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Homogeneous catalytic oxidation of *o*-substituted anilines with dioxygen in the presence of cobalt and manganese complexes

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Abstract. Homogeneous catalytic oxidation of *o*-substituted aniline derivatives by dioxygen under ambient conditions has been studied. Systems exemplifying two fundamental mechanisms are described. Molecular oxygen may enter the catalytic cycle via either dioxygen complex formation, or the generation of $RO_2^{\bullet}$ radicals via oxidation by metal salts. 2-Aminophenol is catalytically converted to 2-aminophenoxazin-3-one (APX) via a series of H-abstraction and addition steps in the presence of triphenylphosphine-cobaloxime(II), which readily forms dioxygen complexes. A methyl-substituted 1,5-benzodiazepine (**13**) derived from *o*-phenylenediamine undergoes a methyl to formyl group oxidation catalyzed by manganese(III) salts via a free-radical process of remarkable selectivity.

INTRODUCTION

Oxidation with dioxygen under mild conditions, catalyzed by transition metal complexes is important with respect to both the modeling of oxygenase enzymes and synthetic applications. In order to be able to design catalyst systems of high activity and selectivity, the elucidation of mechanistic details is of considerable importance. Extensive work has been done on various types of dioxygen activating systems, and catalysts are available for the oxidation of different classes of organic compounds, such as alkanes, alkenes, aromatics, phenols, catechols, thiols, thioethers, amines, phosphines, etc. [1,2]. Complexes of iron, copper, cobalt, ruthenium, rhodium, palladium are most often encountered as catalysts.

There have been numerous attempts to describe catalytic dioxygen activation in terms of various reaction mechanisms. A suitable reaction mechanism should explain how the dioxygen molecule is transformed into a reactive species. The latter may be either a free peroxy radical $RO_2^{\bullet}$ formed from O_2 and a free radical $R^{\bullet}$:

$$R^{\bullet} + O_2 \longrightarrow RO_2^{\bullet} \qquad (1)$$

or it may be a transition metal (M) dioxygen complex (superoxo, **1**, or μ-peroxo, **2**):

$$L_nM + O_2 \rightleftharpoons \underset{(1)}{L_nMO_2} \xrightleftharpoons{L_nM} \underset{(2)}{L_nMO_2ML_n} \qquad (2)$$

where L can be any ligand(s) in the coordination sphere. Dioxygen

activation means that the products of reactions (1) and (2) are capable of reacting with an oxidizable substrate via H-atom abstraction (or electron and proton transfer) steps, *e.g.*

$$RO_2^{\bullet} + SH_2 \longrightarrow ROOH + SH^{\bullet} \quad (3)$$

$$L_nMO_2 + SH_2 \longrightarrow L_nMO_2H + SH^{\bullet} \quad (4)$$

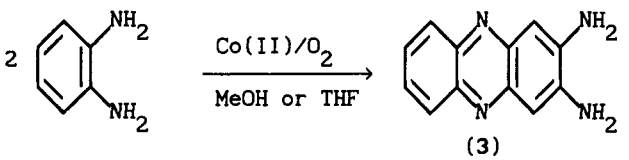
which would initiate free-radical chain reactions or other processes (including oxygen transfer), ultimately leading to catalytic oxidation of the substrate.

Although there is a wide variety of reactions following these initial events, it is a distinctive feature of the given catalytic system whether the interaction between the substrate and the activated form of dioxygen occurs by step (3) or (4).

In this paper we will survey the catalytic oxidation of *o*-substituted anilines and some of their derivatives. Of specific interest is the oxidative aldol condensation discovered in the case of 1,5-benzodiazepine **19**, which is a derivative of *o*-phenylenediamine.

1. OXIDATIVE DEHYDROGENATION OF *o*-PHENYLENEDIAMINE

We have reported that *o*-phenylenediamine (OPD) can be converted to 2,3-diaminophenazine (**3**) in the presence of cobalt(II) salts at room temperature and 1 atm of oxygen [3].



