

# Iron porphyrin catalyzed hydroxylation of ethylbenzene by ozone

Zeev Gross<sup>\*</sup>, Shay Nimri, Liliya Simkhovich

Department of Chemistry, The Technion, Israel Institute of Technology, Haifa 32000, Israel

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## Abstract

The hydroxylation of ethylbenzene by ozone under catalysis of tetramesitylporphyrinato iron(III) complexes with various axial ligands was studied in order to elucidate the principles which determine the efficiency of this biomimetic system. Reaction conditions were carefully chosen to ensure that oxygen-atom transfer from oxidized catalyst to hydrocarbon is rate limiting. The catalyst's proximal ligand was found to affect both the stability and the reactivity of the high-valent iron porphyrin intermediate 1-X, the reactivity pattern being distinctively different from the related epoxidation reactions. The most pronounced and intriguing effect was of methanol, which stabilized the 1-X complex as to completely inhibit its reactivity toward the alkane. Preliminary results for two halogenated-porphyrin iron(III) complexes are presented too, to demonstrate the potential of the present system for practical purposes.

**Keywords:** Iron; Porphyrins; Hydroxylation; Ozone

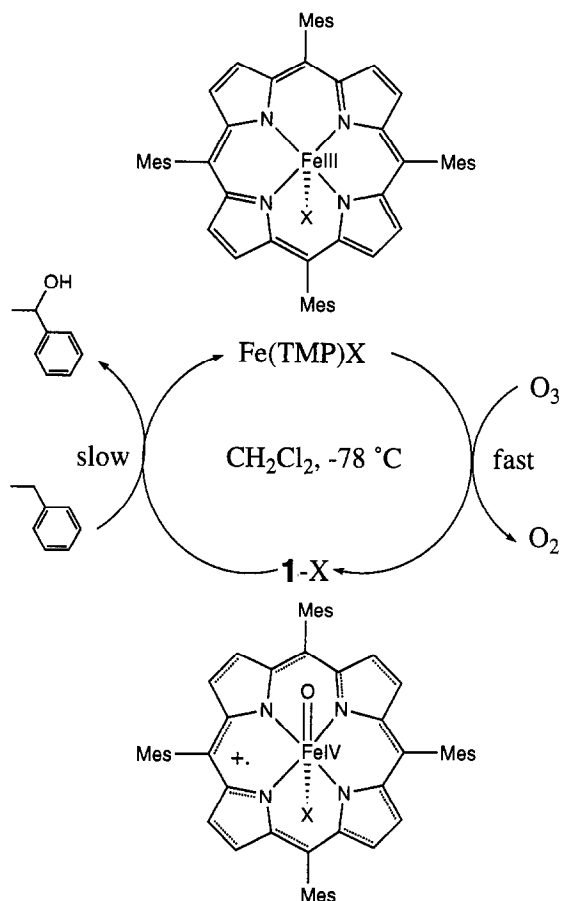
## 1. Introduction

Studies of synthetic metalloporphyrins as model complexes of hemoproteins have led to the development of highly efficient catalysts with enzyme-like activities and to very important insight into their mode of action [1–12]. It is now known that the most reactive intermediates in the catalytic cycles of most of these enzymes and synthetic iron(III) porphyrins are cationic oxoiron(IV) porphyrin cation radical complexes with an axial ligand *trans* to the oxoiron(IV) bond [2,3]. Two unique features of cytochrome P-450 enzymes are the utilization of molecular oxygen for oxygenation of hydrocar-

bons and cysteinylate as proximal ligand. The same proximal ligand is also present in chloroperoxidases [4], which is the only hemo-protein that in combination with exogenous oxidants can be used as effective catalyst for cytochrome P-450-like reactivities [5]. These observations suggest an important role for axial ligands in the last step of catalysis, the oxygen-atom transfer from oxidized catalysts to organic substrates.

We have recently demonstrated a pronounced effect of axial ligands on the oxoiron(IV) bond strengths and the reactivities of synthetic oxoiron(IV) porphyrin cation radical complexes toward olefins [6]. The reactivity studies were however limited to stoichiometric epoxidations, since olefins were oxidized directly by ozone – the oxygen-atom source in these studies – faster

<sup>\*</sup> Corresponding author.



