Radical chemistry of *tert*-butyl hydroperoxide (TBHP). Part 1. Studies of the Fe^{III}–TBHP mechanism

Derek H. R. Barton,*[a] Valérie N. Le Gloahec,*[a,b] Henri Patin[b] and Franck Launay[a]

[a] *Department of Chemistry, Texas A&M University, College Station, TX 77843-3255, USA*
[b] *Ecole Nationale Supérieure de Chimie de Rennes, Beaulieu, 35700 Rennes, France*

By maintaining the iron catalyst in the ferric state, the oxidation of 2,4,6-tri-*tert*-butylphenol with TBHP affords exclusively *tert*-butyl-peroxylated products. Mechanistic interpretation does not require a higher valence state of iron than Fe^{III}.

La chimie radicalaire de l'hydroperoxyde de *tert*-butyle (TBHP). Partie 1. Etudes mécanistiques du système Fe^{III}–TBHP. En maintenant le fer au degré d'oxydation III, l'oxydation du 2,4,6-tri-*tert*-butyl phénol par TBHP conduit à la formation exclusive de produits peroxylés. L'interprétation mécanistique n'implique pas la participation d'une espèce de haute valence de fer.

During our extensive studies of the Gif ketonisation reaction of saturated hydrocarbons, we have developed a coherent theory and have identified the special ligands that are needed.[1] Firstly, an azo-aromatic structure as in picolinic acid and its congeners is essential (two picolinic acids are bonded to each Fe^{III})[2] and secondly, an adequate amount of an unhindered pyridine base such that one equivalent of the base is also coordinated to each Fe^{III}. The oxidant has to be superoxide (addition to Fe^{II}) or hydrogen peroxide (displacement on Fe^{III}).[3] In the absence of the carboxylic acid, the only reaction seen is the formation of oxygen (the catalase reaction).[4]

TBHP is frequently used in oxidation chemistry as an alternant to hydrogen peroxide. In our first studies with TBHP, we tried to accommodate the results within the framework of Gif chemistry even though the KIE (kinetic isotope effect, based on cyclohexane *versus* perdeuterocyclohexane) was about eight (instead of about two as we had always seen with Gif chemistry) and the reactivities toward the hydrocarbons were similar to the standard radical reaction selectivity (but different from the Gif-type selectivity[6]). The helpful intervention of Minisci and his colleagues[7] established that TBHP chemistry was best interpreted as radical although a higher valence state of iron (Fe^{IV}) was also supposed to be involved. Our own studies[1] of alkyl chloride formation, by the reaction of alkyl radicals with Fe^{III}–Cl, confirmed that Minisci was correct about the formation of carbon radicals. In fact, this TBHP-based radical chemistry does not require a carboxylic acid of any kind or a pyridine base: the reaction takes place in any kind of solvent (acetonitrile, acetone, *etc.*) as long as the latter does not trap oxygen-centered radicals (which is the case for example with THF[8]). Thus, it is completely different from Gif ketonisation chemistry as we have already pointed out.[9]

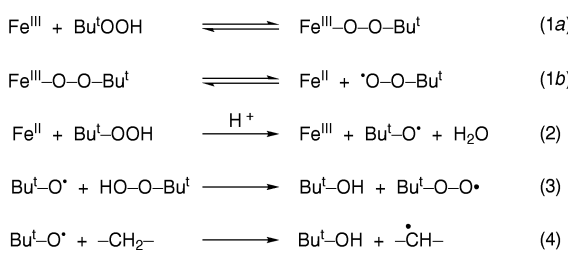
Although the propensity of TBHP to undergo iron-induced radical chemistry is now a well-established fact,[7,10] the mechanistic pathway of its Fe^{III}-catalyzed decomposition remains still under debate. The reaction therefore merited closer scrutiny involving, amongst others, a suitable radical trap that would allow the differentiation between *tert*-butoxyl and *tert*-butylperoxyl radicals.

In agreement with Ingold and co-workers,[11] who have also intervened in this discussion, we consider that there are four important reactions to be considered (Scheme 1). *tert*-Butylperoxyl radicals can be formed from eqn. (1) and (3). For eqn. (3), the excess of TBHP is clearly important. The formation of *tert*-butoxyl radicals is well-accepted [eqn. (2)] and their fate is summarized in eqn. (3) and (4). We note that *tert*-butylperoxyl radicals do not abstract hydrogen from saturated hydrocarbons.[12]

