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Synthesis, structure and catalase-like activity of $Cu(N-baa)_2(phen)$ (phen = 1,10-phenanthroline, N-baaH = N-benzoylanthranilic acid)

József Kaizer^a, Tamás Csay^b, Gábor Speier^{a,b,*}, Marius Réglier^c, Michel Giorgi^c

^a Research Group for Petrochemistry, Hungarian Academy of Sciences at University of Veszprém, 8201 Veszprém, Hungary ^b Department of Organic Chemistry, University of Veszprém, 8201 Veszprém, Hungary

^c Laboratoire de Cristallochimie et Laboratoire de Bioinorganique, Structurale Université Paul, Cézanne Aix-Marseille III F.S.T. Saint-Jérôme, Service 432 Avenue Escadrille Normandie-Niemen, 13397 Marseille cedex 20, France

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Abstract

The mononuclear copper(II) complex $Cu(N-baa)_2$ (phen) is synthesized by the reaction of $Cu(OCH_3)_2$ with N-benzoylanthranilic acid in the presence of 1,10-phenanthroline; the structure and catalase-like activity are investigated. © 2006 Elsevier B.V. All rights reserved.

Keywords: Copper; Carboxylates; N-Benzoylanthranilic acid; Catalase-like activity

Enzymatic antioxidants regulate superoxide concentration by dismutation of superoxide to hydrogen peroxide (SOD), which is then converted to water (peroxidases) or dismuted to water and dioxygen (catalases) [1]. These reactions are important for cell detoxification, and are linked to a variety of pathological consequences such as aging, diabetes and cancer [2]. Besides heme type catalases [3], a number of manganese containing catalases have been isolated and characterized [4-7]. The direct utilization of these natural enzymes as pharmaceutical agents is limited because of low membrane permeability as a consequence of their high molecular weight. So considerable efforts were made in order to obtain non-toxic, low molecular weight biomimetic molecules, which are able to catalyze the dismutation of superoxide anion and/or destroy the forming hydrogen peroxide.

Compared with manganese-containing model systems [8-11], the reported copper-containing systems are rela-

E-mail address: speier@almos.vein.hu (G. Speier).

tively rare [12–15]. Several copper(II) carboxylates of anti-inflammatory drugs such as salicylates [16], indomethacin [17] and lonazolac [18] were studied as SOD mimics, and some binuclear and tetranuclear copper(II) complexes with macrocyclic ligands have been reported as functional models for catalases [13,14]. As a continuity of this topic, binuclear copper complexes $Cu_2(bpy)_2(phga)_4$ (1) and $Cu_2(ba)_4(bpy)_2$ (2), which functionally mimic the catalase enzyme, have been thoroughly investigated and it has been found that the mechanism of their reaction is a direct function of the nature of their ligands associated with the metal ion (Scheme 1) [15]. The observed initial rates for these complexes showed that $Cu_2(bpy)_2(phga)_4$ is almost threefold more reactive than compound $Cu_2(ba)_4(bpy)_2$, and the rate dependence on the catalyst suggested that the (benzoato)copper complex is mainly in the monomeric form, while that of the ketocarboxylato(copper) complex exists in the dimeric form during the catalytic process.

In this communication, we present the synthesis and structural characterization of a new neutral (N-benzoylanthranilato)copper(II) complex with a bidentate ligand 1,10phenanthroline (phen), $Cu(N-baa)_2(phen)(3)$, obtained with

Corresponding author. Address: Research Group for Petrochemistry, Hungarian Academy of Sciences at University of Veszprém, 8201 Veszprém, Hungary. Fax: +36 88 62 4469.

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practically quantitative yield by interaction of $Cu(OCH_3)_2$, *N*-benzoylanthranilic acid, and 1,10-phenanthroline in acetonitrile under argon atmosphere [19]. 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 catalase-like activity was also examined in order to get an insight into the mechanism of these curious reactions.

Complex 1 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 3446 v(NH), 1675 v(CO), 1589, and 1379 $v(CO_2)$ cm⁻¹ [20]. The difference between the asymmetric and symmetric stretching frequencies of the carboxylato group $[\Delta v = v_{as}(CO_2) - v_s(CO_2)]$ is 210 cm^{-1} , rendering these to an asymmetrical carboxylate bonding mode [21]. The stretching vibrations corresponding to those typical of coordinated 1,10-phenanthroline occur at 723, 848, and 1510 cm^{-1} [22]. The electronic spectrum of complex 3 obtained in DMF solution exhibits a very broad absorption band at 680 nm due to d-d transition. The position of this band falls within the range expected for mononuclear copper(II) complexes that contain a $CuN_2O_2 + O_2$ chromophore in a distorted tetragonal geometry [23]. A higher energy band at 316 nm is associated with charge transfer transition. These spectral features are comparable with those of the Cu(phen)(valproate)₂ complex [22].

