DALTON
FULL PAPER

Oxidation of *N*-benzylidene-2-hydroxyaniline by dioxygen catalysed by a dicobalt complex†

Shian Yuh Chang, Yee Hsing Cheng, Bing-Jium Uang and Cheu Pyeng Cheng*

Department of Chemistry, National Tsing Hua University, Hsin-Chu, 30043, Taiwan.
E-mail: cpcheng@faculty.nthu.edu.tw. Fax: 886-3-5721174

Received 10th May 1999, Accepted 8th June 1999

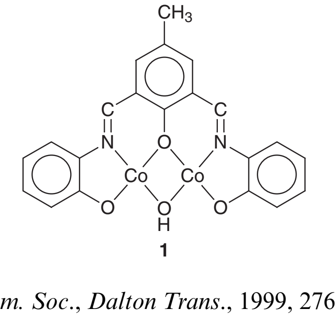
The oxidation of *N*-benzylidene-2-hydroxyaniline and its related derivatives by O_2 catalysed by $[Co_2L(\mu\text{-OH})]$ $\{H_3L = 2,6\text{-bis}[(2\text{-hydroxyphenyl})\text{iminomethyl}]\text{-}4\text{-methylphenol}\}$ in DMF at 363 K was investigated. The oxidation products were the corresponding 2-substituted benzoxazoles. However, a side reaction leading to 2-aminophenoxazine-3-one *via* hydrolysis of the starting compound with water produced in the oxidation, followed by the oxidation of aminophenol, was established. If a dehydrating agent such as anhydrous Na_2SO_4 or 4 Å molecular sieves was present in the reaction mixture the isolated product yields were above 87%. The fact that the reaction rate of the oxidation process in the presence of a radical scavenger was similar to that without suggests that it was a non-radical process. The initial oxidation rates depended linearly on the concentration of catalyst. The rates also depended linearly on the concentration of the organic substrate *N*-benzylidene-2-hydroxyaniline and O_2 pressure when these variables were small ([substrate] < 0.2 M, O_2 pressure < 70 kPa). At high concentration of substrate and O_2 pressure the rate showed saturation behavior. These kinetic data could be satisfactorily accounted for by a mechanism with initial co-ordination of substrate to $[Co_2L(\mu\text{-OH})]$, followed by the co-ordination of O_2 to the catalyst, then the rate limiting step of oxidation of substrate. The formation of the adduct between *N*-benzylidene-2-hydroxyaniline and catalyst at 298 K was characterized by UV-Vis spectroscopy. The variation of the initial rates among the organic substrates could be explained by stereoelectronic effects. Moreover, the influence of acetic acid which slowed the initial rate of oxidation and weak base (2,6-di-*tert*-butylpyridine) which had little effect on the rate could also be satisfactorily accounted for based on the acid–base properties of the proposed reaction intermediates.

Introduction

Cobalt complexes have been widely used in catalysing the reactions of organic substrates with molecular oxygen.[1–20] When dioxygen participates directly in the oxidation reaction the catalytic reaction may involve several different intermediates, such as cobalt–dioxygen adducts, organic free radicals, and organic hydroperoxides. There is also another type of cobalt catalysed dioxygen reaction in which oxygen is used only indirectly. In these reactions[4,7] the co-ordinated nitro group serves as an oxygen donor to oxidize organic substrates. The nitro group is then turned into co-ordinated nitrosyl which can be oxidized by dioxygen to regenerate the nitro group. The organic substrates involved in these catalytic oxidation reactions consist of a variety of functional groups including olefins,[1–7] phenols,[8–10] secondary alcohols,[11] substituted anilines,[12] amines,[13,14] hydrazones,[15] ethers,[3,16] iodo-compounds,[17] naphthalene,[2] anthracene,[2] benzylic compounds[2,18,19] and cyclohexane.[20] To add to this broad range of organic substrates, we report here that *N*-benzylidene-2-hydroxyaniline and its related derivatives can be oxidized by dioxygen to the corresponding benzoxazoles catalysed by a dicobalt complex.

Derivatives of 2-substituted benzoxazole are conventionally prepared by the dehydrative cyclization of the amides formed by the condensation of an aminophenol and a carboxylic acid or its derivative.[21–26] The reaction of aryl halides and an aminophenol under CO atmosphere catalysed by palladium compounds can also lead to the desired amides.[27] Another convenient method of preparing 2-substituted benzoxazole is the oxidation of *N*-benzylidene-2-hydroxyaniline which can be prepared by the condensation of aldehydes and 2-aminophenol. The oxidants that have been used include nickel peroxide,[28] silver oxide,[29] lead(IV) tetraacetate[30,31] and lead(IV) phosphate.[32] Oxygen has also been employed as the oxidant with a copper(I) salt as the catalyst.[33] However, a large amount of catalyst (substrate, 5 mmol; Cu^I, 2 mmol) was required in this Cu^I-catalysed reaction. It is interesting that *N*-alkylidene-2-hydroxyanilines can also be cyclized to the corresponding oxazole photochemically.[34] Alternatively, the reaction between a primary alcohol and 2-aminophenol catalysed by ruthenium complexes[35] above 473 K can also lead to benzoxazole, presumably involving the *N*-benzylidene-2-hydroxyaniline intermediate.

Recently, we showed that the oxidation of PPh_3 using O_2 as oxidant in DMF solution at 353 K can be catalysed by the dicobalt complex **1**, $[Co_2L(\mu\text{-OH})]$ $\{H_3L = 2,6\text{-bis}[(2\text{-hydroxyphenyl})\text{iminomethyl}]\text{-}4\text{-methylphenol}\}$.[36] In solid or solution, each cobalt(II) ion in **1** is expected to be co-ordinated by other ligand(s) including that of solvent molecule(s). Though the detailed structure of **1** is not known exactly, the co-ordination of L to the cobalt(II) ions can be depicted as below based on the structure of $[Cu_2L(\mu\text{-OH})]$ in which a planar $Cu_2N_2O_4$ arrangement was observed.[37]



1

---

† *Supplementary data available*: characterisation data. For direct electronic access see http://www.rsc.org/suppdata/dt/1999/2769/, otherwise available from BLDSC (No. SUP 57583, 2 pp.) or the RSC Library. See Instructions for Authors, 1999, Issue 1 (http://www.rsc.org/dalton).

