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On the Distinction between Radical Chemistry and Gif Chemistry
Competitive Oxidation of Alkanes and *sec.*-Alcohols

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Abstract : By comparing the reactivities of alcohols and alkanes towards TBHP radical oxidation and non-radical Gif oxidation, we bring additional evidence regarding the non-radical nature of Gif chemistry.

As has been already shown by Minisci[1] and by Ingold,[2] as well as by our own investigations,[3] the chemistry of Fe^{II} or Fe^{III} + *tert*-butylhydroperoxide (TBHP) can be explained by the reactivities of *tert*-butoxy and *tert*-butylperoxy radicals. Thus we have agreement on systems where only radical chemistry is involved.

In contrast, the oxidation systems which we have called Gif reactions involve first of all the formation of an iron-carbon bond. We have recognized two manifolds. The first involves Fe^{III}-Fe^{V} chemistry. Here carbon radicals are not seen, except with certain special cases, for example the tertiary position in adamantane. The second manifold is where Fe^{II}-Fe^{IV} chemistry is involved. Here the initial chemistry is also iron-carbon bond formation but in many, but not all, cases the Fe^{IV} species fragments into Fe^{III} and a carbon radical. The latter reacts with $FeCl_3$ in a well-known manner to make an alkyl chloride and Fe^{II}.

As we pointed out some time ago,[4] in radical chemistry, cyclooctane is 2-3 times more reactive per hydrogen than cyclohexane. Recent results published by Ingold[2a] also reach this conclusion. In an overall analysis[5] we have shown that there is a clear difference in reactivity between cyclooctane and cyclohexane for radical reactions as compared with Gif reactions where cyclohexane is slightly more reactive than cyclooctane. For cyclododecane, on the other hand, the difference between radical chemistry and Gif chemistry is not so apparent.

If one starts with Fe^{II} + H_2O_2 in the Fe^{II}-Fe^{IV} manifold, in the presence of chloride ion, with a competitive oxidation of cyclohexane and cyclooctane, the carbon radicals formed make mostly cycloalkyl chloride. However, the Fe^{II} is slowly oxidized to Fe^{III} and then chloride formation stops and normal oxidation chemistry takes over. If one makes a line of normalized C_8/C_6 activity across the whole oxidation process, it is constant at about 0.8. This proves that the reactivity in the Fe^{II}-Fe^{IV} manifold is not initiated by hydroxyl radicals for which, if this were the case, the ratio would be 2 or 3 to 1.

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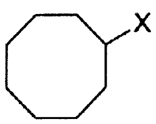
In Gif chemistry, saturated hydrocarbons can be oxidized in the presence of alcohols without significant oxidation of the latter.[6,7] Of course there are far more C-H bonds in the saturated hydrocarbon than in the derived alcohol so the results have to be normalized with one hydrogen for the alcohol and n hydrogens for the alkane. Now it is well known in radical chemistry[8] that primary and secondary alcohols are selectively attacked by oxygen radicals at the hydrogens α to the hydroxyl function. So there should be a difference between alkoxy radical oxidation as with TBHP and real Gif non-radical oxidation of alcohols compared to saturated hydrocarbons.

In Table 1 (two sets of experiments have been carried out and are referred as ***a*** and ***b*** respectively), the oxidation of cyclohexanol and cyclooctane are compared in Entries 1 and 2. At once the normalized results show that the radical oxidant (TBHP) is far more reactive for alcohol oxidation than the Gif system by a factor of about 4. In Entries 3 and 4, a similar comparison is made for cyclooctanol and cyclohexane. Again the radical oxidant is more reactive towards the alcohol than towards cyclohexane by a similar factor.

The data in Table 1 also show that for TBHP radical oxidation, cyclooctane was more reactive than cyclohexane whilst in the oxidation with Gif chemistry the relationship was reversed. This is in accordance with the data cited.[5] However, the rate differences between cyclooctane and cyclohexane were not as great as in the simpler experiments,[5] but so much *sec.*-alcohol was present that binding to iron may have complicated the results to a minor degree.



