Ozone as primary oxidant in iron(III) porphyrin catalyzed hydroxylation of hydrocarbons

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Abstract

Iron porphyrins with halogen substituents at the β-pyrrole positions are found to be poorer catalysts for hydroxylation of ethylbenzene by ozone than the corresponding unsubstituted complexes. For the best catalyst, the chloroiron(III) complex of tetra-(2,6-dichlorophenyl)porphyrin, the initial process proceeds in quantitative yields relative to ozone. Inactivation of the catalytic process after formation of about 100–140 mol alcohol/mol catalyst is attributed to product inhibition.

Keywords: Catalysis; Iron porphyrins; Hydroxylation; Ozone
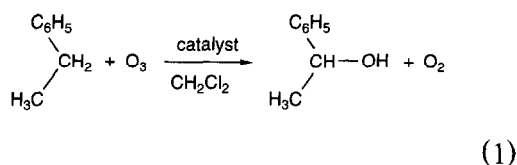
1. Introduction

The extensive studies of synthetic iron porphyrins as model complexes of cytochrome P-450 monooxygenases are devoted to both mechanistic and practical aspects of their utilization as catalysts for oxygenation of inactivated hydrocarbons (for recent review articles, see [1,2]). The mechanistic investigations have led to the conclusion that the most reactive intermediates in the catalytic cycles of the synthetic catalysts and many heme-dependant enzymes are cationic oxoiron(IV) porphyrin cation radical complexes with an axial ligand *trans* to the oxoiron(IV) bond (for other less reactive intermediates, see [3,4,2]). The efficiency of catalysis was remarkably improved over the years by replacing the original metal complexes of tetraphenylporphyrin by derivatives in which the phenyl CH's are substituted by halogens, and complexes in which the β-pyrrole positions are also halogenated were recently introduced [2]. Representative examples of these three generations of catalysts are shown in Scheme 1. The porphyrin ring in the heavily substituted third generation catalysts was shown to be highly distorted, an important factor affecting their steric and electronic features [5,6]. Most important, although improvement of catalytic stability and reactivity was achieved by halogenation of the β-pyrrole positions [7], several lines of evidence are indicative for a significant change in reaction mechanism compared to first and second generation catalysts [8].

As part of an ongoing effort for elucidation of the effect of axial ligands on the reactivity of metalloporphyrin based biomimetic catalysts we have recently reported the catalytic conversion

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of ethylbenzene to the corresponding alcohol by ozone at low temperatures (Eq. (1)) [9,10].

$$C_6H_5 \text{--} \underset{H_3C}{CH_2} + O_3 \xrightarrow[\text{CH}_2\text{Cl}_2]{\text{catalyst}} C_6H_5 \text{--} \underset{H_3C}{CH} \text{--OH} + O_2 \tag{1}$$

The major advantages of that system were: (a) ozone is a clean oxidant; (b) the original axial ligand of the catalyst was not replaced during the reaction; (c) direct reaction of ozone with the alkane was negligible; (d) it was assured that the rate limiting step was reaction of the oxoiron(IV) porphyrin cation radical intermedi-

ate with the alkane. In the previous studies we have concentrated on the *principles* which determine the efficiency of the system by utilizing the limited-potential, but very well characterized, Fe(III)(TMP)X catalysts (see Scheme 1, X = axial ligand). The most important finding was that both the stability and the reactivity of the catalyst were affected by its axial ligand, with the particular case of methanol that stabilized the oxidized form of the catalyst to an extent which completely diminished its reactivity toward the alkane.
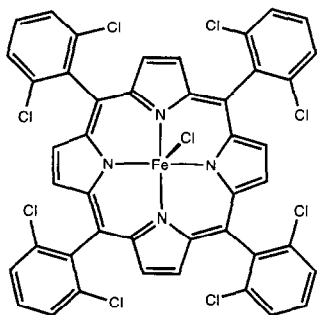
Because of the above mentioned advantages, we have decided to extent the studies to catalysis by more efficient iron porphyrins, in particular by the second and third generation catalysts,
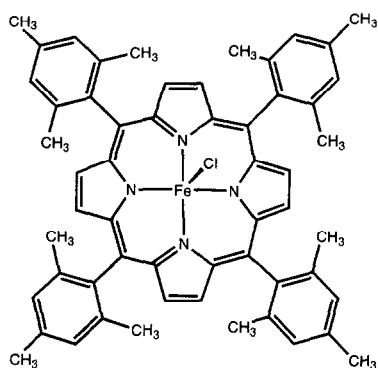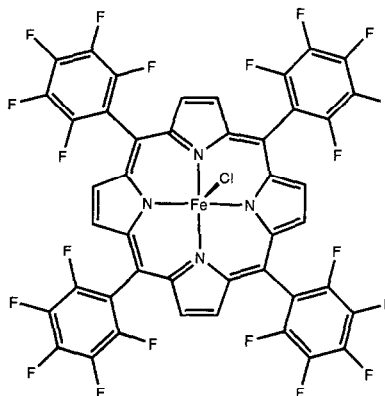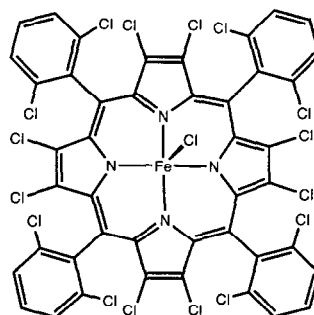

