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Copper-catalyzed oxygenation of 3-hydroxy-2-phenylquinolin-4(1*H*)-one: Synthesis, structure and spectral properties of $[Cu(idpa)(N\text{-baa})]ClO_4$, [idpa = 3,3′-iminobis(*N*,*N*-dimethylpropylamine), *N*-baaH = *N*-benzoylanthranilic acid]

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Abstract

Reaction of one molar equivalent of 3,3′-iminobis(*N*,*N*-dimethylpropylamine (idpa)), *N*-benzoylanthranilic acid (*N*-baaH) and $[Cu(CH_3CN)_4](ClO_4)$ in acetonitrile resulted in the formation of a stable ionic copper(II) complex without additional solvent coordination. The composition and molecular structure of $[Cu(idpa)(N\text{-baa})]ClO_4$ was fully determined by IR, UV–vis, and X-ray crystal analysis. The complex has a distorted square planar CuN_3O core. The oxygenation of 3-hydroxy-2-phenylquinolin-4(1*H*)-one ($QuinH_2$) using $[Cu(idpa)(N\text{-baa})]ClO_4$ as a catalyst results in the oxidative cleavage of the heterocyclic ring to give a *N*-benzoylanthranilic acid and CO as a mimic of quercetinase and 3-hydroxy-1,4-dihydroquinolin-4-one 2,4-dioxygenase action.

Keywords: Copper; 3-Hydroxy-2-phenylquinolin-4(1*H*)-one; *N*-benzoylanthranilic acid; Dioxygenation; Quercetinase

To date, four prokaryotic dioxygenases are known, which catalyze an oxidative C–C bond cleavage with incorporation of two O-atoms into, and release of CO from their substrate [1–4]. Flavonol 2,4-dioxygenase (FDO), which catalyzes the cleavage of flavonol (**1**) to carbon monoxide and phenolic carboxylic acid ester (**3**) was produced by the copper-containing fungi like *Aspergillus flavus* [5], *Aspergillus niger* [6], *Aspergillus japonicus* [7] and the iron-containing protein Yxag from *Bacillus subtilis* [8]. In the course of model studies of FDO numerous copper complexes of flavonol and *O*-benzoylsalicylic acid have been prepared and characterized [9–13]. 3-Hydroxy-2-phenylquinolin-4(1*H*)-one (**2**) $QuinH_2$ which is isoelectronic with flavonol (**1**) is degraded by the enzyme 3-hydroxy-1,4-dihydroquinolin-4-one 2,4-dioxygenase [2,3]. This enzyme does not contain any metallic cofactor. The base-catalyzed oxygenation of 3-hydroxy-2-phenylquinolin-4(1*H*)-one as a functional model showed that these reactions lead to cleavage products, including **4** and carbon monoxide [14].

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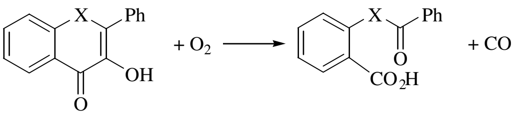

1 X = O
2 X = NH

3 Flavonol 2,4-dioxygenase
4 3-hydroxy-1,4-dihydroquinolin-4-one 2,4-dioxygenase

(1)

In this communication, we present the synthesis and structural characterization of a new ionic (*N*-benzoylanthranilato)copper(II) complex with a tridentate ligand 3,3′-iminobis(*N*,*N*-dimethylpropylamine) (idpa) [Cu(*N*-baa)(idpa)]ClO$_4$ (**5**), obtained with practically quantitative yield by interaction of [Cu(CH$_3$CN)$_4$]ClO$_4$, *N*-benzoylanthranilic acid, and idpa in acetonitrile under dioxygen atmosphere [15]. The determination of its structure was carried out by X-ray single crystal study. In addition IR and UV–vis analysis of the title compound and its dioxygenase-like activity in the oxygenation of 3-hydroxy-2-phenylquinolin-4(1*H*)-one was also examined in order to get insight into the mechanism of these curious reactions.