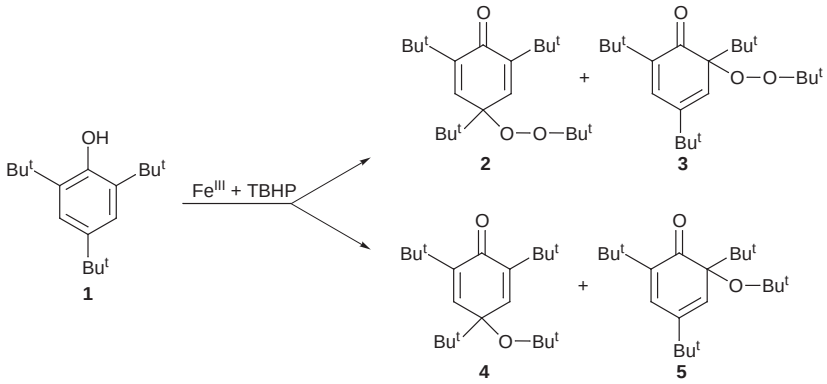
We decided to maintain the valence state of the iron as Fe^{III} or Fe^{II} by the addition of an appropriate oxidant (for Fe^{II}) or reductant (for Fe^{III}). We expected that this would greatly simplify the observed chemistry. In this and the following paper, we show that this is indeed the case.

Firstly, we needed to identify a good trap for *tert*-butylperoxyl radicals. Vitamin E (α-tocopherol) is well-known to inhibit lipid peroxidation. Modelling vitamin E in structure, substituted phenols have received due interest and have been shown to mimic the biological anti-oxidant as a peroxyl radical scavenger.[13–16] The authoritative work of Ingold[17] and his colleagues has established that the inhibition depends on the transfer of a hydrogen atom from α-tocopherol to the peroxyl radical. The phenolic α-tocopherol radical then quenches a further peroxyl radical. With this biogenetic concept in mind, we thought that the readily available 2,4,6-tri-*tert*-butylphenol **1** would be a suitable trap for *tert*-butylperoxyl radicals. It would furnish the peroxyl adducts **2** and **3**, whilst *tert*-butoxyl radicals, if present, would be captured as **4** and **5** (Scheme 2). All of these compounds are well-known and authentic samples were easily prepared. They are also stable under the experimental and work-up conditions.

The results of the oxidation of **1** in varying ratio with respect to an excess of TBHP are summarized in Table 1. The quantification of the products was carried out by ^1H NMR using 1,1,2,2-tetrachloroethane as an internal standard. As the



Scheme 1



Scheme 2 Fe^{III}-catalyzed oxidation of 2,4,6-tri-*tert*-butylphenol

ratio of **1** to TBHP increases, not all *tert*-butoxyl radicals react as in eqn. (3) (Scheme 1) and some are captured by the radical from **1**. Table 1 clearly demonstrates that TBHP, in the presence of Fe^{III}, does indeed furnish peroxyl radicals.

In Table 2, the results of the same type of trapping experiments in the presence of an excess of cyclohexane are summarized. As the concentration of TBHP increases, trapping of the *tert*-butylperoxyl and *tert*-butoxyl radicals is seen. When there is an excess of TBHP (entry 3), the *tert*-butoxyl radicals react to make cyclohexyl radicals (chloride formation from $FeCl_3$) or they are quenched in making additional *tert*-butylperoxyl radicals. It is interesting to note that the rate of the reaction is greatly enhanced when **1** is added to the reaction mixture (entries 1, 2 and 3 compared to entry 4: half-life $t_{1/2} \approx 2$ h instead of 1 day when **1** is not present). This clearly demonstrates the existence of an equilibrium [eqn. (1)], which is displaced to the right in the presence of **1**.

After these preliminary experiments, we now concentrated on finding an oxidant that would rapidly oxidize Fe^{II} into Fe^{III}, but not interfere by oxidation of the TBHP or by over-oxidation of **1**. Diammonium persulfate [one $(NH_4)_2S_2O_8$] rapidly (less than 5 min) oxidized two $FeCl_2$ to Fe^{III}. It did not oxidize the phenol **1** or TBHP. An equally efficient reagent was potassium ferricyanide [$K_3Fe(CN)_6$]. In less than 5 min, one equivalent of Fe^{II} was converted to Fe^{III}. The ferricyanide or the derived ferrocyanide did not titrate for Fe^{II} in the standard 4,7-diphenyl-1,10-phenanthroline titration[18] for Fe^{II}. Clearly, the cyanide ligands are too tightly bound: a blue complex is formed (Prussian Blue, also called 'Turnbull's blue'[19]) but this does not contain any free, titratable Fe^{II}. Of course, the derived ferrocyanide is stable[19] and does not reduce Fe^{III} to Fe^{II}.

Both of these oxidants (Table 3) produced only *tert*-butylperoxyl radical chemistry, in contrast to the equivalent experiments without the reoxidants in which *tert*-butoxyl radicals were easily detected. It is also interesting to note that the more TBHP is added, the faster is the reaction (entries 3 and 6). This confirms the existence of an equilibrium [eqn. (1)] which is displaced to the right when TBHP is used in excess. Diammonium persulfate, as well as potassium ferricyanide, titrate in the standard iodometric titration. As they are used in excess, it is not possible to quantify, at the end of the experiment, how much TBHP is left (because they interfere during the quantification). In Table 3, the mass balance with respect to TBHP is therefore not given.

