Oxene versus Non-oxene Reactive Intermediates in Iron(III) Porphyrin Catalyzed Oxidation Reactions: Organometallic Compounds as Diagnostic Probes

Kaliappan Kamaraj and Debkumar Bandyopadhyay*

Department of Chemistry, Indian Institute of Technology New Delhi-110016, India

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The iron(III) porphyrin catalyzed alkane hydroxylation and olefin epoxidation by oxidants such as MCPBA, C_6H_5IO, C_6F_5IO, H_2O_2, and hydroperoxides have been extensively studied.[1] An almost universally accepted mechanism of these oxidation reactions, except for minor details, is shown in eq 1, where P

$$[PFe(III)]^+ + Ox \overset{fast}{\rightleftharpoons} \underset{\text{(intermediate-A)}}{PFe(III)\text{-}Ox} \xrightarrow{rds} \underset{\text{(intermediate-B)}}{\text{oxene or non-oxene}} \xrightarrow{S} SO + [PFe(III)]^+ \quad (1)$$

is porphyrin dianion, Ox is oxidant, oxene is π cation radical of an oxoiron(IV) porphyrin, non-oxene is *t*-BuOO$^\bullet$ or oxoiron(IV) porphyrin depending upon the oxidants, S is substrate, and SO is oxidized product.[1n,2] Stereoselectivity and stereospecificity, along with the dependence of rate on the nature of oxidant, structure of catalyst, deuterium content, and buffer concentration of the solvent, have been used to suggest the above generalized mechanism. Intermediate B is oxene, when MCPBA and C_6H_5IO are the terminal oxidants as evidenced by Groves et al. (eq 2).[3a] The two types of oxene intermediates generated by

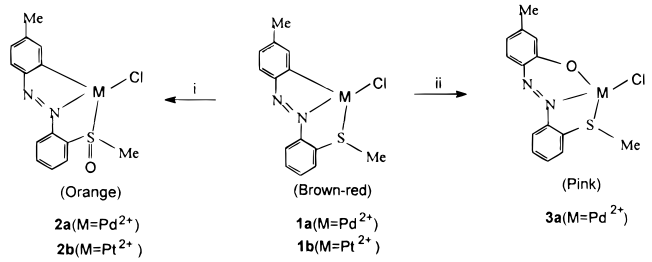
$$[PFe(III)]^+ + ArCO_3H \overset{fast}{\rightleftharpoons} \underset{\text{intermediate-C}}{[PFe(III)]^{+}(O\text{-}C(O)Ar)} + H^+ \xrightarrow{rds} \underset{\text{(oxene)}}{P^{+\bullet}Fe(IV)=O} + ArCO_2H \quad (2)$$

reacting $TMPFe^{III}Cl$ with MCPBA and C_6H_5IO are only different in their axial ligation to iron(IV).[3b] Oxoiron(IV) porphyrin and peroxyl free radicals on the other hand are found to be more rational reactive intermediates in explaining the product profiles where hydroperoxides are terminal oxidants (eqs 3−4).[4,5] In fact, the radical-chain mechanism for alkyl hydroperoxides has been very strongly supported by many others.[6,7] These studies are not in agreement with the proposed heterolytic cleavage of peroxy bonds of all oxidants (peroxides and peracids) to give oxene, which finally oxidizes the substrate.[1k−n] Herein we present the reactions of the above-noted reactive intermediates with organometallic compounds. Our result critically analyzes the nature of reactive intermediates present in solution and brings forward the important role played by the oxene precursor (intermediate C, eq 2) which remained almost unnoticed in these oxidation reactions.

$$ROOH + [PFe(III)]^+ \longrightarrow [P\,Fe(IV)\text{-}OH]^+ + RO^\bullet \quad (3)$$

$$ROOH + [P\,Fe(IV)\text{-}OH]^+ \longrightarrow [P\,Fe(III)\text{-}H_2O]^+ + ROO^\bullet \quad (4)$$

Scheme 1[a]



[a] Reagents and conditions: (i) $F_{20}TPPFe^{III}Cl-C_6F_5IO$ in CH_2Cl_2 at 33 °C. (ii) MCPBA or C_6F_5IO or *t*-BuOO$^\bullet$ or $F_{20}TPPFe^{III}Cl$−MCPBA in toluene.