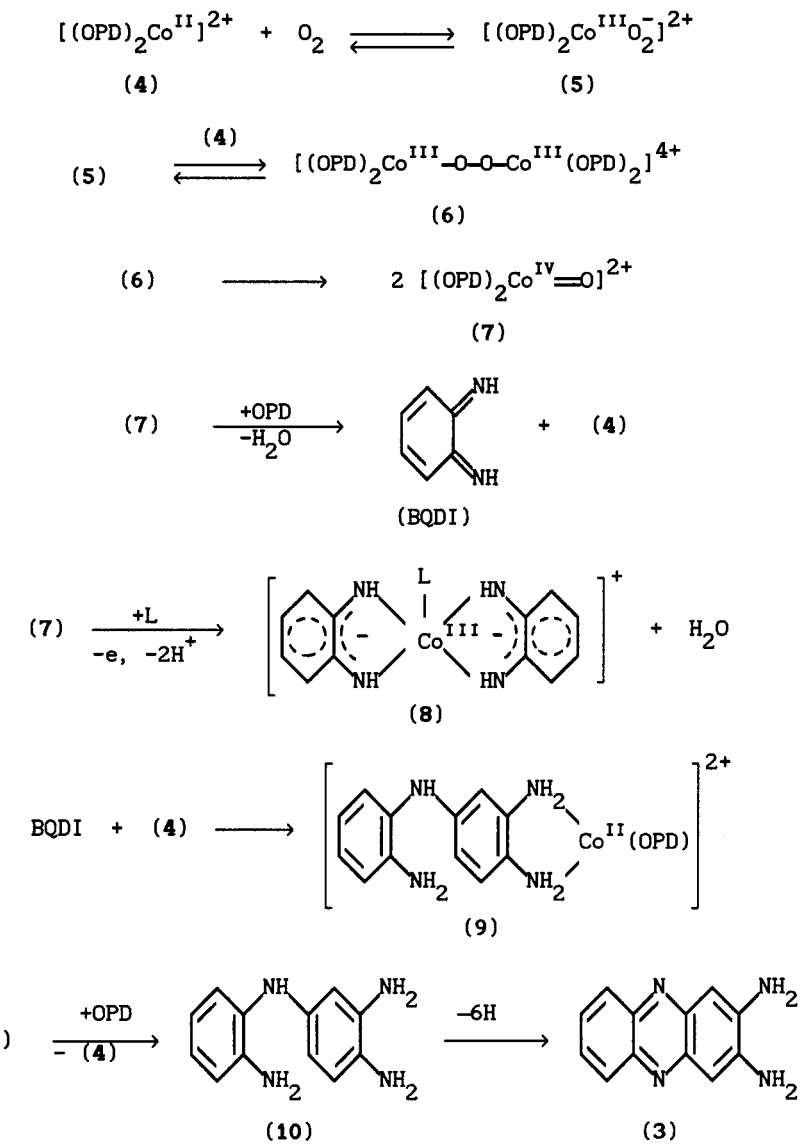
(3) (5)

Reaction (5) occurs via a complex mechanism involving the transient formation of μ-peroxodicobalt(III) (**6**), and oxocobalt(IV) (**7**) complexes, the mixed ligand species **9** and *o*-benzoquinonediimine (BQDI). We suggest Scheme 1 for describing the mechanism of reaction (5). The further dehydrogenation of intermediate **10** to the product (**3**) probably involves H-atom abstractions by the dioxygen complexes **5**, **6** and oxocobalt(IV) species **7**, but no details are known about this multistep process.

The superoxo and μ-peroxo species in the above scheme are analogs of similar dioxygen complexes formed from cobalt(II) complexes of various amino ligands [6], and the proposed oxocobalt(IV) intermediate has precedents in cobaloxime chemistry [7-9].

The oxocobalt(IV) species **7** in Scheme 1 may react in two ways: (i) it may afford coordinated BQDI, which is displaced by free OPD, or (ii) in the presence of added Ph_3P, Ph_3As or Ph_3Sb it produces stable bis(*o*-benzosemiquinonediimine)cobalt(III) complexes (**8**), which have been isolated and the Ph_3P derivative has been characterized by X-ray diffraction [4,5].