Minisci *et al.* have repeatedly suggested[7] that *tert*-butoxyl radicals can be formed from Fe^{III} + TBHP with co-formation of Fe^{IV}. Our results are not in agreement with these views. On the other hand, Minisci and co-workers have already considered,[20] but only in passing, the generation of *tert*-butylperoxyl radicals from the reaction of TBHP with Fe^{III}. However, the most recent literature does not address this possibility.

When TBHP oxidation using Fe^{III} was carried out in the presence of cyclohexane, but without the peroxyl trap **1**, there was formation of cyclohexanone **6** as well as some **7** and **8** (Table 2; Scheme 3). We then examined the formation of oxygen (Table 4). In the absence of hydrocarbon, oxygen was formed by the alkylperoxyl bimolecular self-reaction.[21] In the presence of the hydrocarbon, oxygen was absorbed with con-

Table 1 Oxidation of 2,4,6-tri-*tert*-butylphenol **1** at various concentrations[a]

Entry	x[b]	**1**[c]	**2**[c]	**3**[c]	**4**[c]	**5**[c]	Yield[d]/%	MB_1[e]/%
1	1	n.d.[f]	0.76	0.28	n.d.	n.d.	104	104
2	2.5	n.d.	1.85	0.66	n.d.	n.d.	100	100
3	5	n.d.	3.10	1.10	0.35	0.26	84	96

[a] TBHP (10 mmol); $FeCl_3 \cdot 6H_2O$ (1 mmol); pyridine (30 mL); RT under air; 24 h. [b] Mmol of **1**. [c] Yields with respect to **1** in mmol. [d] Total yield of peroxylated compounds with respect to **1**. [e] Mass balance with respect to **1**. [f] n.d. = not detected.

Table 2 Influence of peroxyl radical trapping on the functionalization of cyclohexane[a]

Entry	x[b]	y[c]	**1**[d]	**2**[d]	**3**[d]	**4**[d]	**5**[d]	**6**[d]	**7**[d]	**8**[d]	TBHP[d]	Bu^{t}OH[d]	$(Bu^tO)_2$[d]	MB_1[e]/%	MB_{TBHP}[f]/%
1	5	2.5	3.14	0.83	0.30	0.56	0.43	n.d.[g]	n.d.	tr.[h]	0.2	0.22	n.d.	105	102
2	5	5	1.80	1.52	0.54	0.69	0.49	n.d.	n.d.	0.19	0.2	1.55	n.d.	101	100
3	5	10	0.23	3.55	1.30	n.d.	n.d.	n.d.	n.d.	1.24	0.4	4.20	n.d.	101	95
4	0	10	—	—	—	—	—	1.05	0.12	0.21	5.6	3.16	0.09	–	89

[a] $FeCl_3 \cdot 6H_2O$ (1 mmol); pyridine (30 mL); cyclohexane (20 mmol); RT under air; 24 h. [b] Mmol of **1**. [c] Mmol of TBHP. [d] Yields in mmol. [e] Mass balance with respect to **1**. [f] Mass balance with respect to TBHP. [g] n.d. = not detected. [h] tr. = trace amount.

Table 3 Influence of a reoxidant on the oxidation of 2,4,6-tri-*tert*-butylphenol[a]

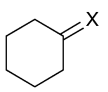
Entry	x[b]	y[c]	z[d]	Time/h	**1** left[e]	**2**[e]	**3**[e]	**4**[e]	**5**[e]	MB_1[f]/%
1*a*	5	2.5	0	20	3.11	1.06	0.36	0.43	0.35	106
1*b*	5	2.5	5	20	2.11	1.54	0.60	tr.[g]	tr.	85
2*a*	2	2	0	2	0.41	0.62	0.24	0.48	0.31	103
2*b*	2	2	5	2	1.63	0.29	0.11	n.d.[h]	n.d.	101
3*a*	5	5	0	5.5	2.52	1.36	0.50	0.34	0.30	100
3*b*	5	5	1	5.5	2.86	1.06	0.38	0.35	0.29	99
3*c*	5	5	3	5.5	2.86	1.11	0.38	tr.	tr.	87
3*d*	5	5	5	5.5	3.27	1.10	0.42	n.d.	n.d.	96
4*a*	5	5	0	24	1.09	1.92	0.68	0.62	0.47	96
4*b*	5	5	3	23.5	2.20	1.78	0.60	0.15	0.11	97
4*c*	5	5	5	24	1.90	1.63	0.58	n.d.	n.d.	82
5*a*	5	5	0	5	3.89	0.71	0.27	0.28	0.20	107
5*b*	5	5	5	5	4.38	0.61	0.22	n.d.	n.d.	104
6*a*	5	2.5	0	5.5	3.14	0.83	0.29	0.35	0.28	98
6*b*	5	2.5	1	5.5	3.61	0.89	0.30	0.10	0.07	96
6*c*	5	2.5	3	5.5	4.21	0.69	0.23	tr.	tr.	103
7*a*	5	2.5	0	26.5	2.85	0.85	0.30	0.37	0.28	93
7*b*	5	2.5	1	26.5	2.73	1.24	0.42	0.18	0.16	95
7*c*	5	2.5	3	24.5	2.72	1.31	0.46	0.10	0.08	93