Fe^{III}(TMP)Cl   Fe^{III}(TPFPP)Cl

Fe^{III}(TDCPP)Cl   Fe^{III}(Cl$_8$-TDCPP)Cl

Scheme 1. Formulas of iron porphyrins of the first (TMP), second (TPFPP and TDCPP) and third (Cl$_8$-TDCPP) generation of catalysts used in the present studies.

Fe(III)(TDCPP)Cl and Fe(III)(Cl$_8$-TDCPP)Cl, respectively. In the present communication we report two very significant observations: (a) Fe(III)(TDCPP)Cl is a much *better* catalyst than Fe(III)(Cl$_8$-TDCPP)Cl in the present system; (b) product inhibition by coordination of the produced alcohol to the catalyst severely limits the catalytic efficiency. All results are explained by the high selectivity of the catalytic system for the biomimetic reaction mechanism on the expense of different reaction pathways.

2. Experimental section

Fe(III)(TDCPP)Cl was available from our previous studies and served for preparation of Fe(III)(TDCPP)ClO$_4$ via ligand metathesis by Ag(ClO$_4$), similar to that of the TMP derivative [10]. Fe(III)(Cl$_8$-TDCPP)Cl was prepared by chlorination of Fe(III)(TDCPP)Cl as previously described, recrystallized from CH$_2$Cl$_2$/n-hexane and analyzed by TLC, UV–vis and ^{1}H NMR [6]. Reaction conditions are given in the legends of the Figures. All other experimental details were identical to those reported in our previous studies [10]. The accuracy of the results is ±5%.

3. Results and discussion

Three variables which determine the effectiveness of iron porphyrin catalyzed ozonolysis of 1.63 M ethylbenzene in CH$_2$Cl$_2$ (Eq. (1)) were investigated by examination of the time dependant turnover numbers (mol product/mol catalyst). The effect of the rate of ozone introduction and of temperature is shown for Fe(III)(TDCPP)Cl catalyzed reactions in Figs. 1 and 2, respectively, while the effect of the porphyrin structure is demonstrated in Fig. 3. The remarkable difference between slopes a and b of Fig. 1 clearly indicates that at 22 mmol O$_3$/h the rate limiting process was supplement of ozone. Only a small increase in catalytic rate

was observed by increasing the rate of ozone introduction from 35 to 150 μmol/h, which shows that this limitation was resolved. Accordingly, in all other experiments the conditions of 150 μmol O$_3$/h were conserved. Under the conditions of slope a, as well as at short reaction times for the conditions of slopes b and c, the yields of product relative to ozone were quantitative. For example, for 35 μmol O$_3$/h and 0.66 μmol catalyst, the highest possible turnover number is 53 and the experimental number was 56. But, at longer reaction times and high concentration of ozone the reaction stopped after formation of 100–120 equivalents of alcohol. Examination of the UV–vis spectrum of the final reaction mixture indicated that all the catalyst was destroyed, and a qualitative correlation between the decease of alcohol formation and the amount of deactivated catalyst was found at all reaction times.