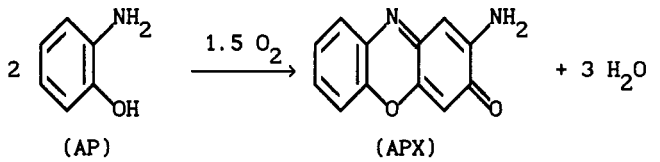
Scheme 1



Free BQDI undergoes 1,4-addition with coordinated OPD, a reaction required to create the skeleton which upon further stepwise dehydrogenation yields 2,3-diaminophenazine (3).

2. OXIDATIVE DEHYDROGENATION OF 2-AMINOPHENOL

We have previously reported that 2-aminophenol (AP) can be catalytically oxidized (dehydrogenated) at room temperature and 1 atm O_2 to 2-aminophenoxazin-3-one (APX) in the presence of cobalt(II) salts [11] or a soluble cobalt(II) phthalocyanine derivative [12].



We now report that another suitable catalyst for the oxidation is *bis*(triphenylphosphine)cobaloxime(II), $(Ph_3As)_2Co(Hdmg)_2$, where $Hdmg^-$ is the dimethylglyoximato monoanion, which readily forms dioxygen complexes in MeOH. We have carried out a detailed kinetic study of this reaction and have found that kinetic equation (6) describes

$$\text{RATE} = \frac{k_1K_1K_2\,[Co]_o[AP]_o[O_2]}{1 + K_1\,[AP]_o + K_2\,[O_2]} \qquad (6)$$

the dependence of the rate on reactant concentrations and O_2 pressure and is consistent with reaction mechanism (7) - (11), where Co stands for $Co(Hdmg)_2$, AP$^\bullet$ is the 2-aminophenoxyl radical, and BQMI is *O*-benzoquinone monoimine.

$$Co^{II} + AP \underset{}{\overset{K_1}{\rightleftharpoons}} (AP)Co^{II} \qquad (7)$$

$$(AP)Co^{II} + O_2 \overset{K_2}{\rightleftharpoons} (AP)Co^{III}(O_2^-) \qquad (8)$$

$$(AP)Co^{III}(O_2^-) \xrightarrow{k} Co^{III}(O_2H^-) + AP^\bullet \qquad (9)$$

$$2Co^{III}(O_2H^-) \xrightarrow{\text{fast}} 2Co^{III}(OH) + O_2 \qquad (10)$$

$$Co^{III}(OH) + AP^\bullet \xrightarrow{\text{fast}} (BQMI) + Co^{II} + H_2O \qquad (11)$$

In this mechanism AP first replaces the axial ligand in $(Ph_3As)Co(Hdmg)_2$ (the first Ph_3As is lost upon dissolution in MeOH), then a superoxocobaloxime derivative is formed, in which the cobalt center mediates the transfer of one electron and a proton from AP to O_2, generating an *o*-aminophenoxyl radical. Reaction (10) leading to the regeneration of $\frac{1}{2}O_2$ serves to explain two important facts. One is that the volumetric dioxygen absorption curves exhibit a sharp break after the uptake of 0.5 mol O_2/mol Co, but, as shown by UV-VIS spectra, at that moment the solution contains only traces of the μ-peroxo-dicobaloxime(III), which would correspond to that stoichiometry. The other fact is that, according to ESR measurements, neither the paramagnetic cobaloxime(II) nor the superoxocobaloxime, $Co^{III}(O_2^{\bullet -})$, can be detected in the reacting system [13]. Thus during the catalytic reaction cobalt is predominantly present as the hydroxocobaloxime(III), Co(OH). It does not activate O_2 in the above fashion, but a slow autocatalytic reaction with AP can be demonstrated in the absence of cobaloxime(II), which starts with the step:

