Catalytic Oxidation of a Trialkyl-Substituted Phenol and Aniline with Biomimetic Schiff Base Complexes

Jutta Knaudt, Stefan Förster, Ulrich Bartsch, Anton Rieker, and Ernst-G. Jäger

Introduction

The catalytic oxidation and oxygenation of organic substrates by biomimetic metal complexes gains more and more in importance in modern chemistry. Such complexes could serve as potential catalysts for the development of new procedures for organic syntheses in an ecologically desirable way, replacing toxic oxidation agents like chromate or lead dioxide by molecular oxygen or hydroperoxide. The catalytic oxidation of substituted phenols and anilines has also proved to be a useful procedure for mechanistic studies [1-3]. In earlier attempts the effect of different central atoms (Co, Mn) and various chelating ligands (Schiff bases, porphyrins, oximes) on the catalytic activity and the product distribution has been investigated.

Detailed mechanistic investigations were carried out with Co(salen) (CoV) and related compounds as catalysts using 2,6-dialkyl-substituted phenols and anilines with different groups in the para-position as substrates [1,2]. In the case of trialkyl-substituted phenols a radical mechanism is discussed with the formation of a phenoxy radical as the active intermediate [1a,b,2b,3]. This species is thought to form the final products of the reaction via a hydroperoxide or a bisquinolperoxide.

However, further investigations [1b] point to the fact that for phenol derivatives the catalytic cycle could also involve the formation of phenolate anions. Hereby, a connection between the redox potentials of the substrates, the potential of the catalyst and the regioselectivity could be noticed. Analogously, it should be possible to influence the product distribution by using the same substrate but different catalysts.

Thus, our attention turned towards the investigation of differences in the catalytic behaviour as a function of the metal complex catalyst, using one and the same phenol and aniline derivative as substrates. The catalysts for this investigation were chosen from a pool of complexes with macrocyclic and open-chain Schiff base ligands, types I – IV (Scheme 1). These compounds are characterised by a high diversity of peripheral substituents which can be used for tuning the electronic features of the central atom – including the redox potentials and the electrophilicity of the vacant axial coordination sites [4]. Distinct central atoms like Mn, Fe and Co were incorporated into these ligands. This renders possible a direct investigation of their influence on the catalytic behaviour under identical conditions. As reference catalyst the well-known Co(salen) complex (type V) was included into the measurements. So, a direct comparison of this complex with derivatives without N,N-condensed aromatic ring or its polycyclic analogues is possible.

As substrates, the 2,4,6-tri-tert-butyl substituted phenol 1 and aniline 2 were chosen out of the great pool of possible compounds, in order to compare the results with those of earlier investigations using these types of substrates.
**Results and Discussion**

**Oxygenation of phenol 1:** A mixture of 1 and the respective catalyst dissolved in dichloromethane was stirred at room temperature under an atmosphere of dioxygen. After filtration through a short silica gel column whereby the complex remains completely adsorbed, the products were separated by TLC yielding mainly the corresponding para- (3) and ortho- (4) quinone and other products containing para-bisquinolperoxide (6) and probably para-quinolhydroperoxide (5) (Scheme 2). Further products occur in very small amounts (Table I).

In the further course of the investigations the separation by TLC was replaced by an identification via $^1$H NMR spectra. If chemical shifts of certain protons have characteristic positions for each compound, it should be possible to determine the product distribution directly from the NMR spectra of the reaction mixture, if for one compound the absolute concentration can be determined by an independent method. Such a quantification of the results from a calibration of the NMR data of the olefinic protons using the photometric...
determination of the amount of ortho-quinone 4 which, as the sole product, possesses a characteristic absorption band in the visible range at $\lambda = 575$ nm, was envisaged. However, some of the compounds which could not have been identified by TLC, like the para-substituted compounds 7 ($\delta = 6.68$) and 8 ($\delta = 6.73$), have almost the same chemical shifts as the peroxide 6 ($\delta = 6.67$), hence, their separate quantification was not possible even by this method. Compound 9 was only found in the presence of CoV and in very small amounts (< 1%). The latter is also true for 7, which could be identified by HPLC, whereas compound 5 ($\delta = 6.57$) could not be detected under these conditions. The olefinic proton shifts of 3-9 are given in the experimental part. For the above reasons, the yields of the para-quinolide products 5 – 8 in Table I are given only summarily.

The results (Table I) show a strong dependence of the catalytic activity as well as of the product distribution on the central atom and the equatorial ligand of the complex.

