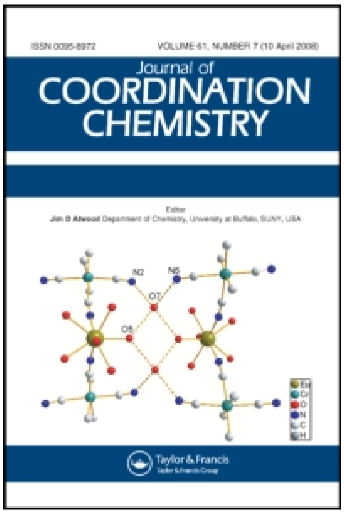

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TRYPTOPHAN 2,3-DIOXYGENASE MODEL RING-OPENING DIOXYGENOLYSIS OF 3-METHYLINDOLE CATALYZED BY $M^{I\ OR\ II}$ (M = Cu, Mn, Fe, OR Co) WITH MONODENTATE LIGAND OR BIDENTATE LIGAND SYSTEMS

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The dioxygenolysis of tryptophan analogues by $M^{I\ or\ II}$ (M = Cu, Mn, Fe, or Co) with monodentate ligand or bidentate ligand (monodentate ligands = pyridine (py) derivatives and bidentate ligands = 2,2'-bipyridine (bpy) derivatives) was studied as a model of tryptophan 2,3-dioxygenase (TDO). The high yields (44–54%) of the oxygenative pyrrole ring cleavage product, *o*-formaminoacetophenone (*o*-FAAP), in the dioxygenolysis of 3-methylindole at 25°C under atmospheric O_2 were obtained in tetrahydrofuran (THF). Among the monodentate ligand tested, electron donating ligands such as py and α-picoline accelerated the reaction high yields of *o*-FAAP. Bidentate ligands such as 2,9-dimethyl-1, 10-phenanthroline (dmphen) with the relatively weak ligation ability also promoted the present dioxygenolysis.

KEYWORDS: dioxygenolysis, tryptophon, Cu, Mn, Fe, CO

INTRODUCTION

The enzymatic action of TDO containing protoheme IX has previously been simulated by the oxidative cleavage of the pyrrole ring in indole derivatives by using transition-metal complexes such as bis(salicylidene)ethylenediaminatocobalt(II) (CoSalen),[1] *meso*tetraphenylporphyrinatocobalt(II) (CoTPP),[2] *meso*-tetraphenylprophyrinatoiron(II or III) ($Fe(py)_2TPP$ or FeC1TPP),[3] manganese(II) phthalocyanine (MnPc).[4] Although dioxygenolysis of 3-substituted indoles with the *in situ* prepared catalytic system of CuCl/py by Balogh-Hergovich *et al.*[5] and Tsuji *et al.*[6]

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or with $FeCl_2$ (or $FeCl_3$)/py/bpy by us[7] has been reported, the composition of metal/monodentate ligand/bidentate ligand for an efficient *in situ* prepared catalytic system has not yet been elucidated and the dioxygenation catalysis (including the substrate (or O_2) activation process) of the catalytic systems remains ambiguous.

In this paper, we wish to report the efficient catalytic system in the ring-opening dioxygenolysis of a tryptophan analogue (3-methylindole) catalyzed by $M^{I\ or\ II}$ (M = Cu, Mn, Fe, or Co) with monodentate ligand or bidentate ligand systems, the reaction intermediates have been investigated by optical absorption, ESR, and ^{1}H-NMR spectroscopy and electrochemistry.

EXPERIMENTAL SECTION

Materials

o-Formaminoacetophenone (*o*-FAAP) and tetrakisacetonitrilecopper(I) perchlorate ($[Cu^I(CH_3CN)_4]ClO_4$) were prepared according to the literature procedures.[8-9] THF and other solvents were dried and distilled before use. All other chemical reagents used were of reagent grade.

Dioxygenolysis of 3-methylindole

No dioxygenolysis products were present for both the tryptophan analogues of 3-methylindole before the reaction. Blank experiments were also performed in the absence of copper(I)/pyridine/2,2'-bipyridine, and no dioxygenolysis products were present before the reaction. A typical dioxygenolysis run was as follows: THF solution (20 cm^3) containing $[Cu^I(CH_3CN)_4]ClO_4$ (65.4 mg; 0.2 mmol), pyridine (0–20.0 cm^3; 0–247 mmol), and 2,2'-bipyridine (0–0.781 g; 0–5 mmol) was maintained at 25 ± 1 °C with magnetic stirring in an O_2 atmosphere. The reation was started by the addition of 3-methylindole (1.0 mmol). After oxygen absorption ceased, the amounts of unreacted substrates and the products were determined spectrophotometrically after separating them from the reaction mixtures by TLC on silica gel (Merck F_{254}).[10] The ring-opening products were identified with authentic samples by ^{1}H-NMR (JEOL, JAERI-MH-100), IR (JASCO, A–100), m.p. measurement and by elemental analysis.

ESR Measurements

ESR spectra were recorded for the Cu^I/py and O_2 system with or without 3-methylindole at −196 °C in the frozen state with a JEOL JES-FE-IX spectrometer with 100 kHz field modulation. As a standard, MgO powder doped with Mn^{II} was used.

