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# THE OXIDATION OF METHYLENE CARBON-CARBON DOUBLE BONDS UNDER $Fe^{III}$-TBHP AND $Fe^{III}$-TBHP-PA CONDITIONS

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**Abstract:** The oxidation of 1,1-diphenylethylene under $Fe^{III}$-TBHP and $Fe^{III}$-TBHP-PA conditions followed a pathway *alkene to intermediate* **A** to *intermediate* **B** to *ketone*. Intermediate **A** could be trapped by $NaN_3$.

Using model compounds to emulate enzymatic activity is an important approach to understanding the mechanisms of biological processes involving the activation of dioxygen.[1] The selective functionalization of non-activated saturated hydrocarbons is of importance in industry, as well as a challange to mechanistic theory. To mimic the non-heme enzymatic oxidation of hydrocarbons, we have developed a family of chemical systems named as Gif systems.[2] All of them involve a pyridine/acetic acid solution of the hydrocarbon being oxidized, an Fe-catalyst and an oxidant. Non-activated methylene groups were ketonized with near quantitative yield at conversions from 15% to 30%. Both $H_2O_2$ and t-butylhydroperoxide (TBHP) were used as the oxidizing reagent. Usually the reaction of TBHP is more efficient. Terminal methylenecarbon-carbon bonds were oxidized to give the corresponding ketones and formaldehyde under Gif conditions. We herein wish to report the oxidation of 1,1-diphenylethylene under $Fe^{III}$-TBHP and $Fe^{III}$- TBHP-PA (picolinic acid) conditions.

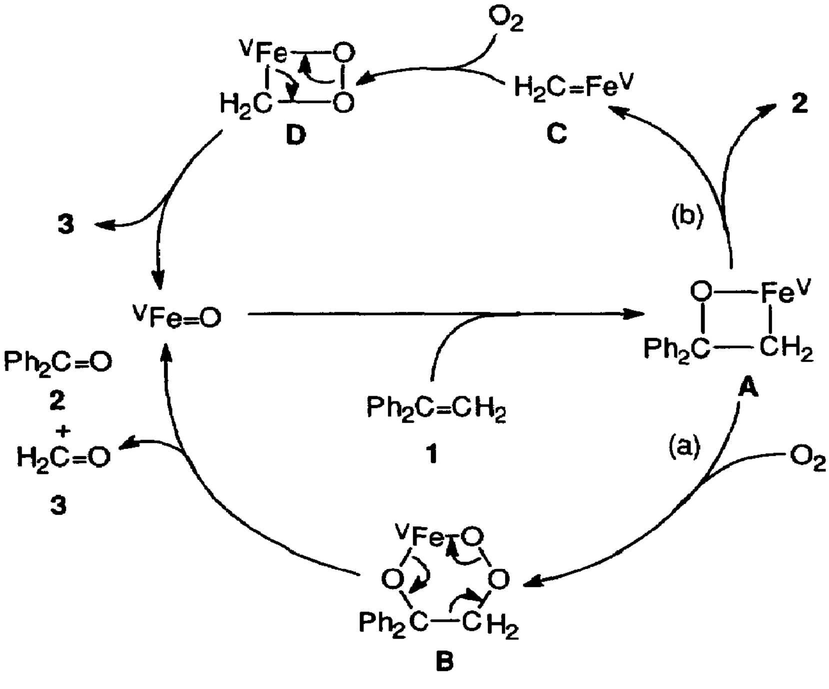
Under $Fe^{III}$-TBHP and $Fe^{III}$-TBHP-PA conditions, 1,1-diphenylethylene **1** was oxidized to give benzophenone **2** in 100% yields (**1** : TBHP : $Fe^{III}$=5 : 5 : 1) when the reactions were run under air. A blank experiment showed that $Fe^{III}$ could not catalyze the oxidation of 1,1-diphenylethylene **1** to benzophenone **2** in the absence of TBHP. Under $Fe^{III}$-TBHP-PA conditions, only 30% of 1,1-diphenylethylene oxide was oxidized to benzophenone **2** and 70% was recovered in 14 h. Thus it was not a reaction intermediate. The half life time for $Fe^{III}$-TBHP and $Fe^{III}$-TBHP-PA reactions were 7 and 4 h respectively. Titration experiments showed that in the $Fe^{III}$-TBHP-PA reaction of 1,1-diphenylethylene **1** under air, 50% of the TBHP was recovered, while 100% of **1** was oxidized. Thus the efficiency of TBHP was 200%. Further study showed that the efficience of TBHP could reach 272% (Table, Entry 2). When the above reaction was run under argon, only 3% of benzophenone **2** was detected, 96% 1,1-diphenylethylene **1** and 83% of the TBHP were recovered (by titration) in 14 h. Therefore oxygen is vital to the formation of **2**. Two possible pathways toward the formation of benzophenone **2** were suggested as shown in Scheme 1. The $^{V}Fe{=}O$ species reacted with the carbon-

Table 1 The Oxidation of 1,1-Diphenylethylene **1** under GoAgg$^V$ Conditions

| Entry | FeCl$_3$ (mmol) | PA(a) (mmol) | **1** (%) | **2** (%) | M.B.(b) (%) |
|---|---|---|---|---|---|
| 1 | 0.2 | 0.6 | 67.6 | 34.2 | 102 |
| 2(c) | 0.2 | 0.6 | 44.6 | 53.2 | 97.8 |
| 3 | 0.5 | 1.5 | 55.6 | 41.4 | 97.0 |
| 4 | 1 | 3 | 53.2 | 44.8 | 98.0 |
| 5(c) | 1 | 3 | 47.4 | 50.6 | 98.0 |
| 6 | 2 | 6 | 64.0 | 33.0 | 97.0 |
| 7 | 3 | 9 | 67.0 | 32.4 | 99.4 |