Regarding the complexes of type I a gradation of the catalytic activity could be observed leading from manganese showing the highest activity via cobalt to iron. The low activity of the iron complex, even at long reaction times, is in contrast to the results which were obtained by studying the catalytic oxidation of hydroquinone with such types of complexes [5] where the highest catalytic activities were observed in the presence of some of the iron containing compounds. Apparently, the mechanisms of the oxidation of the two substrates are different concerning the intermediates formed from the metal(II) complexes and dioxygen: i) In the case of the hydroquinone oxidation with iron complexes like FeI or FeII, oxygen is generally reduced to form $\mu$-oxo derivatives [FeIII–O–FeIII], which seem to be of importance in the catalytic cycle of the hydroquinone oxidation [6]. ii) In the case of phenol oxidation with cobalt complexes a one- or two-electron-reduction to form superoxo or $\mu$-peroxo adducts, respectively, as the active species [7], is usually assumed. If a mechanism similar to i) occurs in the case of phenol oxidation by iron complexes too, their low catalytic activity could well be explained by the very short life-time of such Fe-$\mu$-peroxo complexes. The manganese compounds in general show a very differentiated behaviour against dioxygen [8a] which could be confirmed by our investigations [5a,9]. Depending on the type of ligand most of the oxygen adduct types can occur, including $\mu$-oxo- and $\mu$-peroxo derivatives [8]. For MnI the corresponding oxygen adduct could not be determined clearly [5], the formation of a $\mu$-oxo compound, however, can be excluded. The high activity of this manganese(II) complex is in agreement with earlier investigations where a manganese(III) complex of tetraphenylporphyrin shows a corresponding behaviour [3a].

The cobalt catalysed oxidation of 1: In the case of the cobalt complexes, further investigations were carried out to gain more information on the mechanism of this reaction. UV/Vis – spectrophotometrical investigations show clearly the formation of a deep blue phenoxyl radical catalysed by
the cobalt complex. All used cobalt compounds show the same effect but with different rates of radical formation [10]. Its existence was also confirmed by EPR measurements showing a signal with a g-value of 2.00426 and the coupling of the electron spin with the H nucleons \( (\Delta_{2H} = 0.162 \text{ mT}, \Delta_{9H} = 0.039 \text{ mT}) \) typical of 2,4,6-tri-tert-butyl-phenoxyl. No radical formation can be observed without the cobalt complex under otherwise identical conditions.

Therefore the start of the reaction seems to be the formation of the phenoxyl radical. For CoII and CoIV the mechanism of this reaction could be the same as it is described in literature [3a] since these complexes form superoxo adducts with dioxygen in different solvents. For the other complexes a higher degree of formation of \( \mu \)-peroxo derivatives was proved. In these cases an alternative mechanism including the \( \mu \)-peroxo species could be postulated (Scheme 3).

It is notable that the product distribution varies to a high extend dependent on the complex (Table I). If the catalyst's only function would be to generate phenoxyl radicals which form all other products by secondary reactions, all reactions should lead to the same product distribution, independent of the catalyst. Thus, it can be assumed that in the course of reaction further interactions of the substrate with the complex must take place. Such interactions have recently been described by Wieghardt with various metal catalysts and substituted phenols [11].

This hypothesis is supported by the fact that the absorption maximum of the radical in the UV/Vis spectrum in the presence of (and catalysed by) the cobalt complex is shifted bathochromically \( (\lambda_{\text{max}} = 707 \text{ nm}) \) in comparison to the free phenoxyl radical \( (\lambda_{\text{max}} = 629 \text{ nm}, \text{prepared by oxidation of the phenol by lead dioxide [12]}) \). This can be explained by an interaction between the cobalt catalyst and the phenoxyl radical [13]. However, no information exists up to now about the nature of such a species. The two possibilities of a cobalt(II) complex \( (\text{Co}^{II} \cdot \text{OR}) \) with the radical \( \cdot \text{OR} \) or a cobalt(III) phenolato complex \( (\text{Co}^{III} \cdot \text{OR}) \) could be regarded as contributing forms between which the real structure of the compound could be expected.

If the negative charge would be mainly localised on the substrate (\( \cdot \text{OR} \)), a dependence of the regioselectivity (ortho- or para-substitution) on the redox potential of the complex could be observable. Nishinaga et al. [1b] reported such a dependence of the regioselectivity on the redox potentials of various different substituted phenols. An attempt to prove such a correlation is shown in Fig. 1. For CoI – CoIII and CoV the points show indeed a nearly linear correlation, but the range of ratios is very small. On the other hand, the complex CoIV shows a strong deviation. Therefore a simple interpretation of the mechanism with respect to the potentials is not generally valid. More data must be available for a detailed discussion [10].