All of the compounds shown in Scheme 1 are independently synthesized and are thoroughly characterized as previously described.[8] Compound **1a** shows incredible selectivity toward the reactive intermediates proposed in iron(III) porphyrin catalyzed oxidation reactions (intermediates A and B, eq 1). This is presented in Scheme 1. Throughout this work, we have used iron(III) tetrakis(pentafluorophenyl)porphyrin chloride ($F_{20}TPPFe^{III}Cl$) as the catalyst because all the rates of reactions of various oxidants with this catalyst are known.[1n] That C_6F_5IO C_6H_5IO react with iron(III) porphyrins to give oxene is unanimously concluded.[1n,3,9] Therefore compounds **1a,b** were first reacted with oxene to observe the selectivity. We obtained **2a** and **2b,** respectively, as the only major oxidized products. In a representative experiment,12.8 mg (0.027 mmol) of **1b** was dissolved in CH_2Cl_2 (10 mL) and 0.96 mg (0.0009 mmol) of $F_{20}TPPFe^{III}Cl$ was added at room temperature (33 °C), followed by 8.9 mg (0.028 mmol) of solid C_6F_5IO (97%). The contents were stirred magnetically for only 4 min (until all the oxidant was completely dissolved), and the reaction mixture was added directly at the top of the silica gel column (1 cm × 15 cm) which was preequilibrated in petroleum ether (40:60). The unreacted compound, **1b** (3.2 mg) and a pink yet uncharacterized product (<1%) were first eluted with CH_2Cl_2. The pure orange band of the major product **2b** was eluted next with 0.2% CH_3OH in CH_2Cl_2, the solid compound (9.2 mg) was isolated by evaporation of the solvent *in vacuo*.[10] More polar eluent (5% MeOH in CH_2Cl_2) was used to recover the catalyst (90%) from the column. Compound **1a** under similar treatment yields compound **2a** in 73% isolated yields (based on the amount of starting material consumed), and 68% of the catalyst survived at the end of the reaction. By reacting MCPBA with $TMPFe^{III}Cl$ at −78 °C, we also generated a standard oxene sample as described by Groves et al.[3] Reaction of this authentic oxene

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(10) The yield was 93% based upon the amount of starting material consumed (68% based upon total oxidant).

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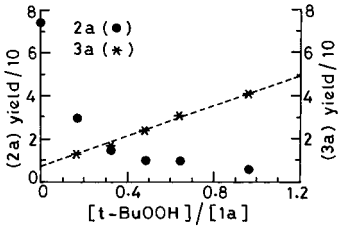


Figure 1. Oxidation of **1a** by oxene in the presence of variable amounts of *t*-BuOOH. In all six independent experiments, concentrations of **1a**, $F_{20}TPPFe^{III}Cl$, and C_6F_5IO were 0.028, 0.0008, and 0.026 mM, respectively. To a dichloromethane solution of **1a** and $F_{20}TPPFe^{III}Cl$ (at 33 °C) was added *t*-BuOOH followed by solid C_6F_5IO, and the mixture was stirred for 3−4 min (until all the solid C_6F_5IO was completely dissolved). Usual workup was then followed to measure the yields of **2a** and **3a** (see text).

sample with **1a** produced only **2a,** and we could not detect any **3a**.[11] These experiments unequivocally demonstrate that oxene efficiently oxidizes **1a** to **2a**.

Next we reacted compound **1a** with oxoiron(IV) porphyrin, the latter one was generated by following the reported method of Balch et al.[12] Compound **1a** remained unchanged.[13] Reaction of **1a** with either MCPBA or C_6F_5IO alone (without any catalyst) gives **3a**, but at relatively slow rate (1.0 and 0.08 M^{-1} s^{-1}, respectively); interestingly, **2a** was *not* formed at all in these reactions even in trace amounts.[8,14] H_2O_2 and *t*-BuOOH do not show any detectable reactivity with **1a** in 48 h. However, a 2:1 mixture of *t*-BuOOH and C_6F_5IO converts **1a** to **3a** in 70% isolated yields within mixing time. Evidently *t*-BuOO$^\bullet$ that is generated by the known reaction of *t*-BuOOH and C_6F_5IO has made this conversion possible.[1l,15]

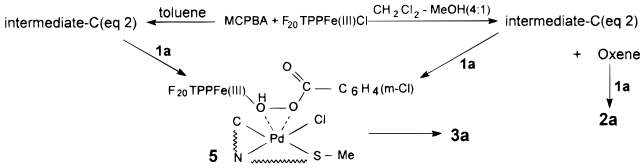
In a separate set of experiment, oxene was generated by reacting $F_{20}TPPFe^{III}Cl$ with C_6F_5IO in CH_2Cl_2 solutions having fixed concentrations of **1a** but variable concentrations of *t*-BuOOH and the measured yields of **2a** and **3a** were plotted against *t*-BuOOH/**1a** (Figure 1). We explain this plot by taking advantage of the following reported rate constants (eqs 5 and 6).[1k,n] In absence of *t*-BuOOH, oxene generated by eq 5 attacks

$$F_{20}PFe(III)Cl + C_6F_5IO \xrightarrow{4000\ M^{-1}s^{-1}} {}^{+\bullet}Fe(IV)=O + C_6F_5I \qquad (5)$$

$$^{+\bullet}Fe(IV)=O + t\text{-BuOOH} \xrightarrow{10^7\ M^{-1}s^{-1}} t\text{-BuOO}^\bullet + [P\,Fe(IV)\text{-}OH]^+ \qquad (6)$$

