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Dual activation process in a copper(II)oxoisoindoline-catalyzed catechol oxidation

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ABSTRACT

The mononuclear [Cu(3′MePyOIND)$_2$] (3′MePyOINDH: 3-(3′-methyl-2′-pyridylimino)isoindoline-1-one) complex has been prepared and characterized by various techniques such as elemental analysis, IR, UV–vis and ESR spectroscopy. The title compound was suitable as catalyst for the catalytic oxidation of 3,5-di-*tert*-butylcatechol (3,5-DTBC-H$_2$) to 3,5-di-*tert*-butyl-1,2-benzoquinone (3,5-DTBQ) (catecholase activity) with dioxygen at ambient condition in good yields. Kinetic measurements revealed first-order dependence on the catalyst and dioxygen concentration and saturation type behavior with respect to the corresponding substrate. It was also found that the complex shows dual effects, acts as a base deprotonating 3,5-DTBC-H$_2$ and also as a redox catalyst, activating O_2 during the oxidation reaction.

1. Introduction

The oxidative degradation of organic substances such as aromatics with dioxygen under mild conditions is of great interest for industrial [1] and synthetic processes both from an economical and environmental point of view [2]. The aromatic rings are first hydroxylated to phenols or diphenols either through successive steps or dihydroxylation, which are the key compounds for either oxidation by dioxygen to *o*-quinones catalyzed by catechol oxidases [3–8] and tyrosinases [10,11], or dioxygenation to ring-cleaved products by catechol dioxygenases [12,13]. Both tyrosinase and catechol oxidase belong to the monophenol oxidase family and possess active sites with two copper atoms, both of which are coordinated by three histidine residues (type 3 copper proteins) [14–17]. Structural information was available for hemocyanins [18], catechol oxidase [9] and very recently for a recombinant tyrosinase [19]. Although comparison of metal coordination region from these structural data evidences high similarities, the functional differences between Tyr, CO and Hc could not be rationalized to date. The mechanism for the catecholase reaction is primarily based on an earlier proposal derived from spectroscopy and theoretical studies [20] and a recent series of crystal structures of the various intermediates of the catechol oxidase. Major differences in the various mechanisms are (1) coordination of catechol as a bidentate or as a bridging ligand and (2) production of H_2O_2 or H_2O from the coordinated peroxide. The mechanism of the catechol oxidation by the natural catecholase enzyme and by the model complexes still also remains far from clear. For example there are only few information about the deprotonation of the substrate catechol. The monodentate binding of the diphenolic substrate to the CuB is suggested from the crystal structure of the catechol oxidase–phenylthiourea inhibitor complex, in which catechol binds after deprotonation of one of the two hydroxyl groups to CuB. Glutamate group, hydrogen bonded to a solvent molecule close to the dimetal center, may assist in deprotonating the substrate. A unique mechanism for the catalytic cycle was proposed by Siegbahn, applying hybrid density functional studies [21]. According to that the availability of several external nearby bases, which could store protons, released during the cycle. Nevertheless, a bidentate bridging of catechol is also proposed [22–24]. The contrasting cofactor dependence of the intradiol and extradiol dioxygenases is intriguing: intradiol dioxygenases utilize a mononuclear iron(III) [25–27] or copper(II) [28] cofactor, whereas the extradiol dioxygenases utilize a mononuclear iron(II) [29–32] or manganese(II) [33–35] cofactor. A fundamental question is arised: what factors control the choice of oxidase vs. dioxygenase or intadiol vs. extradiol specificity [36]? It has been proposed that acid–base behavior of fragment of the enzyme close to the active center is a key factor in extradiol cleavage [37,38]. Studies of a biomimetic model reaction for extradiol cleavage using $FeCl_2$, 1,4,7-triazanonane and pyridine have shown that pyridine has two roles in the reaction: pyridine initially generates the catecholate mono-anion; the pyridinium cation then acts as a proton

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donor to assist the Criegee rearrangement [39]. These observations were consistent with the presence of two acid–base groups in the outer sphere of the extradiol catechol dioxygenases [37]. Contrary, copper-containing dioxygenase enzymes and their model systems mediate only intradiol scission of catechols [40].

Since the catecholase oxidation reaction is widely applied in medical diagnosis for the determination of the hormonally active catecholamines, adrenaline, noradrenaline and dopamine [41] interest in developing small molecular weight copper (II) complexes as models for catechol oxidase has lead to investigate the catecholase activities of several mononuclear and binuclear copper complexes [42–48]. Here we describe a new copper(II)-catalyzed system for the catechol oxidation in which the complex shows dual effects, acts as an acid–base and also as a redox catalyst. The dual effect on the biomimetic catechol oxygenase/oxidase activity is probed with spectroscopic and functional investigations on the prepared copper(II) complex.