[a] $FeCl_3 \cdot 6H_2O$ (1 mmol); pyridine (15 mL); RT under air. Entry 1: addition of z mmol of $(NH_4)_2S_2O_8$ dissolved in 2 mL H_2O. Entries 2–7: addition of z mmol of $K_3Fe(CN)_6$ dissolved in 2 mL H_2O. Entry 5: addition of 20 mmol of cyclohexane. [b] Mmol of **1**. [c] Mmol of TBHP. [d] Mmol of reoxidant. [e] Yields in mmol. [f] Mass balance with respect to **1**. [g] tr. = trace amount. [h] n.d. = not detected.

Table 4 Oxygen formation in the Fe^{III} + TBHP system[a]

Entry	O_2	TBHP left	**6**	**7**	**8**	Bu^tOH	$(Bu^tO)_2$	MB_{TBHP}[b]/%
1	0.85	5.10	—	—	—	4.62	0.16	99
2*a*	−0.45	5.73	1.03	0.13	0.16	4.62	0.06	104
2*b*	—	—	0.90	0.27	0.16	—	—	—

[a] $FeCl_3 \cdot 6H_2O$ (1 mmol); TBHP (10 mmol); pyridine (30 mL); RT under air; 25 h. Entry 1: experiment performed in the absence of hydrocarbon. Entry 2: experiment performed in the presence of 20 mmol of cyclohexane, analyzed after either the usual basic workup (entry 2*a*) or workup with triphenylphosphine (entry 2*b*). All data in mmol except as noted. [b] Mass balance with respect to TBHP.



6 X = O
7 X = H, OH
8 X = H, Cl
9 X = H, $OOBu^t$

Scheme 3 Fe^{III}-catalyzed oxidation of cyclohexane

comitant formation of mainly cyclohexanone with some alcohol and chloride. The consumption of oxygen was equivalent to the oxidation products formed. A work-up with triphenylphosphine was also carried out to verify the amount of hydroperoxide that was produced. As expected, the ketone was formed from the cyclohexyl hydroperoxide and Fe^{II} and not by decomposition of the hydroperoxide during GC analysis.[22]

Table 5 Study of the stability of the mixed peroxide[a]

Entry	Time/days	**6**	**7**	**9**	MB_9[b]/%
1	80	0.01	0.01	0.83	101
2	100	0.05	0.09	0.71	101
3	100	0.05	0.05	0.84	110
4	0.5	0.11	0.01	0.60	86
5	0.5	0.11	n.d.[c]	0.77	105

[a] **9** (0.84 mmol); $FeCl_3 \cdot 6H_2O$ (1 mmol) (entries 2 and 5) or $FeCl_2 \cdot 4H_2O$ (1 mmol) (entries 3 and 4); pyridine (33 mL); RT under argon. Entries 4 and 5: addition of Bu^tOOH (3.9 mmol) to the reaction mixture. All data in mmol except as indicated. [b] Mass balance with respect to **9**. [c] n.d. = not detected.

In addition, it has been proved, thanks to the synthesis of an authentic specimen, that the *tert*-butyl cyclohexyl peroxide **9** was stable under our GC conditions, whatever the work-up procedure. However, the mixed peroxide had been considered previously as a possible precursor to cyclohexanone,[23] so it seemed appropriate to examine the stability of this compound in the presence of Fe^{II} and Fe^{III}. The results are summarized in Table 5. In pyridine, the peroxide was not subject to either basic (entry 1) or Fe^{III}-catalyzed (entry 2) decomposition over periods as long as 80 days. It was also not very reactive towards Fe^{II} (entry 3). Moreover, **9** was recovered almost quantitatively when exposed to either *tert*-butoxyl or *tert*-butylperoxyl radicals generated from the combination of

Table 6 Influence of the addition of potassium ferricyanide on the functionalization of cyclohexane[a]

Entry	$K_3Fe(CN)_6$	TBHP left	**6**	**7**	**8**
1*a*	0	6.5	0.84	0.12	0.12
1*b*	0	0	0.79	0.18	0.16
2*a*	5	—	1.00	0.12	0.13
2*b*	5	0	1.00	0.20	0.18
3*a*	0	7.9	0.49	0.10	n.d.[b]
3*b*	0	0	0.43	0.25	n.d.
4*a*	5	—	0.69	0.13	n.d.
4*b*	5	0	0.55	0.35	n.d.