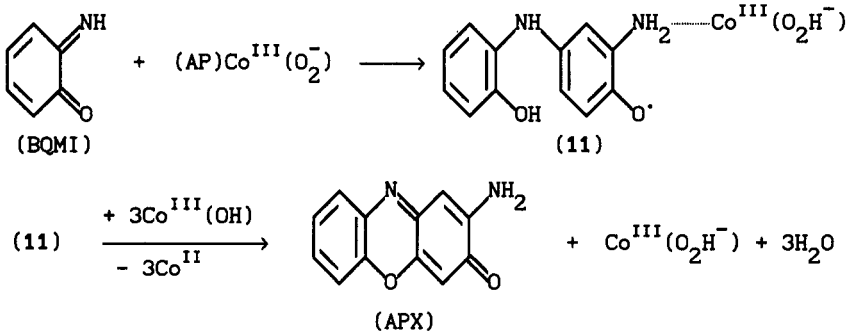
$$Co^{III}(OH) + AP \longrightarrow Co^{II} + AP^\bullet + H_2O \qquad (12)$$

Following this the cobaloxime(II) formed will catalyze the reaction as shown by mechanism (7) - (11).

This catalytic cycle is accessible to kinetic studies only up to the formation of BQMI. There are several further reactions before the product APX is formed. The proposed sequence of steps is shown in Scheme 2.

In Scheme 2 an AP molecule coordinated to cobaloxime(II) in axial position via its N-atom in the ternary complex $(AP)Co^{III}(O_2^-)$ attacks a free BQMI, undergoing 1,4-addition to yield the precursor of intermediate **11**, the corresponding 2-substituted phenol. Intramolecular electron transfer, accompanied with solvent (MeOH) mediated H^+-transfer converts the latter to a coordinated free radical **11**, which we have detected in the reacting mixture by the ESR technique [13]. Further multistep dehydrogenation and ring closure affords the observed product APX.

Scheme 2

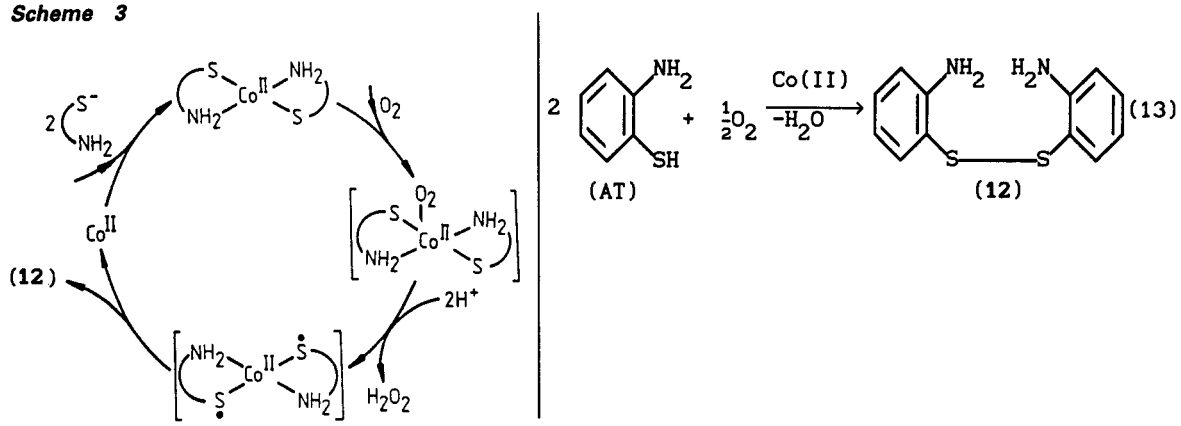


3. OXIDATIVE DEHYDROGENATION OF 2-AMINOTHIOPHENOL

2-Aminothiophenol (AT) is catalytically oxidized by O_2 in MeOH or THF at room temperature in the presence of cobalt(II) [11] to 2,2'-diaminodiphenyldisulfide (**12**).