The effect of temperature for the Fe(III)(TDCPP)Cl catalyzed reaction is shown in Fig. 2. The catalytic rate increased in going from −78 to −63°C, but decreased at higher temperatures. In all cases, the UV–vis spectra indicated that the catalyst was completely destroyed after about 90 min, which is also appar-
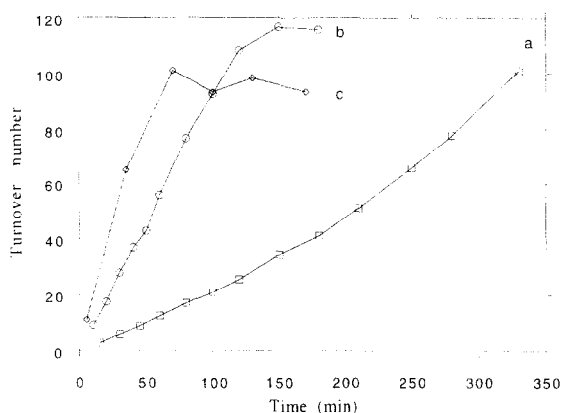

Fig. 1. Time dependant formation of sec-phenethyl alcohol in ozonolysis of 1.63 M ethylbenzene/CH$_2$Cl$_2$ at −78°C in the presence of catalytic amounts of Fe(III)(TDCPP)Cl: (a) 0.56 mM catalyst, 22 μmol O$_3$/h; (b) 0.33 mM catalyst, 35 μmol O$_3$/h; (c) 0.32 mM catalyst, 150 μmol O$_3$/h. At these conditions, selectivity to formation of sec-phenethyl alcohol was very high. Acetophenone was less than 5% of the products.

ent from the decrease of alcohol formation and increase in formation of ketone — the product of non-catalyzed ozonolysis of ethylbenzene. Another very important difference was the color of the reaction mixtures, brilliant green at −78°C, deep red at 0°C, and a mixture of both colors at the other temperatures. The brilliant green and the deep red colors are characteristic of oxoiron(IV) porphyrin cation radicals and oxoiron(IV) porphyrins [3], Fe(IV)(TDCPP$^{+\cdot}$)(O)(Cl) and Fe(IV)(TDCPP)(O), respectively, in the present case. The rate of hydroxylation by Fe(IV)(TDCPP)(O) is expected to be much slower than by Fe(IV)(TDCPP$^{+\cdot}$)(O)(Cl) [3], and since the former complex is a one-electron oxidant, the selectivity for formation of alcohol is expected to decrease. All the observations lead to the conclusion that at temperatures higher than −63°C, the relative importance of Fe(IV)(TDCPP$^{+\cdot}$)(O)(Cl) as major intermediate responsible for the hydroxylation process is decreased, because of its decay to Fe(IV)(TDCPP)(O).

The effect of porphyrin structure is shown in Fig. 3 for Fe(III)(TDCPP)Cl, Fe(III)(Cl$_8$-TDCPP)Cl, and Fe(III)(TDCPP)(ClO$_4$). The ac-
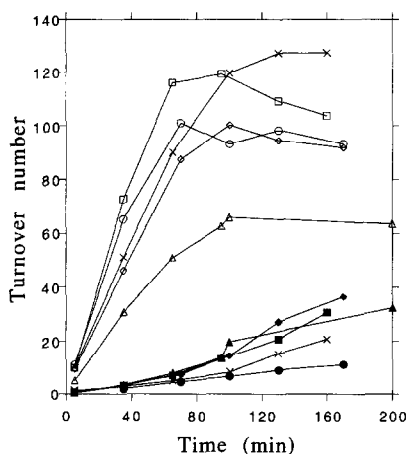

Fig. 3. Time dependant formation of sec-phenethyl alcohol (empty symbols) and acetophenone (filled symbols) in ozonolysis of 1.63 M ethylbenzene/CH$_2$Cl$_2$ by 150 μmol O$_3$/h at −78°C in the presence of 0.12 mM catalyst: (●) Fe(III)(TDCPP)Cl; (▲) Fe(III)(Cl$_8$-TDCPP)Cl; (■) Fe(III)(TDCPP)(ClO$_4$).
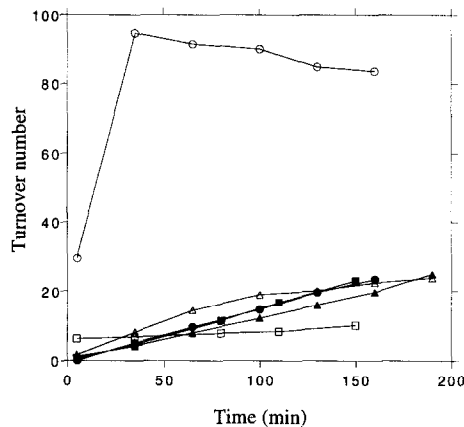

Fig. 2. Time dependant formation of sec-phenethyl alcohol (empty symbols) and acetophenone (filled symbols) in ozonolysis of 1.63 M ethylbenzene/CH$_2$Cl$_2$ by 150 μmol O$_3$/h in the presence of 0.32 mM Fe(III)(TDCPP)Cl: (●) −78°C; (■) −63°C; (×) −42°C; (♦) −23°C; (▲) 0°C.