[a] $FeCl_3 \cdot 6H_2O$ (1 mmol); C_6H_{12} (20 mmol); TBHP (10 mmol); pyridine (30 mL); RT under air; 24 h. Entries *a*: usual basic workup; entries *b*: workup with Ph_3P. Entries 1 and 2: without the addition of H_2O; entries 3 and 4: with the addition of 2 mL of H_2O. [b] n.d. = not detected.

TBHP with Fe^{II} or Fe^{III} salts, respectively (entries 4 and 5). So the involvement of **9** as an intermediate in cyclohexane oxidation was definitively ruled out.

It was of interest to maintain the Fe^{III} species as such during cyclohexane oxidation. Some results are shown in Table 6. The addition of the ferricyanide had a small positive effect on the yield of ketone. The work-up with triphenylphosphine showed that little free hydroperoxide was present. The addition of water reduced significantly the yield of oxidation products. Thus, addition of ferricyanide increased the yield and also increased the concentration of the hydroperoxide, no doubt formed by hydrolysis of the species $Fe^{III}—O—O—C_6H_{11}$.

In conclusion, 2,4,6-tri-*tert*-butylphenol is an efficient trap for oxygen-centered radicals. By the addition of an oxidant that converts Fe^{II} to Fe^{III}, but that otherwise does not participate in the oxidation process, the chemistry can be reduced to a simple and quantitative trapping of the *tert*-butylperoxyl radical by the hindered phenolate radical.

Experimental

^1H and ^{13}C NMR spectra were performed in deuterochloroform with tetramethylsilane (TMS) as an internal reference on a Varian XL 200E spectrophotometer.

Gas chromatographic analysis was carried out on a Hewlett–Packard 5890 series II instrument, equipped with a flame ionization detector with N_2 as a carrier gas and a Hewlett–Packard 3396 A integrator. The columns used were either a DB-Wax (30 m long, 0.25 μm film thickness, 0.32 mm i.d.) or a DB-5 capillary column (30 m long, 25 μm film thickness, 0.32 mm i.d.) from J&W Scientific.

Column chromatography was performed on silica gel (Merck Kieselgel 60, 230–400 mesh).

Unless otherwise stated, all solvents and chemicals were purchased from commercial sources and used, after verification, without any further purification. TBHP was used as a 90% aqueous solution, after its purity had been checked by iodometric titration.

Preparation of the authentic samples

Data for all the compounds are consistent with the proposed structures and are in agreement with those of the literature.[15,24]

Preparation of 2. Compound **2** was prepared according to the procedure of Bickel and Kooyman[15] using the cobalt(III) naphtenate + TBHP system as a source of *tert*-butylperoxyl radicals. Purification by column chromatography over silica gel (hexane) afforded compound **2** as a yellow oil in quantitative yield. **2**: $C_{22}H_{38}O_3$. UV (CH_2Cl_2): $\lambda = 240$ nm ($\varepsilon = 12\,175$ mol L^{-1} cm^{-1}). ^1H NMR (200 MHz, $CDCl_3$): δ 0.96 [s, 9H, $—C(CH_3)_3$]; 1.20 (s, 9H, $—C(CH_3)_3$); 1.25 [s, 18H, 2 × $—C(CH_3)_3$]; 6.70 (s, 2H, 2 × C*H*=C—). ^{13}C NMR (50 MHz, $CDCl_3$): δ 26.1, 26.5, 29.6, 35.0, 40.6, 79.3, 82.5, 141.6, 147.9, 186.7.

Preparation of 4. Compound **4** was prepared by generating *tert*-butoxyl radicals through the thermolysis of *tert*-butyl hyponitrite. The general procedure was as follows: A mixture of *tert*-butyl hyponitrite[25] (0.17 g, 1 mmol) and 2,4,6-tri-*tert*-butylphenol (0.80 g, 3 equiv.) in 10 mL of dry benzene was refluxed for 3 h. Purification by column chromatography over silica gel (hexane) furnished compound **4** as a yellow oil (0.33 g, 49%). **4**: $C_{22}H_{38}O_3$. UV (CH_2Cl_2): $\lambda = 247$ nm ($\varepsilon = 10\,094$ mol L^{-1} cm^{-1}); $\lambda = 654$ nm ($\varepsilon = 57$). ^1H NMR (200 MHz, $CDCl_3$): δ 0.90 (s, 9H, $—C(CH_3)_3$); 1.19 (s, 9H, $—C(CH_3)_3$); 1.24 (s, 18H, 2 × $—C(CH_3)_3$); 6.74 (s, 2H, 2 × C*H*=C—). ^{13}C NMR (50 MHz, $CDCl_3$): δ 25.8, 29.3, 31.0, 34.9, 42.1, 75.6, 77.8, 145.1, 145.7, 186.0.