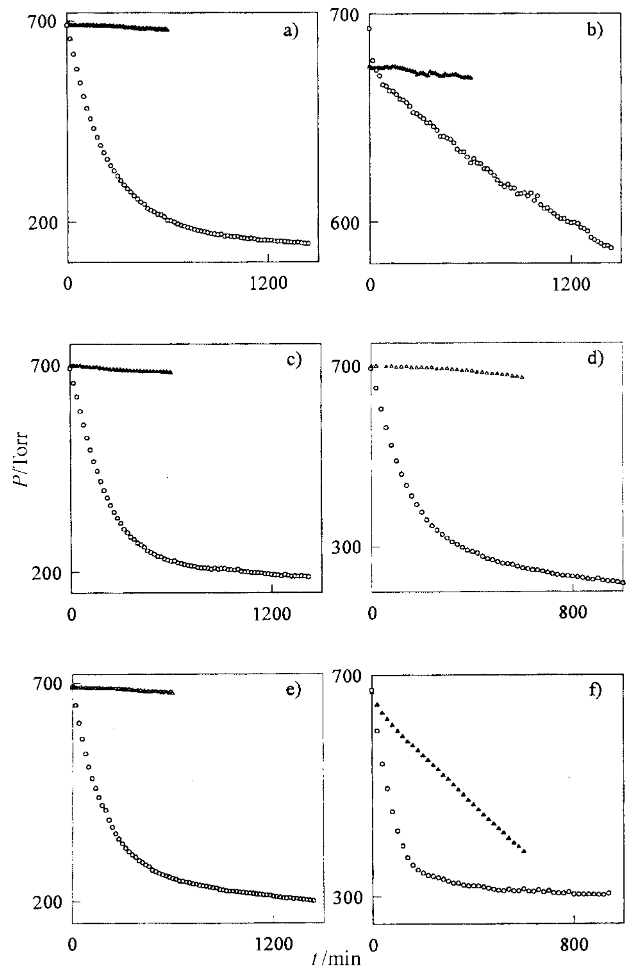


Fig. 1 The oxygen pressure change with (○) and without (▲) the presence of dicobalt catalyst **1** for the substrates **Ia** (a), **Ib** (b), **Ic** (c), **Id** (d), **Ie** (e) and **If** (f). Reaction conditions: $V(O_2) = 0.110$ L at 25 K; reaction mixture 5.0 mmol substrate, 0.050 mmol catalyst in 10.0 mL DMF at 363 K.

In this oxidation a reactive intermediate which is capable of oxidizing olefins to epoxides, alcohols to carbonyl compounds, sulfide to sulfoxide and sulfoxide to sulfone was generated. These substrates can not be oxidized without the presence of PPh_3 under the reported reaction conditions. We have now studied the oxidation of *N*-benzylidene-2-hydroxyaniline by O_2 to benzoxazole catalysed by this dicobalt complex to extend the range of application of this catalytic system. The dicobalt complex was proven to be very effective and gave almost quantitative yield for the oxidation of *N*-benzylidene-2-hydroxyaniline even in the absence of PPh_3. The kinetics of this oxidation reaction is consistent with an initial co-ordination of the organic substrate and O_2 to the catalyst, followed by a rate determining step that leads to the product and water.

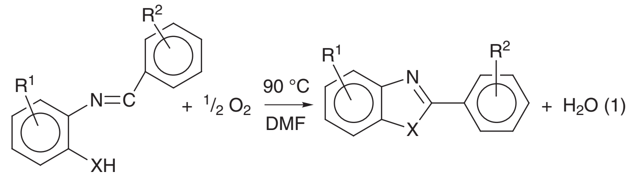
Results and discussion

N-Benzylidene-2-hydroxyaniline **Ia** and its derivatives **Ib**–**Ie** in DMF do not react or react very slowly with O_2 directly at 363 K (Fig. 1). However in the presence of a small amount of dicobalt catalyst **1** an appreciable O_2 pressure drop can be observed. For reactants **Ia** and **Ic**–**Ie** the O_2 pressures decrease rapidly for 600 min, then slow down. The decrease is approximately 65 kPa. The number of moles of *N*-benzylidene-2-hydroxyaniline (5.0 mmol) in the reaction mixture is slightly less than twice the O_2 consumed (2.9 mmol). This stoichiometric relationship indicates that each mol of O_2 can oxidize two mol of organic substrate. Additionally, there is another oxidation reaction in which the stoichiometry requires more oxygen. For **Ib** the rate of oxidation is much slower than for the other compounds (Fig. 1b). In a 24 h reaction period the O_2 pressure decreased by 13 kPa only. As for **If**, which exists as benzothiazoline rather than the structure depicted in eqn. (1), it can be oxidized directly by O_2 at 363 K (Fig. 1f). However, addition of **1** also speeds up the oxidation reaction. The oxygen pressure changes in Fig. 1(c)–1(e) are very similar to that in Fig. 1(a).

Table 1 Yields and initial reaction rates of benzoxazole and its derivatives **IIa**–**IIf** from O_2 oxidation of **Ia**–**If** catalysed by $[Co_2L(\mu\text{-}OH)]^a$

Entry	Product	Yield(%) *b*	Yield(%) *c*	Rate^d/10^{-5} M s^{-1}
1	**IIa**	68	87	3.52
2	**IIb**	21	—	0.427
3	**IIc**	81	96	3.26
4	**IId**	74	93	3.90
5	**IIe**	70	90	3.45
6	**IIf**	88	—	4.55

^{a}Reaction conditions: substrate, 5.0 mmol; catalyst, 50 μmol, in 10 mL DMF at 363 K; P_{O_2} 90.7 kPa, $V(O_2)$ 0.11 L at 298 K. ^{b} Isolated yield for a 24 h reaction period under the conditions in footnote *a*. ^{c} Isolated yield for a 24 h reaction period under the reaction conditions in footnote *a* with the addition of 1.0 g of 4 Å molecular sieves. ^{d} Initial rate is defined as d[substrate]/d*t* obtained from the O_2 pressure change as $\{dP_{O_2}/dt\}\{V(O_2)/RT\}\{1/V(sol)\}$.



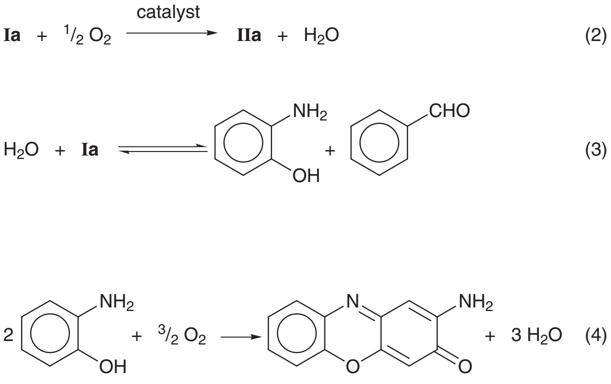
	R1	R2	X
Ia	H	H	O
Ib	5-Cl	H	O
Ic	5-Me	H	O
Id	H	4-Cl	O
Ie	H	4-Me	O
If	H	H	S

	R1	R2	X
IIa	H	H	O
IIb	5-Cl	H	O
IIc	5-Me	H	O
IId	H	4-Cl	O
IIe	H	4-Me	O
IIf	H	H	S

The ^1H NMR spectrum of a sample containing 0.30 mmol **Ia** and 10 μmol **1** in 0.5 mL d_7-DMF solvent in the absence of O_2 (removed by at least three freeze–pump–thaw cycles) indicated that no new compound is formed in a wide temperature range (223 to 363 K) or after prolonged (1 h) heating at 363 K. After O_2 was introduced into the NMR tube and the reaction mixture heated to 363 K, the ^1H NMR spectrum revealed that there was only one organic product, 2-phenylbenzoxazole. Furthermore, a signal at δ 3.5 indicated the formation of water in the reaction. Therefore, the selectivity of the oxidation reaction is close to 100% in the early stages. After the catalytic oxidation had proceeded for 24 h chromatographic separation of the reaction mixture gave a major product **II** for each reactant **I**. The oxidation reactions catalysed by **1** are summarized in eqn. (1).