Complex **5** isolated as a blue solid is stable in air and analyzed satisfactorily for C, H, N. The infrared (IR) spectrum of the complex shows bands corresponding to the coordinated *N*-benzoylanthranilate at 3438 ν(NH), 1670 ν(CO), 1593, 1390 ν(CO$_2$) and 1303 ν(NH) cm^{-1}. The difference between the asymmetric and symmetric stretching frequencies of the carboxylato group [$\Delta\nu = \nu_{as}(CO_2) - \nu_s(CO_2)$] is 203 cm^{-1}, rendering these to a monodentate carboxylate bonding mode [16,17]. The middle band at 3219 cm^{-1} can be rendered to the ν(NH) of the 3,3′-iminobis(*N*,*N*-dimethylpropylamine) ligand. The absorption bands at 1114, 1061 and 624 cm^{-1} can be assigned to the perchlorate anion. The electronic spectrum of complex **5** shows an absorption band at 695 nm due to d–d transition. A higher energy band at 320 nm is associated with charge transfer transition. These spectral features are comparable with those of the [Cu(*O*-bs)(idpa)]ClO$_4$, (*O*-bsH = *O*-benzoylsalicylic acid) [18].

Suitable crystals of **3** were obtained by slow diffusion of diethyl ether into DMF solution of the complex at 20 °C. The molecular structure of [Cu(*N*-baa)(idpa)]ClO$_4$ [19] as well as selected bond lengths and angles are shown in Fig. 1.

The reaction between 3-hydroxy-2-phenylquinolin-4(1*H*)-one and dioxygen in the presence of catalytic amounts of [Cu(*N*-baa)(idpa)]ClO$_4$ were performed in DMF solutions and examined at 130 °C with a ratio between initial concentration of [Cu(*N*-baa)(idpa)]ClO$_4$ (**5**) and 3-hydroxy-2-phenylquinolin-4(1*H*)-one (**2**) from 1:10 to 1:90. We found that the oxygenation of QuinH$_2$ results in oxidative cleavage of the heterocyclic ring to give *N*-benzoylanthranilic acid (**4**) and CO as products [22]. The oxidation is selective, no other products were obtained. 3-Hydroxy-2-phenylquinolin-4(1*H*)-one exhibits its absorption at 372 nm. Spectral changes accompanying addition of dioxygen to the reaction mixture show that the absorption peak at 372 nm decrease, while that at 417 nm increase with time (Fig. 2).