2. Experimental

2.1. Materials

All manipulations were performed under a pure dinitrogen or argon atmosphere unless otherwise stated, using standard Schlenck-type inert-gas techniques [49]. Solvents used for the reactions were purified by literature methods [50] and stored under argon. All other chemicals were commercial products and were used as received without further purification.

2.2. Analytical and physical measurements

Infrared spectra were recorded on an Avatar 330 FT-IR Thermo Nicolet instrument using samples mulled in Nujol between KBr plates or in KBr pellets. Electronic absorption spectra were recorded on a Hewlett–Packard (Agilent) 8452 diode array spectrophotometer over a 190–1100 nm range in quartz cuvettes. Electron spin resonance (ESR) spectra were recorded in a Bruker ELEXYS E500 CW EPR in dmf solution, and simulated by WINEPR SimFonia 2.11 program. GC, GC/MSD analyses were performed on a HP 5830A gas chromatograph equipped with a flame ionization detector and a CIP SIL 8CB column and on a HP5890II/5971 GC/MSD apparatus equipped with a column identical to that used for GC analyses. Single crystals of Cu(3′MePyOIND)$_2$ suitable for an X-ray diffraction study were grown from methanol by ether diffusion. The intensity data were collected with Rigaku R-AXIS Rapid single-crystal diffractometer using Mo Kα radiation (λ = 0.71070 Å) at 295 K. Crystallographic data and details of the structure determination are given in Table 1, whereas selected bond lengths and angles are listed in Table 2. SHELX-97 [51] was used for structure solution and full matrix least squares refinement on F^2. Crystal structure has been deposited at the Cambridge Crystallographic Data Centre (Deposition no. CCDC 716650).

2.3. Synthesis of 3′MePyOINDH

Under anaerobic conditions, 3-imino-1-oxoisoindoline (1.04 g, 7.1 mmol) and 2-amino-6-methylpyridine (0.72 mL, 7.1 mmol) were refluxed in ethanol (20 mL) for 24 h. The precipitated yellow solid was filtered, washed with cold methanol and dried in vacuum to give 0.52 g (31%) of the ligand 3-(3′-methyl-2′-pyridylimino)isoindoline-1-one), mp: 136–138 °C, IR (KBr): 3261 (vs, ν_{NH}), 3079 (m, $\nu_{CH,ar}$), 2958 (w, $\nu_{CH,aliph}$), 2924 (w, $\nu_{CH,aliph}$), 2857 (w, $\nu_{CH,aliph}$), 1732 (vs, ν_{CO}), 1672 (m), 1613 (vs), 1578 (vs), 1537 (vs), 1463 (vs), 1440 (vs), 1293 (m), 1278 (m), 1219 (vs), 1151 (s), 1132 (vs), 1089 (s), 1063 (s), 1026 (m), 899 (w), 823 (w), 779 (m), 711 (s), 677 (m), 654 (m), 548 (w), 536 (w) cm^{-1}. UV–vis (DMF): 290 nm ($\lambda_{max,}$ log ε, 3.753), 300 (3.76), 343 (3.91). ^{1}H NMR (DMSO): δ 2.02 (s, 1H, NH), 2.30 (s, 3H, CH_3), 7.05 (m, 1H, ArH), 7.61 (m, 2H, ArH), 7.68 (d, 1H, ArH), 7.76 (d, 1H, ArH), 7.93 (d, 1H, ArH), 8.24 (d, 1H, ArH). Anal. Calcd. for $C_{14}H_{11}N_3O$: C, 70.87; H, 4.67; N, 17.71. Found: C, 70.53; H, 4.39; N, 17.23%.

Table 1
Summary of the crystallographic data and structure parameters for Cu(3′MePyOIND)$_2$.

