Oxidation of Isopropylbenzene by Iron Tetraphenylporphyrin: Evidence for the Interaction of the Cumyl Radical with Oxygen Donors

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Evidence is presented for an unprecedented oxygen transfer from oxygen donors to a cumyl radical in the oxidation of isopropylbenzene catalysed by tetraphenyl metalloporphyrins.

Hydroxylation of a C–H bonds is the outcome of the reaction of alkanes and alkylaromatic compounds with tetraphenyl metalloporphyrins ($TPPM^{III}$; M = Fe or Mn) in the presence of an oxygen donor (OD; *e.g.* PhIO). The active species is a metal oxo-complex of the porphyrin, indicated as $TPPM^{V}=O$ in Scheme 1, and the reaction is suggested to occur by H atom abstraction followed by 'in cage' hydroxyl radical recombination (oxygen rebound).[1,2]

$$TPPM^{III} \xrightarrow{OD} TPPM^{V}=O$$

$$R\text{–}H + TPPM^{V}=O \rightarrow [R\cdot\ TPPM^{IV}\text{–}OH] \rightarrow R\text{–}OH + TPPM^{III}$$

Scheme 1

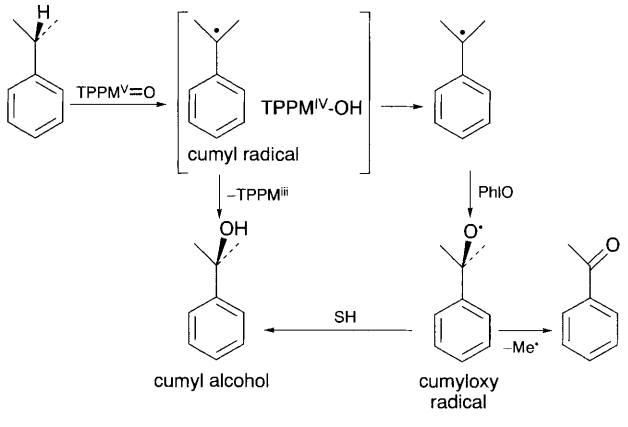
We have now found, however, that in the TPPFe/PhIO activated benzylic hydroxylation of isopropylbenzene, substantial amounts of acetophenone (*ca.* 20% of the overall molar conversion) are formed together with the expected 2-phenylpropan-2-ol (cumyl alcohol).† Thus, when 2.1 mmol of isopropylbenzene were treated with 4.1×10^{-2} mmol of iodosobenzene (PhIO) and 4.3×10^{-3} mmol of TPPFe in 3 ml of benzene, 4.2×10^{-3} mmol of cumyl alcohol (10% yield with respect to PhIO) and 1.2×10^{-3} mmol of acetophenone (3%) were formed. A substantially similar result was obtained when using the corresponding manganese porphyrin.

We checked that the cumyl alcohol product is stable under the reaction conditions, and therefore it is ruled out as the possible source of acetophenone, either by oxidative fragmentation‡ or by water loss to form α-methylstyrene, which might then produce acetophenone by oxidation.[4] Anyway, we also tested that α-methylstyrene is stable under the reaction conditions.

Since it is well known that alkoxy or benzyloxy radicals can undergo β-fragmentation reactions to form carbonyl compounds,[5] it was tempting to hypothesize that oxygen transfer from PhIO to cage escaped 2-phenyl-2-propyl radical (cumyl radical) might occur, resulting in the formation of a cumyloxy radical, which can lead to acetophenone by β-fragmentation and to additional cumyl alcohol by a hydrogen abstraction reaction (Scheme 2; SH is a hydrogen donor, presumably isopropylbenzene).