The yields for compounds **II** are summarized in Table 1. The particularly low yield for **IIb** is not due to any side reaction, but because of the inherent low reactivity of the substrate. After 24 h reaction time a large amount of **Ib** was still unchanged. However, the low isolated yields for **Ia**–**Ie** in Table 1 are probably due to the additional oxidation pathway that requires more O_2 than that in eqn. (1).

To investigate the nature of the additional oxidation pathway we carried out the catalytic oxidation of compound **Ia** in the presence of anhydrous Na_2SO_4 or 4 Å molecular sieves. The total amount of O_2 consumed in the presence of the dehydrating agent is less than that in its absence. Interestingly, the initial rates are exactly the same regardless of whether the dehydrating agent is present or not. Furthermore, the isolated yield for **IIa** increases from 68 to 87% (Table 1). For **IIc**–**IIe** the isolated yields are equal or better than 90%. From these results it is obvious that water plays a key role in the additional oxidation pathway. It is likely that the water generated in the oxidation of **Ia** may cause the hydrolysis of the substrate to benzaldehyde and 2-aminophenol. We have tested the oxidation of benzaldehyde and 2-aminophenol in the presence of **1**. The result indicates that benzaldehyde is not oxidizable, but 2-aminophenol can be oxidized to 2-aminophenoxazin-3-one by consuming more than one half mol of O_2 per mol of reactant as reported.[12] The details of this oxidation reaction will be published elsewhere. Hence the additional oxidation pathway, in the absence of dehydrating agent, is shown in Scheme 1. In eqn. (4) the reaction yields more water which causes more **Ia** to undergo hydrolysis. In support of this mechanism, benzaldehyde was found chromatographically as a product of the oxidation of **Ia** in the absence of dehydrating agent.



Scheme 1

Compound **If** was not tested for the presence of the additional oxidation pathway because the isolated yield for **IIf** was already high in the absence of dehydration agent. This result suggests that the additional oxidation pathway analogous to that in Scheme 1 is not important. This is further evidenced from the amount of O_2 consumed (2.4 mmol), nearly half that of **If** (5.0 mmol) oxidized at the completion of the oxidation reaction as shown in Fig. 1(f).

In the presence of dehydration agent this catalysed oxidation method gives a yield of benzoxazole or its derivatives that is equal or better than any other oxidation method in the literature.[28–33] Based on the isolated yields, the turnover numbers of the dicobalt complex **1** for the oxidation of compound **Ia** in the absence and presence of dehydrating agent are 67 and 87, respectively. We would point out that the C=N bonds in **1** might be susceptible to hydrolysis.[38] However, there is no sign (based on UV-Vis spectroscopy) of the occurrence of this hydrolysis in either dry or wet DMF at 363 K over a period of 24 h. This stability against hydrolysis may be attributed to the conjunction of C=N bonds with the phenyl rings. Since there is no sign of decay of this catalyst, the turnover number should be much more than 100.

When a small amount of galvinoxyl radical [galvinoxyl = 2,6-di-*tert*-butyl-α-(3,5-di-*tert*-butyl-4-oxo-2,5-cyclohexadien-1-ylidene)-*p*-tolyloxy] and 2,6-di-*tert*-butyl-4-methylphenol, which are a known radical scavenger and a chain inhibitor, were added separately to the reaction mixture the oxidation rates were practically the same. This indicates that the reaction does not go through a free radical chain reaction pathway. In fact, the absence of an induction period in Fig. 1 is also consistent with a non-radical reaction pathway. This is in contrast with the radical mechanism when the reaction is catalysed by copper(I) salt.[33] When a small amount of acetic acid (1.0 mmol) was added to the reaction mixture (5.0 mmol **Ia** and 50 µmol **1** in 10 mL DMF) the rate of oxidation was greatly reduced (Fig. 2). Judging from the initial rates of reaction, the presence of acetic acid reduced the rate of the reaction by a factor of 10. The presence of a non-co-ordinating base 2,6-di-*tert*-butylpyridine induced only a small increase in the rate of the oxidation reaction (Fig. 2).

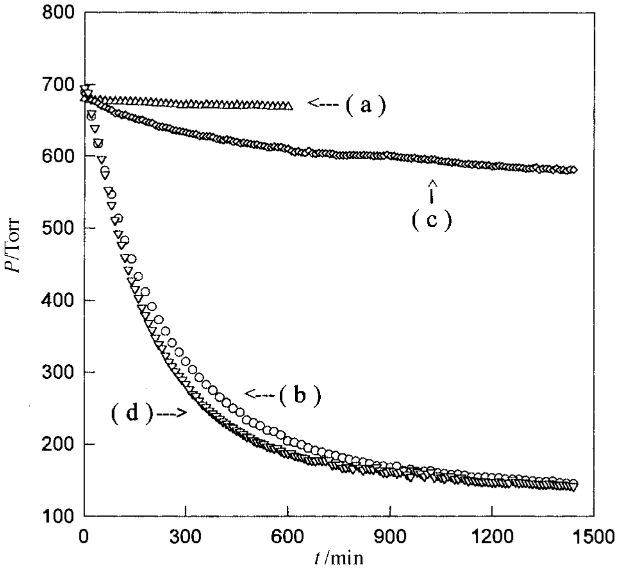


Fig. 2 The oxygen pressure change in the oxidation of compound **Ia** (0.50 M) in DMF at 363 K under various conditions: (a) no catalyst, (b) $[Co_2L(\mu\text{-}OH)] = 5.0$ mM, (c) same as (b) with additional acetic acid (0.10 M), (d) same as (b) with additional 2,6-di-*tert*-butylpyridine (0.10 M).

The kinetics of the catalytic oxidation of compound **Ia** was investigated at 363 K. In Fig. 3(a) the initial rate of oxidation depends linearly on catalyst concentration in the range 0.474×10^{-3} to 7.5×10^{-3} M at an O_2 pressure of 90.7 kPa and **Ia** concentration 0.5 M. The dependence of initial rate on the concentration of **Ia** under the conditions of fixed initial O_2 pressure 90.7 kPa and $[\mathbf{1}] = 5.1 \times 10^{-3}$ M is shown in Fig. 3(b). At low concentration of **Ia** the initial rate depends linearly on [**Ia**]. However for [**Ia**] > 0.2 M the initial rate levels off. This dependence indicates that the co-ordination of **Ia** to the catalyst must be involved in the reaction mechanism. In Fig. 3(c), the initial reaction rate depends linearly on O_2 pressure and shows slight saturation behavior at $[\mathbf{Ia}] = 0.5$ M and $[\mathbf{1}] = 5.1 \times 10^{-3}$ M. This leveling off indicates that O_2 co-ordination to catalyst must also be involved in the reaction mechanism. From these dependencies of initial rates on [**1**], [**Ia**], and P_{O_2}, the rate law (5)

$$\text{rate} = d[\mathbf{Ia}]/dt = b[\mathbf{1}][\mathbf{Ia}]P_{O_2}/(1 + a[\mathbf{Ia}]P_{O_2}) \qquad (5)$$

is initially proposed. According to this rate law the initial rate depends linearly on [**1**], and also linearly on [**Ia**] and P_{O_2} when these two parameters are small, and a saturation behavior is expected when either [**Ia**] or P_{O_2} is large. These dependencies are qualitatively consistent with the experimental observations. The solid curve in Fig. 3(b) is the result of the non-linear least-square curve-fitting analysis of the initial rates *vs.* [**Ia**] according to the rate law (5) with the parameters $b = 1.79(\pm 0.45) \times 10^{-3}$ kPa^{-1} M^{-1} s^{-1} and $a = 0.178(\pm 0.054)$ M^{-1} kPa^{-1}. The solid curves in Fig. 3(a) and 3(c) are calculated from the rate law (5) with these values of *a* and *b*. It is obvious that the fit to the data in Fig. 3(c) is unacceptably poor. To account for the weak dependence of the initial oxidation rate on dioxygen pressure we propose a modified rate law (6). In this

$$\text{rate} = d[\mathbf{Ia}]/dt = b[\mathbf{1}][\mathbf{Ia}]P_{O_2}/(1 + a[\mathbf{Ia}](1 + mP_{O_2})) \quad (6)$$