Formula weight	299.79
Crystal system	Monoclinic
Crystal description	Prism
Space group	*C*2/*c*
Unit cell dimensions	
a (Å)	19.8495(4)
b (Å)	7.7466(2)
c (Å)	15.3227(3)
α (°)	9000
β (°)	100.2(1)
γ (°)	90.00
Volume (Å^3)	2318.86(9)
Z	8
Calculated density (g cm^{-1})	1.717
Crystal size (mm^3)	0.40 × 0.30 × 0.15
Index ranges	$0 \le h \le 27$ $0 \le k \le 10$ $-20 \le l \le 20$
Temperature (K)	293(2)
Radiation	Mo Kα (λ = 0.71073)
Absorption coefficient (mm^{-1})	1.876
F(0 0 0)	1216
Reflections collected	3192
Observed reflections [$I > 2\sigma(I)$]	2777
Goodness-of-fit	1.139
Final *R* indices	R_1 = 0.0457, wR_2 = 0.1557
R indices (all data)	R_1 = 0.0573, wR_2 = 0.1713

2.4. Synthesis of Cu(3′MePyOIND)$_2$

A suspension of 0.38 g (1.3 mmol) of 3′MePyOINDH and 0.08 g (0.65 mmol) of Cu(OCH$_3$)$_2$ in 20 mL CH$_3$CN was refluxed for 24 h. The brown product was collected by filtration, washed with diethyl ether, and dried under vacuum (0.20 g, 60%): UV–vis ($\lambda_{max,}$ DMF): 267 nm (log ε, 4.13), 283 (4.30), 302 (4.31), 351 (4.39), 367 (4.40), 382 (4.39). IR (KBr): 3055 (m, $\nu_{CH,ar}$), 2966 (m, $\nu_{CH,aliph}$), 2920 (w, $\nu_{CH,aliph}$), 2857 (w, $\nu_{CH,aliph}$), 1732 (s, ν_{CO}), 1698 (vs), 1617 (vs), 1585 (vs), 1552 (vs), 1455 (s), 1415 (s), 1368 (m), 1312 (s), 1279 (m), 1234 (m), 1176 (s), 1096 (vs), 1077 (m), 1002 (w, py), 889 (m), 842 (w), 786 (m), 716 (vs), 548 (w), 514 (w) cm^{-1}. ESR (toluene): g = 2.0918, A_{Cu} = 74.3, A_N = 15.43 G. Anal. Calcd. for $C_{28}H_{20}CuN_6O_2$: C, 62.74; H, 3,76; N, 15.68. Found: C, 62.59; H, 3.64; N, 15.75%.

2.5. Spectrophotometric titrations of Cu(3′MePyOIND)$_2$ with $HClO_4$

The titrations of complex Cu(3′MePyOIND)$_2$ were performed by the addition of aqueous $HClO_4$ (70%) in DMF to an anaerobic solutions of the anionic metal complex via a gastight syringe to form the

Table 2
Selected bond lengths (Å) and bond angles (°) for Cu(3′MePyOIND)$_2$.

Cu(1)–N(1)	1.9131(19)	N(2)–C(8)	1.287(3)
Cu(1)–N(3)	2.0235(19)	N(2)–C(9)	1.382(3)
N(1)–C(1)	1.392(3)	C(2)–C(7)	1.382(3)
C(1)–C(2)	1.494(3)	C(7)–C(8)	1.490(3)
C(1)–O(1)	1.210(3)	N(3)–C(9)	1.357(3)
N(1)–C(8)	1.375(3)		
N(1)–Cu(1)–N(1′)	148.59(14)	N(1)–Cu(1)–N(3)	100.86(8)
N(1)–Cu(1)–N(3′)	90.99(8)	N(3)–Cu(1)–N(3′)	135.35(8)

corresponding metal complexes. 2 mL of 0.06 mM of the complex in DMF solution was titrated stepwise (10 μL = 1 equiv.) with a DMF solution of $HClO_4$ (11.8 mM) and the absorbances in the range of 200–600 nm were measured under inert conditions. Back titrations with DMF solution of NEt_3 and titrations with tetrachlorocatechol ($Cl_4Cat\text{-}H_2$) were carried out in a similar manner.

Caution: perchlorate salts of metal complexes with organic ligands are potentially explosive. Only small amounts of material should be prepared, and these should be handle with great care.

2.6. Kinetics of the oxidation of 3,5-di-tert-butylcatechol

In a typical experiment, $Cu(3'MePyOIND)_2$ (5.92×10^{-5} mol dm^{-3}) and the corresponding substrate 3,5-di-*tert*-butylcatechol (3,5-DTBC-H_2) (23.40×10^{-4} mol dm^{-3}) were dissolved in 10 cm^3 of DMF, under argon atmosphere in a thermostated reaction vessel with an inlet for taking samples with a syringe. The solution was then thermostated at the appropriate temperature (20 °C), the argon was replaced by air and the oxidation of 3,5-DTBC-H_2 was followed spectrophotometrically by monitoring the formation of 3,5-DTBQ at 400.5 nm (log $\varepsilon = 3.21$) as function of time (λ_{max} of a typical band of 3,5-DTBQ) (Table 1). The 3,5-DTBQ was also quantified by GC and verified by GC-MS. Dioxygen uptakes were also measured in a constant pressure gas-volumetric apparatus. The amount of H_2O_2 formed during the reactions was determined by iodometry [52]. The volume of absorbed dioxygen was red periodically using a gas burette. The solubility of dioxygen in DMF at 20 °C was taken as 0.938×10^{-3} mol dm^{-3} [53]. The validity of Dalton's law was assumed for the calculation of dioxygen concentration at different partial pressures [54].

