid is not as reactive in pyridine as it is in other solvents (i.e. acetonitrile). We then investigated the oxidation of other substrates to determine the potential of this oxidizing system. The results are listed in Table 1.

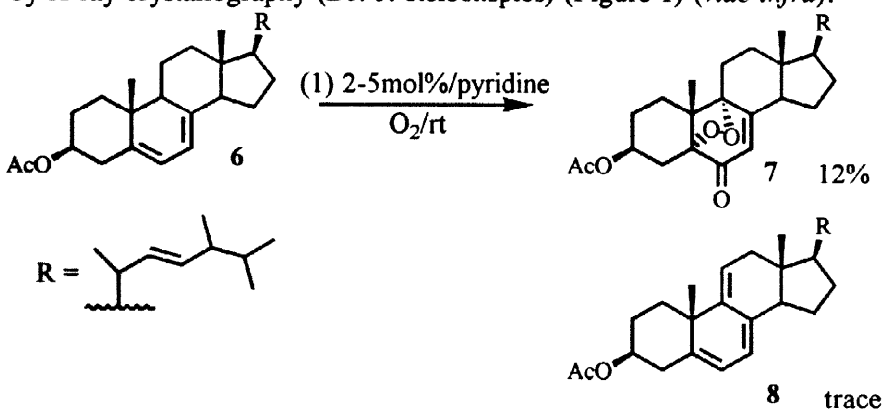
Table 1: Catalytic oxidation of organic substrates with **1** and H_5IO_6.[a]

Entry	Substrate	Product[b]	Yield	Time (min)
1	2,4-di-*t*-butylphenol	2,2'-dihydroxy-3,3',5,5'-tetra-*t*-butylbiphenyl	90%[c]	120
2	α-terpinene	*p*-cymene	>95%[d]	60
3	γ-terpinene	*p*-cymene	90%[d]	180
4	di-*n*-butylsulfide	di-*n*-butylsulfone di-*n*-butylsulfoxide	53%[d] 8%	60
5	di-*n*-butylsulfide	di-*n*-butylsulfone	>95%[c,e]	60
6	diphenylsulfide	diphenylsulfone	trace[d]	over night
7	diphenylsulfoxide	diphenylsulfone	88%[c]	8h
8	2,6-di-*t*-butylphenol	3,3',5,5'-tetra-*t*-butyldiphenoquinone	80%[c]	over night
9	styrene	no reaction	n/a	over night
10	cyclohexane	no reaction	n/a	over night
11	Ergosterol acetate	peroxide (**7**)	12%[c]	60

a) Reactions were carried out with **1** (2-5mol%) in pyridine 30ml. b) All products were identified by comparison with authentic samples. c) Isolated yield. d) Yield determined by GC. e) Two equivalents of periodic acid.

Alkyl sulfides were found to be readily oxidized. With only one equivalent of oxidant the major product was the sulfone, indicating that the sulfoxide was more reactive than the sulfide. With two equivalents of oxidant the sulfone was formed quantitatively. Surprisingly, diphenylsulfide did not react under these conditions although diphenylsulfoxide was smoothly converted to the sulfone. A curious observation in the oxidation of dibutylsulfide was that only a trace of oxidation had occurred after 30min, but after 60min only the sulfone was present. There appeared to be an induction period between **1** and periodic acid. The implication of this observation will be discussed later. 2,6-Di-*t*-butylphenol gave

3,3',5,5'-tetra-*t*-butyldiphenoquinone, not the mono-quinone, in good yields although the rate of the reaction was much slower than for the 2,4-isomer. Styrene gave no reaction under these conditions. With hydrogen peroxide and **1**, styrene gave the epoxide which gives support to the theory that bleaching and epoxidation probably involve two different intermediates.[2] As expected, cyclohexane did not afford any products from oxidation. An unexpected reaction was observed with the diene ergosterol acetate (**6**). When **6** was treated with either hydrogen peroxide or periodic acid in the presence of **1**, the peroxide **7** was isolated in low yield. The structure was determined from its spectral data and it was identical to the product obtained from ergosterol acetate by treatment with $FeCl_3$ and hydrogen peroxide. The structure of the latter was elucidated by X-ray crystallography (Dr. J. Reibenspies) (Figure 1) (*vide infra*).