Scheme 1.

than by the catalyzed pathway. A similar conclusion was reached by attempted ozonolysis of olefins under catalysis of much more robust iron porphyrin complexes, where only 0.4–12% of the products were formed via the catalyzed pathway (5–42% for manganese porphyrins) [7].

We describe now the *catalytic* hydroxylation of ethylbenzene by ozone, utilizing various  $\text{Fe}^{\text{III}}(\text{TMP})\text{X}$  complexes (TMP = tetramesitylporphyrinato, X = axial ligand;  $\text{F}^-$ ,  $\text{Cl}^-$ ,  $\text{AcO}^-$ ,  $\text{CF}_3\text{SO}_3^-$  (trif),  $\text{ClO}_4^-$ , Scheme 1). Ozone was chosen as primary oxidant, since both ozone and molecular oxygen – the precursor and the reduced product of ozone – are not potential ligands for the high-valent iron complex. It thus

provides the unique opportunity of studying the effect of axial ligands on the reactivity of the catalysts. The choice of ethylbenzene as alkane representative was based on its structural similarity to styrene, to enable the comparison with the previous epoxidation studies [6]. Since only with tetramesitylporphyrin, but not for the more reactive and robust halogenated porphyrins [8], the characterization of oxoiron(IV) porphyrin cation radical complexes with various axial ligands is possible [6], the emphasis in the present study was placed on this rather limited catalyst. The most important findings were that ozone can be used as the oxygen atom source without non-catalyzed direct ozonolysis of the alkane, that axial ligands have a distinctively different effect on hydroxylation and epoxidation catalysis, and that methanol – which would be the hydroxylation product of methane – has an inhibitory effect on the catalyst's activity. Preliminary results for catalysis by more robust iron porphyrins are presented too, for comparison with the  $\text{Fe}^{\text{III}}(\text{TMP})\text{X}$  complexes.

## 2. Experimental section

### 2.1. Materials

Dichloromethane (Lab-Scan, HPLC grade) was dried by distillation over  $\text{CaH}_2$ . Ethylbenzene (Aldrich) was purified by repeated washing with concentrated  $\text{H}_2\text{SO}_4$ , until the aqueous layer was colorless, followed by washing with aqueous  $\text{K}_2\text{CO}_3$  and water. The material was dried by  $\text{MgSO}_4$  and distilled twice over Na.  $\text{CD}_3\text{OD}$ ,  $\text{C}_6\text{D}_6$ ,  $\text{CDCl}_3$ , and  $\text{CD}_2\text{Cl}_2$  (Aldrich products) were used as received.

#### 2.1.1. Iron porphyrins

The iron(III) tetramesitylporphyrin complexes with various axial ligands were available from our previous studies [6], thus only a brief description of their preparation is appropriate here. Tetramesitylporphyrin was prepared by