3. Results and discussion

3.1. Synthesis and characterization of $Cu(3'MePyOIND)_2$

The complex $Cu(3'MePyOIND)_2$ has been prepared by treating $Cu(OCH_3)_2$ with the appropriate amount of 3-(3′-methyl-2′-pyridylimino)isoindoline-1-one) in acetonitrile. Single crystals of $Cu(3'MePyOIND)_2$ suitable for an X-ray diffraction study were grown from methanol by ether diffusion. As shown in Fig. 1, the central copper(II) atom is coordinated with two pyridine and two pyrrole nitrogen atoms of the two oxoisoindoline ligands. The 3′MePyOIND is a bidentate and monoanionic ligand, which results in a neutral copper complex. The X-ray crystallography symmetry imposes that the two ligands are oriented in a *trans* configuration. The geometry around copper(II) may be best described as distorted tetrahedron in an N_4 donor set. The Cu–N distances involving the pyridine nitrogen atoms (Cu(1)–N(3) 2.0235(19) Å), are significantly longer than that involving the pyrrole nitrogen atom (Cu(1)–N(1) 1.9131(19) Å).

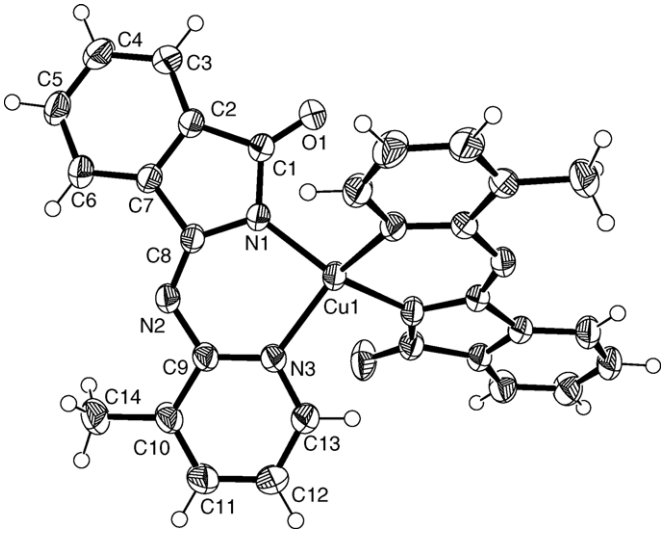
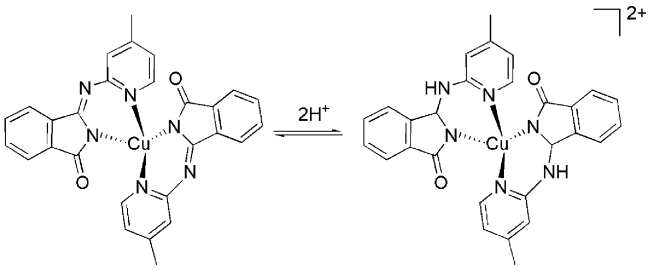


Fig. 1. Ellipsoid drawing of $Cu(3'MePyOIND)_2$ with the atom numbering scheme.

3.2. Oxidation of 3,5-di-tert-butylcatechol (catecholase activity)

3-(3′-Methyl-2′-pyridylimino)isoindoline-1-one (3′MePyOINDH) has been found to be useful as a chromophoric probe of pH owing to the distinct spectral features obtained when it is neutral or its proton is dissociated. Coordinated 3′MePyOIND to copper(II) resulted in a brawn color with absorption peaks at λ_{max} = 351, 367, 382 and 406 nm in DMF. When $HClO_4$ was added to their solution, the brown color disappeared. This suggested that the bidentate coordinated oxoisoindoline ligands may be protonated according to Eq. (1).