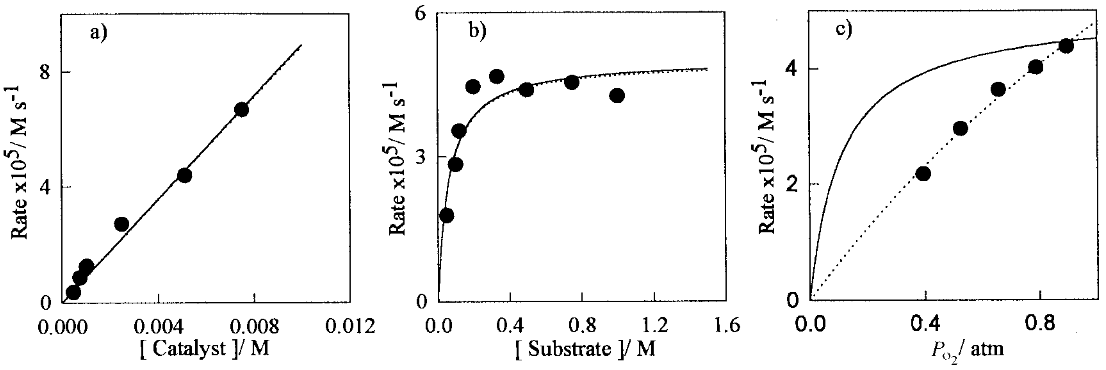
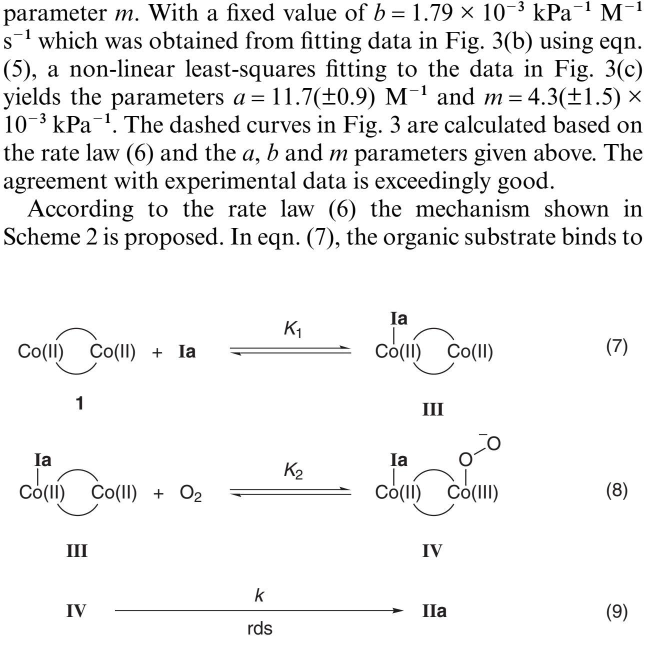


Fig. 3 Kinetics of the catalysed oxidation of compound **Ia** in DMF at 363 K: (a) initial rate as a function of [Co_2L(μ-OH)], [**Ia**] = 0.50 M, P_{O_2} = 90.7 kPa; (b) initial rate as a function of [**Ia**], [Co_2L(μ-OH)] = 5.0 mM, P_{O_2} = 90.7 kPa; (c) initial rate as a function of P_{O_2}, [Co_2L(μ-OH)] = 5.0 mM, [**Ia**] = 0.50 M. The solid curves are calculated based on the rate law (5) and parameters obtained from Fig. 3(b) by non-linear least-squares curve-fitting analysis. The dashed curves are calculated based on the rate law (6) and parameters obtained from Fig. 3(b) and 3(c) by non-linear least-squares curve-fitting analysis.

proposed rate law both the linear dependence of the initial rate on P_{O_2} and slight saturation can be accounted for by the new parameter *m*. With a fixed value of $b = 1.79 \times 10^{-3}$ kPa^{-1} M^{-1} s^{-1} which was obtained from fitting data in Fig. 3(b) using eqn. (5), a non-linear least-squares fitting to the data in Fig. 3(c) yields the parameters $a = 11.7(\pm 0.9)$ M^{-1} and $m = 4.3(\pm 1.5) \times 10^{-3}$ kPa^{-1}. The dashed curves in Fig. 3 are calculated based on the rate law (6) and the *a*, *b* and *m* parameters given above. The agreement with experimental data is exceedingly good.

According to the rate law (6) the mechanism shown in Scheme 2 is proposed. In eqn. (7), the organic substrate binds to the dicobalt complex **1** to form adduct **III** with an equilibrium constant K_1. Dioxygen then co-ordinates to **III** to form adduct **IV** in eqn. (8) with an equilibrium constant K_2. The oxidation state of the cobalt co-ordinated by O_2 increases from +2 to +3 and the co-ordinated O_2 becomes negatively charged. This oxidation state change is well documented both in the artificial oxygen transport systems of cobalt complexes[39,40] and in heme systems related to O_2 transport.[39,40] In eqns. (7) and (8), simplified notations for **1**, **III** and **IV** were used. Co-ordination of DMF solvent to some of the cobalt ions in these species must occur. Since the exact picture of solvent co-ordination is not known we adopt these simplified notations for **1**, **III**, **IV** and other species in the following paragraphs just for convenience without any implication that they represent the exact co-ordination spheres of the cobalt centers. In eqn. (9) the co-ordinated **Ia** in **IV** transfers two protons and two electrons to the co-ordinated dioxygen, and transforms into product **IIa**. What happens after the rate determining transfer of electrons and protons may be very complicated. Several questions, such as does the O–O bond break or does H_2O_2 form and how the catalyst returns to its original state, may be raised. No matter what are the answers to these questions, the mechanism in Scheme 2 yields a rate law (10) consistent with the experimental rate law (6).



Scheme 2

$$d[\mathbf{Ia}]/dt = kK_1K_2[\mathbf{1}][\mathbf{Ia}]P_{O_2}/(1 + K_1[\mathbf{Ia}](1 + K_2P_{O_2})) \quad (10)$$

Using the values of *a*, *b* and *m* deduced from the data in Fig. 3 according to the rate law (6), *k*, K_1 and K_2 are calculated to be $3.6(\pm 2.1) \times 10^{-2}$ s^{-1}, $11.7(\pm 0.9)$ M^{-1} and $4.3(\pm 1.5) \times 10^{-3}$ kPa^{-1}, respectively at 363 K. The magnitude of the equilibrium constants K_1 and K_2 provides a clue to answer the question why O_2 can co-ordinate to **III**, eqn. (8), but there is no indication of the existence of the O_2–**1** adduct in the rate law. Let's make the reasonable assumption that O_2 co-ordinates to **1** with an equilibrium constant approximately equal to K_2, then [O_2–**1**]/[**III**] is 7.4×10^{-2} under the conditions [**Ia**] = 0.5 M and P_{O_2} = 100 kPa. This small value indicates that [O_2–**1**] is negligible. If O_2 also binds to **1** with a large equilibrium constant, then one would expect an extra term related to P_{O_2} in the denominator of eqn. (6). The absence of this term shows that our rate law and the parameters are consistent with each other in this regard.

