How much do we know about Aerobic Oxidations?

Ive Hermans[1]*

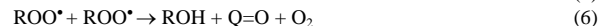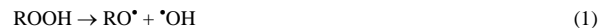[1]*ETH Zurich, Wolfgang-Pauli-Strasse 10, 8093 Zurich (Switzerland)*
*hermans@chem.ethz.ch

Introduction

Oxygenated compounds are used as building blocks in nearly all branches of chemical industry, ranging from polymer synthesis to medicinal chemistry.[1] This industrial interest explains the massive increase in the number of scientific publications dealing with selective oxidations in the later half of the 20th century. The importance of oxidations, coupled with the obvious need for improvement, especially with regards to process sustainability, has transported this domain to the forefront of chemical and chemical engineering research.
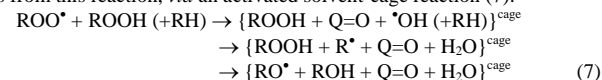
Directly using oxygen (air) instead of other oxidants would not only reduce the cost, it would also eliminate many environmental problems. Unfortunately the scope of molecular oxygen as an oxidant is, at present, still narrow. This is related to the kinetic inertness of hydrocarbons towards triplet O_2, and to the higher oxidizability of the reaction products compared to the parent hydrocarbon. One type of O_2 based oxidation which is already applied on a very large scale in industry is autoxidation. In this reaction type, the active oxidants are not O_2 molecules but reactive peroxyl radicals. These ROO$^\bullet$ species cause a radical chain reaction, responsible for the production of all observed products. Although these chain reactions occur in absence of a catalyst, very often small amounts of transition metal ions are added to initiate the chain reactions and to increase the reaction rate. A general problem with these autoxidations is the fact that they are difficult to control, *viz.* the desired products are easily over-oxidized. In order to get more control over on the selectivity it is important to know the precise reaction mechanism.

It was generally assumed [1-3] that (initially added) hydroperoxide molecules dissociate into O-centered radicals (1), initiating a radical reaction. These oxy (RO$^\bullet$) and hydroxyl ($^\bullet$OH) radicals react rapidly with the alkane substrate (2 & 3), generating alkyl radicals (R$^\bullet$). These C-centered radicals react diffusion controlled with oxygen (4), yielding peroxyl radicals (ROO$^\bullet$) which, upon reaction with the substrate, regenerate alkyl radicals (5). ROO$^\bullet$ radicals repeat this propagation cycle several times (4 & 5)before they are destroyed in a mutual chain termination reaction (6).This last reaction has been assumed for decades to be the origin of alcohol (ROH) and ketone (Q=O). Additionally, in case of cyclohexane autoxidation, over-oxidation of the ketone product was assumed to be the major source of ring-opened by-products.

$$ROOH \rightarrow RO^\bullet + {}^\bullet OH \tag{1}$$
$$RO^\bullet + RH \rightarrow ROH + R^\bullet \tag{2}$$
$${}^\bullet OH + RH \rightarrow H_2O + R^\bullet \tag{3}$$
$$R^\bullet + O_2 \rightarrow ROO^\bullet \tag{4}$$
$$ROO^\bullet + RH \rightarrow ROOH + R^\bullet \tag{5}$$
$$ROO^\bullet + ROO^\bullet \rightarrow ROH + Q{=}O + O_2 \tag{6}$$

Results and Discussion

The overall product distribution identifies the hydroperoxide as being the exclusive primary product, whereas alcohol and ketone/aldehyde are secondary products, formed in similar quantities as the ROOH product. [4] Clearly this observation cannot be explained by the textbook-mechanism. In addition to the propagation reaction (5), peroxyl radicals were found to react even faster with the ROOH product, provided that the latter features an αH-atom. [4,7] This reaction was identified as a straightforward source of ketone. Also, alcohol originates from this reaction, *via* an activated solvent-cage reaction (7).

$$ROO^\bullet + ROOH\ (+RH) \rightarrow \{ROOH + Q{=}O + {}^\bullet OH\ (+RH)\}^{cage}$$
$$\rightarrow \{ROOH + R^\bullet + Q{=}O + H_2O\}^{cage}$$
$$\rightarrow \{RO^\bullet + ROH + Q{=}O + H_2O\}^{cage} \tag{7}$$

The RO$^\bullet$ radicals co-produced in this step normally react with the substrate (2). However, in the case of cyclohexane oxidation (R = Cy), the CyO$^\bullet$ radicals can also ring-open. This reaction could unambiguously be identified as the predominant source of by-products, rather than the over-oxidation of cyclohexanone.[8]

Addition of Co(acac)$_2$ results in a very similar product distribution as for the thermal autoxidation.[9] Indeed, Co$^{2+/3+}$ ions take over the role of ROO$^\bullet$ as a fast ROOH reaction partner, yielding similar products. This Co + ROOH reaction was furthermore kinetically quantified by *in situ* UVVIS spectroscopy, yielding an activation energy of 13.3 kcal/mol, in good agreement with a B3LYP/LANL2DZ predicted value of 13.0 kcal/mol (for R = *t*-butyl). The reaction is first order in Co and ROOH up to a certain Co concentration after which inhibition occurs. The reasons for this inhibition as well as its consequences for the catalysis will be discussed.

Significance

Despite decades of academic and industrial research, a solid mechanism for autoxidations was still missing. This work provides a molecular understanding, based on extensive experimental investigations and quantum chemical calculations.

References

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