Cyclic Voltammetry Measurements

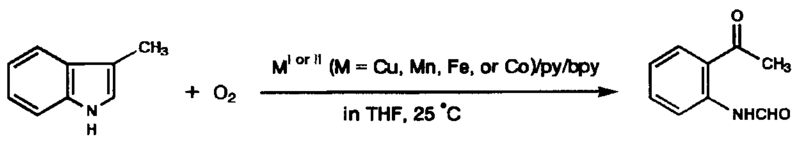
Electrochemical measurements of $[Cu^I(CH_3CN)_4]ClO_4$ (1.0×10^{-3} mol dm^{-3}) in the presence (or absence) of pyridine (0.15 mol dm^{-3}), bipyridine (1.0×10^{-2} mol dm^{-3}) and 3- methylindole (5.0×10^{-3} mol dm^{-3}) were performed in a Pyrex cell

(10 cm^3) equipped with a Pt working electrode, a Pt counter electrode and a saturated calomel electrode (SCE) at 25°C in acetonitrile. Solutions were deoxygenated by bubbling with nitrogen the supporting electrolyte was 0.1 mol dm^{-3} tetrabutylammonium perchlorate. The cyclic voltammetric apparatus utilizes a Hokuto Denkou HA-301 potentiostat and a Hokuto Denkou HB-107A function generator. Voltammetric data were recorded on a National Vp-6414A X-Y recorder.

RESULTS AND DISCUSSION

Dioxygenolysis of 3-methylindole by in situ Prepared Catalytic System of $M^{I\ or\ II}$ (M = Cu, Mn, Fe, or Co)/pyridine/2,2'-bipyridine

When the dioxygenolysis of 3-methylindole (5.0×10^{-2} mol dm^{-3}) was carried out with an *in situ* prepared catalytic system of $M^{I\ or\ II}$ (M = Cu, Mn, Fe, or Co (0.01–0.5 mol dm^{-3}))/py (0–4.0 mol dm^{-3})/bpy (0–0.1 mol dm^{-3} in THF at 25°C



(1)

Equation 1 Ohkubo, Sagawa, Takano, Hata, Kobayashi.

under atmospheric oxygen, the ring-opening oxygenated product was mainly a keto-amide product (*o*-FAAP) as shown in Eqn. 1. Although other ring-opening products such as *o*-aminoacetophenone and *o*-isocyanoacetophenone were also detected, the amounts were negligible as compared with that of *o*-FAAP. The experimental results are given in Table 1 for the dioxygenolysis of 3-methylindole with several complex systems of Cu^I, Cu^{II}, Mn^{II}, Fe^{II}, or Co^{II}/py/bpy.

The catalytic efficiency of the metal complexes for the present reaction followed the order $Cu^I >> Cu^{II} \sim Fe^{III} Co^{II} > Fe^{II} Mn^{II}$. The activity order of the low-valent state complexes, $Cu^I > Co^{II} > Fe^{II} > Mn^{II}$, is related to the order of the reactivity toward O_2, as reflected by the potential order of the HOMO (or SOMO) *d*-orbitals, Cu^I ($d_x 2_{-y} 2$)> Co^{II} ($d_x 2_{-y} 2$ or $d_z 2$)> Fe^{II} (d_{yz} or d_{xz})>Mn^{II} (d_{yz} or d_{xz}). Namely, the low-valent state metal complexes exhibit catalytic activity after oxidation with O_2.

$$M^{IorII}(M = Cu,Co,Fe,orMn) + O_2 \rightarrow M^{IIorIII}\text{---}O_2^- or M^{IIorIII} + O_2^- \qquad (2)$$

In the highly active CuCl/py system, $CuCl_2 \cdot CuO$ formed partly by reaction of CuCl wuth O_2, previously reported by Tsuji *et al.*,[11] was found to generate a dimerized product (3,3'-dimethyl-3, 3'-bi-3H-indole) in the 3-methylindole dioxygenolysis with $CuCl_2 \cdot CuO$ in CH_2Cl_2.[6] Therefore, the catalytically active species generated from the $Cu^I Cl$/py/bpy or $[Cu^I(CH_3CN)_4]ClO_4$/py/bpy systems for the formation of the ring-opening product (*o*-FAAP) in an O_2 atmosphere correspond to a high-valent Cu^{II} complex. The high-valent state Cu^{II} or M^{III} (M = Co, Fe, or

Table 1 Catalytic activities of *in situ* prepared transition-metal/pyridine/2, 2'-bipyridine complexes for the dioxygenolysis of 3-methylindole[a]

