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Study of a New Reaction : Trapping of Peroxyl Radicals by TEMPO

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Abstract : The reaction of 2,2,6,6-tetramethylpiperidinyloxy (TEMPO) with *t*-butyl hydroperoxide, in the presence of catalytic amounts of Fe^{III} yields oxygen. This reaction, which has never been described in the literature so far, led us to envisage a totally new concept, involving the reaction of TEMPO with oxygen-centered radicals. The formation of an intermediate has been detected during the course of the reaction. A mechanism based on the experimental facts and literature data is proposed. © 1998 Elsevier Science Ltd. All rights reserved.

The stable nitroxide free radical 2,2,6,6-tetramethylpiperidinyloxy (TEMPO) is a well-known carbon radical scavenger[1] and is extensively used as a radical probe for the mechanistic investigation of unknown reactions. During the course of our study of Fe/TBHP chemistry,[2] it seemed logical to investigate the effect of carbon radical scavengers on the Fe^{III}-catalyzed oxidation of cyclohexane. As expected, the presence of TEMPO induced an inhibition of the formation of ketone and alcohol, with the concomitant formation of cyclohexyl-TEMPO and methyl-TEMPO (Me-TEMPO) coupling products. The latter arising from the trapping of methyl radicals, generated from the β-scission of *t*-butoxyl radicals. More surprisingly, this investigation led us to discover that under these specific conditions a significant amount of dioxygen was formed. The bimolecular self reaction[3] of peroxyl radicals has already been reported in the literature in which an intermediate tetraoxide has been proposed which subsequently decomposes to give dioxygen. Our experimental observation therefore led us to envisage a similar concept, which involves the reaction of *t*-butyl peroxyl radicals with TEMPO.

In order to further explore this new reaction, cyclohexane was omitted from the reaction mixture, allowing us to only focus on the reaction of TEMPO with oxygen-centered radicals. We have studied the influence of the different parameters (Fe^{III}, TBHP, TEMPO) on oxygen formation.[4] The amount of TBHP only affected the yield and the rate of the reaction. Working with a large excess of TEMPO had no effect on the reaction (Table 1). In the same manner, the iron was only needed in catalytic amounts.

As expected, the formation of oxygen was found to be proportional to the disappearance of TBHP. However, it was observed that the rate of the reaction decreased with time : after 24 hours the formation of dioxygen stopped although 40% of oxidant, quantified by iodometric titration, remained in the solution (Table 1, entry 2). On the other hand, if a second portion of 5 mmol of TBHP was added, the oxygen formation started again.

Table 1 : Influence of the amount of TEMPO on the Oxygen Formation

Entry	x	O_2	Me-TEMPO	Residual oxidant	*t*-BuOH	*t*-BuO*Ot*-Bu
1	0	0.05	-	~ 3	1.39	0.07
2	1.0	0.89	0.19	1.92	2.79	0.14
3	2.2	1.09	0.24	2.46	2.26	0.13
4	5.0	0.89	0.19	3.06	1.47	0.10

1 mmol of $FeCl_3.6H_2O$*; 15 mL of pyridine; 5 mmol of TBHP; x mmol of TEMPO; RT; 24 hrs.*

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Table 2 summarizes this experimental observation by reporting the results of an experiment carried out over a period of one week with regular addition of *t*-butyl hydroperoxide. Under these conditions, oxygen was formed almost quantitatively for each additional portion of TBHP. A blank experiment has showed that TEMPO did not affect the iodometric titration. This led us to envisage that the remaining 40% of oxidant, titrated in the reaction mixture, corresponded mainly to the intermediate TEMPO-OO*t*-Bu. The decomposition of the latter possibly being favored in the presence of an excess of *t*-butyl hydroperoxide. The TLC of a typical reaction indicated the presence of an additional compound, more polar than TEMPO. However, attempted isolation by flash chromatography afforded only traces of the compound. In contrast, TEMPO was recovered quantitatively. It therefore appeared that the postulated intermediate decomposed during the course of the isolation step. Spectroscopic analyses have been however carried out on the isolated compound. It exhibited IR and ^{1}H NMR spectra close to the ones found for TEMPO. By GC, it decomposed into three products; one being TEMPO, one not identified and the third one being the 2,2,6,6-tetramethylpiperidine. In addition, the preparation at -60°C of such trioxides ROOOR has already been described in literature,[5] which supports the proposed theory. Such compounds would be expected to be reduced by HI.

Table 2 : Oxygen Formation

Time (days)	O_2 (total)	Addition of TBHP (total)	Residual Oxidant
1	1.2	5	1.6
2	3.0	10	2.4
3	4.8	15	2.9
4	7.2	20	2.3
5	9.3	25	3.5

1 mmol of TEMPO; 1 mmol of $FeCl_3.6H_2O$*; 15 mL of pyridine; RT.*

We have also studied the effect of the addition of 2,4,6-tri-*t*-butyl phenol, a suitable trap for oxygen-centered radicals.[2,6] Its presence inhibited the formation of dioxygen and this result therefore confirmed our working hypothesis, involving the reaction of TEMPO with oxygenated radicals. Although all the phenomena associated with *t*-butyl hydroperoxide have been explained by the reaction of *t*-butoxyl and *t*-butyl peroxyl radicals,[2,7] under these specific conditions, *t*-butoxyl radical species are only involved to a small extent. Indeed, as we have already pointed out, the addition of a suitable oxidant, which confines the iron as Fe^{III} allows the exclusive generation of *t*-butyl peroxyl radicals from TBHP[2]. This is the case encountered in the present study since TEMPO has shown the ability[8] to oxidize very rapidly Fe^{II} into Fe^{III}. The reaction of *t*-butoxyl radicals with TEMPO will therefore not be considered in our mechanistic proposal.