Reaction conditions: **1** 5 mmol, Pyridine 30 mL, TBHP 1 mmol, time 14 h.
(a) Picolinic acid (b) Mass balance, calculated from **1** + **2**; (c) 100 psi oxygen.

carbon double bond to form intermediate **A**; (a) Dioxygen inserted into the $^V$Fe-C bond to form intermediate **B**, which decomposed to give benzophenone **2**, formaldehyde **3**[3] and the $^V$Fe=O species. (b) Intermediate **A** decomposed to form benzophenone **2** and carbene **C**, which reacted with dioxygen to give intermediate **D**, whose decomposition afforded formaldehyde **3** and $^V$Fe=O species. Both pathways can explain why TBHP is catalytic, but the fact that the reaction under argon did not give much benzophenone **2** suggested that pathway (a), not (b), was followed.



Scheme 1

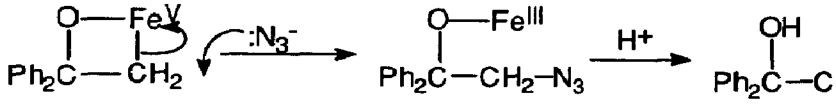
Table 2 Azidation of **1** under $Fe^{III}$-TBHP-PA Conditions

| Entry | t<br>min | **1**<br>% | **2**<br>% | **4**<br>% | M.B.<br>% |
|---|---|---|---|---|---|
| 1(a) | | 85.1 | trace | 10.8 | 96.0 |
| 2(b) | 0 | 71.4 | 0 | 26.6 | 97.8 |
| 3(b) | 5 | 65.4 | 0 | 31.2 | 96.6 |
| 4(b) | 10 | 27.2 | 0 | 70.8 | 98.0 |
| 5(b) | 30 | 18.6 | 3.6 | 74.2 | 96.4 |

**Reaction Conditions: 1 5 mmol, Pyridine 30 mL, $FeCl_3 \cdot 6H_2O$ 1 mmol, Picolinic acid, 3 mmol, (a) $NaN_3$ was added and the reaction mixture was stirred for 5 h , THBP 10 mmol; (b) TBHP 5 mmol; After t min, $NaN_3$ (10 mmol) was added; The reaction mixture was stirred for 14 h at 20 °C under argon and worked up.**

When the GoAgg$^{V}$ reaction was run under 100 psi oxygen pressure, similar results were obtained. The results in Table 1 showed that when 20% catalyst was used, the reaction gave the best yield when the reaction was run under air. When the reactions were run under 100 psi oxygen, the amount of $Fe^{III}$ was not important (Entry 2, 5).The $Fe^{III}$- TBHP-PA reaction could be run in water. When pyridine was replaced by the same amount of water, 50% of benzophenone was obtained at 20 °C after 14 h, although the 1,1-diphenylethylene **1** was insoluble.

$NaN_3$ is a strong nucleophile. When it was submitted to the Gif reaction mixture, the formation of the ketone was diverted toward the formation of alkyl azides by trapping the $^{V}Fe$-C bond of the reaction intermediate.[1] When the reactions of diphenylethylene **1** under $Fe^{III}$-TBHP-PA conditions were run under argon in the presence of $NaN_3$, β-hydroxyl azide **4**[4,5] was detected. A blank experiment showed that 1,1-diphenylethylene oxide did not react with $NaN_3$ to afford **4** under $Fe^{III}$-TBHP-PA conditions. Therefore **4** must be formed from the reaction of intermediate **A** with azide anion (Scheme 2). Azidation under $Fe^{III}$-TBHP-PA conditions was slow. The reaction was complete in 5 days and afforded **4** in 80% yield.[7] Under $Fe^{III}$-$H_2O_2$-PA-$NaN_3$ conditions, 15% of **4** and 44% of **2** (40% of **1**) were found after 14 h, thus intermediate **A** was also formed.



**A** **E** **4**

Scheme 2

When the reaction was started by the addition of the TBHP, the later $NaN_3$ was added, themore azide **4** was found (Table 2). Incubation with $NaN_3$ before the addition of TBHP gave less **4**

(Entry 1).This suggested that a possible ligand exchange occurred to afford a new complex, which was not so efficient.

A general procedure for $Fe^{III}$-TBHP reactions: A mixture of 1,1-diphenylethylene **1** (5 mmol)and $FeCl_3 \cdot 6H_2O$ (1 mmol) and picolinic acid (3 mmol) were dissolved in pyridine (30 mL) in a 125 mL Erlenmeyer flask. TBHP was added dropwise to the mixture with stirring and the mixture was stirred for some time and worked up.

In conclusion, an $^{V}Fe$-C bond was also formed in the oxidation of 1,1-diphenylethylene **1** under $Fe^{III}$-TBHPand $Fe^{III}$-TBHP-PA conditions as in the usual reactions in Gif systems. Oxygen gas was necessary to complete the fission of intermediate **A** to give benzophenone. We have always considered[2,3] the possible role of carbon radicals[8] in Gif chemistry. When oxygen is removed from the system, carbon radicals, if formed, would couple with the pyridine.[2] There was no indication of coupling to pyridine in any of this work. Effort toward the further identification and even isolation of the reaction intermediate **B** bearing an $^{V}Fe$-C bond is being continued.

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5 **4** could be reduced by $NaBH_4$ in refluxed i-propanol to afford 1,1-diphenyl-2-aminoethanol in 70% yield. The melting point and $^1H$, $^{13}C$ NMR spectra are the same as that prepared according to the literature[6] procedure.

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7 The reaction afforded **4** in 27% yield in 14 h.

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