the Lindsey procedure [9] and  $\text{Fe}^{\text{III}}(\text{TMP})\text{Cl}$  was obtained by its reaction with elemental iron in glacial acetic acid and subsequent washing with 10% HCl.  $\text{Fe}^{\text{III}}(\text{TMP})(\text{OSO}_2\text{CF}_3)$  and  $\text{Fe}^{\text{III}}(\text{TMP})(\text{OCIO}_3)$  were obtained from the chloride complex by treatment with the corresponding dried Ag(I) salt in toluene solution.  $\text{Fe}^{\text{III}}(\text{TMP})\text{OAc}$  was obtained by treating **2-CI** with KOH/MeOH, followed by recrystallization from AcOH. **2-F** was formed by treating  $\text{Fe}^{\text{III}}(\text{TMP})\text{Cl}$  with  $n\text{-Bu}_4\text{NF}$ . All compounds were recrystallized prior to use and examined by  $^1\text{H}$  NMR to confirm their purity, especially in terms of contamination by  $\text{Fe}^{\text{III}}(\text{TMP})\text{Cl}$ . The complexes of  $\text{trif}^-$  and  $\text{ClO}_4^-$  must be crystallized from benzene, whose low hygroscopy ensured that water was not present as sixth ligand [10]. For the same reason, and also to avoid reaction with residual HCl present in chlorinated solvents, the NMR data were recorded in benzene- $d_6$ .  $^1\text{H}$  NMR ( $\text{C}_6\text{D}_6$ , RT):  $\text{Fe}^{\text{III}}(\text{TMP})\text{F}$ :  $\delta$  81.5 (*pyr.*-H, 8H), 12.8 and 11.7 (*m*-H, 8H), 3.4 (*p*- $\text{CH}_3$ , 12H).  $\text{Fe}^{\text{III}}(\text{TMP})\text{Cl}$ :  $\delta$  80.3 (*pyr.*-H, 8H), 15.4 and 13.9 (*m*-H, 8H), 3.9 (*p*- $\text{CH}_3$ , 12H).  $\text{Fe}^{\text{III}}(\text{TMP})\text{OAc}$ :  $\delta$  79.6 (*pyr.*-H, 8H), 13.9 and 12.7 (*m*-H, 8H), 3.6 (*p*- $\text{CH}_3$ , 12H).  $\text{Fe}^{\text{III}}(\text{TMP})(\text{OSO}_2\text{CF}_3)$ :  $\delta$  52.6 (*pyr.*-H, 8H), 15.3 and 14.2 (*m*-H, 8H), 4.4 (*p*- $\text{CH}_3$ , 12H).  $\text{Fe}^{\text{III}}(\text{TMP})(\text{OCIO}_3)$ :  $\delta$  29.2 (*pyr.*-H, 8H), 14.1 and 13.4 (*m*-H, 8H), 4.2 (*p*- $\text{CH}_3$ , 12H).

The chloroiron(III) porphyrin complexes of 5,10,15,20-tetra(2,6-dichlorophenyl)porphyrinato (TDCPP) and 2,3,7,8,12,13,17,18-octabromo-5,10,15,20-tetramesitylporphyrinato ( $\text{Br}_8\text{-TMP}$ ) were prepared in accord with published procedures, recrystallized from  $\text{CH}_2\text{Cl}_2$ /hexanes and analyzed by UV-Vis and  $^1\text{H}$  NMR [11].

## 2.2. Instruments

The  $^1\text{H}$  NMR spectra were recorded on a Bruker AM 200, operating at 200 MHz. Chemical shifts are reported relative to residual hydrogens in the deuterated solvents (7.20, 7.26 and 5.32 for  $\text{C}_6\text{D}_5\text{H}$ ,  $\text{CHCl}_3$  and  $\text{CHDCl}_2$ , respec-

tively). A HP 8452A diode array spectrophotometer was used for electronic spectra. Ozone was produced by electric discharge of oxygen with an ozonolyzer, manufactured by Welsbach. The amount of  $\text{O}_3$  (mole vs. time) was determined by introduction of the  $\text{O}_3/\text{O}_2$  stream into an aqueous KI solution and subsequent titration of  $\text{I}_3^-$  with  $\text{Na}_2\text{S}_2\text{O}_3$  [12]. Alternatively, dry-ice/acetone-cooled  $\text{CH}_2\text{Cl}_2$  solutions containing excess tetrabutylammonium iodide were treated with ozone and the concentration of  $\text{I}_3^-$  was determined by its UV-Vis spectrum ( $\lambda_{\text{max}} = 364 \text{ nm}$ ,  $\epsilon = 27000 \text{ M}^{-1} \text{ cm}^{-1}$ ). Identical results were obtained by both methods.

## 2.3. Oxidation reactions

The reaction mixtures were introduced into a 3 ml reaction vessel, which had a small side arm above the solution level which leads to a smaller vial (about 0.5 ml). Both parts were kept in a dry-ice acetone bath. A slow stream of  $\text{O}_3$  in  $\text{O}_2$  (60 ml total gas/min) was introduced into the reaction mixture by flexible capillary Teflon tubing. Under these conditions the incoming gas ensured efficient stirring of the reaction mixture. Small aliquots ( $\approx 0.05 \text{ ml}$ ) were transferred into the empty side arm of the reaction vessel at measured times and quenched by excess tetrabutyl ammonium iodide, still at  $-78^\circ\text{C}$ . The aliquots were used for product analysis without any further treatment.