Scheme 2

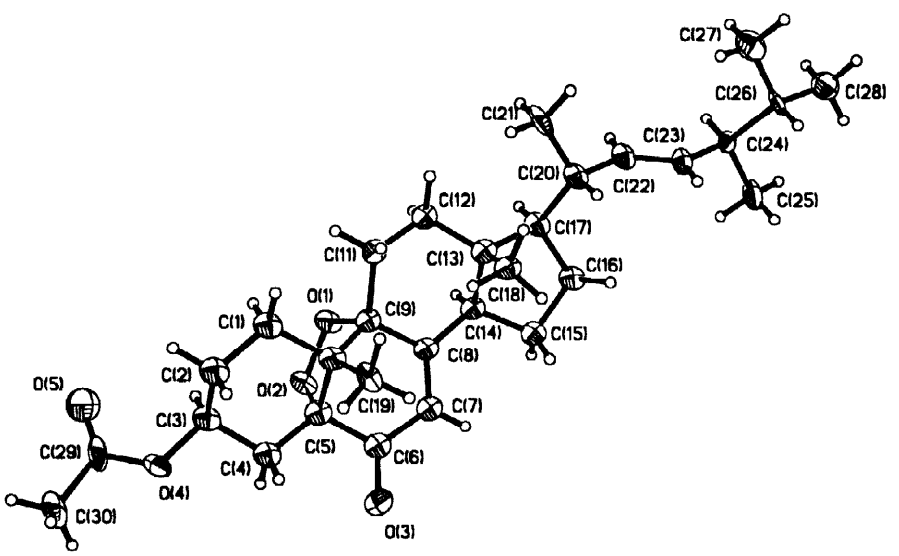


Figure 1

Traces of dehydroergosterol acetate[5] (**8**) were also detected by ^1H and ^{13}C nmr spectral analysis of the product mixture. Oxygen was needed for the reaction to proceed as no reaction was observed when the reaction was carried out under argon. However, when oxygen was bubbled through the reaction mixture **6** was rapidly consumed. This indicated that the peroxide bridge of **7** comes from oxygen. The oxidation of

6 with mercuric acetate is known to give the dehydro derivative (**8**) through the formation of a carbon-mercury bond. The formation of **7** is believed to involve a similar pathway which will be discussed later.

We suspected that the manganese was being oxidized to a higher oxidation state and we may have been expected to observe epoxidation of alkenes if a $Mn^{V}=O$ species was formed similar to those reported by Jacobsen.[6] As this was not the case we suspected that a $Mn^{VI}=O$ species may be the actual oxidant. To test this we investigated oxidation with potassium manganate. Very little has been published on oxidation reactions with potassium manganate and, reportedly, the latter disproportionates in basic solutions.[7] The reactions of various substrates with potassium manganate in pyridine/water (5:1) are summarized in Table 2. Addition of the oxidant gave a blue solution which rapidly turned brown, presumably as a result of the formation of manganese dioxide. The results show very similar reactivity to the reactions with **1** and periodic acid. It is conceivable that the oxidation is a result of disproportionation to potassium permanganate which may be the actual oxidant, but oxidation of 2,4-di-*t*-butylphenol (**2**) with permanganate under the conditions used gave a mixture of products. In contrast, manganate gave only the biphenyl compound **3**.

Table 2: Oxidation of organic substrates with K_2MnO_4.[a]

Entry	Substrate	Product	Yield	Time (min)
1	α-terpinene	*p*-cymene	60%[b]	150
2	γ-terpinene	*p*-cymene	90%[b]	150
3	2,4-di-*t*-butylphenol	2,2'-dihydroxy-3,3',5,5'-tetra-*t*-butylbiphenyl	90%[c]	90
4	di-*n*-butyl sulfide	di-*n*-butylsulfone	20%[c,d,e]	180
5	diphenylsulfoxide	diphenylsulfone	70%[b] 95%[c]	80 o/n
6	2,6-di-*t*-butylphenol	3,3',5,5'-tetra-*t*-butyldiphenoquinone	88%[c,d]	120
7	Ergosterol acetate	peroxide (**7**)	0	-

a) Reactions run in pyridine/water (5:1) unless otherwise stated. b) Yield determined by GC. c) Isolated yield. d) Two equivalents of K_2MnO_4. e) Potassium manganate appears to disproportionate to give a purple solution of permanganate.

As mentioned previously, the reactions appeared to have an induction period. By studying the catalase reaction we observed similar behavior. The reaction of **1** with hydrogen peroxide at pH=10 resulted in the slow formation of oxygen, presumably via the catalase reaction ($\tau_{1/2}$~25min). Addition of a second portion of hydrogen peroxide gave the calculated amount of oxygen in half the time ($\tau_{1/2}$~12min). On additional treatment with hydrogen peroxide the rate of formation of oxygen was increased until the half-life for the reaction was constant at 4 min. The complex could also be activated with Oxone® which gave 0.93mmol of oxygen when 1mmol of hydrogen peroxide was added to the solution. However, this also showed an induction period as there was no gas evolution for ~20min followed by rapid formation of oxygen which was complete after 3min. The addition of another 1mmol of Oxone® to the solution followed by 1mmol of

hydrogen peroxide resulted in the almost instantaneous formation of 1.02mmol of oxygen ($\tau_{1/2}$~30sec). This could be repeated numerous times with the same results. Periodic acid was not used in this case as hydrogen peroxide does not react with Oxone®, while it does react with the periodate to generate oxygen. This led us to believe that the complex was not the actual species being oxidized and that it was being transformed to another species which was activated by the oxidant. Similarly, Hage and Feringa recently reported that **1** was a better catalyst in the oxidation of benzyl alcohol when it was treated with excess hydrogen peroxide before the addition of the alcohol.[4] Epr spectroscopy indicated a Mn^{III}-Mn^{IV} species was being formed.

