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# BENZYLIC OXIDATION BY THE GIF$^{IV}$ SYSTEM

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*<u>Summary</u>. Oxidation of ethylbenzene, diphenylmethane and benzylcyclopropane affords, in each case, the corresponding ketone as unique product. There is no detectable attack on the aromatic rings and only traces of phenol are formed from benzene. The oxidation of cumene affords acetophenone and 2-phenyl-2-hydroxypropane in nearly the same proportions as in a Gif$^{IV}$ oxidation of cumene hydroperoxide. An explanation is given.*

Much effort is currently devoted to the selective substitution of saturated hydrocarbons.[1] Emphasis is placed on $P_{450}$ models.[2] There is considerable agreement that an iron-oxo species is present, which behaves like an alkoxyl radical.[3]

Our own contribution to this field is the Gif type systems, which have the interesting property of oxidizing saturated hydrocarbons to ketones in preference to attacking tertiary and primary positions. They also show unusual chemoselectivity. Saturated hydrocarbons are oxidized faster than primary or secondary alcohols, or easily autoxidizable ethers.

Radical chemistry is a minor component of the reactivity seen.[4,5] We explain the unusual substitution and chemoselectivity by an $^{V}$Fe oxenoid species which inserts itself into the C-H bond to form an iron-carbon sigma bond.[6]

Olefins also show unusual behaviour in Gif type systems. 1,2-Di and tri-substituted olefins are converted to the corresponding unsaturated ketones, with no sign of epoxide formation. 1,1-Di-substituted olefins, on the other hand, are cleaved to nor-ketones (and formaldehyde) with no sign of unsaturated ketone formation or of epoxidation.[7]

We decided to examine the behaviour of benzylic hydrocarbons using the $Gif^{IV}$ system, the ingredients of which are specified under Table I. We started, however, with benzene, since a facile reaction with the phenyl ring would complicate the products obtained. In fact, only trace amounts of phenol were produced. We isolated and characterized the phenol by bromination to 2,4,6-tribromophenol (Table I). It is well known that hydroxyl radicals react rapidly with benzene and its congeners.[8] As before, hydroxyl radical behaviour is not seen and no doubt the solvent pyridine removes effectively any that are formed.[9]

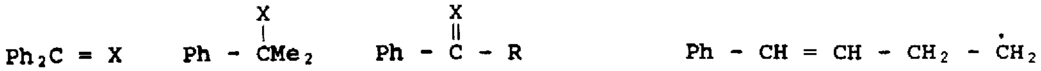
The oxidation of ethylbenzene gave a single product, acetophenone 4 (Table II). No other compound could be detected by g.l.c. The ease of this reaction is comparable to the oxidation of cyclohexene to cyclohexenone.[4]

The oxidation of diphenylmethane 1 likewise gave benzophenone (Table III) as the sole product. The oxidation of cumene (isopropylbenzene) was more complicated. It afforded a mixture of 2-phenyl-2-hydroxypropane 5 and acetophenone 4. The cleanness of the reaction was comparable with that of ethylbenzene.

According to our theory[4,5] an iron-carbon sigma bond is formed at the tertiary position in cumene. Because it is benzylic as well as tertiary, this bond is very weak so it breaks down into radicals. The capture of these radicals by oxygen and further reduction affords the hydroperoxide 6. This is reduced further to the carbinol 5 or cleaved in a Fenton manner by $^{II}Fe$ to give acetophenone 4 and a methyl radical.[10] Support for the latter stage of this mechanism was secured by submitting the hydroperoxide 6 to $Gif^{IV}$ conditions. This gave the alcohol 5 (49%) and acetophenone (45%). This was close to the results found for the oxidation of cumene (1.3:1 for 5 and 4 respectively). These oxidations at the benzylic position would be far more efficient if the Gif-Orsay electrochemical system were used.[7]

Finally, we oxidized benzylcyclopropane 7 under $Gif^{IV}$ conditions. This gave the ketone 8 as the only detectable product (5%, mass balance > 95%). This experiment suggests again that a secondary benzyl radical is not involved, as such a radical would open to give the radical 9.[11] Similarly, oxidation of 7 under $Gif^{III}$ conditions[4] gave the ketone 8 as the sole product (7.5%, mass balance > 95%).