Catalytic activity in this system is due to the formation of $Co(AT)_2$ complexes from cobalt(II) ions and AT, which is deprotonated and S,N-bonded to cobalt(II). No stable superoxocobalt(III) complex can be detected in this system owing to its short lifetime. The catalytic cycle shown in Scheme 3 is proposed to describe product formation from coordinated, S-centered free radicals, which are also too reactive to be detected.

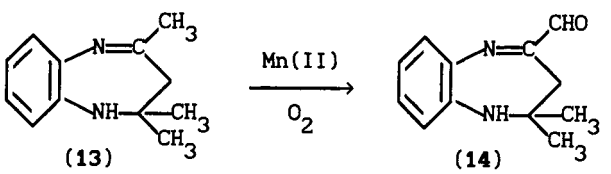
Scheme 3



4. OXYGENATION OF AN ACTIVATED METHYL GROUP CATALYZED BY MANGANESE SALTS

Activation of hydrocarbons attracts increasing interest due to the remarkable insight that working model catalysts provide into the mechanisms operative in enzymatic systems. Catalyst systems effective under ambient conditions most often include iron, cobalt, ruthenium or copper complexes [1]. The following example describes a manganese(II,III) redox catalyst which generates free radicals under very mild conditions from the *o*-phenylenediamine derivative **13**, and effects its oxygenation to aldehyde **14** without intervention of dioxygen complexes.

The catalytic oxygenation of the 4-methyl group of 1,5-benzodiazepine derivative **13**, eq. (14), to the corresponding aldehyde **14** takes place at 25°C and 1 atm of O_2 in the presence of manganese(II) salts in MeOH or acetone [14]. Reaction (14) is followed by a novel oxidative aldol type condensation between **13** and **14**, whose product has been characterized by X-ray diffraction [15].

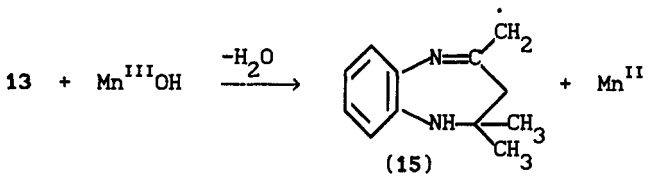


(13) (14) (14)

There is a long induction period before reaction (14) starts. The rate of O_2-uptake increases rapidly, indicating an autocatalytic behavior. Added manganese(III) acetate eliminates the induction period. The mechanism proposed to interpret these observations is shown in eqs (15) - (19).

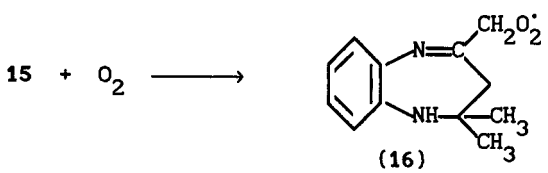
$$Mn^{II} \xrightarrow[\text{very slow}]{O_2,\ 2H^+} Mn^{III}OH \qquad (15)$$

(several steps)



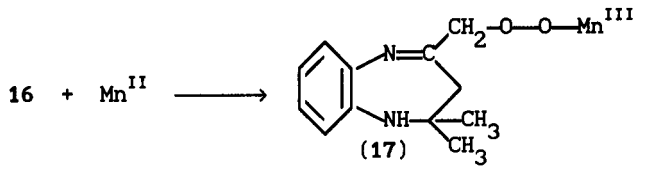
(15) (16)

(15)

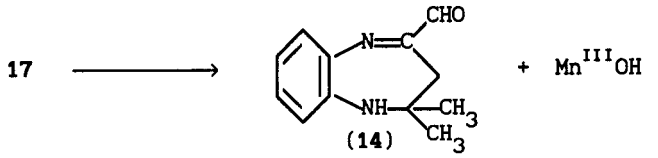


(16) (17)

(16)



(18)



(19)

The exact mechanism of the very slow oxidation of added Mn(II) ions, eq. (15), is not known at present, but adventitious hydroperoxides are likely to be involved, generating Mn^{III} species via the reactions:

$$ROOH + Mn^{II} \xrightarrow[\text{slow}]{\text{very}} RO^{\cdot} + Mn^{III}OH \qquad (20)$$