(1)

To check this and to prove the reversibility of the protonation, spectrophotometric titration of complex $Cu(3'MePyOIND)_2$ with $HClO_4$ was carried out. The spectra taken during the titration of $Cu(3'MePyOIND)_2$ can be seen in Fig. 2. It shows that bands at 367, 382 and 406 nm diminish upon the addition of $HClO_4$, exhibiting two isobestic points at 291 and 357 nm, indicating a direct conversion of deprotonated oxoisoindoline to the protonated, neutral ligand. At a $Cu(3'MePyOIND)_2/HClO_4$ ratio of 1:2, the oxoisoindoline complex is totally protonated because of disappearance of the absorption peaks at 367, 382 and 406 nm, and the appearance of new peaks at 344, 359 and 382 nm ($\Delta\nu = 23$ nm). To check the reversibility of the protonation reaction, back-titration

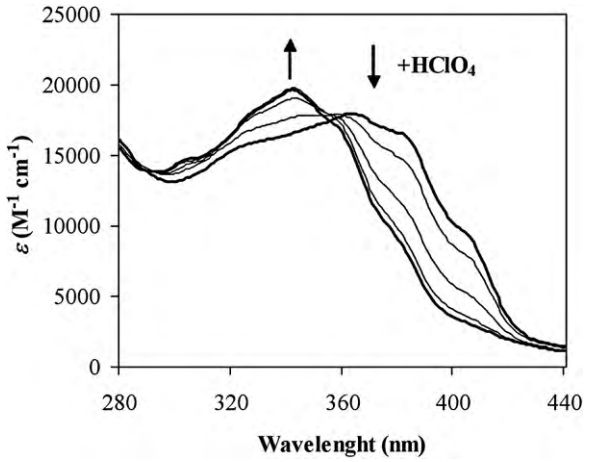


Fig. 2. Spectra during the titration of $Cu(3'MePyOIND)_2$ with $HClO_4$ (0.0, 0.5, 1.0, 2.0 equiv.) in DMF at 20 °C. [$Cu(3'MePyOIND)_2$] = 0.06 mM, [$HClO_4$] = 11.8 mM (10 μL = 1 equiv.).

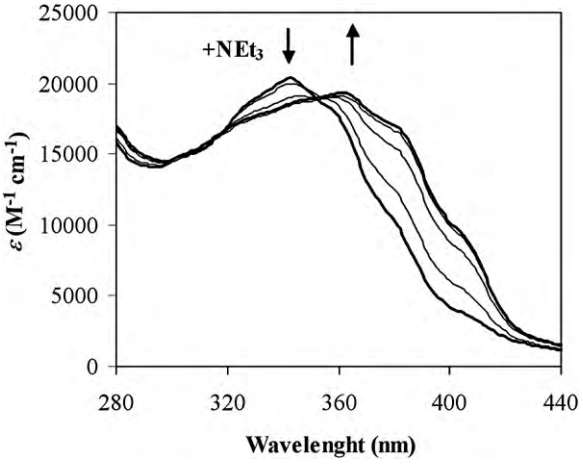


Fig. 3. Dependences of the absorbances of $[Cu(3'MePyOINDH)_2]ClO_4$ as a function of added NEt_3 (0.0, 0.5, 1.0, 2.0 equiv.) during the titration in DMF at 20 °C. $[[Cu(3'MePyOIND)_2]ClO_4] = 0.06$ mM, $[NEt_3] = 11.8$ mM (10 μL = 1 equiv.).

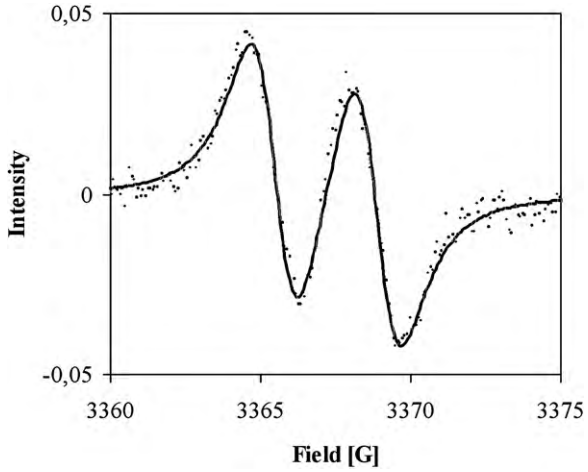


Fig. 5. Measured and simulated ESR spectra of 3,5-di-*tert*-butyl-1,2-semiquinone anion radical (3,5-DTBSQ$^{\bullet -}$) detected in the reaction mixture ($g_0 = 2.0044$, $a_H = 3.39$ G).

of the protonated complex with NEt_3 was also carried out. The spectrophotometric back-titration showed the very same feature in the electronic spectrum proving unequivocally the true reversible nature of the protonation of $Cu(3'MePyOIND)_2$ (Fig. 3). Similar behavior has been found in the presence of $Cl_4Cat\text{-}H_2$ as a slow substrate under argon atmosphere, suggesting that the oxoisoindoline-containing complex $Cu(3'MePyOIND)_2$ can function as a base during the catechol oxidation process (Fig. 4).