Oxidation of aniline 2: Contrary to phenolic substrates, the oxidation or oxygenation of anilines with cobalt containing catalysts does not generally take place with molecular oxygen [1c]. However, such an activity could be observed in the presence of MnI and FeII under long reaction times (29 h). In the case of MnI 50% of the aniline was converted. Only the corresponding nitrosobenzene \( (10; \text{yield 2.5%}) \) and the iminoquinone \( (11; \text{yield 2%}) \) could be isolated from a mixture of at least seven products. In contrast with these findings the reaction was nearly complete and showed a high selectivity with FeII as catalyst. So, only 1% of the aniline, but 10% of nitrosobenzene \( (10) \) and 37% of ortho-quinone \( (4) \) were found in the reaction mixture (Scheme 4). The high reactivity of the Fe-complex corresponds probably more to a reaction mechanism like in the hydroquinone than in the phenol oxidation [5a].
According to literature a higher reactivity could be observed by using tert-butylhydroperoxide (TBHP) as oxidising agent [1c,2a]. Therefore, the catalyst, the substrate 2 and TBHP were dissolved in dichloromethane and stirred until the reaction was completed. The catalyst was separated by filtration through a short silica gel column and the products were isolated by TLC yielding the corresponding iminoquinone (11) [14] and the nitro derivative (13) [15] (Scheme 5). The results are summarised in Table II.

**Table II. Catalytic oxidation of 2 with tert-butylhydroperoxide.**

<table>
<thead>
<tr>
<th>Catalyst</th>
<th>Time [min]</th>
<th>Conversion [%]</th>
<th>Product yield[a]</th>
</tr>
</thead>
<tbody>
<tr>
<td>MnI</td>
<td>15</td>
<td>100</td>
<td>26, 50</td>
</tr>
<tr>
<td>FeI</td>
<td>1440b</td>
<td>100</td>
<td>8, 45</td>
</tr>
<tr>
<td>FeII</td>
<td>15</td>
<td>100</td>
<td>11, 37</td>
</tr>
<tr>
<td>CoI</td>
<td>45</td>
<td>100</td>
<td>26, 40</td>
</tr>
<tr>
<td>CoII</td>
<td>120</td>
<td>97</td>
<td>29, 42</td>
</tr>
<tr>
<td>CoV</td>
<td>900</td>
<td>89</td>
<td>34, 31</td>
</tr>
</tbody>
</table>

[a] Isolated yield referred to the yield of the educt; b sum of 11 and 12; c no complete conversion after a reaction time of 300 min.

Most of the complexes show a very strong catalytic activity. Thus, no distinct dependence on the central atom could be observed for this type of reaction. Only in the case of CoV a total conversion could not be achieved. The highest activities were observed with MnI and FeII where the conversion was completed after 15 minutes.

In contrast to the phenol oxidation only a few products could be isolated and identified from 2. Furthermore, the oxidation of the aniline leads only to relatively slight differences in the product distribution on changing the complex. It is striking, however, that for the iron complexes the yield of 11 + 12 was much lower than in the case of the cobalt and manganese compounds.

The active species in the TBHP/CoL oxidation of 2 is assumed to be the tert-butylperoxy radical.
(tBu–OO–) or the tert-butoxy radical (tBu–O–) which result from the homolytic cleavage of the M–O-Bond in the initially formed M

III–OO–
tBu-Complex [1c]. Since the reactivity and the product distribution for the other two central atoms do not differ significantly compared to the cobalt containing catalysts – apart from the above mentioned differences – it can be assumed that such a species is also present for manganese and iron complexes. This could be the reason for the very high activities of the iron containing complexes with aniline as substrate in contrast to the phenol oxidation by molecular oxygen.

Conclusions

The investigations show that Schiff-base complexes of the type I–IV, with the exception of the iron complexes, catalyse the oxidation of phenol with higher reactivity than that of the well-known Co(salen) complex (CoV). Among the investigated Co-compounds, the complexes CoII and CoIV show the highest reactivity, whereas the Mn-complex is the most reactive one out of the compounds with the same ligand but different central atoms.

In the case of cobalt compounds a phenoxy radical formed by a Co-catalysed reaction with dioxygen could be proved as an intermediate. Since the distribution of the secondary product from this radical varies for each catalyst it can be assumed that the cobalt complexes are not only responsible for the formation of the phenoxy radical but are also involved in the further course of the reaction.

Remarkable is the catalytic oxidation of the substituted aniline with some of the complexes, which could be observed for the first time.

Experimental Part

General: All solvents were dried and distilled before use by standard methods. The complexes MnI [5a], FeI [4c], FeII [17], CoI [16], CoII [17], CoIII [16], CoIV [16] and CoV [18] were prepared as reported in the literature. 1 and 2 were purchased from Aldrich and recrystallised from ethanol before use.