$[Mn^{III}\text{-}Mn^{IV}(L')_2O_2](ClO_4)_3.2H_2O$ **9**

L' =

$[Mn^{III}\text{-}Mn^{IV}O_2L"](PF_6)_2$ **10**

L" =

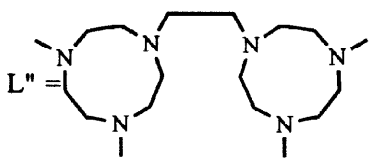
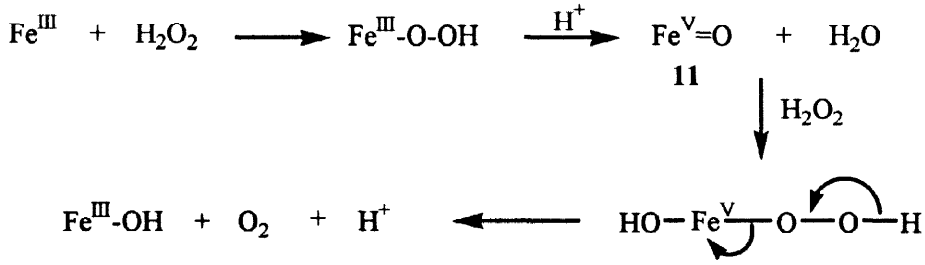


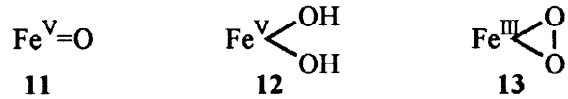
Figure 2

To test this we looked at the reactions of two Mn^{III}-Mn^{IV} complexes **9** and **10** (Figure 2). Both showed rapid oxygen formation when treated with hydrogen peroxide in pyridine or in water at pH=10 with no induction period detected. In water the half-life was less than 30sec and gas evolution appeared to occur in the first 10 seconds. Both complexes also showed the same activity towards the oxidation of the 2,4- and 2,6-di-*t*-butylphenol, but at a much faster rate than with **1**. For example, the reaction of the 2,6- derivative is complete in ~8h with **1**, while with **9** and **10** the reaction is complete in ~3h. This would then indicate that the reactive intermediate is a Mn^{V}-Mn^{IV} species. The addition of 1 equivalent of **9** to **2** showed some reaction, although only a trace of **3** was formed by ^{1}H-nmr spectral analysis indicating that the complex itself is not the oxidizing species. This gave support to our theory of a Mn^{V}=O compound. Brudvig and Crabtree[8] also postulated such a species from the reaction of Mn^{III}-Mn^{IV} complexes with Oxone®. The Mn^{V}=O species either reacts with Oxone® or itself to generate oxygen. We also observe oxygen formation with **9** and Oxone® in water. These results indicate that the active oxidant is a Mn^{V}=O-Mn^{IV} species.

It is always of interest to compare the oxidation of substrates with manganese complexes with that produced by iron based congeners. The selective functionalization of saturated hydrocarbons under Gif conditions requires the presence of ligands like picolinic acid and pyridine or suitable substituted pyridines.[9,10] Without both of these ligands the reaction of Fe^{III} and H_2O_2 affords almost exclusively oxygen (the catalase reaction).[11] We have presented evidence for the simple analysis in Scheme 3 to explain this model catalase reaction.[12] An Fe^{V} species is written as an Fe^{V} oxenoid (**11**), but could also be represented as **12** and even **13** (Figure 3). Be this as it may, we found good evidence that **11** could also oxidize sulfides to sulfoxides and that this reaction was in competition with the formation of oxygen. The total oxidation, allowing 2 H_2O_2 for oxygen formation and 1 H_2O_2 for the formation of **11** to give sulfoxide, was always constant.



