# Iron Catalyst for Oxidation in Water: Surfactant-type Iron Complex-catalyzed Mild and Efficient Oxidation of Aryl Alkanes Using Aqueous TBHP as Oxidant in Water

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Surfactant-type iron(III) complex, $Fe_2O(DS)_4$, was found to be effective for benzylic oxidation of simple aryl alkanes using aqueous *t*-butyl hydroperoxide (TBHP) as an oxidant.

Recently increasing attention has been paid to the development of environmentally benign, sustainable, chemical processes. Use of ubiquitous metals, especially iron, as catalysts for organic synthesis is important in the development of such processes.[1] Utilizing water as an alternative to toxic and harmful organic solvents is also important and has been extensively studied.[2] Thus, the combination of iron catalyst and water as a solvent seems to be very attractive from a viewpoint of green sustainable chemistry.[3] In the course of our studies on Lewis acid surfactant-combined catalysts (LASC) for organic reactions in water,[4] related $\mu$-oxo-dinuclear iron(III) complex $Fe_2O(DS)_4$ (DS = *n*-$C_{12}H_{25}OSO_3$–) (**1**)[5] was found to be effective for benzylic oxidation of simple aryl alkanes in water. Although the combination of iron salts and peroxides for oxidation of alkanes has been well recognized as the Gif system established by Barton and Doller,[6] the system requires the use of pyridine or acetonitrile and acid additives, and benzylic oxidation of simple aryl alkanes has not been well studied.[7] Recently Nakanishi and Bolm focused on the Gif-type system for benzylic oxidation, where pyridine solvent and high temperature were still required and the yields of oxidation products from non-activated hydrocarbons were moderate.[8] Here, we report mild and efficient benzylic oxidation[9] of simple aryl alkanes without additives in water.

Initially we examined several reaction conditions using 1-phenyloctane (**2a**) as a model substrate (Table 1). The reaction of **2a** with 3 equiv of aqueous *t*-butyl hydroperoxide (TBHP) in the presence of 2.5 mol % of the iron catalyst **1** in water, which made a micellar solution, produced the corresponding heptyl phenyl ketone (**3a**) in 40% yield (Entry 1). Use of 5 equiv of TBHP resulted in a much higher yield of the product (Entry 2). Simple iron(II) salts were not effective under the same conditions (Entries 3 and 4). Although $Fe(acac)_3$ did not catalyze the reaction, water-soluble $Fe^{III}$ salts such as $FeCl_3$ and $K_3[Fe(CN)_6]$ showed some catalytic activity (Entries 5–7), even if somewhat lower than that of complex **1**. These results indicate the importance of both valency of iron and surfactant-type ligand. Cummen hydroperoxide or hydrogen peroxide as an oxidant did not give the product at all (Entries 8 and 9). In these cases evolution of gas was observed, and decomposition of the oxidants might occur in the presence of the iron catalyst under the conditions. Finally we obtained 72% yield of the desired ketone after 50 h (Entry 10). Prolonged reaction time or higher catalyst loading did not improve the yield (Entries 11 and 12). In the latter case, an excess of the solid catalyst retarded effective formation of the micellar solution.

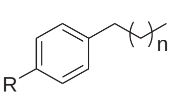
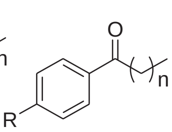
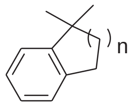
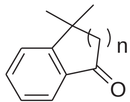
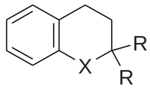
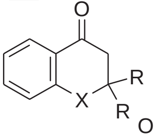
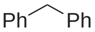
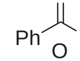
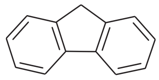
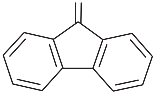
**Table 1.** Optimization of reaction conditions[a]

| Entry | Fe cat./mol % | Oxidant (equiv) | Time/h | Yield/%[b] |
|---|---|---|---|---|
| 1 | $Fe_2O(DS)_4$ (**1**) (2.5) | TBHP (3) | 24 | 40 |
| 2 | **1** (2.5) | TBHP (5) | 24 | 53 |
| 3 | $Fe(OAc)_2$ (5) | TBHP (5) | 24 | 0[c] |
| 4 | $FeSO_4$ (5) | TBHP (5) | 24 | 12 |
| 5 | $Fe(acac)_3$ (5) | TBHP (5) | 24 | 0[c] |
| 6 | $FeCl_3$ (5) | TBHP (5) | 24 | 34 |
| 7 | $K_3[Fe(CN)_6]$ (5) | TBHP (5) | 24 | 26 |
| 8 | **1** (2.5) | $PhCMe_2O_2H$ (5) | 24 | 0[c] |
| 9 | **1** (2.5) | $H_2O_2$ (5) | 24 | 0[c] |
| 10 | **1** (2.5) | TBHP (5) | 50 | 72 |
| 11 | **1** (2.5) | TBHP (5) | 85 | 71 |
| 12 | **1** (5) | TBHP (5) | 50 | 56 |

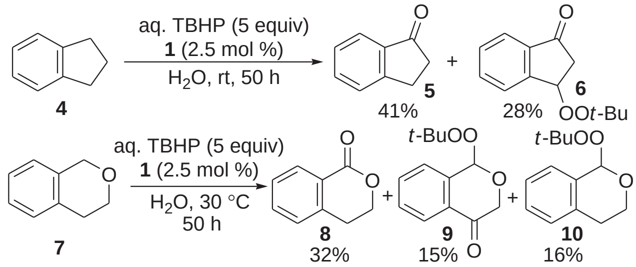
[a]The reaction was carried out with **2a** (0.5 mmol) in $H_2O$ at rt. [b]Determined by $^1H$ NMR analysis. [c]**2a** was recovered quantitatively.