Isolation of the adducts 3 and 5. To a solution of $FeCl_3 \cdot 6H_2O$ (0.27 g, 1 mmol, 1 equiv.) and 2,4,6-tri-*tert*-butylphenol **1** (1.32 g, 5 equiv.) in pyridine (30 mL), was slowly added, at room temperature, *tert*-butyl hydroperoxide (0.25 mL, 2.5 equiv.). The reaction mixture was stirred at ambient temperature until **1** was completely consumed (typically overnight). The reaction was quenched with a 20% aqueous solution of sulfuric acid. The aqueous phase was extracted three times with diethyl ether. The combined organic layers were washed with a saturated solution of sodium bicarbonate, dried over magnesium sulfate, filtered, and concentrated under reduced pressure. Purification by column chromatography (hexane) gave, in addition to **4** and **2**, **3** and **5**. **3**: $C_{22}H_{38}O_3$. ^1H NMR (200 MHz, $CDCl_3$): δ 0.93 (s, 9H, $—C(CH_3)_3$); 1.17 (s, 9H, $—C(CH_3)_3$); 1.20 (s, 9H, $—C(CH_3)_3$); 1.23 (s, 9H, $—C(CH_3)_3$); 6.11 (d, 1H, $J = 2.5$ Hz, —C*H*=C—); 6.77 (d, 1H, $J = 2.5$ Hz, —C*H*=C—). ^{13}C NMR (50 MHz, $CDCl_3$): δ 25.0, 26.6, 29.0, 29.4, 31.5, 34.7, 41.1, 79.4, 88.1, 132.1, 134.1, 143.0, 145.5, 201.2. **5**: $C_{22}H_{38}O_3$. ^1H NMR (200 MHz, $CDCl_3$): δ 0.87 (s, 9H, $—C(CH_3)_3$); 1.11 (s, 9H, $—C(CH_3)_3$); 1.16 (s, 9H, $—C(CH_3)_3$); 1.18 (s, 9H, $—C(CH_3)_3$); 6.23 (d, 1H, $J = 2.3$ Hz, —C*H*=C—); 6.82 (d, 1H, $J = 2.3$ Hz, —C*H*=C—).

Preparation of *tert*-butylcyclohexylperoxide. The peroxide **9** was obtained from the corresponding mesylate according to the following procedure. Methane sulfonyl chloride (8 mL, 1.05 equiv.) was added slowly at −10 °C to a solution of cyclohexanol (96 g, 96 mmol, 1 equiv.) and triethylamine (20 mL, 1.5 equiv.) in dichloromethane (150 mL). The mixture was worked up 2 h later as reported in the literature[26] to afford a yellow oil (100% yield), which was used without further purification in the following step.

Dropwise addition of 50% aqueous potassium hydroxide (11 mL, 1.05 equiv.) to the solution of the obtained mesylate (16.91 g, 95 mmol, 1 equiv.) and 90% aqueous *tert*-butyl hydroperoxide (11 mL, 1.05 equiv.) in isopropyl alcohol (50 mL) was carried out at 0 °C. The resulting mixture was worked up 4 days later. The solvent was partially evaporated and the resulting residue, diluted with diethyl ether, was washed successively with a 10% aqueous solution of hydrochloric acid and brine. Purification by chromatography (hexane) gave the pure peroxide **9**, which was authenticated by comparison of its NMR data with those furnished by Bloodworth and Courtneidge[27]. **9**: $C_{10}H_{20}O_2$. ^1H NMR (200 MHz, $CDCl_3$): δ 1.10–2.00 (m, 10H, $—CH_2—$); 1.23 (s, 9H, $—C(CH_3)_3$); 3.83 (m, 1H, $—CH—OO(CH_3)_3$). ^{13}C NMR (50 MHz, $CDCl_3$): δ 24.1, 25.8, 26.4, 30.7, 79.6, 81.5.

Typical experimental procedures

Reactions with 1. To a solution of **1** (*x* mmol) and $FeCl_3 \cdot 6H_2O$ (1 mmol) in pyridine (30 mL) was added TBHP (*y* mmol) with stirring at room temperature. At the end of the reaction (typically 24 h), the reaction was quenched with a 20% aqueous solution of sulfuric acid. The aqueous phase was extracted three times with diethyl ether. The combined organic layers were washed with a saturated solution of sodium bicarbonate, dried over magnesium sulfate, filtered, and concentrated under reduced pressure. Quantification was carried out by ^1H NMR using 1,1,2,2-tetrachloroethane as an internal standard.

Reactions with Fe^{III}–TBHP. To a solution of $FeCl_3 \cdot 6H_2O$ (1 mmol) and cyclohexane (20 mmol) in pyridine (30 mL) was added TBHP (10 mmol) with stirring at room temperature. After 24 h, an aliquot (1 mL) of the reaction mixture was added to a saturated solution of aqueous sodium bicarbonate (5 mL). The aqueous solution was extracted with diethyl ether

(10 mL). The organic layer was dried over $MgSO_4$ and filtered. Naphthalene solution (1 mL, 0.08 M in diethyl ether) was added as an internal standard to the filtrate. The products were analyzed by gas chromatography.