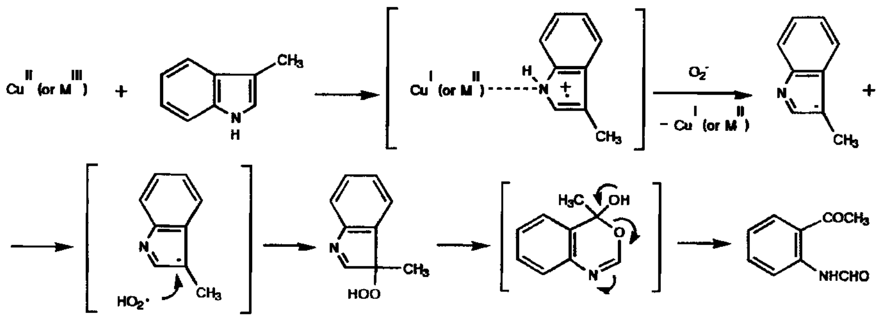
transition-matal	(mol dm^{-3})	py	bpy	reaction time (h)	substrate conv.	o-FAAP yield
		mol dm^{-3}	mol dm^{-3}		%	%
$[Cu^I(CH_3CN)_4]ClO_4$	(0.01)	4.0	0	1	100	50
Cu^ICl	(0.01)	4.0	0	1	100	25
$Cu^{II}(CH_3COO)_2H_2)$	(0.01)	4.0	0	5	36	13
$Cu^{II}SO_4$	(0.01)	4.0	0	5	10	trace
$Cu^{II}(ClO_4)_2 \cdot 6H_2O$	(0.01)	4.0	0	5	18	trace
$[Cu^I(CH_3CN)_4]ClO_4$	(0.01)	4.0	0.02	5	100	34
$[Cu^I(CH_3CN)_4]ClO_4$	(0.01)	1.5	0.01	1	61	17
$[Cu^I(CH_3CN)_4]ClO_4$	(0.025)	0.32	0.01	7	93	44
Cu^ICl	(0.025)	0.32	0	1	83	27
Cu^ICl	(0.025)	0	0.025	1	88	29
Cu^ICl	(0.025)	0.32	0	3	100	73[b]
$Cu^{II}Cl_2 \cdot 2H_2O$	(0.05)	1.15	0.1	9	35	7
$Fe^{II}Cl_2$	(0.05)	1.15	0.1	9	16	4
$Fe^{II}Cl_3$	(0.05)	1.15	0.1	9	34	6
$Co^{II}Cl_2$	(0.05)	1.15	0.1	9	26	trace
$Mn^{II}Cl_2$	(0.05)	1.15	0.1	9	13	n.d.[c]

[a]The reaction was carried out with 3-methylindole (5.0×10^{-2} mol dm^{-3}) in THF under atmospheric O_2 at 25°C. [b]Ref 6 (in CH_2Cl_2). [c]Not detected.

Mn) complexes undergo oxidative addition of the substrate to afford the reactive radical intermediate which is then converted into the ring-opening species of o-FAAP *via* an indolenyl hydroperoxide (discussed later), as shown in Scheme 1.

The catalytic efficiency of the $[Cu^I(CH_3CN)_4]ClO_4$/py or $[Cu^I(CH_3CN)_4]$ ClO_4/py/bpy system for the dioxygenolysis in THF was examined by varying the concentrations of py and/or bpy (Figure 1). The yield of o-FAAP maximized at molar ratio of py/Cu^I = 400 in the absence of bpy (Figure 1 (a)); py promotes the present ring-opening dioxygenolysis, but excess py inhibits coordination of the substrate to copper and depresses the reaction.

The efficiency of the catalytic $[Cu^I(CH_3CN)_4]ClO)_4$/py system for the dioxygenolysis of 3-methylindole was also affected by the solvent (Table 2), with the dioxygenolysis varying inversely with dielectric constant (ε) of the weakly basic



Scheme 1 Ohkubo, Sagawa, Takano, Hata, Kobayashi.