To support this unprecedented rationalization, independent preparation of the cumyl radical was carried out, and its reaction with PhIO or with other oxygen donors was investigated. Cumyl radicals were generated through the reaction of isopropylbenzene with *tert*-butoxy radicals, deriving from the thermal decomposition of di-*tert*-butyl peroxalate ($Bu^tO_3C\text{-}CO_3Bu^t$).§ When this peroxyester was decomposed at 50 °C in a carefully degassed benzene solution containing isopropylbenzene, bicumyl was obtained, as expected, by coupling of the cumyl radical intermediates, accompanied by traces of cumyl alcohol, α-methylstyrene and acetophenone. However, when this thermolysis was repeated in the presence of PhIO, the amounts of acetophenone and of cumyl alcohol significantly increased, while the yield of bicumyl dropped, as shown in Table 1. More importantly, it has to be noted that the yield of acetophenone, with respect to the oxidant, is significantly higher than that found in the biomimetic oxidation, where most of the intermediate cumyl radical undergoes in cage oxygen rebound. Similar and consistent results were obtained (Table 1) when PhIO was replaced by 2-nitroimidazole or by 4-cyanopyridine *N*-oxide, which indicates the feasibility of oxygen transfer to a cumyl radical from other oxygen donors as well.

An additional support to the hypothesis that oxygen transfer from PhIO to the cumyl radical may take place during the oxidation reaction of isopropylbenzene induced by metalloporphyrins, comes from the observation that when the latter substrate was reacted with TPPFe and PhIO in a 5:1 benzene:$CBrCl_3$ medium, only 0.25×10^{-3} mmol of acetophenone were formed (instead of 1.2×10^{-3} mmol, as reported before for the reaction in neat benzene), whereas the yield of cumyl alcohol (4.0×10^{-3} mmol) was almost unchanged. It is very likely, that the cage escaped cumyl radical efficiently abstracts bromine from $CBrCl_3$, and this step competes with the oxygen donation from PhIO leading to cumyloxy radical (Scheme 3) and eventually to acetophenone. Conversely, the in cage oxygen rebound (Scheme 2) to form cumyl alcohol is largely unaffected, as expected.

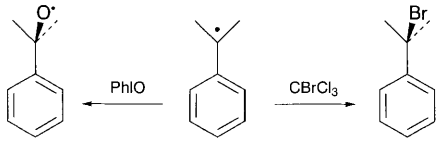


Scheme 2

Table 1 Thermolyses of di-*tert*-butyl peroxalate in degassed benzene in the presence of isopropylbenzene, with and without oxygen donors[a]

	Reaction products[c]		
Oxygen donor[b]	Bicumyl	Cumyl alcohol	Acetophenone (% yield)[d]
None	0.048	0.0006[e]	0.001[e] (1)
PhIO	0.022	0.006	0.012 (12)
2-Nitroimidazole	0.026	0.002	0.007 (7)
4-Cyanopyridine *N*-oxide	0.025	0.011	0.011 (11)

[a] Reaction conditions: 0.1 mmol of peroxyester and 0.94 mmol of isopropylbenzene in 1 ml of benzene for 3 h at 50 °C. [b] Added in 0.1 mmol amounts. [c] Amounts in mmol. [d] With respect to the molar amount of the oxygen donor. [e] Possibly due to residual traces of oxygen in the solvent.



Scheme 3

The possibility that oxygen transfer occurs from the oxygen donor to the carbon radical intermediate in a metalloporphyrin-catalysed oxidation of hydrocarbons, is very likely to depend on the stability of the carbon radical itself, which should be high enough to allow substantial cage escape. Thus, it is plausible that such a reaction has become observable for the first time in the oxidation of isopropylbenzene because in this process a fairly stable tertiary benzylic radical is formed.

A tentative rationale for this unprecedented oxygen donation, in the case of PhIO, might be the formation of an iodine-centred radical adduct, PhIOR,[6] which could fragment to PhI and ·OR.

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Footnotes

† Acetophenone was not reported among the reaction products in a recent study of the oxidation of isopropylbenzene by TPPFe, under the same conditions used in the present work:[3] it is likely that it escaped GC detection, due to its elution time being very close to that of cumyl alcohol, even on a capillary column.

‡ We thank one of the referees for this suggestion.

§ Di-*tert*-butyl peroxalate was prepared (CAUTION: explosive!) by the reaction of *tert*-butyl hydroperoxide with oxalyl chloride.[5]

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