To confirm the existence of complex **III** in eqn. (7) this equilibrium reaction was investigated by UV-Vis spectroscopy (Fig. 4a) at 298 K. At fixed concentration of **1**, the absorbance in the 420–500 nm range increased with the concentration of **Ia** (spectra 1–5). Since substrate **Ia** did not absorb in this region (spectrum 6), the variations in absorbance were attributed to the formation of **III**. The absorbances at 438 nm were further analysed quantitatively. After straightforward mathematical analysis, the relation (11) between absorbance *A* and concentration of **Ia** was obtained, where *l* is the cell pathlength. ε_1 and ε_{III} are the molar absorptivities of cobalt complex **1** and **III**, respectively, C_0 and L_0 are the initial concentrations of **1** and **Ia**, respectively, and K_1 is the equilibrium constant in eqn. (7). The analysis by the non-linear least-squares fitting of ΔA ($A - \varepsilon_1 l C_0$) *vs.* concentration of substrate **Ia** (Fig. 4b) yielded $K_1 = 1.5(\pm 0.3) \times 10^3$ M^{-1} and $\varepsilon_{III} - \varepsilon_1 = 2.0(\pm 1.4) \times 10^3$ M^{-1} cm^{-1} from the data at 438 nm. The large standard deviation in K_1 is due to the similarity of the spectra of **1** and **III** in the region which is suitable for quantitative analysis. Furthermore, the small difference in molar absorptivity between **1** (1.47×10^4) and **III** ($1.67(\pm 0.14) \times 10^4$ M^{-1} cm^{-1}) prevents us from obtaining large values of $A - \varepsilon_1 l C_0$ for accurate numerical analysis. Though there are limitations in the

$$A = \varepsilon_1 l C_0 + (1/2)(\varepsilon_{III} l - \varepsilon_1 l)\{(C_0 + L_0 + K_1^{-1}) - [(C_0 + L_0 + K_1^{-1})^2 - 4C_0L_0]^{1/2}\} \quad (11)$$

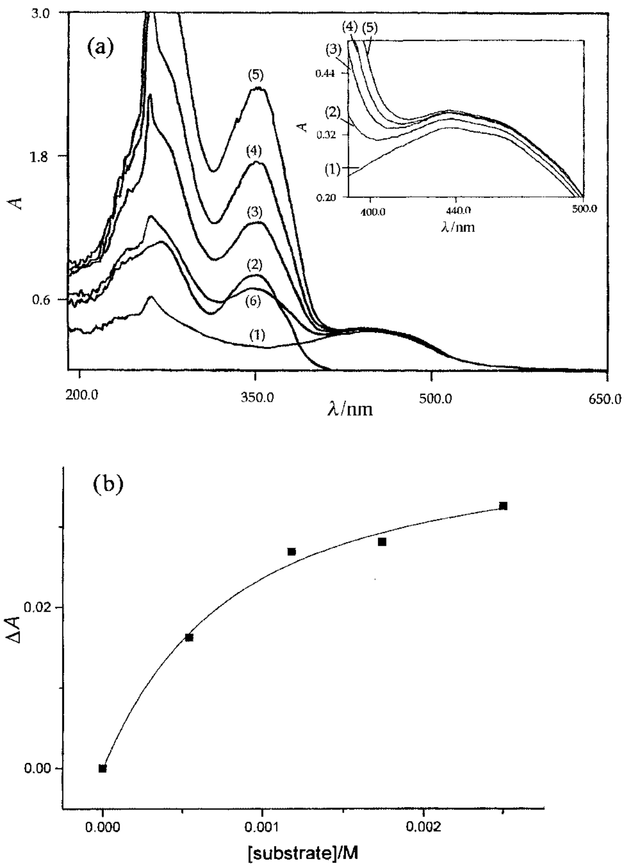


Fig. 4 (a) UV-Vis spectra of catalyst **1** (2.68×10^{-4} M) and **Ia** ((1) 0.0, (2) 5.41×10^{-4}, (3) 1.18×10^{-3}, (4) 1.74×10^{-3}, (5) 2.50×10^{-3} M) in DMF under N_2 in a 0.100 cm cuvette at 298 K. Spectrum (6): **Ia** (8.38×10^{-4} M) in DMF without **1**. Inset: spectra magnified in the range 390–500 nm. (b) Analysis of the absorbance difference as a function of [**Ia**] according to eqn. (11) using a non-linear least-squares curve-fitting method.

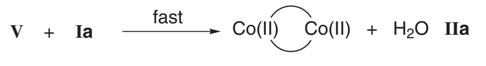
precision of K_1, the presence of the equilibrium relation (7) is unequivocal. Comparing with the K_1 value of 11.7(±0.9) M^{-1} deduced from the kinetic data at 363 K, ΔH^0 is estimated to be −67.1(±2.9) kJ mol^{-1}. We stated before that the ^1H NMR spectrum of **Ia** and **1** in d_7-DMF indicates no new compound is formed. This seems to contradict the fact that **III** exists. Actually there is no contradiction because the ^1H NMR spectrum of **1** and **III** can not be detected since cobalt(II) ions in **1** as well as in **III** are paramagnetic.

An attempt to study the equilibrium (8) by UV-Vis spectroscopy was also carried out. We observed that the spectrum of complex **1** was indistinguishable whether under O_2 (1 atm) or N_2. Furthermore, the spectra of **1** and **Ia** (0.05 M) were insensitive to the presence of O_2. Hence we suspected that UV-Vis spectroscopy could not furnish additional data concerning O_2 binding in eqn. (8). Nevertheless, we still carried out systematic investigations following the procedure used to study the equilibrium under N_2 in the hope that there is significant difference in K_1 that may allow us to characterize the effect of O_2. From a reaction solution containing **1** (2.68×10^{-4} M) and **Ia** (0–3.2×10^{-3} M) at 298 K under air we obtained $K_1 = 1.8(\pm1.0) \times 10^3$ M^{-1}. Under O_2 the experimental data yielded $K_1 = 2.9(\pm0.7) \times 10^3$ M^{-1}. For the air and O_2 systems, the differences in molar absorptivity are $1.5(\pm0.2) \times 10^3$ and $1.4(\pm0.1) \times 10^3$ M^{-1} cm^{-1}, respectively. Indeed, these K_1 values are equal to that under nitrogen within experimental error. It is impossible to extract any reliable information on K_2. Therefore, we were unable to characterize the binding of O_2 in eqn. (8) in more detail. This is probably because of the small equilibrium constant K_2 and the small differences in the molar absorptivities of **1**, **III** and their dioxygen adducts. This failure to observe the effect of O_2 binding in eqn. (8) by UV-Vis spectroscopy is not unique. For example, we observed that the UV-Vis spectrum of **1** in DMF in the 420–500 nm range was independent of the amount of PPh_3 added to the solution, though PPh_3 would co-ordinate to the cobalt ions in **1** (details will be presented elsewhere).