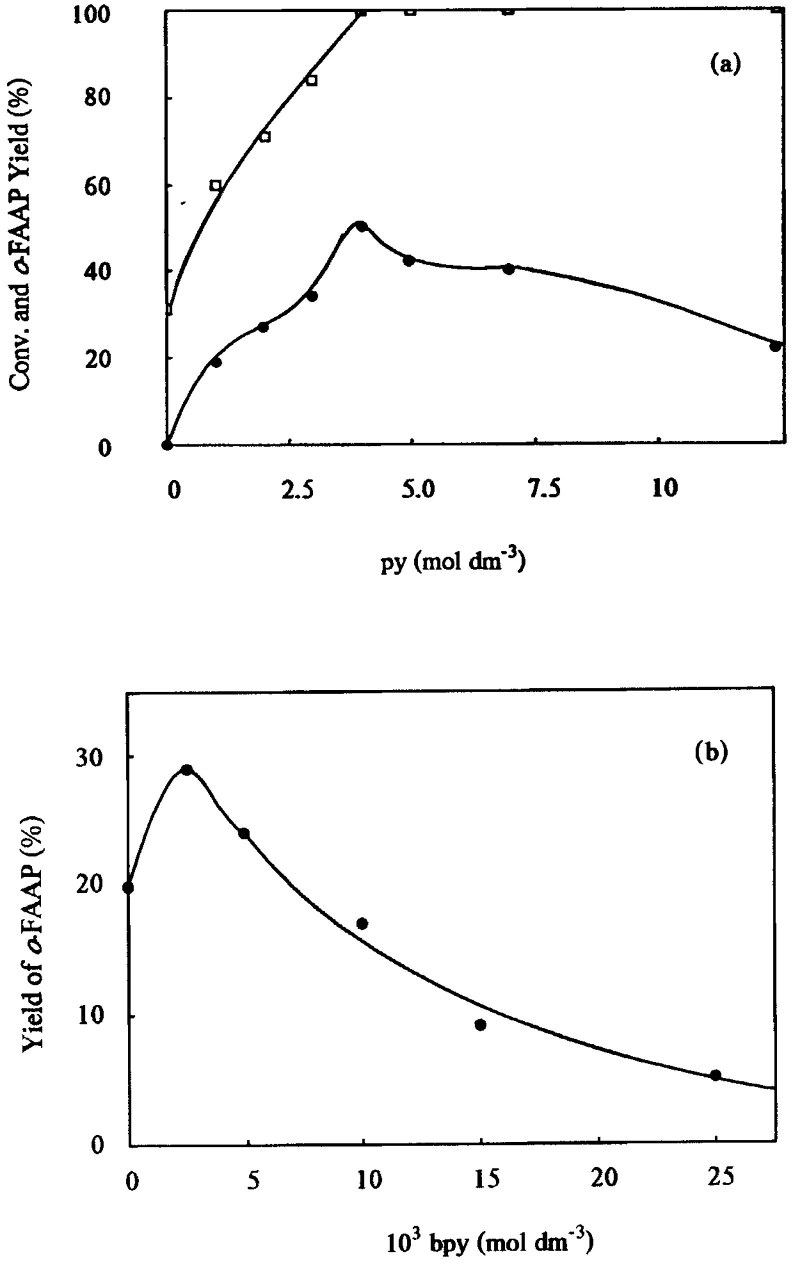


Figure 1 Concentration effects of (a) py on the catalytic efficiency of $[Cu^I(CH_3CN)_4]ClO_4$ (1.0×10^{-2} mol dm^{-3})/py (0–12 mol dm^{-3}) and (b) bpy on that of $[Cu^I(CH_3CN)_4]ClO_4$ (1.0×10^{-2} mol/dm^{-3})/py (1.5 mol dm^{-3})/bpy (0–0.025 mol dm^{-3}) for the conversion (□) and o-FAAP yield (•) in the 3-methylindole (5.0×10^{-2} mol dm^{-3}) dioxygenolysis in THF under atmosphric O_2 at 25°C for 1h.

Table 2 Solvent effects on the dioxygenolysis of 3-methylindole by the $[Cu^I(CH_3CN)_4]ClO_4$/py system under atmospheric O_2 at 25°C for 1 h[a]

solvent	O_2-uptake	substrate conv.	*o*-FAAP yield
	mmol	%	%
THF	0.97	100	50
C_6H_6	100	100	40
CH_3OH	1.18	100	18
DMF	0.85	69	7
DMSO	0.75	n.d.	n.d.

[a] The reaction was carried out with 3-methylindole (5.0×10^{-2} mol dm^{-3}), $[Cu^I(CH_3CN)_4]ClO_4$ ($1.0 \times 10^{-}$ mol dm^{-3}), and py (4.0 mol dm^{-}).

solvents tested, as shown by the order of DMSO (ε46.45) < DMF (36.71) < CH_3OH (32.66) < C_6H_6 (2.27) < THF (7.58).

Monodentate ligand effects on dioxygenolysis of 3-methylindole

The effects of various monodentate nitrogen donor ligands on the catalytic efficiency of the $[Cu^I(CH_3CN)_4]ClO_4$/monodentate ligand system for the dioxygenolysis were examined in the oxygenative pyrrole ring-opening of 3-methylindole by Cu^I/monodentate ligand (molar ratio of 1/400) in THF, and the yields of *o*-FAAP are listed in Table 3, together with the conversion of the reaction.

Among the monodentate ligands tested, triethylamine (pK_a = 10.7) and benzylamine (pK_a = 9.4), which do not have π-conjugation and are quite basic compared to py (pK_a = 5.2), were not as effective. The π-conjugative ligand imidazole (pK_a = 7.20) was also not effective. The bulky ligands of quinoline (pK_a = 5.0) and isoquinoline (pK_a = 5.4), which have almost the same pK_a value as py, were also not effective with $[Cu^I(CH_3CN)_4]ClO_4$, presumably because of their steric hindrance preventing substrate coordination to the Cu^I complex. Among the *o*, *m*, or *p*-substituted pyridine ligands, the electron donating methyl substituted ones (α, β,

Table 3 Monodentate ligand effects on the dioxygenolysis of 3-methylindole by $[Cu^I(CH_3CN)_4]ClO_4$/monodenate ligand system[a]

monodentate ligand	substrate conv.	*o*-FAAP yield
	%	%
pyridine	100	50
α-picoline	100	54
β-picoline	100	43
γ-picoline	92	42
4-cyanopyridine	7	0
imidazole	n.d.	n.d.
quinoline	trace	trace
isoquinoline	trace	trace
triethylamine	6	0
benzylamine	19	n.d.

[a] The reaction was carried out with 3-methylindole (5.0×10^{-2} mol dm^{-3}), $[Cu^I(CH_3CN)_4]ClO_4$ (1.0×10^{-2} mol dm^{-3}), and monodentate ligand (4.0 mol dm^{-3}) in THF under atmospheric O_2 at 25°C for 1 h.

or γ-picoline (pK_a = 5.9, 5.8, or 6.0, respectively)) were suitable for generating *o*-FAAP in the relatively high yield (42–54%), as compared with the *o*-FAAP yield (50%) for py. However, 4-cyanopyridine with the electron withdrawing cyano group did not act as an effective π-conjugation ligand and made the dioxygenolysis reaction very slow with no *o*-FAAP produced. Therefore, appropriate electron donation and π-conjugative ability of monodentate ligands such as py and picolines are necessary for the effective ring-opening dioxygenolysis of 3-methylindole.