Scheme 3



11 12 13

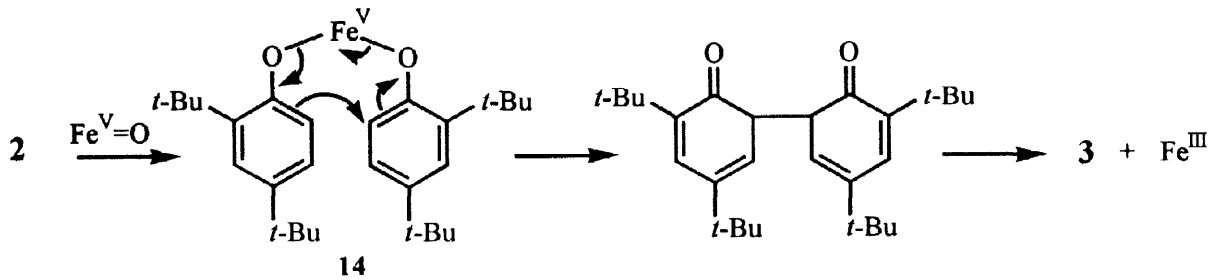
Figure 3

The chemistry of **11** is remarkably selective, similar to that observed with the Mn complexes. The oxidation of 2,4-di-*t*-butylphenol with **11** was a fast reaction ($\tau_{1/2}$ ~3min) affording the biphenyl **3** and approximately 1 mmol of oxygen (Table 3, Entry 2). Traces of 2,4-di-*t*-butyl quinone were also formed. Entry 1 was a blank experiment. It was also shown that the yield of **3** was unaffected when the reaction was carried out under a current of argon or of oxygen. This makes the formation of phenolate radicals, which react rapidly with oxygen, improbable.[13] We believe that the reaction proceeds as indicated in Scheme 4, where an Fe^{V} intermediate (**14**) is postulated affording **3** *via* ionic coupling.

Table 3: Oxidation of 2,4-di-*t*-butylphenol (**2**) with $FeCl_3/H_2O_2$.[a]

Entry	H_2O_2 (mmol)	Temp.	Time	Products (mmol)	
				3	2,4-di-*t*-butyl quinone
1	0	RT	over night	0.07	trace
2	4	0°	60min	0.59	0.15
3[b]	4	0°	60min	0.69	0.13
4[c]	4	0°	60min	0.68	0.15

a) $FeCl_3$ (1mmol), 2 (5mmol) H_2O_2 (Xmmol) and pyridine (33ml). b) Reaction conducted under a current of argon. c) Reaction conducted under a current of oxygen.



14

Scheme 4

Similarly to the $Mn^{V}=O$ species, Fe^{V} reacts rapidly with α-terpinene **4** to yield *p*-cymene **5**. As expected γ-terpinene also afforded *p*-cymene in a similar reaction. Selected data are presented in Table 4.

Entries 1 and 2 are blank reactions which show no reaction with only $FeCl_3$ or hydrogen peroxide. Entry 3 shows that 10 equiv. of α-terpinene completely suppresses oxygen formation and increases *p*-cymene formation (about 75% efficiency assuming 1 H_2O_2 makes 1 Fe^V which makes 1 *p*-cymene). As with manganese, the corresponding reaction with γ-terpinene is slower than for the α derivative. Some oxygen is formed in competition with *p*-cymene formation making the overall efficiency nearly 100%. One difference between the manganese and iron was that diphenylsulfide reacts rapidly with the oxidized species. This is shown in the competition between oxygen formation, dehydrogenation to *p*-cymene and oxidation of diphenylsulfide to its sulfoxide. The respective efficiencies were 83, 83 and 94%. All these data demonstrated well that all the reactions took place with the same Fe^V species. Another difference between the two systems exists in that no sulfone was detected. The iron species appears to be selective for sulfides where the Mn species is more reactive towards sulfoxides.

Table 4: Oxidation of α-terpinene **4** with $FeCl_3/H_2O_2$.[a]

Entry	$FeCl_3$ (mmol)	**4** (mmol)	Ph_2S (mmol)	H_2O_2 (mmol)	O_2 (mmol)	Products (mmol)	
						5	Ph_2SO
1[b]	0	2	0	5	n.d	trace	n/a
2[b]	3	10	0	0	n.d	trace	n/a
3	1	10[c]	0	4	n.d	3.05	n/a
4	1	10	0	4	0.69	2.57	n/a
5[d]	1	2	10	4	0.54	1.11	1.24
6[d]	1	5	10	4	n.d	2.20	1.22
7[d]	1	10	10	4	n.d	2.85	1.09

a) All reactions were carried out in pyridine (33ml) at 0° unless otherwise stated. b) Reaction carried out at room temperature. c) γ-Terpinene. d) The ratios of *p*-cymene:Ph_2SO were 0.90, 1.80 and 2.62 in entries 5,6 and 7 respectively.