Use of $(NH_4)_2S_2O_8$ and $K_3Fe(CN)_6$ as reoxidants. To a solution of $FeCl_2 \cdot 4H_2O$ (1 mmol) in pyridine (15 mL) was added z mmol of the reoxidant [$z = 0.5$ and 1 for $(NH_4)_2S_2O_8$ and $K_3Fe(CN)_6$, respectively] with stirring at room temperature. After 1 min, a titration of Fe^{II} was carried out,[17] which did not detect any Fe^{II}.

To a solution of $(NH_4)_2S_2O_8$ or $K_3Fe(CN)_6$ (5 mmol) in pyridine (15 mL) was added TBHP (5 mmol) with stirring at room temperature. The disappearance of TBHP was followed in time by iodometric titration (*vide infra*). (The iodometric titrations of the persulfate and the ferricyanide were previously carried out and taken into account in the quantification of the residual TBHP.) In both cases, TBHP was shown to be stable under the conditions of the reaction (even after 18 h, 100% of TBHP was recovered).

General procedures for quantification

NMR quantification. The quantification of derivatives **1**, **2**, **3**, **4** and **5** was done by ^1H NMR according to the following procedure. An aliquot (10 mL) of the reaction mixture was added to aqueous H_2SO_4 (25%, 50 mL) at 0 °C and extracted with diethyl ether (3 × 100 mL). The combined organic phases were washed with a saturated solution of sodium bicarbonate, dried over $MgSO_4$, filtered and concentrated under reduced pressure. A known amount of 1,1,2,2-tetrachloroethane was added as an internal standard and the mixture was analyzed by ^1H NMR using deuterated chloroform as solvent.

GC quantification. The quantification of **6**, **7**, **8** and **9** was done by GC after a basic workup. The general procedure was as follows. An aliquot (1 mL) of the reaction mixture was added to a saturated solution of aqueous sodium bicarbonate (5 mL). The aqueous solution was extracted with diethyl ether (10 mL). The organic layer was dried over $MgSO_4$ and filtered. Naphthalene solution (1 mL, 0.08 M in diethyl ether) was added as an internal standard to the filtrate. The products were analyzed by gas chromatography. The quantification of Bu^tOH and $(Bu^tO)_2$ was performed by GC according to the following procedure.[28] An aliquot (1 mL) of the reaction mixture, 0.1 mL of 1,1,1,3,3,3-hexamethyldisilazane and 0.05 mL of chlorotrimethylsilane were mixed and stood for 15 min at room temperature. The mixture was analyzed by gas chromatography after the usual basic workup (*vide supra*).

Determination of residual oxidizing power. An aliquot (1 mL) of the reaction mixture was added to a solution of water (5 mL) and acetic acid (5 mL) containing KI (0.5 g). After having stood at room temperature under an argon atmosphere for 30 min, the I_2 that had formed was titrated with a $Na_2S_2O_3$ solution (40 mM, starch as indicator) until the solution became colorless.

Determination of the amount of oxygen evolved. The reaction system was gas-tight and connected to a manometric burette filled with brine, which was saturated with oxygen (air) prior to use. During the readings, the pressure was always equilibrated, using a separating funnel, by adjusting the brine levels to the same heights. Also, the appropriate temperature and atmospheric pressure were taken into account before each reading and considered in the calculations using the ideal gas law.

