

Hydroxylation of Simple Alkanes by Iodosylbenzene is Catalyzed more Efficiently by Second than by Third Generation Iron(III) Porphyrins

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Abstract: The catalytic activities of aryl-chlorinated iron tetraarylporphyrins with and without chloro substituents at the β -pyrrole positions— third and second generation catalysts, respectively— were compared for the hydroxylation of ethylbenzene and cyclohexane by iodosylbenzene. The results reveal that despite the somewhat larger stability of the former complexes to the oxidative reaction conditions, they are less efficient catalysts than the corresponding unsubstituted complexes, which catalyze the transformation of the alkanes into their oxygenated products with almost 80% yield at more than 10% conversion. It is proposed that for the third generation catalyst the extremely short life time of the most potent intermediate is responsible for the relatively low efficiency in catalysis. © 1998 Published by Elsevier Science Ltd. All rights reserved.

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We have recently reported the iron(III) porphyrin catalyzed hydroxylation of ethylbenzene by ozone at low temperatures,^{1, 2} by both so-called second generation (ortho-phenyl substituted tetraphenylporphyrins) and third generation catalysts (achieved by β -pyrrole halogenation of the former complexes).^{3, 4} Surprisingly, we have not found any beneficial effect of β -pyrrole halogenation of the porphyrins on the efficiency of the process. The brominated complex **2** was not a better catalyst than derivative **1**, and while up to 120 turnovers were obtained with complex **3** as the catalyst, the maximum turnover number with the chlorinated complex **5** was only 20 (see Scheme 1 for the structures). We have now decided to investigate this surprising phenomenon under more conventional reaction conditions, hydroxylation of alkanes by iodosylbenzene at ambient temperature.⁵

Scheme 1. The iron porphyrins mentioned in the text.

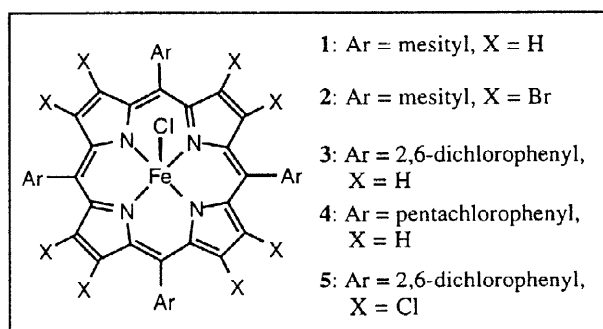


Table 1. Oxidation of ethylbenzene by iodosylbenzene, catalyzed by **3**, **4**, and **5**.^a

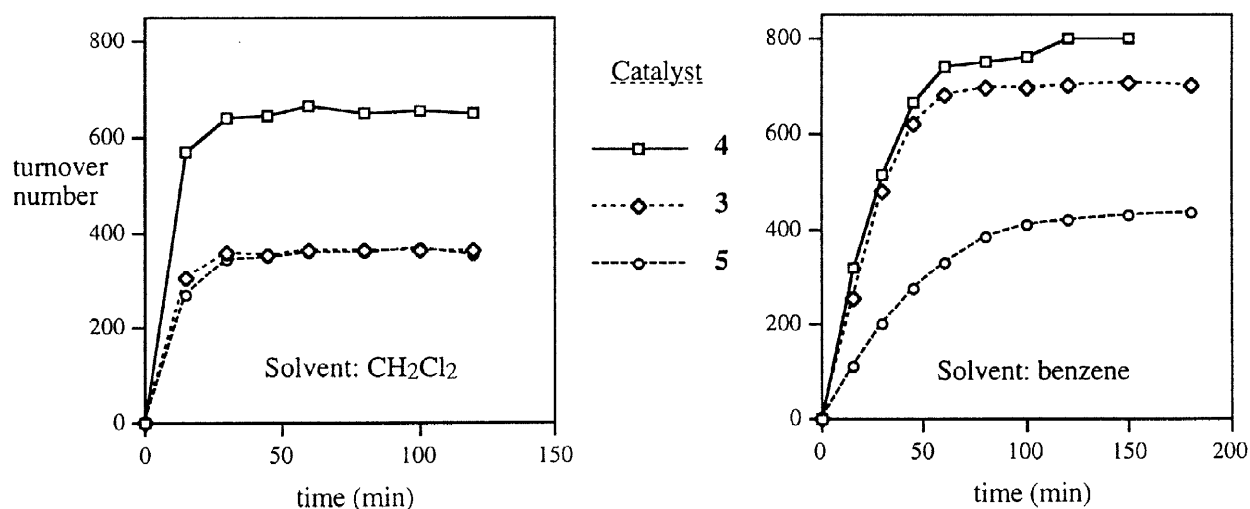
Catalyst/Solvent	Alcohol ^b	Ketone ^b	conversion ^c	yield ^d
3 /CH ₂ Cl ₂	361	92	5.3	27.3
4 /CH ₂ Cl ₂	637	158	9.6	47.7
5 /CH ₂ Cl ₂	351	78	5.0	25.4
3 /benzene	703	324	11.3	67.6
4 /benzene	799	375	12.9	77.5
5 /benzene	439	145	6.1	36.5