We briefly examined the possible oxidation of the organic bases diethylamine, triethylamine and 1,1,3,3-tetramethylguanidine. The general effect was to form rapidly a quantitative yield of oxygen. In competition with Ph_2S and α-terpinene only trace amounts of the sulfoxide and small yields of *p*-cymene were formed. Not only were the amines not oxidized, they speeded up the catalase reaction. This can be understood in terms of the acidity of hydrogen peroxide (Scheme 3). The (partial) anion from H_2O_2 must add to the species **11** more rapidly to make oxygen. Less of **11** is available for other oxidative processes.

The Fe^V oxenoid species studied above does not react with simple olefins like cyclohexene. It also does not react with conjugated dienes like 2,3-dimethylbutadiene. However, like the Mn species, Fe^V reacts readily with ergosterol acetate (**6**). The experiments with ergosterol acetate and activated $FeCl_3$ are summarized in Table 5. When a mixture of $FeCl_3$ and **6** in pyridine was treated with hydrogen peroxide under air at 0° the same peroxide **7** that was isolated from the manganese reaction was formed in about 40% yield. When the experiment was repeated under argon the formation of **7** was less and some

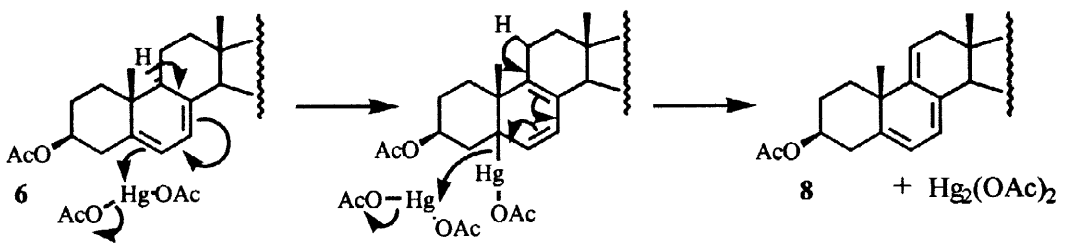
dehydroergosterol acetate **8** was formed (14%, Entry 2). However, dehydroergosterol acetate **8** was not the precursor of the peroxide **7** which was shown by the appropriate experiment (Entry 3).

Table 5: Oxidation of Ergosterol Acetate.[a]

Entry	Substrate (mmol)	H_2O_2 (mmol)	**7** (mmol)	**8** (mmol)
1	Ergosterol Acetate **6**	4	0.41	trace
2[b]	Ergosterol Acetate **6**	4	0.21	0.14
3	Dehydroergosterol Acetate **8**	4	0	0.69

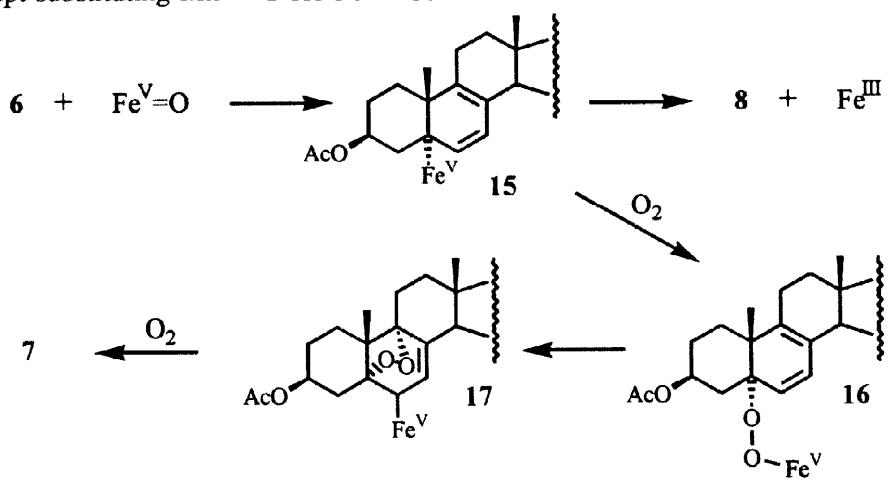
a) Reactions carried out with $FeCl_3$ (0.3mmol) in pyridine (33ml) under an atmosphere of air unless otherwise stated. b) Reaction carried out under a stream of argon.

The mechanism for the mercuric acetate dehydrogenation of ergosterol acetate is considered to be as in Scheme 5. In this Scheme, if the $Hg(OAc)_2$ was replaced by $Fe^V=O$ then we would postulate a 5α-Fe^V-carbon bond instead of a Hg^{II}-carbon bond which would lead to **15** and then to **8** and Fe^{III} as in Scheme 6.



Scheme 5

Also, as in Scheme 6, the insertion of oxygen into the iron-carbon bond of **15** would furnish **16** and then by rearrangement the peroxide **17** could be transformed into the final product **7**. As the same product is formed with complex **1** and hydrogen peroxide, it is believed that **7** is formed by the same or a similar mechanism, except substituting $Mn^V=O$ for $Fe^V=O$.