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References

1 D. H. R. Barton, B. Hu, D. K. Taylor and R. U. Rojas-Wahl, *J. Chem. Soc., Perkin Trans. II*, 1996, 1031.
2 D. H. R. Barton, B. Hu, R. U. Rojas-Wahl and D. K. Taylor, *New J. Chem.*, 1996, **20**, 121.
3 D. H. R. Barton, B. Hu, T. Li and J. Mackinnon, *Tetrahedron Lett.*, 1996, **37**, 8329.
4 D. H. R. Barton and B. Hu, *Tetrahedron*, 1996, **52**, 10313.
5 D. H. R. Barton and W. Chavasiri, *Tetrahedron*, 1994, **50**, 19 and references cited therein.
6 D. H. R. Barton, E. Csuhai, D. Doller, N. Ozbalik and N. Singlet, *Tetrahedron Lett.*, 1990, **31**, 3097.
7 (*a*) F. Minisci and F. Fontana, *Tetrahedron Lett.*, 1994, **35**, 1427. (*b*) F. Minisci, F. Fontana, S. Araneo and F. Recupero, *ibid.*, 1994, **35**, 3759. (*c*) F. Minisci, F. Fontana, S. Araneo and F. Recupero, *J. Chem. Soc., Chem. Commun.*, 1994, 1823. (*d*) F. Minisci, F. Fontana, S. Araneo, F. Recupero, S. Banfi and S. Quici, *J. Am. Chem. Soc.*, 1995, **117**, 226. (*e*) F. Minisci, F. Fontana, S. Araeno, F. Recupero and L. Zhao, *Synlett*, 1996, **6**, 119.
8 L. A. Tavadyan, V. A. Mardoyan and M. V. Musaelyan, *Int. J. Chem. Kinet.*, 1996, **28**, 555.
9 D. H. R. Barton, *Synlett*, 1997, **7**, 229.
10 M. Newcomb, P. A. Simakov and S. Park, *Tetrahedron Lett.*, 1996, **37**, 819.
11 (*a*) I. W. C. E. Arends, K. U. Ingold and D. D. M. Wayner, *J. Am. Chem. Soc.*, 1995, **117**, 4710. (*b*) D. W. Snelgrove, P. A. MacFaul, K. U. Ingold and D. D. M. Wayner, *Tetrahedron Lett.*, 1996, **37**, 823. (*c*) P. A. MacFaul, I. W. C. E. Arends, K. U. Ingold and D. D. M. Wayner, *J. Chem. Soc., Perkin Trans. II*, 1997, 135.
12 (*a*) J. A. Howard and K. U. Ingold, *Can. J. Chem.*, 1968, **46**, 2655. (*b*) J. H. B. Chenier, D. A. Holden and J. A. Howard, *ibid.*, 1978, **56**, 170.
13 T. W. Campbell and G. M. Coppinger, *J. Am. Chem. Soc.*, 1952, **74**, 1469.
14 C. E. Boozer, G. S. Hammond, C. E. Hamilton and J. N. Sen, *J. Am. Chem. Soc.*, 1955, **77**, 3233.
15 A. F. Bickel and E. C. Kooyman, *J. Chem. Soc.*, 1953, 3211.
16 A. Brovo, F. Fontana and F. Minisci, *Chem. Lett.*, 1996, 401.
17 (*a*) G. W. Burton and K. U. Ingold, *Acc. Chem. Res.*, 1986, **19**, 194. (*b*) J. T. Banks, K. U. Ingold, J. Lusztyk and L. Valgimigli, *J. Am. Chem. Soc.*, 1995, **117**, 9966. (*c*) C. Evans, J. C. Scaiano and K. U. Ingold, *ibid.*, 1992, **114**, 4589 and references cited therein.
18 (*a*) L. J. Clark, *Anal. Chem.*, 1962, **34**, 348. (*b*) See also D. H. R. Barton, V. N. Le Gloahec and H. Patin, Part 2 (following paper).
19 A. G. Sharpe, *Inorganic Chemistry*, Longman Group, London, 1981, p. 587.
20 (*a*) F. Minisci, E. Vismara and F. Fontana, *Heterocycles*, 1989, **28**, 489. (*b*) F. Minisci, F. Fontana and E. Vismara, *J. Heterocycl. Chem.*, 1990, **27**, 79.
21 (*a*) G. A. Russell, *J. Am. Chem. Soc.*, 1957, **79**, 3871. (*b*) H. S. Blanchard, *ibid.*, 1959, **81**, 4548. (*c*) A. Factor, C. A. Russell and T. G. Taylor, *ibid.*, 1965, **87**, 3692. (*d*) T. G. Traylor and C. A. Russell, *ibid.*, 1965, **87**, 3698.
22 D. H. R. Barton, E. Csuhai, D. Doller and G. Balavoine, *J. Chem. Soc., Chem. Commun.*, 1990, 1787.
23 H. C. Tung, C. Kang and D. T. Sawyer, *J. Am. Chem. Soc.*, 1992, **114**, 3445.
24 (*a*) E. C. Horswill and K. U. Ingold, *Can. J. Chem.*, 1966, **44**, 269. (*b*) K. Maruyama, T. Kusukawa, T. Mashino and A. Nishinaga, *J. Org. Chem.*, 1996, **61**, 3342. (*c*) K. Omura, *ibid.*, 1996, **61**, 7156. (*d*) A. Nishinaga, K. Nakamura and T. Matsuura, *Tetrahedron Lett.*, 1978, **38**, 3557. (*e*) M. Frostin-Rio, D. Pujol, C. Bied-Charreton, M. Perrée-Fauvet and A. Gaudemer, *J. Chem. Soc., Perkin Trans. I*, 1984, 1971.
25 D. G. Mendenhall, *Tetrahedron Lett.*, 1983, **24**, 451.
26 R. K. Crossland and K. L. Servis, *J. Org. Chem.*, 1970, **35**, 3195.
27 A. J. Bloodworth and J. L. Courtneidge, *J. Chem. Soc., Perkin Trans. I*, 1982, 1797.
28 *Handbook of Derivatives for Chromatography*, ed. K. Blau and J. Halket, W. A. Benjamin, New York, 2nd edn., 1993, p. 59.

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