EPR Spectroscopy has been widely used to characterize the binding of O_2 to some cobalt(II) complexes.[41] No EPR signals were detected for a sample containing **1** ($\approx 10^{-2}$ M) and **Ia** ($\approx 10^{-2}$ M) under O_2 which was then frozen to 77 K. This negative EPR result does not rule out the existence of **IV**. This is because if **IV** exists one may expect some EPR signal from the $Co^{III}–O_2^-$ moiety. However, the presence of a nearby paramagnetic cobalt(II) ion will render the expected EPR signal too broad to be detected. Therefore, EPR spectroscopy can not be used to characterize the binding of O_2 to the dicobalt complex **1**. Therefore, the presence of this reasonable complex **IV** is based mainly on kinetic data.

We propose two possible pathways for the transformation of O_2 and catalyst in eqn. (9). In the first, after the transfer of protons and electrons from co-ordinated **Ia**, the O–O bond is cleaved to yield water as in eqn. (12). The other oxygen is proposed to be still co-ordinated to **1** to form an intermediate **V**. This intermediate, if it exists, is likely to be the same as that generated in the catalysed O_2 oxidation of PPh_3.[36] The intermediate **V** then oxidizes another molecule of **Ia** to form **IIa** and the catalyst returns to the original state as in eqn. (13).

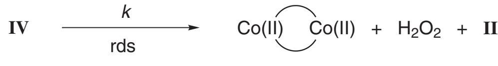
$$\mathbf{IV} \xrightarrow[\text{rds}]{k} \mathbf{V} + H_2O + \mathbf{IIa} \qquad (12)$$



$$\mathbf{V} + \mathbf{Ia} \xrightarrow{\text{fast}} \mathrm{Co(II)}\ \mathrm{Co(II)} + H_2O\ \mathbf{IIa} \qquad (13)$$

According to this mechanism the k in rate law (10) should be $2k$. The value of k is $1.8(\pm1.0) \times 10^{-2}$ s^{-1}.

In the second proposed mechanism H_2O_2 is produced and the catalyst returns to its original state as in eqn. (14). We have



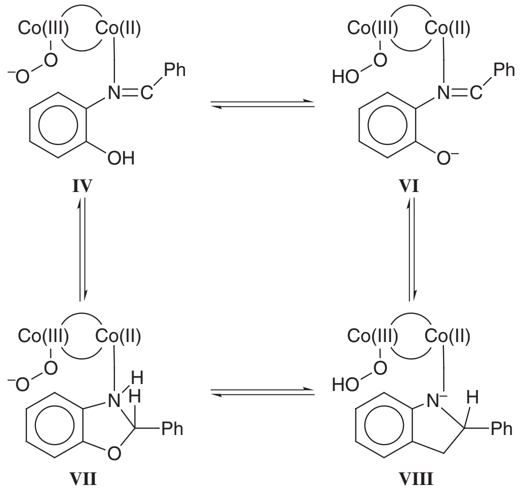
$$\mathbf{IV} \xrightarrow[\text{rds}]{k} \mathrm{Co(II)}\ \mathrm{Co(II)} + H_2O_2 + \mathbf{IIa} \qquad (14)$$

observed that the dicobalt complex catalyst **1** can function as a very effective catalase, *i.e.* it converts H_2O_2 into H_2O and O_2 as in eqn. (15).

$$H_2O_2 \xleftarrow[1]{\text{fast}} H_2O + \tfrac{1}{2}O_2 \qquad (15)$$

A competition experiment with an additional substrate besides **Ia** can be used to distinguish these two pathways. We chose *trans*-stilbene, which can't be oxidized directly under the reaction conditions for the oxidation of **Ia**, and it can be co-oxygenated to *trans*-stilbene oxide with PPh_3.[36] If stilbene can't be co-oxidized, then the pathway with the reactive intermediate **V** is highly unlikely. This argument is valid only when **V** can oxidize **Ia** with a rate constant comparable or less than that with stilbene. This condition can easily be established with a concentration of stilbene higher than that of **Ia**. In view of the expected complicated elementary reactions in the hypothetical reaction between **V** and **Ia**, it is reasonable to assume that this rate constant is smaller than that between **V** and PPh_3. We carried out the following experiment. In a reaction flask containing 10 mL DMF solution of **1** (50 µmol), **Ia** (5.0 mmol), 4 Å molecular sieves (1.0 g) and stilbene (10 mmol) under 92.0 kPa of O_2 pressure at 363 K (conditions similar to that used in eqn. (1)), the amount of O_2 consumed is independent of the amount of stilbene (0, 1.0 and 2.0 M) present. This co-oxygenation experiment certainly indicates that a reactive intermediate which is capable of oxidizing a large excess of stilbene was not produced in the oxidation of **Ia**, and the pathway with the formation of H_2O_2 is more likely.

The structure of intermediate **IV** is not certain. We propose a likely structure and its transformation in Scheme 3. The reactant **Ia** can exist in *cis* and *trans* geometries with *trans* being more stable.[34] The co-ordinated **Ia** in **IV** may lose a proton to the co-ordinated superoxide to form **VI**. Further cyclization of the organic moiety in **VI** forms **VIII**. Alternatively, **Ia** in **IV** may also first cyclize to **VII**, then the proton of the co-ordinated benzoxazoline may be transferred to the co-ordinated superoxide to form **VIII**. There is no direct evidence in favor of any species as the key intermediate in Scheme 3. However, it is known that benzoxazoline is not stable, hence **VII** may play only a minor role. Also, when **Ia** in **IV** loses the phenolic proton, the enhanced nucleophicity of phenoxide in **VI** should facilitate the cyclization reaction for form **VIII**. This reasoning indicates that the pathway **IV** ⟶ **VI** ⟶ **VIII** may be the major transformation pathway of the organic substrate in the initial stage. The oxazoline anion in **VIII** then transfers two electrons and one proton to the co-ordinated superoxide to give the product. In **VIII** the protonated superoxide may facilitate electron transfer from the co-ordinated benzoxazoline anion on the basis of charge considerations.

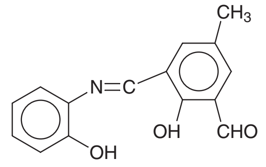


Scheme 3

The reason that compound **If** can react directly with O_2 in the absence of catalyst is probably that it exists in the form of benzothiazoline[34] which is more stable than the structure depicted in eqn. (1). Therefore, it is reasonable to expect that the formation of oxazoline assisted by the dicobalt catalyst is an important aspect in this catalysed oxidation reaction. This point has been taken into account in Scheme 3. The enhanced oxidation rate of **If** in the presence of dicobalt catalyst may be due to the formation of a species such as **VIII**. The co-ordinated O_2H is more susceptible to accept an electron from the co-ordinated benzothiazoline anion which is more electron rich than its neutral form. Therefore, with the proposed mechanism, the accelerated oxidation of **If** in the presence of the dicobalt catalyst **1** can be rationalized.