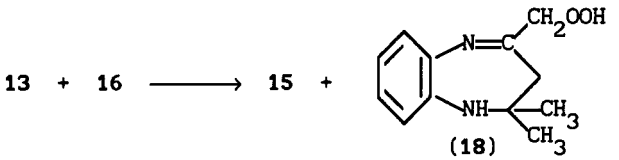
$$RO^{\cdot} + RH \longrightarrow R^{\cdot} + ROH \qquad (21)$$

$$R^{\cdot} + O_2 \longrightarrow RO_2^{\cdot} \qquad (22)$$

$$RO_2^{\cdot} + Mn^{II} \longrightarrow ROOMn^{III} \qquad (23)$$

$$ROOMn^{III} \longrightarrow RO^{\cdot} + Mn^{III}OH \qquad (24)$$

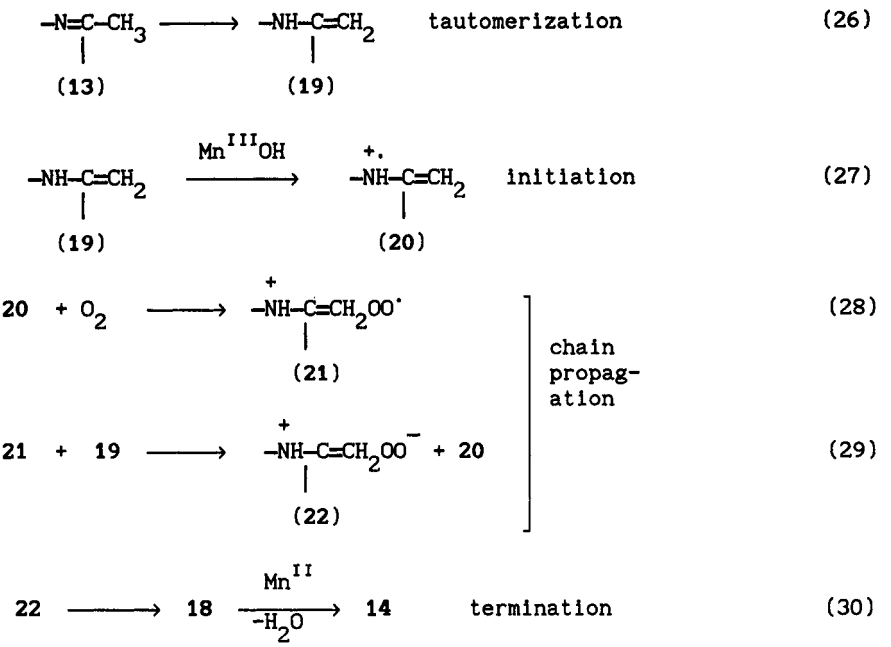
The autocatalytic behavior is apparently due to the much faster regeneration of $Mn^{III}OH$ via steps (17) - (19) than is its formation by reaction (20). Also, the formation of a hydroperoxide (18) via reaction (25) with subsequent manganese-assisted decomposition as in eqs (21) - (24) might contribute to the observed autocatalytic acceleration.



(25)

According to the above mechanism, the methyl group adjacent to a C=N double bond is readily oxidized to a free radical (15), which binds O_2 to form an alkylperoxy radical (16). Oxidative addition of 16 to Mn^{II} yields an alkylperoxomanganese(III) complex (17), eq. (18). Heterolytic O—O bond cleavage in 17 affords the aldehyde and regenerates the active $Mn^{III}OH$ intermediate, eq. (19).

The oxidation of 13 to 14 can also be described by an alternative mechanism, which assumes initial tautomerization (eq. 26) to an enamine (19) followed by electron abstraction from the N-atom. The cation radical formed (20) initiates a chain reaction, eqs (28) - (29), ultimately affording hydroperoxide 18, which is reduced by Mn(II) to aldehyde 14 [16].



Work is in progress on further details of the catalytic oxidation of aromatic derivatives of the type discussed in this paper.

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