Effects of bidentate ligand on dioxygenolysis of 3-methylindole

When bpy was added to the catalytic Cu(I)/py system $[Cu^I(CH_3CN)_4]ClO_4$ (1.0×10^{-2} mol dm^{-3})/py (1.5 mol dm^{-3}) in the concentration range of 0–0.025 mol dm^{-3}, the ring-opening dioxygenolysis of 3-methylindole was most enhanced at the molar ratio of Cu^I/py/bpy = 4/600/1, as shown in Figure 1 (b). Since the *in situ* prepared Cu^I complexes generated with Cu^I/py/bpy = 400/600/1 presumably include the catalytic systems of Cu^I/py/bpy and Cu^I/py, the effects of bidentate ligands on the dioxygenolysis of 3-methylindole were then examined in the Cu^I/py/bidentate ligand (molar ratio of 1/150/1) system.

From the equilibrium constant (K) determined for the ligation of the bidentate ligands to $[Cu^I(CH_3CN)_4]ClO_4$ by monitoring the absorbance change of the Cu^I/bidentate ligand complex around 450 nm in CH_3CN (Table 4), the smaller values of log K resulted in higher catalytic activity in the order: dmphen (2,9-dimethyl-1, 10-phenanthroline) > tmbpy (4,4',6,6'-tetramethylbipyridine) > bpy > dmbpy > (4,4'-dimethylbipyridine) > phen >> en. This result may indicate that the strongly coordinating ligands tend to form bis-bidentate complexes Cu(bidentate ligand)$_2$ $(py)_2^+$ suppressing the substrate-coordination to the Cu^I complex.

Spectroscopic Measurements ring opening dioxygenolysis of the Reaction Intermediates and Reaction Process

The addition of bpy to $[Cu^I(CH_3CN)_4]ClO_4$/py in degassed CH_3CN caused the appearance of a new band (λ_{max} = 435 nm) which has been assigned as a dπ (d_{xz} or

Table 4 Bidentate ligands effects on the dioxygenolysis of 3-methylindole by $[Cu^I(CH_3CN)_4]ClO_4$/py/bidentate ligand system[a]

bidentate ligand	log K[b]	substrate conv. %	*o*-FAAP yield %
dmphen	5.45	75	42
tmbpy	6.13	64	35
bpy	6.60	61	17
dmbpy	6.87	36	20
phen	6.89	35	17
en		6	0

[a]The reaction was carried out with 3-methylindole (5.0×10^{-2} mol dm^{-3}), $[Cu^I(CH_3CN)_4]ClO_4$ (1.0×10^{-2} mol dm^{-3}), py (1.5 mol dm^{-3}) and bidentate ligand ($1.0 \times 10 dm^{-3}$) in THF under atmospheric O_3 at 25°C for 1h. [b]K = equilibrium constant for the bidentate ligand ligation to $[Cu^I(CH_3CN)_4]ClO_4$.

d_{yz}) → π^* (MLCT) transition between copper(I) and bpy[12] of the bpy coordinated complex (Figure 2).

However, the slight change of UV absorption intensity (435 nm) of the Cu^I/py/bpy mixture upon bubbling with O_2 did not positively indicate the O_2 adduct of the Cu^{II}/py/bpy complex. Coordination of O_2 to *meso*-tetraphenylporphyrinatomanganese(II) (Mn^{II}TPP) which possesses catalytic activity for the 3-methylindole dioxygenolysis, was observed spectrophotometrically by UV absorption change of the Soret band for the porphyrin ligand.[10]

To test for an O_2 coordinated Cu^I/py/bpy or Cu^I/py/pby/3-methylindole complex, the ESR spectrum of the [Cu^I(CH$_3$CN)$_4$]ClO$_4$/py,[Cu^I(CH$_3$CN)$_4$]ClO$_4$/py/bpy or [Cu^I(CH$_3$CN)$_4$]ClO$_4$/py/bpy/3-methylindole mixtures bubbled with O_2 for 20 min indicated a typical signal for the Cu^{II} complex over a broad range around g = 2.[13] The signal typical for O_2^- in Cu^{II}-O_2^- or 3-methylindole-Cu^{II}-O_2^- (g = 2.006) (Figure 3); was not observed the recently reported phenoxo-bridged dicopper(I) complex is able to generate Cu^{II}-O_2^- at g = 2.006,[14] and Mn^{II}TPP also indicates the ESR signal (g = 2.004) of the O_2^- in the presence or absence of 3-methylindole for Mn^{III}-O_2^- Therefore, the presence Cu^I/py/bpy or Cu^I/py/bpy/3-methylindole system in an O_2 atmosphere transformed O_2 into O_2^- without the formation of a stable Cu^{II}-O_2^- (or 3-methylindole-Cu^{II}-O_2^-) complex. If the superoxide O_2^-, once formed, participates in the direct formation of the *o*-FAAP product without substrate activation by the Cu^{II} complex *via* the reaction process expressed in Scheme 2, the