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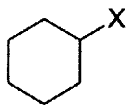
2 X = O
3 X= OH
4 X= o-pyr
5 X= *p*-pyr



6 X = Cl
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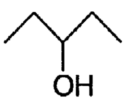

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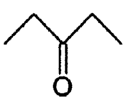

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Recently[9] we have used 3-pentanol as a trap for cumyloxy radicals. We decided to compare TBHP radical chemistry with Gif chemistry in the same way. As seen in Table 2, the TBHP chemistry is much more efficient in the oxidation of 3-pentanol than is Gif chemistry. Entries 1 and 3 again give us information on the activation step in Gif chemistry. If the hydrocarbon in Entry 3 was being activated by an oxygen radical, then, we would expect the ratio of alkane activation to alcohol activation to be the same. In fact the ratio for Entry 1 shows three times more activation for the alcohol whilst for Entry 3, the activation of the alcohol is only 0.7 times that of the alkane. In Entry 2, the ratio of alcohol to alkane activation is again three whilst in Entry 4 alkane activation is greater than alcohol oxidation. The situation is summarized in the final column of Table 2 where the radical oxidation chemistry of TBHP in Entries 1 and 2 is shown to be different from Gif oxidation by an overall factor of about five.

Table 1 : Comparison between the Competitive Reactivity of Alkanes and Alcohols

Entry	Oxidant	1	2	3	6	7	8	Ol/Ane *	ΣAne*
1a	TBHP	1.28	0.11	0	0	2.56	7.06	29.5	1.39
1b		0.66	0.09	0	0	2.52	6.66	50.4	0.80
2a	H_2O_2/PA	0	0.51	0.02	0	0.33	9.18	9.9	0.53
2b		0	0.51	0.05	0	0.30	8.47	8.6	0.56
3a	TBHP	0	3.27	5.60	0.67	0.11	0	50.3	1.04
3b		0	3.29	5.24	0.47	0.06	0.01	73.1	0.72
4a	H_2O_2/PA	0	0.96	8.41	0	0.73	0.10	14.0	1.11
4b		0	0.90	8.52	0	0.55	0.03	18.6	0.77

1 mmol of $FeCl_3.6H_2O$; 10 mmol of RH; 10 mmol of ROH; 3 mmol of PA (when present); 30 mL of pyridine; 5 mmol of H_2O_2 or TBHP; 0°C → RT or RT respectively; Air; 24 hrs. Entries 1 and 2 : $C_6H_{11}OH$ versus C_8H_{16}. Entries 3 and 4 : $C_8H_{15}OH$ versus C_6H_{12}. The results are given in mmol . : The results are normalized per hydrogens. Ol/Ane : Amount of oxidized alcohol over amount of oxidized alkane. ΣAne : Amount of oxidized alkane. Pyridine coupling products were not detected.*

Table 2 : Use of 3-Pentanol 11 as a Radical Probe - Comparison between TBHP and Gif Chemistries

Entry	Conditions	6	7	8	9/10	12	12/(6+7+8+9+10)
1	Fe^{II}/TBHP	0.18	0	0	tr./tr.	0.61	40.7
2	Fe^{III}/TBHP	0.41	0.21	tr.	0/0	1.86	36.0
3	Fe^{II}/H_2O_2/PA	0.34	0	0	0.12/0.05	0.25	5.9
4	Fe^{III}/H_2O_2/PA	0	0.81	0.05	0	0.60	8.4

1 mmol of $FeCl_3.6H_2O$ or $FeCl_2.4H_2O$; 20 mmol of 3-pentanol; 20 mmol of C_6H_{12}; 30 mL of pyridine; 3 mmol of PA (when present). Entries 1 and 3 : 1 mmol of TBHP or H_2O_2; RT or 0°C → RT (respectively); 1 minute. Entries 2 and 4 : 5 mmol of TBHP or H_2O_2; RT or 0°C → RT (respectively); 12 hrs.

Stavropoulos, in a monumental paper,[7] has also noted the reluctance of adaman-2-ol and other alcohols in Gif oxidation as compared with the facility of alkane oxidation.

Acknowledgments

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