Suitable crystals of **3** were obtained from DMF solution of the complex at 20 °C. The molecular structure of $Cu(N-baa)_2(phen)$ (**3**) [24] as well as selected bond lengths and angles is shown in Fig. 1.

Molecule 3 is monomeric in the solid state. The overall geometry around the four-coordinate copper ion is described as a distorted tetragonal geometry, which contains *trans*-CuN₂O₂ + O₂ chromophore.

Catalase activity of complex **3** was performed in DMF solution and examined at 20 °C with a ratio of 1:20–175 between initial concentration of $Cu(N-baa)_2$ (phen) and H_2O_2 (Table 1) [27]. On the basis of kinetic experiments, a Michaelis–Menten type kinetics could be observed for the catalytic disproportionation of hydrogen peroxide (Fig. 2). For complex **3**, values of $k_{cat} = 6.62 \times 10^{-2} \text{ s}^{-1}$, $K_M = 52 \text{ mM}$, and $k_{cat}/K_M = 1.27 \text{ s}^{-1} \text{ M}^{-1}$ have been obtained. A straight line was obtained in a plot of the reaction rate ver-



Fig. 1. Molecular structure of $Cu(N-baa)_2(phen)$ (3) with crystallographic numbering. Hydrogen atoms are omitted for clarity. Relevant bond lengths (Å) and angles (°): Cu(1)-O(1) 1.945(3), Cu(1)-O(2) 2.626, Cu(1)-N(1) 2.023(3), O(1)-C(1) 1.274(4), O(2)-C(1) 1.242(4), O(3)-C(8) 1.226(4), C(1)-C(2) 1.498(5), N(2)-C(7) 1.394(4), N(2)-C(8) 1.367(4), O(1)-Cu(1)-O(1) 95.61(16), O(1)-Cu(1)-N(1) 173.21(11), N(1)-Cu(1)-N(1) 82.04(17), C(1)-O(1)-Cu(1) 106.7(2), C(15)-N(1)-Cu(1) 129.4(3), C(19)-N(1)-Cu(1) 112.3(2), C(8)-N(2)-C(7) 129.3(3).

Table 1 Kinetic data

Kinetic data for the $Cu(N-baa)_2$ (phen)-catalyzed decomposition of hydrogen peroxide

Expt. no.	$10^{-3}[Cu]^a (M)$	$10^{-1} [H_2 O_2]^b \ (M)$	$10^{-5} V_{\rm in} ({\rm M \ s^{-1}})$
1	1.12	1.64	2.23
2	1.53	1.64	8.48
3	1.95	1.64	12.5
4	2.25	1.64	20.0
5	2.79	1.64	30.1
6	3.05	1.64	36.2
7	1.54	0.31	3.78
8	1.54	0.46	4.54
9	1.54	0.62	6.04
10	1.54	0.96	7.50
11	1.54	1.30	7.95
12	1.54	1.64	7.80
13	1.54	1.98	7.27
14	1.54	2.28	7.97
15	1.54	2.62	8.13

^a In 30 ml DMF at 20 °C.

^b The amount of residual H₂O₂ was determined by iodometric titration.



Fig. 2. Initial rate of decomposition of hydrogen peroxide as a function of $[H_2O_2]$ in DMF at 20 °C. Inset: plots of V_{in} versus $[Cu(N-baa)_2(phen)]^2$.

sus the initial concentration of Cu $(N-\text{baa})_2(\text{phen})$ (3) to establish a rate law of $d[O_2]/dt = k_{app}[\text{Cu}(N-\text{baa})_2(\text{phen})]^2$ (Fig. 2). This result supports the fact that the active form of the (carboxylato)copper complex 3 similar to the compound 2 is dimeric during the catalytic process.

A variation of H_2O_2 concentration revealed saturation behavior with K_{ass} value of about 20 M⁻¹. These two phenomena indicated that under the condition of steady-state turnover, the binding of hydrogen peroxide to the Cu(II)– Cu(II) center is much more favored compared to its monomeric form.

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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. 2006.06.005.

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