### 2.3.1. Catalysis by $\text{Fe}^{\text{III}}(\text{TMP})\text{X}$ complexes

The reaction mixtures consisted of 0.8 ml  $\text{CH}_2\text{Cl}_2$ , 0.2 ml ethylbenzene (1.63 M), 0.47–0.53 mg  $\text{Fe}^{\text{III}}(\text{TMP})\text{X}$  (0.54 mM), and 0.21  $\mu\text{l}$  nitrobenzene (2  $\mu\text{mol}$ , internal standard). Ozone was supplied at 6  $\mu\text{mol O}_3/\text{h}$ , which corresponds to conversion of ethylbenzene by a maximum of 0.37%/h. The reactions were examined for 2–3 h. The yields of sec-phenethyl alcohol were in the range of 1.7–5.6  $\mu\text{mol}$ , which are 0.1–0.34% relative to ethylbenzene and 13–31% relative to ozone, the product-limiting oxidant.

### 2.3.2. Catalysis by $Fe^{III}(TMP)Cl$ and $Fe^{III}(Br_8-TMP)Cl$

Two different reaction conditions were applied for these comparative studies; in ethylbenzene only (1 ml), and in a mixture of 0.8 ml  $CH_2Cl_2$  and 0.2 ml ethylbenzene (1.63 M). The other variables were identical: 0.54 mM of catalyst, 4  $\mu$ mol of nitrobenzene, and 22–26  $\mu$ mol  $O_3$ /h. The yields of sec-phenethyl alcohol relative to ozone after 3 h were almost identical for both catalysts, about 14% for the reactions in ethylbenzene and about 7% in the  $CH_2Cl_2$ /ethylbenzene mixture (corresponding to 0.13% and 0.33%, respectively, relative to ethylbenzene).

### 2.3.3. Catalysis by $Fe^{III}(TDCPP)Cl$

The reaction mixtures consisted of 1.6 ml  $CH_2Cl_2$  and 0.4 ml ethylbenzene (1.63 M). Reaction conditions for reaction ■ in Fig. 2 were: 0.56 mM catalyst, 4  $\mu$ mol nitrobenzene, and 22  $\mu$ mol  $O_3$ /h. Reaction conditions for reaction □ in Fig. 2 were: 0.33 mM catalyst, 4  $\mu$ mol nitrobenzene, and 35  $\mu$ mol  $O_3$ /h, which leads to a maximum conversion rate of 1% ethylbenzene/h. After two hours, the yields of sec-phenethyl alcohol was 2%, corresponding to quantitative yields relative to the product-limiting ozone.

### 2.3.4. $^1H$ NMR investigation of catalysis by $Fe^{III}(TMP)Cl$

Two identical NMR solutions of oxidized catalyst were obtained by bubbling ozone at  $-78^\circ C$  for 30 s (6  $\mu$ mol  $O_3$ /min, 1.1 equiv.) into solutions of 2.6  $\mu$ mol of  $Fe^{III}(TMP)Cl$  in 0.6 ml  $CD_2Cl_2$ , followed by purging with  $N_2$  (70 ml/min) for 1 min. Into one of the tubes, 30  $\mu$ l  $CD_3OD$  (5%) was added. 19.5  $\mu$ l (100 equiv.) of styrene was added to both tubes and the reactions were followed by NMR spectroscopy at  $-80^\circ C$ . Clean and gradual conversion of the oxidized catalyst to  $Fe^{III}(TMP)Cl$  was observed in the absence of  $CD_3OD$ , and GC analysis after 12 h showed the presence of sec-phenethyl alcohol. For the 5%  $CD_3OD$  solution, the initial spectrum of [1- $CD_3OD$ ] (see

Ref. [6] and [13]) did not change upon addition of styrene, even in the course of 8 h. GC analysis after 12 h revealed no organic products.

### 2.3.5. Product analysis

Gas chromatographic analysis were performed on a HP 5710A GC coupled to a HP 3392A integrator, with He as carrier gas, a packed Carbowax 5% column, and a TC detector. In later studies a HP 5890 GC linked to the HP Chem-Station (HP 3365) with a DB-5 capillary column and FID detector was utilized. The reaction products were analyzed by comparison of their retention times with authentic samples (Aldrich). Yields were determined by using nitrobenzene as internal standard.