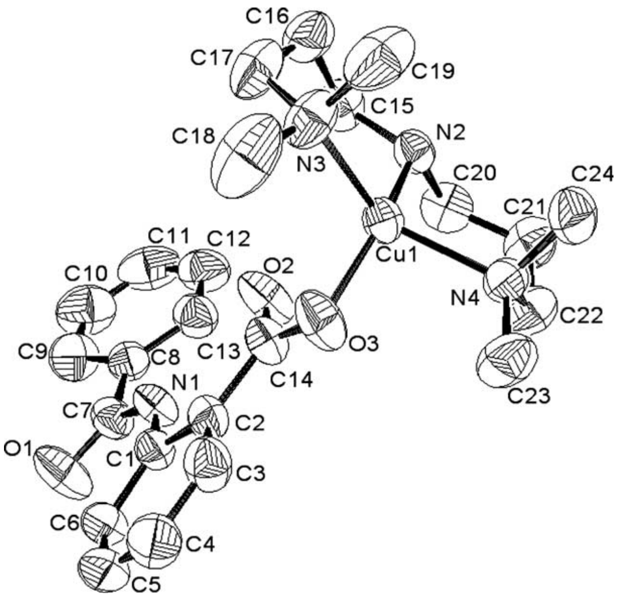

Fig. 1. Molecular structure of [Cu(*N*-baa)(idpa)]$^+$(**5**) with crystallographic numbering. Hydrogen atoms are omitted for clarity. Relevant bond lengths (Å) and angles (°): Cu(1)–N(2) 1.994(2), Cu(1)–N(3) 2.073(3), Cu(1)–N(4) 2.063(3), Cu(1)–O(3) 1.949(2), O(3)–C(14) 1.265(4), C(14)–O(2) 1.246(4), N(1)–C(7) 1.354(4), N(1)–C(1) 1.393(4), C(7)–O(1) 1.223(3). O(3)–Cu(1)–N(2) 152.42(9), N(3)–Cu(1)–N(4) 138.22(11), O(3)–Cu(1)–N(4) 93.27(10), O(3)–Cu(1)–N(3) 95.72 (12), N(3)–Cu(1)–N(2) 95.97(11), O(2)–C(14)–O(3) 120.0(3), Cu(1)–O(3)–C(14) 102.75(19). The molecule is monomeric in the solid state. The overall geometry around the four-coordinate copper ion is described as an distorted square planar geometry. Three nitrogen atoms of the tridentate ligand idpa and the oxygen atom of the monodentate carboxylate group occupy basal positions. The Cu–O bond distance 1.949 Å and Cu–N bond distances average 2.04 Å, which are in the normal range [11,18].

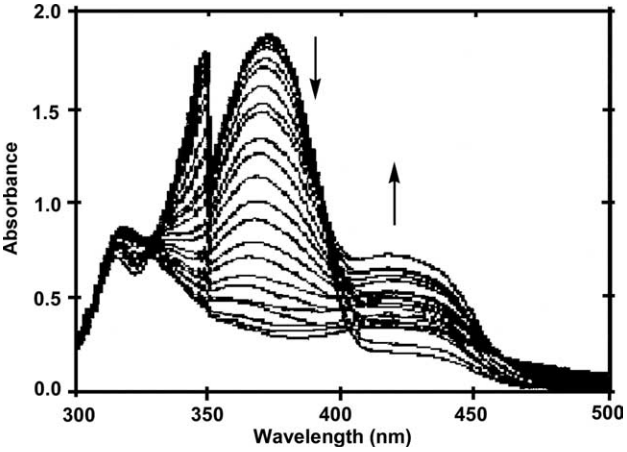

Fig. 2. Spectral changes accompanying the [Cu(*N*-baa)(idpa)]ClO$_4$-catalyzed oxygenation of QuinH$_2$. [[Cu(*N*-baa)(idpa)]ClO$_4$]$_0$ = 2.67×10^{-5} M; [QuinH$_2$]$_0$ = 2.4×10^{-3} M, under dioxygen at 130 °C in 50 cm^3 DMF.

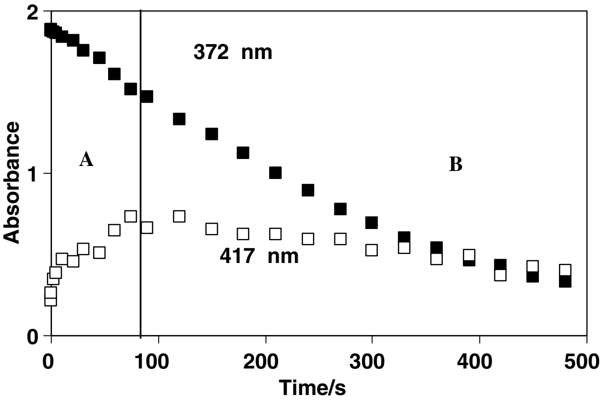

Fig. 3. Spectral changes accompanying the [Cu(*N*-baa)(idpa)]ClO_4-catalyzed oxygenation of $QuinH_2$ at 372 and 417 nm. [[Cu(*N*-baa)(idpa)]ClO_4]$_0$ = 2.67×10^{-5} M; [$QuinH_2$]$_0$ = 2.4×10^{-3} M, under dioxygen at 130 °C in 50 cm^3 DMF.

Plots of the time dependence of the absorptions show two segments, indicating that there are at least two processes occurring consecutively [23]. The initial gradient (part **A**) hints to a slower process, while the second one (part **B**) may be considered as the actual oxygenation process of the coordinated 3-hydroxy-2-phenylquinolin-4(1*H*)-one ligand (Fig. 3). The first one is believed to correspond to a slow conversion of the [Cu(*N*-baa)(idpa)]ClO_4 to [Cu(idpa)(QuinH)]ClO_4, which then reacts with dioxygen to the end-product. This reaction resembles the enzyme action on 3-hydroxy-2-phenylquinolin-4(1*H*)-one to give the cleavage product as shown earlier (Eq. (1)).

Acknowledgement

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version at doi:10.1016/j.inoche.2005.06.007.