Several working hypotheses have been considered. Each of them involve the initial reaction of TEMPO with *t*-butyl peroxyl radicals to give intermediate **1**; they differ subsequently only by the mode of decomposition.

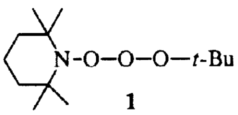

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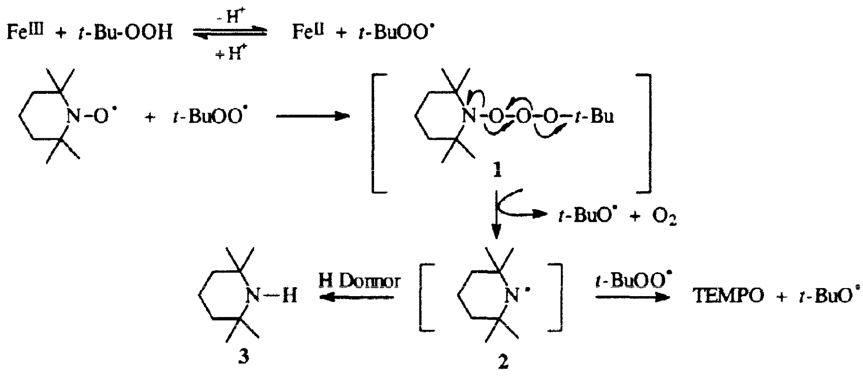
Figure 1 : Structure of the proposed intermediate

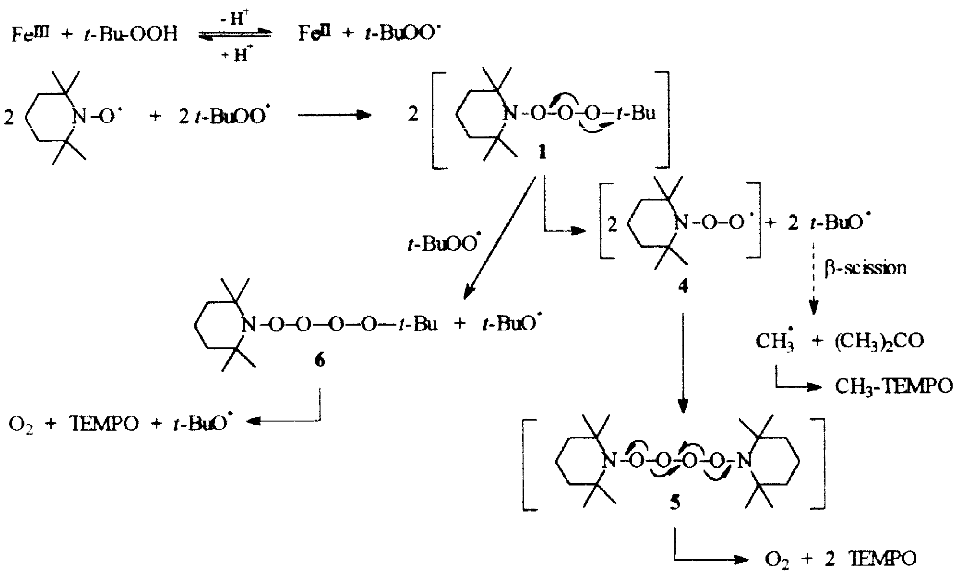
Since the formation of the coupling product *t*-butyl TEMPO was not detected during the course of the experiment, we were able to refute the hypothesis of the involvement of *t*-butyl radicals, generated from the homolytic scission of the intermediate **1**, with concomitant formation of oxygen and regeneration of TEMPO. Professor McKee[9] has kindly suggested an alternative mechanism. He proposed the scission of the N-O bond in the intermediate **1** with the concomitant formation of 2,2,6,6-tetramethylpiperidyl **2** (Scheme 1). TEMPO could be regenerated by combination with another *t*-butyl peroxyl radical and subsequent decomposition as expected. This hypothesis would explain all the experimental facts and more particularly the stoichiometry of the reaction (two moles of TBHP are consumed for the formation of one mole of oxygen). However, the formation of the nitrogen radical is, according to us, not involved since the 2,2,6,6-tetramethylpiperidine **3** has never been detected.



Scheme 1 : McKee Proposal

A third hypothesis which is preferred involves the homolysis of intermediate **1** to generate *t*-butoxyl radicals and another adduct **4** (Scheme 2). The latter has already been observed by ESR[10] and its involvement in the mechanism is therefore likely. It could possibly dimerize to form the corresponding tetraoxide which, by analogy to the bimolecular reaction of two peroxyl radicals described by Blanchard[2b] would yield oxygen and regenerate TEMPO. This mechanistic hypothesis is in agreement with the previously reported experimental facts, since it explains why TEMPO is needed only in catalytic amounts. In addition, the observation of transient species such as **1** and **4** having been already described in literature[3,7] confirm the validity of our theory. An alternative mechanism is represented in scheme 2, which would simply illustrate the need of an excess of TBHP in the reaction mixture for the decomposition of the intermediate **1**.

In conclusion, we have found that TEMPO, a well-known carbon radical scavenger, reacts with peroxyl radicals to catalyze the formation of dioxygen. We have postulated the formation of a trioxide intermediate (**1**) which has been detected by TLC during the course of the reaction. Although the proposed mechanism to account for the formation of dioxygen remains still speculative, we believe in the involvement of the described intermediate species which are supported by several literature reports.



Scheme 2 : Proposal 2

Acknowledgments

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