3,5-DTBC-H_2 has been widely employed as a substrate in tyrosinase and catechol oxidase model complex studies. Owing to its low redox potential, the substrate is readily oxidized and the bulky substituents prevent further reactions. The catecholase-like activity of the complex $Cu(3'MePyOIND)_2$ was examined in DMF at 20 °C. According to parallel electron spectroscopic, iodometric and gas-volumetric measurements (Fig. S1), the stoichiometry of the oxidation reactions corresponds to Eq. (2). No other oxidation products could be detected.

$$3,5\text{-DTBC-}H_2 + O_2 = 3,5\text{-DTBQ} + H_2O_2 \quad (2)$$

The reaction mixture exhibit the ESR signal shown in Fig. 5, corresponding to the intermediate 3,5-di-*tert*-butyl-1,2-semiquinone anion radical (3,5-DBSQ$^{\bullet -}$), as supported by the simulated signal.

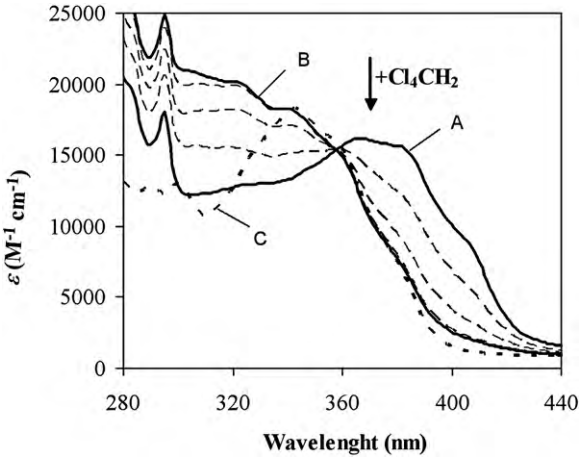


Fig. 4. Spectra during the titration of $Cu(3'MePyOIND)_2$ with $Cl_4Cat\text{-}H_2$ under Ar ((A) $Cu(3'MePyOIND)_2$; (B) $Cu(3'MePyOIND)_2$ + 2.0 equiv. $Cl_4Cat\text{-}H_2$; (C) 3′MePyOINDH) in DMF at 20 °C. $[Cu(3'MePyOIND)_2] = 0.06$ mM, $[Cl_4Cat\text{-}H_2] = 11.8$ mM (10 μL = 1 equiv.).

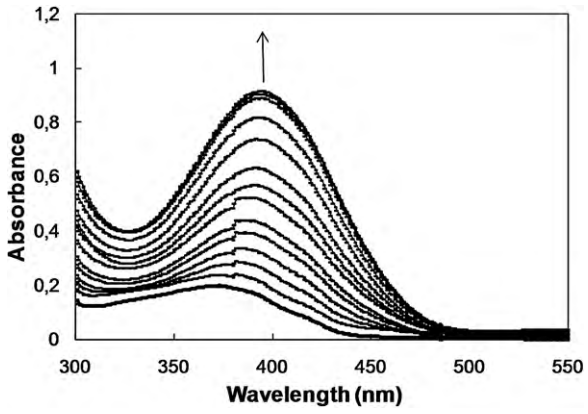


Fig. 6. Time sequence of the increase in the absorption band of 3,5-DTBQ in the catechol oxidation reaction catalyzed by $Cu(3'MePyOIND)_2$. The reactions were performed in DMF: $[3,5\text{-DTBC-}H_2]_0 = 9.37 \times 10^{-3}$ M, $[Cu(3'MePyOIND)_2] = 5.92 \times 10^{-5}$ M under air at 20 °C ($\Delta t = 1$ h).