In the presence of acetic acid the superoxide in **IV** may be protonated, and the formation of **VI** is then hindered. Another possible effect of the acid is that the negatively charged nitrogen in **VIII** may be protonated and therefore the subsequent transfer of an electron from the co-ordinated benzoxazoline to the co-ordinated superoxide may be suppressed. Hence the rate of oxidation is reduced. A weak base, such as 2,6-di-*tert*-butylpyridine, exerts negligible effect on **VI** and **VIII** because it can not extract the proton that has been bonded to the superoxide. This is clear since the acid dissociation constant[42] of pyridinium ion (5.9×10^{-6}) is 6 orders larger than that of H_2O_2 (2.2×10^{-12}) which should be a good model for the co-ordinated hydrogen superoxide. The small dissociation constant of H_2O_2 further supports our viewpoint concerning the significance of pathway **IV** ⟶ **VI** ⟶ **VIII** in Scheme 3. The question why the rate of oxidation of **Ib** is particularly slow can also be answered based on Scheme 3. The electron withdrawing chloro group in **Ib** reduces the nucleophilicity of the phenoxide oxygen in **VI**, and disfavors the formation of **VIII** in the equilibrium between **VI** and **VIII**. Furthermore, the chloro group can also reduce the effective negative charge on the nitrogen of **VIII** and impede the subsequent electron transfer. Both factors render the rate of oxidation slow.

Since the substituents on benzylidenes in compounds **Id** and **Ie** are far away from the co-ordinated nitrogen in **VIII**, these were anticipated to have minimum effect on the rate of oxidation. Indeed, this is confirmed experimentally, the rates of oxidation of **Id** and **Ie** being similar to that of **Ia**. However, when **IX** was used as a substrate it did not oxidize to the corresponding benzoxazole under the standard conditions that [**1**] = 5.0×10^{-3} M, $P_{O_2} = 101$ kPa at 363 K.



IX

The explanation is that the strong electron donating effect of the hydroxy group in the benzylidene renders the carbon atom unfavorable to attack by the nucleophile in the hydroxyaniline moiety, and the corresponding species **VIII** are not formed. The formation of species such as **VIII** is also sterically hindered. Furthermore, the ionization of the additional phenolic proton may also impede the formation of intermediate **VI**. Therefore, no oxidation product was isolated.

This non-reactivity of compound **IX** may be interpreted as indicating that the oxidation mechanism is non-radical. Suppose the mechanism is related to the formation of a phenoxyl radical, then one expects to detect typical oxidation products such as derivatives of benzoquinone or diphenylquinone.[8–10] These quinone products are not detected in the oxidation of **Ia**–**If**. Therefore, a mechanism involving an unco-ordinated phenoxyl radical is highly unlikely in this catalytic system.

Conclusion

Dicobalt complex **1** was shown to be an effective catalyst in the oxidation of derivatives of *N*-benzylidene-2-hydroxyaniline to the corresponding 2-substituted benzoxazoles. These oxidation reactions were carried out using dioxygen as oxidant and under mild conditions. The product yields are about the best ever reported for the preparation of 2-substituted benzoxazoles by the oxidation processes. The high yields were achieved when a dehydrating agent was present. Its function is to prevent hydrolysis of the reactant. This environmentally friendly high yield oxidation process may be of practical importance because derivatives of benzoxazole have been patented as a useful component[43] of organic light emitting diode (OLEDs). The kinetics of this dioxygen reaction can be studied thoroughly. The catalysed reaction undergoes a non-radical pathway because the presence of radical scavenger had a negligible effect on the reaction rate. The rate law indicates that the dicobalt catalyst **1** serves the purpose of binding to the organic substrate and dioxygen simultaneously to initiate the oxidation reaction. There is no evidence to indicate that the co-ordinated dioxygen undergoes O–O bond cleavage to yield water after accepting two protons and two electrons from the co-ordinated organic substrate. Instead, a more likely transformation is that hydrogen peroxide is produced. This is then decomposed into water and oxygen by **1** which possesses catalase activity. The transformation of the co-ordinated dioxygen induced by the co-ordinated *N*-benzylidine-2-hydroxyaniline is in direct contrast with that induced in the oxidation of PPh_3. In PPh_3 oxidation, after $Ph_3P{=}O$ is formed, a reactive intermediate, which was not formed in the oxidation of *N*-benzylidine-2-hydroxyaniline, is formed as mentioned in the Introduction. The different transformation pathways of co-ordinated dioxygen demonstrate the complexity of oxidation by dioxygen. Further extension of this work to other organic substrates is underway.

Experimental

Synthesis of *N*-benzylidene-2-hydroxyaniline and its derivatives Ia–If

These compounds were synthesized following the same procedure. Using *N*-benzylidene-2-hydroxyaniline as an example, a 30 mL methanol solution of 2-hydroxyaniline (0.05 mol) was added slowly to a 15 mL methanol solution of benzaldehyde (0.05 mol). After refluxing for 3 h and subsequent cooling, the mixture was stored in a refrigerator for 6 h. The precipitated product was collected by filtration. The product remaining in the filtrate was obtained by stripping off the solvent followed by recrystallization using diethyl ether as solvent. The compounds **Ia**–**If** were characterized by mass, ^{1}H NMR spectra and melting points (Supplementary Material Table 1, SUP 57583).

Preparation of dicobalt catalyst [$Co_2L(\mu\text{-}OH)$] 1

The preparation of this catalyst follows the literature method.[36] Its composition is confirmed by the results of elemental analysis (Found: C, 50.70; H, 3.72; Co, 23.6; N, 5.42. Calc. for [$Co_2L(\mu\text{-}OH)$]·H_2O ($C_{21}H_{18}Co_2N_2O_5$): C, 50.81; H, 3.63; Co, 23.8; N, 5.65%).

Catalytic oxidation of *N*-benzylidene-2-hydroxyaniline and its derivatives by O_2 catalysed by dicobalt complex

The reactions were carried out in a closed system. Substrate (5.0 mmol) and catalyst (50 μmol) were dissolved in 10 mL DMF which was maintained at the reaction temperature (363 ± 1 K). The flask containing the DMF solution was connected to a thermostatted (298 K) glass vessel containing O_2 at the desired initial pressure. The volume of the glass vessel (0.11 L) was calibrated. The pressure in the glass vessel was measured by a model PT-15V pressure transducer (Asuryu Co., Japan). The digital pressure reading was calibrated against a mercury barometer, and was stored in a PC as a function of time.

After a desirable reaction period (≈24 h), DMF was distilled off under reduced pressure at 313 K. The solid residue was dissolved in the minimum volume of CH_2Cl_2 and chromatographed on a Silica Gel 60 (70–230 mesh, Merck) column (15 cm long, 3.5 cm ID) using dichloromethane as eluent. The initial portion of the yellowish solution from the column was collected. After stripping off the solvent and drying under vacuum, products **IIa**, **IIc**–**IIf** were obtained.

Since the oxidation reaction rate of compound **Ib** was slow, the CH_2Cl_2 solution collected after chromatographic separation was still a mixture. Further TLC separation on Kieselguhr PF 254 used ethyl acetate–*n*-hexane (1 : 15) as eluent. Product **IIb** was obtained at $R_f = 0.48$. The products **IIa**–**IIf** were characterized by mass, ^{1}H and ^{13}C NMR spectral as well as melting points (Supplementary Material Table 2, SUP 57583).