## 3. Results and discussion

### 3.1. Catalysis by $Fe^{III}(TMP)X$ complexes, $X = F^-, Cl^-, AcO^-, CF_3SO_3^-, ClO_4^-, MeOH$

The reactions were initiated by introducing a stream of  $O_3/O_2$  into  $CH_2Cl_2$  solutions at  $-78^\circ C$ , containing 1.63 M ethylbenzene and 0.54 mM of  $Fe^{III}(TMP)X$  (Scheme 1). The rate of ozone introduction was optimized to a value of 6  $\mu$ mol  $O_3$ /h as to minimize destruction of the catalysts, while still assuring that enough oxidant is provided to keep the catalysts in their active state. Under these reaction conditions, *no organic products were formed in the absence of the catalysts*. Shortly after starting the ozone stream, the color of the reaction mixtures changed from brown to brilliant green, the characteristic color of the oxoiron(IV) porphyrin cation radical complexes,  $Fe^{IV}(TMP^+)(O)(X)$  (1-X in Scheme 1). This behavior indicates that the rate-limiting step was oxygen-atom transfer from the 1-X complexes to the organic substrate, a conclusion which was further supported by NMR investigations under stoichiometric conditions (vide infra). For the more stable catalysts –  $Fe(TMP)Cl$  and  $Fe(TMP)(trif)$  – the green color persisted during the reactions and

gradually returned to brown only after termination of the ozone stream, while for Fe(TMP)F, Fe(TMP)OAc, and Fe(TMP)(ClO<sub>4</sub>) the color changed to black with time. Examination of the solutions at the end of the reactions by UV–Vis showed significant bleaching of the last three catalysts, and also served to ensure that the original axial ligand of all Fe<sup>III</sup>(TMP)(X) catalysts remained intact. Finally, in the presence of 5% MeOH a very different behavior was observed. Regardless of the particular catalyst (checked for Fe(TMP)Cl, Fe(TMP)(trif), and Fe(TMP)(ClO<sub>4</sub>)), the reaction mixture remained green for many hours after stopping the ozone stream and no organic products were formed (entry 6 in Table 1).

Product analysis of the reaction mixtures by GC as a function of time revealed the formation of sec-phenethyl alcohol and only small amounts (< 8%) of acetophenone. The reactions were followed up to formation of about 11 equivalents of alcohol, which ensured that the decrease in substrate concentration was negligible (< 0.4%) and had no effect on the catalytic rates. In Table 1, the numerical results for all catalysts are presented in terms of catalytic rates (turnover/h) and stability. Lack of stability was recognized as a decrease in the turnover number with time. The effect of the axial ligands on both the reactivity and stability of the catalysts is further demonstrated in Fig. 1, where the reaction profiles in the presence of Fe(TMP)Cl and Fe(TMP)F are compared. The greater slope of the Fe(TMP)F catalyzed reaction is due to

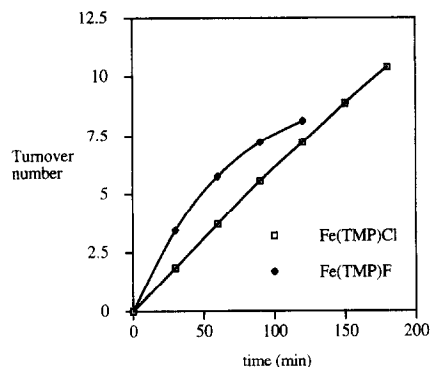


Fig. 1. Time dependent evolution (in turnover numbers, mol alcohol/mol catalyst) of sec-phenethyl alcohol in ozonolysis of ethylbenzene in the presence of catalytic amounts of Fe<sup>III</sup>(TMP)Cl and Fe<sup>III</sup>(TMP)F.

the higher reactivity of this catalyst, while the significant curvature reflects its rather low stability.