Scheme 6

The oxidation of α-terpinene to *p*-cymene may follow a similar mechanism as we suggest for the formtion of dehydroergosterol acetate (**8**) from ergosterol acetate. The analogy extends to the oxidation with mercuric acetate which also affords *p*-cymene and mercurous acetate in high yield.

In conclusion, we have demonstrated the use of dinuclear manganese complexes to catalyze the oxidation of organic substrates, presumably through an $Mn^{V}=O$ species. These complexes require Mn^{III} and Mn^{IV} ions for fast and efficient oxidation. Also we have provided evidence for the existence of an iron species which is not Fe^{III} and, in the context of all the evidence must be Fe^{V}. However, these species in the absence of a carboxylate ligand have an unusual selectivity for organic substrates. Apart from 2,4-di-*t*-butylphenol and various sulfides, the only compounds which show good reactivity are two cyclohexadienes: α-terpinene and ergosterol acetate. Presumably coordination of the two double bonds to the metal species must be an important factor in this special reactivity.

EXPERIMENTAL

General:

Chemicals were purchased from Aldrich Chemical Co., except for pyridine (Mallinckrodt); diethyl ether, $MgSO_4$ and H_2O_2 (Fisher Scientific Co.). Unless otherwise stated, all solvents and chemicals were after verification used as purchased. H_2O_2 was used as 30% in H_2O.

Gas chromatography analysis was performed on a Hewlett Packard 5890 series II instrument equipped with flame ionization detector and Hewlett Packard 3396A integrator. Purified N_2 was used as the carrier gas. The columns used were DB-WAX (30m, 0.32mm i.d., 25mm film thickness), DB-5 (30 m, 0.32mm i.d., 25mm film thickness) or DB-1 (15m, 0.32mm i.d., 25mm film thickness) capillary columns from J&W Scientific.

Gas chromatography-mass spectrometry (GC-MS) analysis was carried out on a Hewlett Packard 5890 series II gas chromatograph coupled with a Hewlett Packard 5971 series quadropole mass-selective detector (40 eV, electron impact). Helium was used as the carrier gas. The column used in the GC-MS was a HP-5MS (30m, 0.25mm i.d., 0.25mm film thickness).

^{1}H-NMR and ^{13}C-NMR spectra were performed on Varian XL-200E or Varian Gemini 200 with tetramethylsilane (TMS) as the internal reference. Ultraviolet (UV) spectra were determined on a Beckman DU-7 spectrophotometer. Infrared (IR) spectra were recorded on a ATI Mattson Genesis Series FTIR. Melting points were determined an a Thomas hot-stage melting point apparatus and are uncorrected.

Typical work-up procedure: An aliquot (1ml) was taken from the reaction mixture and added to 25% H_2SO_4 (2ml) at 0°, and extracted 3 times with diethyl ether (5ml each time). The combined organic extracts were washed with a saturated solution of $NaHCO_3$ and water, dried over $MgSO_4$ and added with 1ml naphthalene solution (0.08M in diethyl ether) as an internal standard. The products were analyzed by gas chromatography.

Method for the measurement of O_2 evolved: The reaction system was made gastight and connected to a manometric burette filled with saturated brine solution which was saturated with oxygen (air) prior to use. The volume of O_2 gas evolved from the Gif reactions was measured. During the readings, the pressure was always equilibrated using a separation funnel by adjusting the brine levels to the same heights. Also, the

appropriate temperature and atmospheric pressure were taken into account before each reading and considered in the calculations using the ideal gas law.

Typical experiment for the catalytic oxidation of organic substrates with manganese complexes **1**, **9** or **10**.

A solution of periodic acid (2.37g, 10.2mmol) in pyridine (20ml) was added dropwise to a solution of 2,6-di-*t*-butylphenol (1.03g, 5mmol) and the catalyst (2-5 mol%) in pyridine (10ml) and the progress of the reaction monitored by tlc (reactions with terpinenes, sulfides and sulfoxides were monitored by GC). On the consumption of the phenol the solution was added to an ice/water slurry and acidified with conc. HCl. The mixture was extracted with dichloromethane (3x25ml), the extracts dried and evaporated to give the crude product which was recrystallized from hexanes to give 3,3',5,5'-tetra-*t*-butyldiphenoquinone as lustrous purple needles in 88% yield. mp.= 252-253° (lit.[14] mp.= 245-246°)

Typical experiment for the oxidation of organic substrates with potassium manganate (K_2MnO_4).