Mass spectra were obtained with a FINNIGAN MAT SSQ 710 apparatus. NMR spectra were recorded on a Bruker AC-200 (1H, 13C NMR) spectrometer. UV/Vis-spectra were obtained with a VARIAN CARY 5 spectrophotometer at 293 K.

EPR spectra were recorded in frozen solutions with a conventional X-band spectrometer (EPS 300E, Bruker) at a temperature of 77 K.

Catalytic oxygenation of 2,4,6-tri-tert-butylaniline

1: A typical batch includes 0.45 mmol (0.118 g) of 1 and 0.09 mmol of the catalyst dissolved in 10 ml of CH2Cl2 under argon. The experiments were carried out at room temperature. The oxidation was effected by pure dioxygen under atmospheric pressure. The catalysis was started with the addition of the dioxygen and stopped after 3 h or when no further reaction (TLC control) could be observed. The catalyst was removed from the reaction mixture by column chromatography (silica gel, solvent: CH2Cl2).

i) The products were separated by preparative TLC (silica gel/CaSO4; CH2Cl2 : 2n-hexane = 3 : 1). The product yields were determined gravimetrically and the products were characterised by mass spectra and NMR spectroscopy. The spectral and analytical data were checked against literature values: 3 [3a], 4 [19], 5 [3a], 6 [20].

ii) A Vis-spectrum was recorded of the reaction mixture to determine the amount of ortho-quinone 4 (λmax = 575 nm, ε = 48.61 · mol–1 · cm–1, CH2Cl2). With the aid of the position of the olefinic protons in the 1H NMR spectrum of the mixture the products could be characterised. (1: δ = 7.19; 3: δ = 6.49; 4: δ = 6.9 (d, J = 2.3 Hz), δ = 6.2 (d, J = 2.3 Hz); 5: δ = 6.57; 6: δ = 6.67; 7: δ = 6.68; 8: δ = 6.73; 9: δ = 6.57 (the signal of the O–H proton (δ = 1.05) is in the range of the signals of the protons of the tert-butyl groups). The quantification ensues from the integration of these peaks and a calibration with the amount of ortho-quinone 4.

Catalytic oxidation of 2,4,6-tri-tert-butylaniline

2: a) Oxidation with dioxygen: In a typical batch 0.1 mmol of the catalyst and 0.131 g (0.5 mmol) of 2 were dissolved in 25 ml of CH2Cl2. The solution was exposed to pure oxygen over a period of 2 h at the beginning of the reaction and after a reaction time of 24 h again. The reaction was stopped after 29 h. The products were isolated and characterised as described above.

b) Oxidation with TBHP: All samples were handled under an atmosphere of argon. To a solution of 2 (0.118 g, 0.45 mmol) in CH2Cl2 (10 ml) containing 0.09 mmol of the catalyst was added 3.6 mmol of TBHP (80% in (tert-BuO)2). After the reaction was completed as monitored by TLC the mixture was filtered through a column of silica gel and eluted with CH2Cl2 (50 ml altogether). Evaporation of the eluent followed by TLC separation of the resulting mixture gave the products
11 and 13. Under the conditions used in this investigation no isolation of 12 was possible due to the degradation of this compound during the reaction and on silica gel resulting in the formation of 11. For spectral and analytical data see [1c].

Investigation of the phenoxyl radical: 0.45 mmol of phenol 1 and 0.09 mmol of the cobalt complex were dissolved in 5 ml of CH$_2$Cl$_2$ under anaerobic conditions. For the start of the reaction, the solutions were set under an atmosphere of dioxygen. These mixtures were taken for UV/Vis- and EPR-spectroscopic measurements. The „classical“ synthesis of the phenoxyl radical was performed according to [12], using lead dioxide as oxidising agent under an argon atmosphere.

Acknowledgements

We are obliged to the Deutsche Forschungsgemeinschaft, the Fonds der Chemischen Industrie and the Freistaat Thüringen for financial support.
[12] a) E. Müller, K. Ley, Chem. Ber. 87, 922 (1954);
[13] It was verified in a separate experiment that the observed signal resulted really from an interaction of the phenoxy radical with the catalyst: Phenoxyl radicals generated with lead dioxide were mixed with the catalyst leading to the same signal in UV/Vis spectrum with a maximum at $\lambda = 707$ nm.
[14] The product 12 which was also formed in the catalytic cycle could not be isolated due to its decomposition during the reaction and on the silica gel column being turned into the iminoquinone 11.
[15] Recent investigations [1c] have shown that the nitrobenzene (13) is formed by oxidation of the primary product nitrosobenzene (10) by an excess of TBHP.
[16] a) E.-G. Jäger, P. Renner, Z. Chem. 17, 189 (1977);
[19] a) S. Berger, A. Rieker, Chem. Ber. 109, 3252 (1976);