The results clearly indicate that the effect of the axial ligands in the present system is twofold. They affect both the reactivity of the catalyst toward the organic substrate and its stability toward bleaching. Bleaching is apparent from the curvature in the plot of percentage of products vs. time and was in perfect correlation with the earlier mentioned examination of the reaction mixtures by UV–Vis. For instance, while Fe(TMP)F appeared to be the most reactive catalyst, it suffered most from bleaching. After about one hour, alcohol production decreased and the UV–Vis spectrum of the reaction mixture indicated that most of the catalyst was destroyed (the intensity of the Soret band decreased to 20% of its original value). On the other hand, the somewhat less reactive Fe(TMP)Cl and Fe(TMP)(trif) catalysts were still active after more than two hours and their electronic spectra was unaffected. Because of the dual effect of the axial ligands it is not possible at the present stage to draw detailed mechanistic conclusions from the data of most reactions. But, comparing the relative reactivities of oxygen-atom transfer from the various 1-X complexes to ethylbenzene and styrene is most revealing. In the epoxidation of styrene,

Table 1

The reactivity and stability of the various catalysts in hydroxylation of ethylbenzene by ozone in CH<sub>2</sub>Cl<sub>2</sub> at -78°C

Entry	Fe <sup>III</sup> (TMP)X X =	Turnovers/h	Stability (min) <sup>a</sup>
1	F <sup>-</sup>	6.8	30
2	Cl <sup>-</sup>	3.7	120
3	AcO <sup>-</sup>	2.0	< 30
4	trif <sup>-</sup>	4.8	120
5	ClO <sub>4</sub> <sup>-</sup>	5.6	< 60
6	MeOH	0	> 120

<sup>a</sup> For the definition of stability, see text.

we have previously found a reactivity pattern of  $1\text{-F} > 1\text{-Cl} > 1\text{-OAc} > 1\text{-trif} \gg 1\text{-ClO}_4$  [6]. While the complex  $1\text{-ClO}_4$  did not produce any organic product in its reaction with styrene, it was the second most reactive catalyst for hydroxylation of ethylbenzene. It is thus apparent that the mechanistic aspects of hydroxylation and epoxidation by the same complexes are distinctly different, reinforcing our earlier conclusions from studies of internal competitive hydroxylation and epoxidation of cyclohexene [14].

### 3.2. The inhibitory effect of methanol on catalysis by the $\text{Fe}^{\text{III}}(\text{TMP})(\text{X})$ complexes

The most surprising result was the inhibitory effect of MeOH in the present system. The reactions of entries 2 and 6 of Table 1 were performed in identical ways, besides the presence of 5% MeOH in the latter case. Under these conditions, it is well known that the active form of the catalyst is an oxoiron(IV) porphyrin cation radical complex with MeOH as axial ligand ( $1\text{-MeOH}$ ) [13]. Besides the fact that in the epoxidation of olefins,  $1\text{-MeOH}$  is more reactive than  $1\text{-Cl}$  [6,15], this apparent inhibitory effect of MeOH on hydroxylation could have additional implications. Since the green color due to  $1\text{-MeOH}$  persisted even after the ozone stream was stopped, it appears that coordination of MeOH to the oxoiron(IV) ion decreased its reactivity toward the alkane. To confirm this conclusion and to rule out other possibilities, such as MeOH-induced reduction to the much less reactive  $\text{Fe}^{\text{IV}}(\text{TMP})(\text{OCH}_3)_2$  or  $\text{Fe}^{\text{IV}}(\text{TMP})(\text{O})$  complexes [16], the reaction was also studied by  $^1\text{H}$  NMR under stoichiometric conditions. Two solutions of  $1\text{-Cl}$  were prepared at  $-80^\circ\text{C}$ , but to one of the tubes were added 5%  $\text{CD}_3\text{OD}$  to form a  $1\text{-CD}_3\text{OD}$  solution<sup>1</sup>. The

same amount of ethylbenzene was then added to both solutions and the reaction mixtures were inspected by NMR. While the  $1\text{-Cl}$  solution converted cleanly and completely to  $\text{Fe}^{\text{III}}(\text{TMP})\text{Cl}$  in the course of about 4 h with concurrent production of sec-phenethyl alcohol (GC), the  $1\text{-CD}_3\text{OD}$  solution remained unchanged for over 8 h and no organic products were formed. This comparative experiment served not only to ensure the inhibitory effect of MeOH, but also confirmed that in the catalytic reactions the formation of oxoiron(IV) porphyrin cation radical complexes was not rate limiting.