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[15] Synthesis of [Cu(idpa)(*N*-baa)]ClO_4: [Cu(CH_3CN)$_4$]ClO_4 (0.328 g, 1 mmol), *N*-benzoylanthranilic acid (0.241 g, 1 mmol) and 3,3′-iminobis(*N*,*N*-dimethylpropylamine) (0.186 g, 1 mmol) were dissolved in 20 cm^3 of acetonitrile and refluxed under dioxygen for 6 h. The product was collected by filtration, washed with diethyl ether and dried in vacuum (0.53 g, 90%). M.p. 183–187 °C. IR (KBr) cm^{-1}: 3438 m, 3219 m, 3144 w, 3101 w, 2939 w, 2880 w, 1670 s, 1593 s, 1505 vs, 1452 m, 1390 vs, 1303 s, 1260 m, 1114 vs, 1061 s, 1043 s, 899 w, 863 w, 829 w, 761 m, 713 m, 624 s, 590 w, 538 w, 455 w. UV–vis (DMF) λ_{max} ($\log \varepsilon/dm^3\ mol^{-1}\ cm^{-1}$): 320 (3.92); 695 (2.50). Anal. Calc. For $C_{24}H_{35}ClCuN_4O_7$: C, 48.81; H, 5.97; N, 9.49. Found: C, 48.31; H, 6.05; N, 9.23%.

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[19] Crystal data for **2**: $C_{24}H_{35}ClCuN_4O_7$, 590.55 g mol^{-1}, monoclinic, *P21/c*, $a = 12.7890(2)$ Å, $b = 12.0840(1)$ Å, $c = 17.8870(2)$ Å, $\beta = 93.6500(5)$ (°), $Z = 4$, $V = 2758.69(6)$ Å^3, μ(Mo Kα) = 0.937 mm^{-1}, $d_{calc} = 1.422$ g cm^{-3}, $T = 293(2)$ K, $F(000) = 1236$. The intensity data were collected with a Nonius Kappa CCD single-crystal diffractometer using Mo Kα radiation ($\lambda = 0.71073$). Reflections collected = 21473, reflections total = 5340, reflections unique = 4764. The structure was refined to $R = 0.0465$ (0.0529) and $wR_2 = 0.1267$ for the reflections with $I > 2\sigma(I)$ (all data) and max. resd. density = 0.487e Å^{-3}. The computer program used were SHELXL97 [20]. The structure was solved by direct and difmap methods (SIR92) [21]. CCDC reference number: 271100.

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[22] [Cu(idpa)(*N*-baa)]ClO_4-catalyzed oxygenation of 3-hydroxy-2-phenylquinolin-4(1*H*)-one: 3-hydroxy-2-phenylquinolin-4(1*H*)-one (0.0360 g, 0.15 mmol) and [Cu(idpa)(*N*-baa)]ClO_4 (0.0044 g, 0.0075 mmol) were dissolved and stirred at 130 °C in 5 cm^3 DMF for 12 h under dioxygen atmosphere. Diazomethane solution (2 cm^3) (in diethyl ether) was added to 0.5 cm^3 of the reaction mixture at r.t. and the conversion (75%) of 3-hydroxy-2-phenylquinolin-4(1*H*)-one into *N*-benzoylanthranilic acid was determined by GC as the methylated derivative.

[23] The [Cu(idpa)(*N*-baa)]ClO_4-catalyzed oxygenation of 3-hydroxy-2-phenylquinolin-4(1*H*)-one was followed by UV–vis spectroscopy too. In a typical experiment 3-hydroxy-2-phenylquinolin-4(1*H*)-one and [Cu(idpa)(*N*-baa)]ClO_4 was dissolved under argon atmosphere in a thermostated reaction vessel with an inlet for taking samples with a syringe, and connected to mercury

manometer to regulate constant dioxygen pressure. The solution was then heated to appropriate temperature and the argon was replaced by dioxygen. The concentration of 3-hydroxy-2-phenylquinolin-4(1*H*)-one was determined by measuring the absorbance of the reaction mixture at 372 nm (log ε 3.96) (λ_{max} of a typical band of 3-hydroxy-2-phenylquinolin-4(1*H*)-one).