We have also carried out experiments where either Na_2SO_4 or 4 Å molecular sieves were added to the reaction mixture. Both solid reagents were carefully dried, Na_2SO_4 at 373 K for 24 h and 4 Å molecular sieves at 473 K for 24 h. The amount of Na_2SO_4 or 4 Å molecular sieves used was 1.0 g in each run. Products **IIa**, **IIc**–**IIe** were isolated by extraction instead of column separation. After DMF solvent was removed from the reaction mixture by distillation under reduced pressure at 313 K, diethyl ether was used to extract the benzoxazole product. Then the product was obtained after diethyl ether was removed and the solid dried in a vacuum oven.

The kinetics of the oxidation of compound **Ia** was established by the initial rate method. The non-linear least-squares curve-fitting analyses of the kinetic data according to the rate laws (5) and (6) and fitting of UV-Vis data using eqn. (11) were accomplished by using the commercially available program Origin, Version 5.0 (Microcal Software Inc., Northampton, MA, USA).

Acknowledgements

We thank the National Science Council of Taiwan ROC for financial support (NSC 87-2113-M-007-029).

References

1 M. D. Reddy, T. Punniyamurthy and J. Iqbal, *Tetrahedron Lett.*, 1995, **31**, 159.
2 C. C. Maikap, D. Guhathakurta and J. Iqbal, *Synlett.*, 1995, 189.
3 M. T. Reetz and K. Töllner, *Tetrahedron Lett.*, 1995, **36**, 9461.
4 C. Ercolani, A. M. Paoletti, G. Pennesi and G. Rossi, *J. Chem. Soc., Dalton Trans.*, 1991, 1317.
5 J. D. Koola and J. K. Kochi, *J. Org. Chem.*, 1987, **52**, 4545.
6 T. Okamoto and S. Oka, *J. Org. Chem.*, 1984, **49**, 1589.
7 B. S. Tovrog, S. E. Diamond and F. Mares, *J. Am. Chem. Soc.*, 1979, **101**, 270; B. S. Tovrog, S. E. Diamond, F. Mares and A. Szalkiewicz, *J. Am. Chem. Soc.*, 1981, **103**, 3522; S. E. Diamond, F. Mares, A. Szalkiewicz, D. A. Muccigrosso and J. P. Solar, *J. Am. Chem. Soc.*, 1982, **104**, 4266.
8 I. Sasaki, A. Chiaroni, A. Gaudemer, D. Pujol and C. Riche, *Polyhedron*, 1987, **6**, 2103.
9 A. Zombeck, R. S. Drago, B. B. Gorden and J. H. Gaul, *J. Am. Chem. Soc.*, 1981, **103**, 7580.
10 M. Perrée-Fauvet and A. Gaudemer, *J. Chem. Soc., Chem. Commun.*, 1981, 874.
11 S. J. S. Kalra, J. Iqbal and T. Punniyamurthy, *Tetrahedron Lett.*, 1994, **35**, 4847.
12 L. I. Simandi, T. Barna, Z. Szeverenyi and S. Nemeth, *Pure Appl. Chem.*, 1992, **64**, 1511; Z. Szeverenyi, E. R. Milaeva and L. I. Simandi, *J. Mol. Catal.*, 1991, **67**, 251; L. I. Simandi, S. Nemeth and N. Rumelis, *J. Mol. Catal.*, 1987, **42**, 357.
13 A. Nishinaga, T. Matsuura and S. Yamazaki, *Tetrahedron Lett.*, 1988, **29**, 4115.
14 A. K. Basak and A. E. Martell, *Inorg. Chem.*, 1986, **25**, 1182.
15 A. Nishinaga, T. Matsuura and S. Yamazaki, *Chem. Lett.*, 1986, 505.
16 P. Li and H. Alper, *J. Mol. Catal.*, 1992, **72**, 143.
17 T. Bamhaoud and J. Prandi, *Chem. Commun.*, 1996, 1229.
18 T. Punniyamurthy and J. Iqbal, *Tetrahedron Lett.*, 1994, **35**, 4003.
19 R. Boca, *J. Mol. Catal.*, 1981, **12**, 351.
20 J. G. D. Schulz and A. Onopchenko, *J. Org. Chem.*, 1980, **45**, 3716.
21 A. Ladenburg, *Ber. Dtsch. Chem. Ges.*, 1875, **8**, 677; 1877, **10**, 1124; 1878, **11**, 826.
22 D. W. Hein, R. J. Blheim and J. J. Leavitt, *J. Am. Chem. Soc.*, 1957, **79**, 427.
23 Y. Kanaoka, T. Hamad and O. Yonemitsu, *Chem. Pharm. Bull.*, 1970, **18**, 587.
24 H. O. Hankovszky and K. Hideg, *Tetrahedron Lett.*, 1965, 2365.
25 M. Terashima, M. Ishii and Y. Kanaoka, *Synthesis*, 1982, 484.
26 R. M. Acheson, *An Introduction to the Chemistry of Heterocyclic Compounds*, 3rd edn., Wiley, New York, 1977, p. 353.
27 R. J. Perry, B. D. Wilson and R. J. Miller, *J. Org. Chem.*, 1992, **56**, 2883.
28 K. Nakagawa, H. Onoue and J. Sugita, *Chem. Pharm. Bull.*, 1964, **12**, 1135.
29 M. Yoshifuji, R. Nagase, T. Kawashima and N. Inamoto, *Heterocycles*, 1978, **26**, 274.
30 F. F. Stephens and J. D. Bower, *J. Chem. Soc.*, 1949, 2971.
31 F. F. Stephens and J. D. Bower, *J. Chem. Soc.*, 1950, 1722.

32 M. S. A. El-Meligy and S. A. Mohamed, *J. Prakt. Chem.*, 1974, 316.

33 G. Speier, *J. Mol. Catal.*, 1987, **41**, 253.

34 K. H. Grellmann and E. Tauer, *J. Am. Chem. Soc.*, 1973, **95**, 3104.

35 T. Kondo, S. Yang, K.-T. Huh, M. Kobayasi and M. Watanabe, *Chem. Lett.*, 1991, 1275.

36 Y. H. Hwang and C. P. Cheng, *J. Chem. Soc., Chem. Commun.*, 1992, 317.

37 Y. H. Hwang and C. P. Cheng, unpublished work.

38 A. K. Basak and A. E. Martell, *Inorg. Chem.*, 1986, **25**, 1182.

39 E. C. Niederhoffer, H. H. Timmons and A. E. Martell, *Chem. Rev.*, 1984, **84**, 137.

40 I. Bertini, H. B. Gray, S. J. Lippard and J. S. Valentine, *Bioinorganic Chemistry*, University Science Books, California, 1994, ch. 5.

41 See, for example S. J. Dzugan and D. H. Busch, *Inorg. Chem.*, 1990, **29**, 2528; K. A. Lance, K. A. Goldsby and D. H. Busch, *Inorg. Chem.*, 1990, **29**, 4537.

42 D. A. Skoog, D. M. West and F. J. Holler, *Fundamentals of Analytical Chemistry*, 7th edn., Saunders College Publishing, New York, 1996, Appendix 3.

43 S. A. VanSlyke and C. W. Tang, *U.S. Pat.*, 4 539 507, 1985.

Paper 9/03699G