With the optimized conditions in hand, we then investigated substrate generality of the present reaction system (Table 2). A variety of aryl alkanes bearing methoxy, fluoro, *t*-butyl and phenyl functional groups at the para position gave the corresponding aryl alkyl ketones in moderate to good yields (Entries 1–5). It is noteworthy that the present catalytic system can be ap-

**Table 2.** Iron-catalyzed oxidation in water[a]

| Entry | Substrate **2** | Product **3** | | Yield/%[b] |
|---|---|---|---|---|
| 1 |  |  | **a**: R = H, n = 6 | 72 |
| 2 | | | **b**: R = OMe, n = 6 | 84 |
| 3 | | | **c**: R = F, n = 6 | 52 |
| 4 | | | **d**: R = *t*-Bu, n = 6 | 77 |
| 5 | | | **e**: R = Ph, n = 3 | 71 |
| 6 | | | **f**: R = $NO_2$, n = 0 | 90 |
| 7 | | | **g**: R = OTf. n = 0 | 86 |
| 8 |  |  | **h**: n = 1 | 91 |
| 9 | | | **i**: n = 2 | 87 |
| 10 |  |  | **j**: X = O<br>R = $CH_3$ | 87 |
| 11 | | | **k**: X = $NSO_2Ph$<br>R = H | 84 |
| 12[c] |  |  **l** | | 94 |
| 13[c] |  |  **m** | | 99 |

[a]Conditions: **1** (2.5 mol %), TBHP (5 equiv), $H_2O$, 30 °C, 50 h. [b]Isolated yield. [c]Room temperature for 24 h.

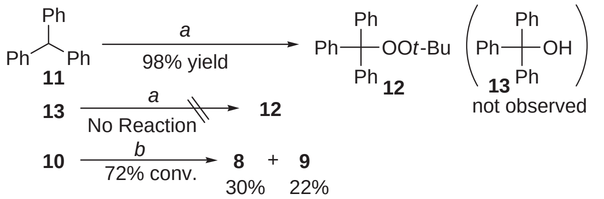


**Scheme 1.** Oxidation of aryl alkanes bearing two benzylic positions.

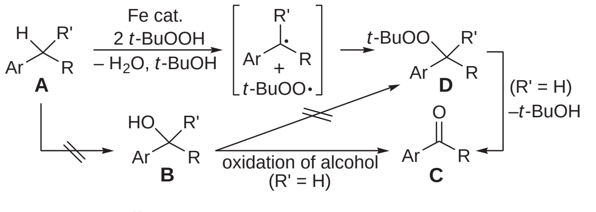
plied to aryl alkanes with strong electron-withdrawing groups on the aromatic rings, which are known as unreactive substrates in aerobic benzylic oxidation mediated by heterogeneous catalysts[10] or NHPI/$Co^{II}$ system[11] (Entries 6 and 7). Not only acyclic but also cyclic aryl alkanes were efficiently oxidized under the conditions to give the corresponding cyclic ketones in high yields without affecting oxygen- and nitrogen-containing functionalities (Entries 8–11). Diarylmethane derivatives also underwent the benzylic oxidation under the present conditions to give diarylketones in excellent yields after 24 h (Entries 12 and 13).

We then applied this system to substrates possessing two benzylic positions as shown in Scheme 1. Although the desired 1-indanone (**5**) was obtained by the oxidation of indane (**4**), 3-(*t*-butylperoxy)-1-indanone (**6**) was also isolated as a side-product in low yield.[12] Formation of by-products was also observed in the oxidation of isochromane (**7**), which produced isochromanone (**8**) along with mixed-peroxides **9** and **10**.[13] Formation of these by-products strongly suggested the presence of *t*-butylperoxy radical in the reaction mixture.

The reaction of triphenylmethane (**11**) gave us further mechanistic information. Thus, the reaction of **11** afforded peroxide **12** instead of alcohol **13** in quantitative yield. A control experiment clearly denied the pathway from **13** to **12**. We also confirmed that peroxide **10** was the intermediate for the formation of **8** and **9** (Scheme 2). From these observations, we concluded that the present oxidation reaction proceeded not via alcohol **B** (Path **A**–**B**–**C**, Scheme 3) but via a radical intermediate. This kind of mechanism has been proposed in iron-catalyzed oxidation systems using the combination of TBHP and $Fe^{III}$ salts in organic solvents.[7] The reaction of TBHP and aryl alkanes **A** in the presence of the iron catalyst produces *t*-butylperoxo radical and benzyl radical,[14] whose recombination gives peroxide **D** followed by elimination of *t*-butanol to afford aryl alkyl ketone.



**Scheme 2.** Oxidation of triphenylmethane and peroxide **10**. Conditions: (a) **1** (2.5 mol %), aq. TBHP (5 equiv), $H_2O$, 30 °C, 50 h. (b) **1** (2.5 mol %), aq. TBHP (3 equiv), $H_2O$, rt, 24 h.



**Scheme 3.** Possible mechanism.

In summary, we have developed mild and efficient iron-catalyzed benzylic oxidation of simple aryl alkanes in water. Organic solvents and/or additives are not required for this catalytic system. Further investigations into the use of surfactant-type iron complexes in other organic reactions in water are now in progress in our laboratory.

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