Potassium manganate (197mg, 1mmol) was added to a solution of 2,4-di-*t*-butylphenol (203mg, 1mmol) in pyridine/water (6ml, 5:1). On consumption of **2**, (90min), the reaction was worked up as described above to give the crude product which was purified by flash chromatography to give **3** as a cream colored solid in 90% yield. mp.= 192-193° (lit.[15] mp. 194.5-195.5°)

Reaction of hydrogen peroxide with manganese complexes **1**, **9** or **10** (Catalase reaction).

The manganese complex **1** (~0.025mmol) was dissolved in a solution of 1M $NaHCO_3$ (20ml) in a round bottom flask which was attached to an apparatus to measure gas formation. The apparatus was flushed with oxygen prior to the addition of the solution and after. Hydrogen peroxide (2mmol) was introduced to the closed system and the amount of oxygen formed and the rate of formation was determined. After gas formation had stopped the pressure was equalized and another portion of hydrogen peroxide (2mmol) was added and the amount and rate of gas formation was again determined. This process was repeated until the rate of gas formation became constant.

Activation of **1** with Oxone® and reaction with hydrogen peroxide.

Complex **1** (808mg, 1mmol) was dissolved in water (20ml) in the apparatus to measure gas formation described above. Oxone® (615mg, 1mmol) was added followed by hydrogen peroxide (1mmol). No gas was evolved for ~20min when rapid started. Oxygen (~1mmol) was formed in 3min. The pressure was equalized and Oxone® (1mmol) was added to the solution. Hydrogen peroxide (1mmol) was introduced and oxygen was evolved rapidly ($\tau_{1/2}$~30s). This procedure could be repeated with the same result.

Typical experiment for the oxidation of 2,4-di-*t*-butylphenol with $FeCl_3/H_2O_2$.

$FeCl_3.6H_2O$ (270mg, 1mmol) and 2,4-di-*t*-butylphenol (**2**) (1.03g, 5mmol) were dissolved in pyridine (33ml) under a stream of argon. The solution was cooled to 0° and H_2O_2 (0.4mL, 4mmol) added dropwise (30s to 1min). The solution was kept under argon at this temperature for 1h. The remaining 2,4-di-*t*-butylphenol and the biphenyl **3** formed were quantified by GC after typical acidic work-up using AcOEt

instead of Et_2O to do the extraction. The rest of the reaction mixture was reduced by the addition of Zn (1g) and AcOH (3ml) under argon. After 30min, another aliquot (1ml) was taken and added into to 2 mL of acetic anhydride. It was kept under argon for 3h and worked up by typical procedure using AcOEt as solvent. The 3,5-di-*t*-butyl-*o*-benzoquinone was transformed into 1,2-diacetoxy-3,5-di-*t*-butyl benzene and quantified by GC.

Typical experiment for the oxidation of α-terpinene with $FeCl_3/H_2O_2$.

$FeCl_3.6H_2O$ (270mg, 1mmol) and α-terpinene **4** (1.362g, 10mmol) were dissolved in pyridine (33ml). The solution was cooled to 0° and H_2O_2 (0.4ml, 4mmol) added dropwise (30s to 1min). The solution was kept at this temperature for 1h, then allowed to gradually come to room temperature. The products were quantified by GC after typical work-up.

Oxidation of ergosterol acetate (**6**) with $FeCl_3/H_2O_2$.

$FeCl_3.6H_2O$ (81mg, 0.3mmol) and ergosterol acetate (**6**) (438mg, 1mmol) were dissolved in pyridine (33ml). The solution was cooled to 0° and H_2O_2 (0.4ml, 4mmol) added dropwise after which stirring was continued for 1h. The reaction mixture was added to H_2SO_4 (25%) at 0° and extracted with dichloromethane (2x50ml). The extracts were dried and evaporated to give the crude peroxide. The peroxide was isolated from traces of ergosterol acetate and dehydroergosterol acetate by column chromatography (Silica, hexanes:dichloromethane). The peroxide **7** was obtained pure after recrystallizing twice from $CHCl_3$/EtOH to give white needles melting 128-130°. $[\alpha]_D^{24}$ = -16.2° (*c* 5.0, $CHCl_3$); UV ($CHCl_3$): λ_{max} 239 nm (ε 1.39 ∞ 10^4); IR (KBr): ν_{max} 2956, 2871, 1739, 1692, 1461, 1384, 1368, 1052, 1018, 971 cm^{-1}; ^{1}H-NMR : δ 5.91 (d, 1H, *J* 2.6 Hz), 5.22-5.15 (m, 2H), 5.10-4.90 (m, 1 H), 2.55-0.70 (m, 37H), 0.65 (s, 3H); ^{13}C-NMR : δ 195.0, 170.2, 161.4, 134.7, 132.7, 124.5, 90.4, 85,7, 69.2, 56.8, 55.5, 53.4, 53.2, 42.8, 42.4, 40.1, 36.1, 33.0, 31.5, 28.4, 27.8, 26.9, 22.8, 21.2, 19.9, 19.6, 17.5, 15.8, 14.1, 12.3. Anal Calc. for $C_{30}H_{44}O_5$: C, 74.34; H, 9.15. Found: C, 73.30; H, 9.10.