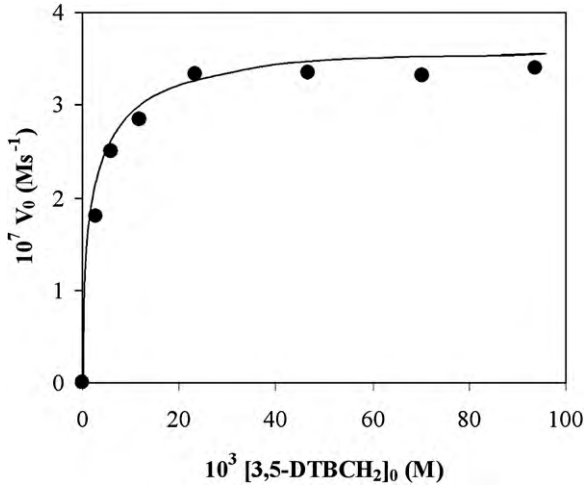


Fig. 7. Dependence of the reaction rates on the 3,5-DTBC-H_2 concentrations for the oxidation reaction catalyzed by $Cu(3'MePyOIND)_2$. The reactions were performed in DMF $[Cu(3'MePyOIND)_2]_0 = 5.92 \times 10^{-5}$ M, under air at 20 °C.

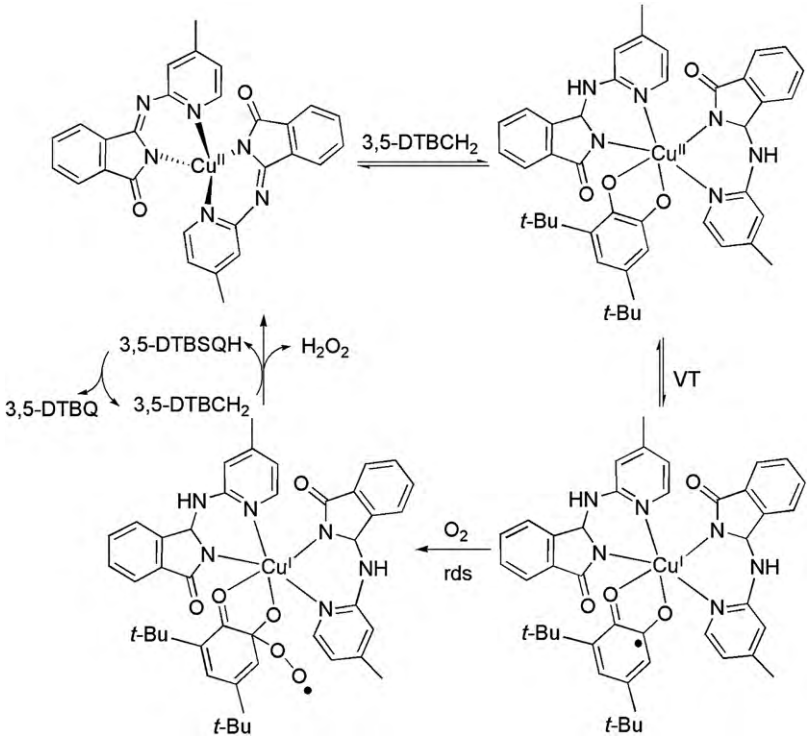
Table 3
Kinetic data for the Cu(3′MePyOIND)$_2$-catalyzed oxidation of 3,5-DTBC-H$_2$ in DMF.

Experiment no.	T (°C)	10^3 [O_2] (M)	10^5 [Cu] (M)	10^4 [3,5-DTBC-H$_2$] (M)	10^7 V_0 (M s^{-1})
1	20	0.938	5.92	2.70	1.80 ± 0.05
2	20	0.938	5.92	5.86	2.50 ± 0.04
3	20	0.938	5.92	11.7	2.84 ± 0.03
4	20	0.938	5.92	23.4	3.33 ± 0.05
5	20	0.938	5.92	46.8	3.34 ± 0.06
6	20	0.938	5.92	70.3	3.31 ± 0.04
7	20	0.938	5.92	93.7	3.40 ± 0.06
8	20	0.938	–	93.7	0.25 ± 0.004[a]
9	20	0.938	1.58	23.4	0.76 ± 0.01
10	20	0.938	2.96	23.4	1.59 ± 0.02
11	20	0.938	4.44	23.4	2.49 ± 0.05
12	20	2.350	5.92	23.4	4.39 ± 0.08
13	20	0.223	5.92	23.4	1.07 ± 0.02
14	20	0.446	5.92	23.4	1.58 ± 0.03
15	20	0.670	5.92	23.4	2.11 ± 0.04

[a] With free ligand [3′MePyOINDH]$_0$ = 5.92 × 10^{-5} M.