tivity of Fe(III)(TPFPP)Cl and Fe(III)(TDCPP)Cl in 5% CH$_3$OH solutions was as low as that of Fe(III)(TDCPP)(ClO$_4$); almost no alcohol was formed and the amount of ketone was identical to that of a reaction without any catalyst. Our explanation for these very surprising results is based on the assumption that the only important active form of the catalysts is the oxoiron(IV) porphyrin cation radical intermediate. This raises the following three questions: (a) Can such intermediates be formed? (b) How reactive are they toward the alkane? (c) How stable are they with respect to destruction by excess ozone? The answer to the first question is definitely positive for all catalysts besides Fe(III)(Cl$_8$-TDCPP)Cl, since their oxidized form was previously characterized [11]. The reactivity toward alkane is expected to increase in the order of Fe(III)(Cl$_8$-TDCPP)Cl > Fe(III)(TPFPP)Cl > Fe(III)(TDCPP)(Cl), which is very different from the current results. From UV–vis inspection of the reaction mixtures it became clear that destruction of the catalyst is the major effect. The reason behind this phenomenon, as well as the large difference in stability between Fe(III)(TDCPP)(Cl) and Fe(III)(TDCPP)(ClO$_4$) or Fe(III)(TDCPP)(Cl) in 5% MeOH solutions is however intriguing.
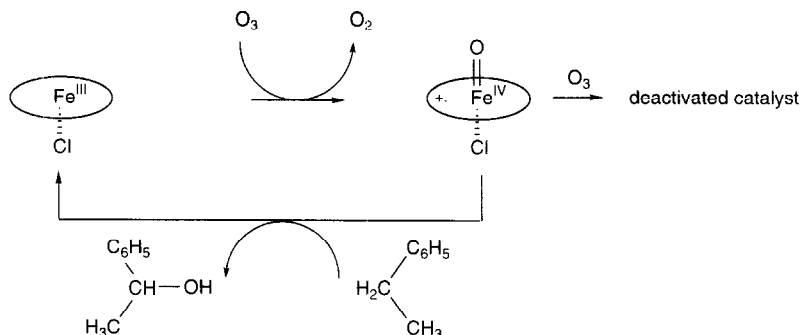
Scheme 2. Reaction mechanism of the iron porphyrin catalyzed hydroxylation of ethylbenzene by ozone.

In our previous studies with Fe(III)(TMP)Cl we have proven that the retarding effect of McOH was due to very low reactivity of the MeOH-coordinated oxoiron(IV) porphyrin cation radical toward the alkane [10]. The pronounced deactivating effect of MeOH in the present system, led us to investigate the possibility that the alcohol formed in the reactions had a similar effect. We thus examined the oxygenation reaction of ethylbenzene by ozone under Fe(III)(TDCPP)(Cl) catalysis in a solution which contained already 100 equivalents of the product, sec-phenethyl alcohol. The results were highly revealing indeed; only 50 additional equivalents of product were formed and the catalyst was almost completely destroyed after 5 min. This contrasts with the regular results, where the catalyst was active for 35 min and 100 equivalents of products were formed. We thus conclude that the product reduced the reactivity of the active intermediate toward the alkane, similar to the effect of MeOH. Because of that, an alternative destructive pathway becomes dominant (Scheme 2). The phenomenon of product inhibition is probably responsible for the rest of the results as well. It explains the limitation of the current system to a total turnover number of 100–120 mol product/mol catalyst, despite the fact that at early times the yields are very high. The very low activity of Fe(III)(TDCPP)(ClO$_4$) is attributed to easy displacement of the perchlorato ligand by alcohol. Similarly, in the electron deficient Fe(III)(Cl$_8$-TDCPP)(Cl) and Fe(III)(TPFPP)(Cl) complexes

coordination by alcohol is expected to be very efficient.

In summary, we have shown that ozone can be utilized as the primary oxidant in iron porphyrin catalyzed hydroxylation of an alkane, that Fe(III)(TDCPP)(Cl) is much more effective than the third generation catalyst Fe(III)(Cl$_8$-TDCPP)(Cl), and that a highly significant product inhibition process is involved. Preliminary results show that similar phenomena are also important in the standard iron porphyrin catalyzed hydroxylation of hydrocarbons by iodosylbenzene at room temperature.

Acknowledgements

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