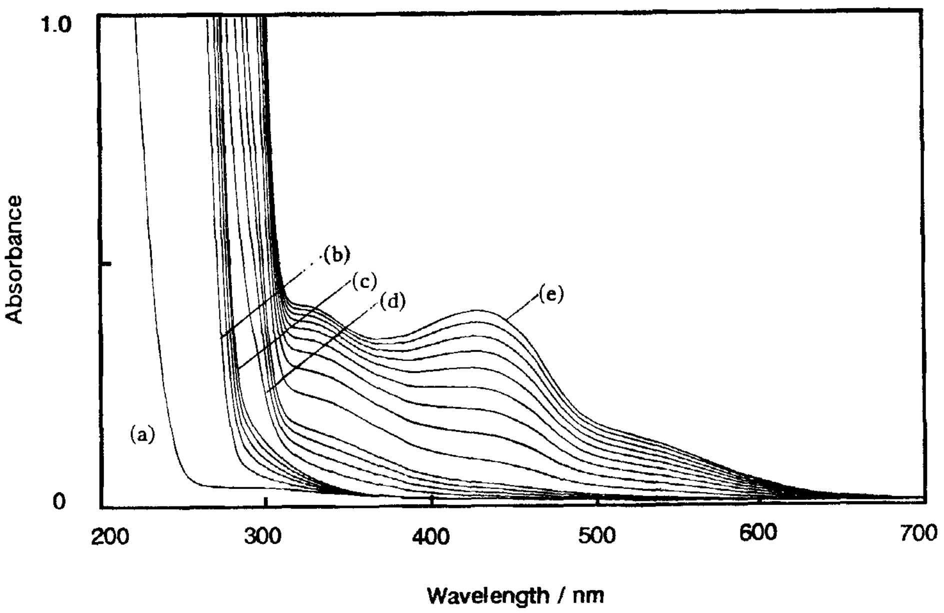


Figure 2 Absorption spectral changes from the addition of py and bpy to [Cu^I(CH$_3$CN)$_4$]ClO$_4$ (1.50×10^{-4} mol dm^{-3}) in degassed CH$_3$CN. The concentrations of py and bpy were (a) [py] = [bpy = 0 mol dm^{-3}, (b) [py] = 4.50×10^{-3} mol dm^{-3}, [bpy] = 0 mol dm^{-3}, (c) [py] = 2.25×10^{-2} mol dm^{-3}, [bpy] = 0 mol dm^{-3}, (d) [py] = 2.25×10^{-2} mol dm^{-3}, [bpy] = 3.75×10^{-5} mol dm^{-3}, and (e) [py] = 2.25×10^{-2} mol dm^{-3}, [bpy] = 1.50×10^{-3} mol dm^{-3}.

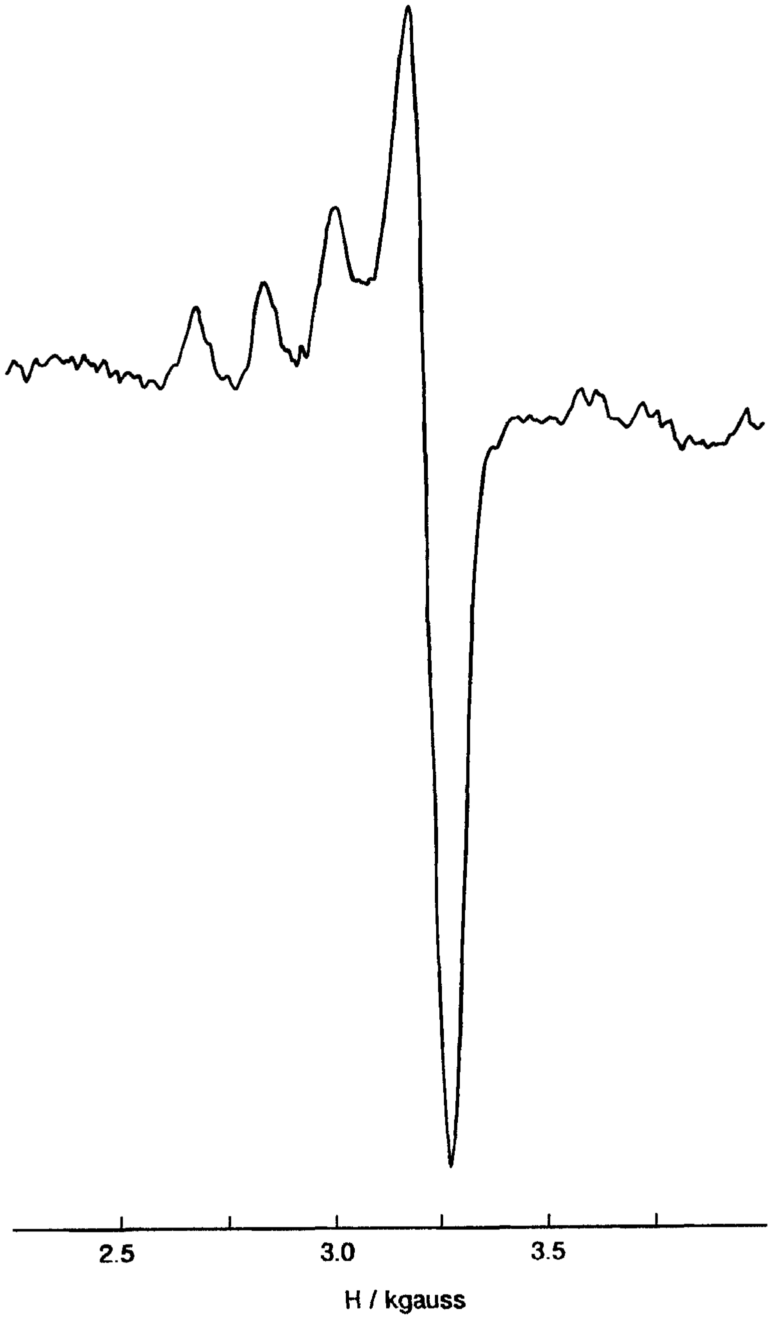
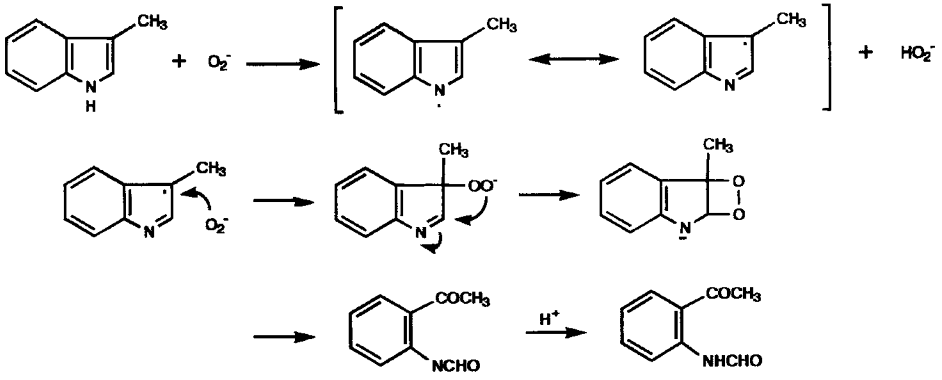