^a 0.18–0.20 M catalyst, 8300–8500 equivalents ethylbenzene, and 2000 equivalents iodosylbenzene. ^b alcohol = *sec*-phenethyl alcohol, ketone = acetophenone, in mol product/mol catalyst. ^c % of products, relative to ethylbenzene. ^d relative to iodosylbenzene, taking into account that 2 equivalents of iodosylbenzene are required for the formation of acetophenone.

Two second generation iron(III) porphyrins (**3** and **4**) and one third generation complex (**5**) were examined as catalysts for the hydroxylation of ethylbenzene and the less reactive cyclohexane. An additional important research goal was the development of reaction conditions for high catalytic turnovers at significant conversion of the hydrocarbons into their oxygenated products, in contrast to most reports which were limited to 20 - 100 catalytic turnovers and sub-percentage of conversions.³⁻⁶ Also, most commonly the yields are only reported in terms of products vs. consumed oxidant. The results of the current investigation were obtained by addition of 2000 equivalents of iodobenzene to solutions which contained 0.2 mM catalyst and about 8500 equivalents of substrate. Also present in the solutions were 50 equivalents of nitrobenzene as an internal standard, which allowed the determination of the absolute efficiency of the reactions (% conversion), in addition to the yields relative to the oxidant. Accordingly, the reactions are driven toward maximal values of 23% conversion and 2000 catalytic turnovers.

The results for hydroxylation of ethylbenzene by iodobenzene in two solvents (CH_2Cl_2 and benzene, Table 1 and Figure 1) disclose several significant phenomena: a) The initial slopes are larger in CH_2Cl_2 , i.e. the reactions are faster therein. b) The plateau is reached earlier in CH_2Cl_2 , which indicates that the lifetimes of the catalysts are larger in benzene. c) The final product yields are higher in benzene than in CH_2Cl_2 , clear evidence that of the two above mentioned opposite effects the second is more beneficial for effective catalysis. d) The least efficient catalyst was the third generation complex **5**. For example, the chemical yields relative to ethylbenzene (yields relative to the oxidant are given in the parentheses) in the reactions performed in benzene were 12.9 (78), 11.3 (68), and 6.1 (36) % with catalysts **4**, **3**, and **5**, respectively. e) At the end of the reactions the catalysts were almost completely bleached (UV-vis), including the more robust **5**. The seemingly relative long lifetime of **5** (best seen in Fig. 1b) is misleading, since at identical times less iodobenzene was consumed by this catalyst. For example, 15 min after initiation of the reactions performed in benzene, 18.5, 25, and 11.7% of iodobenzene were formed with catalysts **3**, **4**, and **5**, respectively.

Figure 1. Time dependent formation of *sec*-phenethyl alcohol in the **3** - **5** catalyzed reaction of ethylbenzene with iodobenzene.



The beneficial effect of aromatic vs. chlorinated solvents was already appreciated in our earlier studies, including with chiral metalloporphyrins.⁷ The reduced yields in CH_2Cl_2 may be attributed to two effects; participation of CH_2Cl_2 as an oxidizable substrate and the formation of chlorine radicals, which destroy the

catalysts. The faster rates in CH_2Cl_2 probably have no mechanistic significance, as the rate limiting step is the formation of an active iron porphyrin intermediate, which in turn is governed by the low solubility of iodosylbenzene in the solvents. But, the relatively poor results with **5** as catalyst are very surprising in the context of the attempts to improve the efficiency of metalloporphyrin catalyzed hydroxylation of alkanes. Accordingly, oxidation of the less reactive cyclohexane was also investigated.

The results for the **3** - **5** catalyzed oxidation of cyclohexane are provided in Table 2, and Figure 2 shows the comparison between **3** and **5**. Again, the beneficial effect of benzene vs. CH_2Cl_2 as solvent is quite pronounced, and the effectiveness of the catalysts in terms of final chemical yields increases in the order of $5 < 3 < 4$. Inspection of Figure 2 shows that after 80 min with **3** as catalyst the iodosylbenzene is quantitatively transformed into iodobenzene, with 73% selectivity toward formation of cyclohexanol and cyclohexanone. At the same time and identical reaction conditions with **5** as catalyst, 56% of iodobenzene is formed with only 63% selectivity.

Figure 2. Time dependent formation of iodobenzene (O), cyclohexanol (\diamond), and cyclohexanone (Δ) in the **3** (full lines) and **5** (broken lines) catalyzed reaction of cyclohexane with iodosylbenzene in benzene.