1a to give **2a** as only product, but in presence of *t*-BuOOH, the latter one gets oxidized to *t*-BuOO$^\bullet$ by eq 6, well before any additional reactive intermediate is generated by the reaction of *t*-BuOOH and $F_{20}TPPFe^{III}Cl$, because these two react with each other at a relatively slower rate.[1n] The concentrations of **1a**, C_6F_5IO, and *t*-BuOOH are so chosen that some excess amount of oxene was always present in solution to convert **1a** to **2a**. The *t*-BuOO$^\bullet$, generated by eq 6, and also by the reaction of C_6F_5IO and *t*-BuOOH, is easily detected by its observed reaction on **1a** giving **3a**. Thus with the increase of *t*-BuOOH, the yield of **2a** goes down and that of **3a** goes up. Compound **1b** shows similar reduction of the yield of **2b**, when the former was reacted with oxene in the presence of variable concentrations of *t*-BuOOH (not shown). This experiment establishes that the coexistence of *t*-BuOO$^\bullet$ and oxene in solution can even be detected by compound **1a**.

Scheme 2



Now we compared the yields of **2a** and **3a** from the reactions of **1a** with MCPBA in the presence of $F_{20}TPPFe^{III}Cl$ in two solvent systems. In pure toluene, we obtained 94% **3a** with 70% recovery of the catalyst and no trace of **2a** was noted. This experiment clearly indicates that oxene is *not* the reactive intermediate in this case.[16] Here, the total yield of **3a** is contributed by independent reaction of the oxidant on the substrate, and we strongly believe that part of oxygen transfer to the substrate takes place from intermediate C (eq 2) as is theoretically predicted by Bach et al. in the case of hydroperoxides.[17] However, the possibility of any radical-chain homolytic path can also not be overruled.[6,7] The formation of oxene by the reaction of $F_{20}TPPFeCl$ and MCPBA in hydroxylic solvent has now been demonstrated by conducting the same reaction in CH_2Cl_2−MeOH (4:1) solvent. We obtained 31% **3a** and 28% **2a** when the experiment was conducted at 33 °C, whereas in the same polar solvent system, we got 48% **3a** and only 10% **2a**, when the experiment was conducted at −78 °C. These results strongly suggest that in the case of MCPBA oxygen transfer to substrate takes place from intermediate C, and even in hydroxylic solvent systems (commonly used in most studies), this possibility cannot be overruled.

The high yield chemoselective conversion of **1a** to **3a** by MCPBA, C_6F_5IO, *t*-BuOO$^\bullet$, and $F_{20}TPPFe^{III}$−MCPBA in toluene suggests that this oxidation process passes through a common type of intermediate. The kinetics of oxidation of **1a** to **3a** by MCPBA have indicated that the oxidant first coordinates to Pd(II) to give a pentacoordinated Pd(II) species, and oxygen transfer to the Pd−C bond takes place therefrom in a concerted manner.[8] Such type of intermediate formation is only possible by the oxidants which are nucleophilic in nature (unlike oxene, which is electrophilic). Structure **5** (Scheme 2) shows the possible structure of intermediate for the oxidation of **1a** to **3a** by $F_{20}TPPFe^{III}Cl$−MCPBA in toluene. This type of intermediate formation is not possible for $F_{20}TPPFe^{III}$−C_6F_5IO due to steric reasons. In the latter case, oxene (formed by eq 5) reacts with compound **1a** to give **2a** as the exclusive product.

The competitive oxidizing power of oxene and its precursor (intermediate C, eq 2) is established, and a method of identifying reactive intermediates (like oxene, oxoiron(IV) and *t*-BuOO$^\bullet$) has been developed. These observations demand reviewing of the generalized mechanism of oxidation (eq 1) of organic substrates by oxene only! The importance of this conclusion is that we are encouraged to investigate methods of generating oxene and the precursors from various oxidants and compare the product ratios in various solvent systems (used in most published works). In our opinion, this will be the most rational way to resolve the dichotomy remaining in early literature.

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Supporting Information Available: Results of selective oxidation of **1a** and additional scheme (2 pages). See any current masthead page for ordering and Internet access instructions.

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(11) The yield of **2a** and survival of hemin were more in CH_2Cl_2 than those in CH_2Cl_2−MeOH (4:1).

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(16) This conclusion has been further supported by the observation that **1a** was exclusively converted to **2a** (68% yield) by an unequivocal oxene sample in toluene where no **3a** was formed.

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