Figure 3 ESR spectra of $[Cu^I(CH_3CN)_4]ClO_4$/py/bpy/3-methylindole in CH_3 CN under atmospheric O_2 at −196°C. $[[Cu^I(CH_3CN)_4]ClO_4] = 2.26 \times 10^{-6}$ mol dm^{-3}, [py] $= 3.36 \times 10^{-4}$ mol dm^{-3}, [bpy] $= 2.25 \times 10^{-5}$ mol dm^{-3}, and [3-methylindole] $= 1.13 \times 10^{-5}$ mol dm^{-3}.



Scheme 2 Ohkubo, Sagawa, Takano, Hata, Kobayashi.

failure to observe the O_2^- complex requires the excess amount of the *in situ* prepared Cu^Ipy/bpy complex for the generation of O_2^-.

The $g_{\parallel}$ and $A_{\parallel}$ parameters in the ESR spectrum observed from the addition of the pyridine, bipyridine, and 3-methylindole to Cu^I in the presence of O_2 (Figure 3) were found to be 2.134 and 178×10^{-4} cm^{-1} respectively. These parameters which

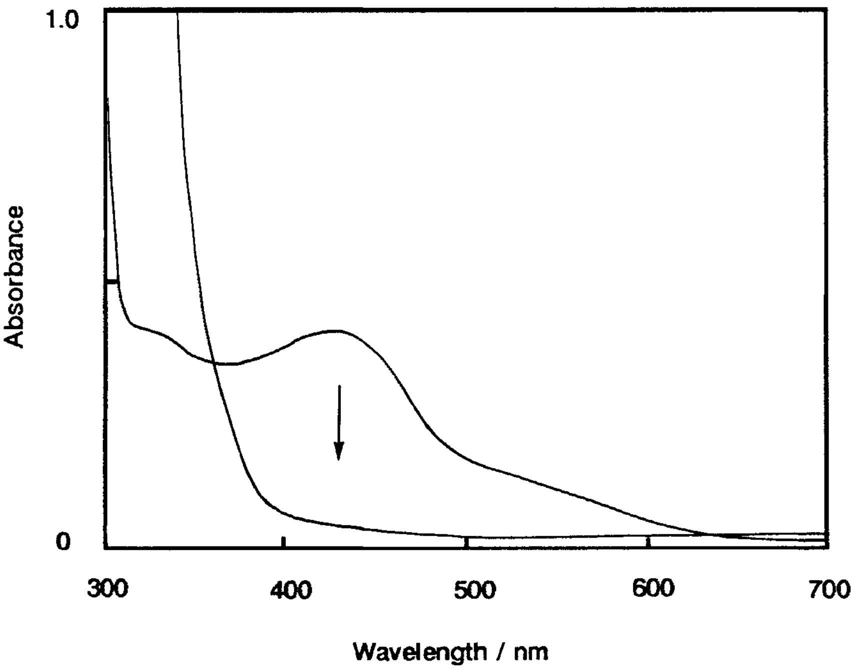


Figure 4 Absorption spectral changes from the addition of 3-methylindole (1.5×10.6^{-6} mol) to $[Cu^I(CH_3CN)_4]ClO_4$ (3.0×10^{-7} mol)/py (4.5×10^{-5} mol) bpy (3.0×10^{-6} mol) in CH_3CN (2 cm^3) under an O_2 atmosphere.

are similar to those previously reported for structurally well-characterized complexes of Cu^{II} might reflect the degree of square planar distortion.[15] At present, however, we do not have enough evidence to characterize the exact structure of the catalyst, the geometry of the *in situ* prepared complex may be square planar by pyridine, bipyridine, and 3-methylindole ligation to Cu^{II}.