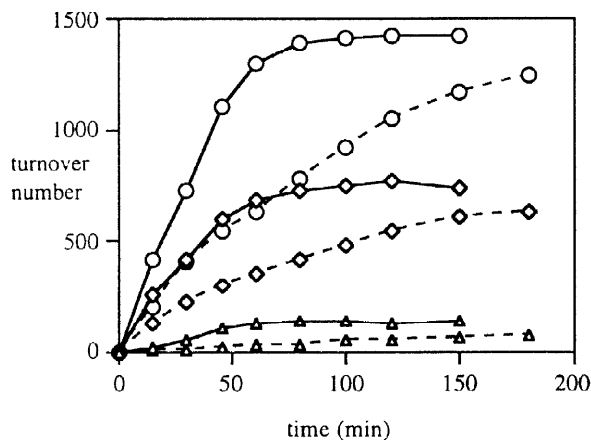


Table 2. Oxidation of cyclohexane by iodosylbenzene, catalyzed by **3**, **4**, and **5**.^a

Catalyst/Solvent	Alcohol ^b	Ketone ^b	conversion ^c	yield ^d
3 / CH_2Cl_2	282	29	3.6	17.0
4 / CH_2Cl_2	540	77	6.9	34.7
3 /benzene	874	249	11.6	68.6
4 /benzene	895	253	13.9	70.0
3 /benzene ^e	740	140	3.6	72.9
5 /benzene ^e	637	79	2.8	56.8

^a 0.19-0.22 M catalyst, 8500-9000 equivalents cyclohexane, and 2000 equivalents iodosylbenzene. ^b alcohol = cyclohexanol, ketone = cyclohexanone, in mol product/mol catalyst. ^c % of products, relative to cyclohexane. ^d relative to iodosylbenzene, taking into account that 2 equivalents of iodosylbenzene are required for the formation of cyclohexanone. ^e 0.08 M catalyst, 24,500 equivalents cyclohexane, and 1400 equivalents iodosylbenzene.

From these results we may conclude that the third generation complex **5** is a significantly poorer catalyst than the second generation complexes **3** and **4**, both in terms of total turnover numbers and in turnover/time. Several reasons for this quite unexpected result may come to mind. It is well known that the porphyrin ring in the heavily substituted third generation catalysts is highly distorted, an important factor affecting their steric and electronic features.⁸ Also, several lines of evidence are indicative of a significant change in reaction mechanism between first and second generation catalysts under certain conditions.⁹ The simple substrates employed in this study almost certainly rule out steric effects, and the quite similar alcohol/ketone ratio obtained with all three catalysts are supportive of oxometal species as the main intermediates with all catalysts.

The conflict of the current investigation with the various reports about the superiority of third generation catalysts in terms of catalytic stability, reactivity, and selectivity is most probably only artificial. Our results were obtained at conditions which lead to much higher turnovers (> 1000) and conversions (> 10%) than most other investigations, which were limited to less than 100 turnovers and sub percentage conversions.³⁻⁶ If we examine

our results at short reaction times, a seemingly superior selectivity of **5** over **3** and **4** is indeed apparent. For example, in the reaction of ethylbenzene with iodosylbenzene in benzene, the alcohol/ketone ratio after 15 min is 5.4, 4.2, and 3.3 for catalysts **5**, **4**, and **3**, respectively. These numbers are however misleading, since the **5** catalyzed reaction proceeds only to about half the extent of those catalyzed by **3** and **4** (see Figure 1). Similarly, at the end of the reactions the product ratios are lower with all catalysts, with practically identical numbers in the **3** and **4** catalyzed reactions (2.16 and 2.13, respectively), and an alcohol/ketone ratio of 3.03 in the reaction catalyzed by **5**. But, the last reaction proceeds to approximately half the extent of the two other (see Table 1).

We conclude that for significant conversion of simple unactivated alkanes into their oxygenated products there is no real advantage in using the much less accessible third generation iron porphyrins. A simple solvent change from the most commonly used CH_2Cl_2 to benzene is much more beneficial. This situation is very different from that of the analogous manganese complexes, for which the third generation porphyrins are clearly superior.^{3,10} This contrariety is most probably related to the differences in the structure of their most reactive intermediates, oxoiron(IV) porphyrin radical vs. oxomanganese(V) porphyrin. As for iron, but not for the manganese complexes, the porphyrin has to be oxidized during catalysis, excessive substitution by electron withdrawing groups on the porphyrin periphery eventually prohibits the formation of the key intermediate.¹¹ Accordingly, we propose that the increased difficulty in obtaining the oxoiron(IV) porphyrin radical intermediate of **5** is responsible for the low turnover/time, and that the exceedingly large reactivity of that intermediate leads to non productive pathways which are responsible for the relatively low number of total turnovers.

Acknowledgments

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