### 3.3. Catalysis by the chloroiron(III) complexes of TDCPP and $\text{Br}_8\text{-TMP}$

As mentioned in the introduction, metal complexes of TMP are probably the best system for systematic studies of the variables which were discussed in the previous sections. But, their catalytic activity is known to be low, compared to derivatives which are halogenated at either the phenyl rings or the  $\beta$ -pyrrole positions [7,11]. Thus, it was of interest to compare the ozonolysis of ethylbenzene under  $\text{Fe}(\text{TMP})\text{Cl}$  catalysis to that of the representatives of each class. For that purpose we chose the chloroiron(III) complexes of TDCPP and  $\text{Br}_8\text{-TMP}$ . Since we expected the two last mentioned catalysts to be more robust, as well as more reactive, the rate of ozone introduction was increased to 22–26  $\mu\text{mol/h}$ . The results of this investigation are shown in Fig. 2, in which the filled  $\blacksquare$ ,  $\blacklozenge$ , and  $\blacktriangledown$  symbols stand for the reactions catalyzed by  $\text{Fe}(\text{TDCPP})\text{Cl}$ ,  $\text{Fe}(\text{Br}_8\text{-TMP})\text{Cl}$ , and  $\text{Fe}(\text{TMP})\text{Cl}$ , respectively.

The comparison between  $\text{Fe}(\text{TMP})\text{Cl}$  and  $\text{Fe}(\text{Br}_8\text{-TMP})\text{Cl}$  ( $\blacktriangledown$  and  $\blacklozenge$ , respectively, in Fig. 2) clearly shows that the latter is not a better catalyst than the former. The rate of alcohol production was actually about two time faster for  $\text{Fe}(\text{TMP})\text{Cl}$ , and only because of the somewhat higher stability of  $\text{Fe}(\text{Br}_8\text{-TMP})\text{Cl}$ , the total amount of produced alcohol was similar

<sup>1</sup> Obtained by bubbling ozone at  $-78^\circ\text{C}$  for 30 s (6  $\mu\text{mol}$   $\text{O}_3$  /min, 1.1 equiv.) into a solution of 2.6  $\mu\text{mol}$  of  $\text{Fe}(\text{TMP})\text{Cl}$  in 0.6 ml  $\text{CD}_2\text{Cl}_2$ , followed by purging with  $\text{N}_2$  (70 ml/min) for 1 min.

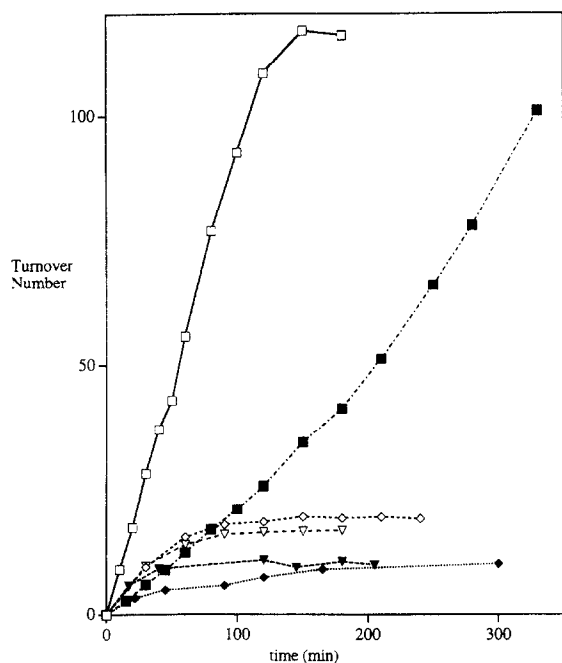


Fig. 2. Time dependant formation of sec-phenethyl alcohol in ozonolysis of ethylbenzene in the presence of catalytic amounts of the chloroiron(III) complexes of TDCPP (■), Br<sub>8</sub>-TMP (◆), and TMP (▼). The open symbols stand for the same catalysts under modified reaction conditions, as outlined in the text.

for both catalysts (about 10 equiv.). UV–Vis inspection of the aliquots which were removed from the reaction mixture for product analysis revealed that the decrease in alcohol production was accompanied by a parallel decrease of the Soret band of the iron porphyrins. In both cases, the porphyrin was destroyed at the end of the reaction. This was not the case for the much more efficient Fe(TDCPP)Cl catalyst (■ in Fig. 2), whose Soret band was almost unchanged even after 5 h.