For the 3-methylindole coordinated Cu^{II} complex which might be necessary for the present catalytic reaction, the addition of 3-methylindole to Cu^{I}/py/pby in O_2 changed the UV spectrum of the Cu^{I}/py/bpy giving a new UV absorption peak of the *o*-FAAP product at 318 nm (Figure 4). The addition of pyridine and bipyridine to $[Cu^{I}(CH_3CN)_4]ClO_4$ resulted in the reduction of the oxidation potential of the Cu^{I}/Cu^{II} ($E_p^{I/II}$) from + 1.08 V *vs.* SCE to +0.08 V *vs.* SCE ($E_p^{I/II}$ of Cu^{I}, Cu^{I}/py, Cu^{I}/py/pby and Cu^{I}/py/bpy/3-methylindole were +1.08, +0.47, +0.08 and +0.08 V

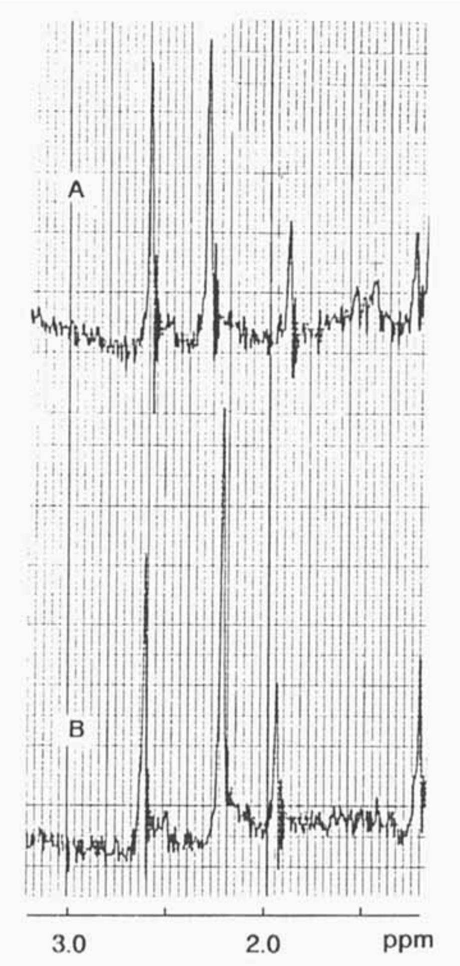


Figure 5 NMR spectral change of 3-methylindole by mixing with $[Cu^{I}(CH_3CN)_4]ClO_4$/py and O_2 in $CDCl_3$: (A) 1 h after mixing; (B) 3 h after addition of CF_3 CO_2H.

vs. SCE respectively). Thus, the pyridine and bipyridine are functioning as ligands to Cu^I and their role may be to reduce the $E_p^{I/II}$ to promote this 3-methylindole dioxygenolysis. The addition of 3-methylindole to Cu^I/py/bpy in O_2 changed the $E_p^{I/II}$ from +0.08 V *vs.* SCE to +0.06 V *vs.* SCE (after O_2 bubbling of the $[Cu^I(CH_3CN)_4]ClO_4$/py/bpy/3-methylindole mixture, the solution was deoxygenated by bubbling with nitrogen during the measurement). Relative intensities of the ESR signals under an O_2 atmosphere (Figure 3) of the Cu^I (0.00, no signal), Cu^I/py (0.230), Cu^I/py/bpy (0.235) and Cu^I/py/bpy/3-methylindole (1.00) mixtures indicated that the most stable coordination system of Cu^I/py/bpy/3-methylindole was the one in a square planar type Cu^{II} complex. The ESR spectrum of the Cu^I/py/bpy/3-methylindole system in O_2 did not clearly indicate the peroxyl radical ($g = 2.016$) at the 3-C position in 3-methylindole; for comparison; Mn^{II}TPP results in an ESR signal of the peroxyl radical ($g = 2.016$) in the reaction of 3-methylindole with O_2.[10] Therefore, the present catalytic reaction seems to be characterized by the formation of the indolenyl hydroperoxide through attack of a $HO_2\cdot$radical (generated by the abstraction of the NH proton in 3-methylindole by O_2^- of the carbon radical at the 3-C position in the substrate (see Scheme 1).

The dioxygenolysis of 3-methylindole by $[Cu^I(CH_3CN)_4]ClO_4$/py in $CDCl_3$ in an NMR tube at 25°C resulted in gradual disappearance of the methyl signal in the substrate (2.30 ppm) with the appearance of the methyl signal of indolenyl hydroperoxide (1.45 ppm[10]) and of the ring-opened product (2.60 ppm), as shown in Figure 5, the addition of CF_3CO_2H (a hydroperoxide decomposition reagent) to the reaction mixtures at 60°C extinguished the resonance at 1.45 ppm.

The intramolecular rearrangement of the indolenyl hydroperoxide resulted in the ring-opening product of *o*-FAAP.

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