Oxidation of α-terpinene by mercuric acetate:

α-Terpinene (**4**) (409mg, 3mmol) in chloroform (3ml) and $Hg(OAc)_2$ (956mg, 3mmol) in acetic acid (20ml) were mixed together at room temperature. The resulting solution was stirred for 1 day. The precipitate, $Hg_2(OAc)_2$ (800mg, 1.54mmol), formed was filtered and the products were quantified by GC after typical work-up procedure. *p*-Cymene (**5**) (1.50mmol) was detected.

ACKNOWLEDGMENTS

We thank Unilever, Quest Intl., the Welch Foundation and the Schering-Plough Corporation for the support of this work and the generous gifts of manganese complexes (Unilever). We appreciate the excellent work of Dr. J. Reibenspies in the determination of the structure of **7** by X-ray crystallography. Details of this work will be published elsewhere (*Acta Crystallographica*, submitted for publication).

REFERENCES

1. Brudvig, G.W., Beck, W.F. and de Paula, J.C., *Ann. Rev. Biophys. Biophys. Chem.*, **1989**, *18*, 25; Thorpe, H.H. and Brudvig, G.W., *New J. Chem.*, **1991**, *15*, 479.

2. Hage, R., Iburg, J.E., Kerschner, J., Koek, J.H., Lempers, E.L.M., Martens, R.J., Racherla, U.S., Russel, S.W., Swarthoff, T., van Vliet, M.R.P., Warnaar, J.B., van der Wolf, L. and Krijnen, B., *Nature*, **1994**, *369*, 637.
3. Teterd, D., Rabion, A., Verlhac, J-B. and Guilhem, J., *J. Chem. Soc., Chem. Commun.*, **1995**, 531; Menage, S., Collomb-Dunand-Suathier, M-N., Lambeaux, C. and Fontecave, M., *J. Chem. Soc., Chem. Commun.*, **1994**, 1885; Vincent, J.M., Menage, S., Lambeaux, C. and Fontecave, M., *Tetrahedron Lett.*, **1994**, *34*, 6287.
4. Zondervan, C., Hage, R. and Feringa, B.L., *J. Chem. Soc., Chem. Commun.*, **1997**, 419.
5. Windaus, A. and Linsert, O., *Ann.*, **1928**, *465*, 148.
6. Zhang, W., Loebach, J.L., Wilson, S.R. and Jacobsen, E.N., *J. Am. Chem. Soc.*, **1990**, *112*, 2801; Zhang, W. and Jacobsen, E.N., *J. Org. Chem.*, **1991**, *56*, 2296.
7. Záhonyi-Budó, É. and Simándi, L.I., *Inorg. Chim. Acta.*, **1995**, *237*, 173.
8. Limburg, J., Brudvig, G.W. and Crabtree, R.H., *J. Am. Chem. Soc.*, **1997**, *119*, 2761.
9. Barton, D.H.R., Hu, B., Taylor, D.K. and Rojas Wahl, R.U., *J. Chem. Soc., Perkin Trans. 2*, **1996**, 1031.
10. Barton, D.H.R., Hu, B., Li, T. and MacKinnon J., *Tetrahedron Lett.*, **1996**, *37*, 8329.
11. (a) Horswill, E.C. and Ingold, K.U., *Can J. Chem.*, **1966**, *44*, 269. (b) Cook, C.D., Woodworth, R.C. and Flanu, P., *J. Am. Chem. Soc.*, **1956**, *78*, 4159. (c) Cook, C.D. and Woodworth, R.C., *J. Am. Chem. Soc.*, **1953**, *75*, 6242. (d) Hatchard, W.R., Lipscomb, R.D. and Stacey, F.W., *J. Am. Chem. Soc.*, **1958**, *80*, 3636.
12. Barton, D.H.R. and Hu. B., *Tetrahedron*, **1996**, *52*, 10313.
13. (a) Lichtenberger, F., Nastainczyk, W. and Ullrich, V., *Biochem. Biophys. Res. Commun.*, **1976**, *70*, 939. (b) Groves, J.T., Nemo, T.E. and Myers, R.S., *J. Am. Chem. Soc.*, **1979**, *101*, 1032.
14. Taimr, L. and Pospísil, J., *Tetrahedron Lett.*, **1971**, *16* 2809.
15. Müller, E., Mayer, R., Narr, B., Rieker, A. and Scheffler, K., *Liebigs Ann. Chem.*, **1961**, *645*, 25.