Professor D. T. Sawyer has kindly informed us that he has also oxidized ethylbenzene to acetophenone as sole product using his modifications of the Gif type systems.[12]



$Ph_2C = X$ $\quad Ph - \overset{X}{\overset{|}{C}}Me_2$ $\quad Ph - \overset{X}{\overset{\|}{C}} - R$ $\quad Ph - CH = CH - CH_2 - \dot{C}H_2$

1 $X = H_2$ $\quad$ 3 $X = H$ $\quad$ 4 $X = O$, $R = CH_3$ $\quad$ 9

2 $X = O$ $\quad$ 5 $X = OH$ $\quad$ 7 $X = H_2$, $R$ = cyclopropyl

6 $X = OOH$ $\quad$ 8 $X = O$, $R$ = cyclopropyl

TABLE 1 OXIDATION OF BENZENE BY THE GIF$^{IV}$ SYSTEM[a]

| Entry | Benzene ml (mmol) | TBP[b] (mg) | Phenol mmol | Chem. Yield % | Coulombic Yield %[c] |
|---|---|---|---|---|---|
| 1 | 1.0 (11) | 16 | 0.05 | 0.4 | 0.2 |
| 2 | 5.0 (55) | 19 | 0.06 | 0.1 | 0.3 |
| 3 | 10.0 (110) | 20 | 0.06 | 0.05 | 0.3 |

[a] Benzene, zinc powder (1.3 g, 20 mg-at) and pyridine (28 ml) were placed in a 125 ml Erlenmeyer flask. To this mixture, a solution of $Fe(OAc)_2$ (40 mg, 0.23 mmol) in AcOH acid (2.3 ml, 40 mmol) was added. The latter was prepared freshly by dissolving iron powder in AcOH at reflux (1 hr.) under an argon atmosphere. The mixture was then stirred open to air (16 hrs.) at RT. The resulting brown solution was treated with 11 ml of 10% w/v NaOH. The white precipitate formed was filtered and washed with water. The filtrate was evaporated to dryness under reduced pressure. The residue was dissolved in AcOH (25 ml) and treated with $Br_2$ until the red color persisted (~0.1 ml). After 10 minutes of stirring, 1N sodium bisulfite (20 ml) was added and the solution was extracted with ether (2 x 50 ml). The ether extracts were dried ($MgSO_4$) and evaporated to dryness. The solid was sublimed to give pure 2,4,6-tribromophenol, mp. 93-94°.

[b] 2,4,6-Tribromophenol

[c] Calculated on the standard $P_{450}$ equation.

TABLE 2 OXIDATION OF ETHYLBENZENE BY THE GIF$^{IV}$ SYSTEM[a]

| Entry | Catalyst (mmol) | Ethylbenzene ml (mmol) | 4 mmol | Chemical Yield (%) | Coulombic Yield (%) | Catalyst Turnover |
|---|---|---|---|---|---|---|
| 1 | $Fe(OAc)_2$ (0.27) | 0.25 (2.0) | 0.14 | 7.0 | 1.4 | 0.5 |
| 2 | $Fe(OAc)_2$ (0.27) | 5.0 (41) | 0.92 | 2.2 | 9.2 | 0.9 |
| 3 | $Fe(OAc)_2$ (0.45) | 10.0 (82) | 1.5 | 1.8 | 15.0 | 3.3 |
| 4 | $FeCl_2.4H_2O$ (0.25) | 0.25 (2.0) | 0.14 | 7.0 | 1.4 | 0.5 |
| 5 | $FeCl_2.4H_2O$ ($5x10^{-3}$) | 0.25 (2.0) | 0.19 | 9.4 | 1.9 | 38.0 |

[b] The Gif$^{IV}$ reaction was performed as described in Table 1.

TABLE 3 OXIDATION OF DIPHENYLMETHANE AND ISOPROPYLBENZENE BY THE GIF$^{IV}$ SYSTEM[a, b]

| Entry | Substrate (mmol) | Products(%) | Coulombic Yield (%) | Catalyst Turnover |
|---|---|---|---|---|
| 1 | 1 (1.0) | 2(11) | 1.1 | 0.4 |
| 2 | 3 (2.0) | 4(5.4),5(6.9) | 1.3 | 1.0 |
| 3 | 3 (10) | 4(2.9),5(3.9) | 3.4 | 2.7 |

[a] $FeCl_2.4H_2O$ was used as catalyst.
[b] Gif$^{IV}$ reaction conditions are described in Table 1

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10. When this reaction was run in pyridine-$d_5$-$CH_3CO_2D$ $\alpha$-(15%) and $\gamma$-(8%) picolines were detected thus confirming the presence of methyl radicals.
11. Based on analogy the rate constant for the opening of this benzyl radical can be estimated to be about $1x10^6$ $sec^{-1}$. at 25°; see Newcomb, M.; Glenn, A. G. *J. Am. Chem. Soc.* **1989**, *111*, 275. Friedrich, E. C.; Holmstead, *J. Org. Chem.* **1971**, *36*, 971; Corey, E. J.; Nagata, R. *Tetrahedron Lett.* **1987**, *28*, 5391.
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