Several possible reasons for the low efficiency of Fe(Br<sub>8</sub>-TMP)Cl as catalyst and its instability were considered; (a) low selectivity for ethylbenzene vs. CH<sub>2</sub>Cl<sub>2</sub> oxidation is responsible for the low yields. (b) oxidation of CH<sub>2</sub>Cl<sub>2</sub> produces Cl radicals which deactivate the catalyst. (c) the reactive state of the catalyst, an oxoiron(IV) porphyrin radical complex, is not formed by ozonolysis of Fe(Br<sub>8</sub>-TMP)Cl. The last possibility can be ruled out, despite the

fact that the characteristic green color of oxoiron(IV) porphyrin radicals was not observed, because of the formation of alcohol as major product. In the absence of catalyst, only acetophenone was formed under otherwise identical reaction conditions. Thus, the formation of alcohol most probably indicates that some of the extremely short-lived reactive state of the catalyst was trapped by ethylbenzene.

In order to check the other two postulates, the reaction of the two catalysts were checked in neat ethylbenzene. The absence of CH<sub>2</sub>Cl<sub>2</sub> eliminates the major source of Cl radicals, as well as the possible competition of ethylbenzene and CH<sub>2</sub>Cl<sub>2</sub> for the active form of the catalysts. Thus if postulates a or b are correct, the catalysis should become more efficient. The results, presented as the ▽ and ◇ symbols in Fig. 2, clearly show that the yields of the reactions increased for both catalysts. The comparison of the curves for Fe(Br<sub>8</sub>-TMP)Cl and Fe(TMP)Cl shows that their reactivity is about the same (the initial slopes), but that the stability of the first is somewhat larger, i.e. the plateau is reached after longer reaction times. The conclusion from the comparison of the reactions with and without CH<sub>2</sub>Cl<sub>2</sub> is that the stability of Fe(Br<sub>8</sub>-TMP)Cl is slightly higher than that of Fe(TMP)Cl, but that the selectivity for ethylbenzene vs. CH<sub>2</sub>Cl<sub>2</sub> oxidation is higher for Fe(TMP)Cl.

Finally, we have noted that the Fe(TDCPP)Cl catalyzed reaction showed a somewhat S-shaped behavior, which suggests that in this case the reaction is limited by ozone supplement. This was shown to be true by slightly modifying the reaction conditions (35 μmol O<sub>3</sub>/h, 0.66 μmol catalyst, 1.6 ml CH<sub>2</sub>Cl<sub>2</sub>, 0.4 ml ethylbenzene). In this case (□ in Fig. 2) the reaction was extremely efficient for the first two hours (2% conversion of ethylbenzene), after which significant bleaching occurred. For the first 100 min, however, the amount of alcohol produced increased linearly with time. Furthermore, the turnover numbers during that stage corresponded to formation of the alcohol in about 100% yields relative to ozone.

#### 4. Summary

In this study we have shown that ozone can be utilized as the primary oxidant in iron porphyrin catalyzed hydroxylation of an alkane, that a significant axial ligand effect – different from that of the related epoxidation reactions – does exist, and that MeOH has an inhibitory effect on the reactivity of the catalyst. The utilization of ozone is very important in the context of the increasing demand for utilization of ‘clean’ – free of problematic byproducts – oxidants [17], while the axial ligand effect has mechanistic significance. Interestingly, since MeOH would be the hydroxylation product of methane, the fact that MeOH inhibits the active form of the catalyst might have a serious impact on attempts to mimic methane monooxygenase activity [18] by model systems of cytochrome P-450. The limited investigation of the iron(III) complexes of two halogenated porphyrins suggests that halogenation of the phenyl rings improves both the reactivity and the robustness of the catalyst more than halogenation of the pyrrole hydrogens. Based on the knowledge acquired from the present study, we are currently investigating the catalytic applications of a large variety of phenyl- and  $\beta$ -pyrrole-halogenated metalloporphyrins with emphasis on derivatives in which both positions are halogenated.

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