The kinetic studies on the oxidation of 3,5-DTBC-H$_2$ were carried out by the method of initial rates by monitoring the increase in the characteristic quinone (3,5-DTBQ) absorption band at 400.5 nm as a function of time (Fig. 6). The reactivity studies were performed in DMF solution at 20 °C (Table 3). Since the base-catalyzed oxidation of 3,5-DTBC-H$_2$ to 3,5-DTBQ by O_2 is known to take place in the presence of various N-bases, the blank test of the reaction was performed without adding the catalyst in the presence of the free ligand 3′MePyOINDH. The reaction rate of the Cu(3′MePyOIND)$_2$-catalyzed reaction was found to be more than one order of magnitude faster than that of using only the free ligand, suggesting that not only the basicity of the coordinated ligand is responsible for the two electron oxidation.

To determine the dependence of the rates on the substrate concentration, solutions of the complex Cu(3′MePyOIND)$_2$ were treated with increasing amounts of 3,5-DTBC-H$_2$. Under this experimental condition, saturation kinetics was found for the initial rates vs. the 3,5-DTBC-H$_2$ concentrations (Fig. 7). Carrying out the kinetic experiments by varying the Cu(3′MePyOIND)$_2$ concentration, the reaction rate is linearly dependent on the concentration of the complex, indicating a first-order dependence on catalyst concentration (Fig. S2). Experiments made at different dioxygen pressures show that P_{O2} appreciably influences the rate of the reaction. Kinetic measurements of the reaction rate with respect to the dioxygen concentration indicate first-order dependence too (Fig. S3). These facts above indicate that an intermediate complex-substrate adduct Cu(3′MePyOINDH)$_2$(3,5-DTBC) is formed, and thereafter, as a result of valence tautomerism (VT) the forming Cu(3′MePyOINDH)$_2$(3,5-DTBSQ) complex reacts with the dioxygen in the rate-determining step of the catalytic cycle. Fig. S4 is an another proof for the catechol coordination. By adding non-oxidizable catechol such as tetrachlorocatechol into the reaction mixture during the oxidation of 3,5-DTBCH$_2$ the reaction was stopped, supporting the inhibition effect of the coordinated Cl$_4$Cat-H$_2$. Then the oxygenated species reacts with 3,5-DTBC-H$_2$ in a fast step to the semiquinone (3,5-DBSQ$^{\bullet-}$) and HO$_2$ which



Scheme 1. Proposed mechanism of the catechol oxidation catalyzed by Cu(3′MePyOIND)$_2$.

after disproportionation give the quinone 3,5-DTBQ and H_2O_2 (Scheme 1).

The complex displays moderate catecholase activity. An analysis of the data based on the Michaelis–Menten model, originally developed for enzyme kinetics, was applied. The results evaluated from Lineweaver–Burk plots are $V_{max} = 3.53 \times 10^{-7}$ M s^{-1}, $K_M = 0.26$ mM, $k_{cat} = 5.96 \times 10^{-3}$ s^{-1} and $k_2(k_{cat}/K_M) = 23.37$ M^{-1} s^{-1}. The turnover rate of 21.5 h^{-1} is comparable to those values reported for other model systems, but significantly lower than those recently reported for the binuclear copper complexes (k_{cat} = 200–6000 h^{-1}), and at least three orders of magnitude less active than the enzyme (8250) itself [55]. On the basis of the k_{cat} values above, it can be said that the binuclear complexes show higher reactivity than the mononuclear complexes due to the fact that this kind of mechanism requires two metal ions in close proximity.

4. Conclusion

A new oxoisoindoline ligand 3′MePyOINDH, and its copper(II) complex Cu(3′MePyOIND)$_2$ were synthesized and characterized. The crystal structure of this complex shows that the central part of the molecule forms a distorted tetrahedron with the two ligands in the *trans* configuration. This mononuclear complex is able to oxidize 3,5-di-*tert*-butylcatechol to the respective *o*-quinone with molecular oxygen. In our model reactions, hydrogen peroxide is produced, which shows high similarity to the copper loaded S100B protein which has catecholase activity and also produces H_2O_2. Kinetic measurements revealed first-order dependence on the catalyst and dioxygen concentration and saturation type behavior with respect to the corresponding substrate. It was also found that the complex shows dual effects, acts as a base and also as a redox catalyst during the oxidation reaction. These results have led to new insights into one of the critical part of the oxidative cycle, wherein the ligand needs to deprotonate to bind to the copper ion.

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Appendix A. Supplementary data

Supplementary data associated this article can be found, in the online version, at doi:10.1016/j.molcata.2010.06.020

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