Nitrosalicylatocopper(II) complexes with chelating pyridine derivatives

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Abstract: Three new nitrosalicylatocopper(II) complexes have been prepared and characterized. Compounds of the composition $Cu(5\text{-}NSal)_2(2\text{-}ampy)_2$ **(1)**, $Cu(5\text{-}NSal)_2(2\text{-}hmpy)_2$ **(2)** and $Cu(3,5\text{-}DNSal)_2(2\text{-}hmpy)_2$ **(3),** where 2-ampy = (2-aminomethyl)pyridine, 2-hmpy = (2-hydroxymethyl)pyridine, 5-NSal = 5-nitrosalicylate anion and 3,5-DNSal = 3,5-dinitrosalicylate anion, were characterized by elemental analyses, EPR and IR spectroscopy. EPR spectra are consistent with the d_{x2-y2} ground electronic state. Spectral properties have shown "classic" monodentate coordination of 5-nitrosalicylate anion. Similarly, bonding mode of the 3,5-dinitrosalicylate anion in **(3)** is assumed to be unidentate via the carboxyl group, which is surprising compared with the previously studied complex, where the preferred coordination via the phenolate group anion was observed.

Keywords: nitrosalicylatocopper(II) complexes, (2-aminomethyl)pyridine, (2-hydroxymethyl)pyridine, spectral properties

Introduction

The study of Cu(II) complexes with bioligands as potential SOD mimetics was an important part of the research. For instance, superoxide radical dismutation by Cu(II) complexes with non-steroidal anti-inflammatory drugs has been widely studied in the last decades (Daier et al., 2016). It is well known, that superoxide radicals are reactive oxygen species (ROS) causing oxidative stress, which is associated with numerous pathological changes in the human body (Wang et al., 2011).

Due to its high molecular weight (32 kDa) and low molecular permeability, superoxide dismutase enzyme is pharmacologically inapplicable; therefore, the preparation of Cu(II) complexes with presumed SOD mimetic activity has become of great importance (Kovala-Demertzi et al., 2004; O'Connor et al., 2012). SOD mimetics should fulfil some essential properties: they should support coordination of the superoxide radical by the central atom and the exchange of molecules in the axial position has to be fast (Abuhijleh et al., 2010). Distorted structure of the central atom polyhedron should favor geometrical changes, which is essential for the catalytic reaction; in other words, mimetics have to have free coordination place to bind $O_2^{\bullet-}$ (Kaim et al., 2013). Based on the fact that Cu(II) ion is surrounded with N- and O-donor ligands, some 2-substituted derivatives of pyridine as 2-(aminomethyl)pyridine (2-ampy) and 2-(hydroxymethyl)pyridine (2-hmpy) were choosen, which can stabilize the structure of complexes with their chelating properties. However, thanks to higher stability and rigidity, dismutation properties may decline. To compensate for this unwanted situation, 5-nitrosalicylic (5-NSalH) and 3,5-dinitrosalicylic (3,5-DNSalH) acids were chosen to provide more soluble complexes. In most Cu(II) complexes, 2-ampy and 2-hmpy precipitate as bidentate chelating ligands, bonding with amino-imine (2-ampy) (Barquín et. al., 2009) or hydroxide-imine (2-hmpy) groups (Yilmaz et al., 2002). Salicylate anions offer a wider range of bonding modes from the most common monodentate (Icbudak et al., 2003; Devereuxe et al., 2007; Repická et al., 2012; Mirzaei et al., 2012), through bidentate-chelating (Mirzaei et al., 2012; Gembicky et al., 2008) and bridging (Mei et al., 2010), to chelating-bridging (Mukherjee et al., 2012; Palanisami et al., 2006). This paper is focused on the preparation and spectral properties of 5-nitrosalicylatocopper(II) and 3,5-dinitrosalicylatocopper(II) complexes with 2-(aminomethyl)pyridine and/or 2-(hydroxymethyl) pyridine. The influence of reaction conditions on the formation and composition of the obtained compounds was studied and the formation of three complexes of the composition $Cu(5\text{-}NSal)_2(2\text{-}ampy)_2$ (**1**), $Cu(5\text{-}NSal)_2(2\text{-}hmpy)_2$ (**2**), $Cu(3,5\text{-}DNSal)_2(2\text{-}hmpy)_2$ (**3**) is presented here as a part of a wider approach to study the SOD activity and the factors influencing SOD.

Materials and Methods

Synthesis

All complexes were prepared by the following method: 2-(aminomethyl)pyridine or 2-(hydroxymethyl)pyridine (1 mmol) were added to the mixture of copper(II) acetate (2 mmol) and 20 ml of the relevant solvent (water-ethanol, ethanol, acetonitrile) under stirring. In the next step, 5-nitrosalicylic acid or 3,5-dinitrosalicylic acid (2 mmol) was added to the mixture with the necessary amount of the relevant solvent. The formed precipitates were filtered and let to dry at ambient temperature. The samples were characterized by secondary analytical methods and the mother liquors were left to crystalize at laboratory temperature. However, single crystals were not available for the X-ray analysis.

Apparatus and physical measurement

Carbon, hydrogen and nitrogen analyses were carried out on a CHNSO FlashEA^{TM} 1112 Automatic Elemental Analyzer.

Infrared spectra (4000—400 cm^{-1}) were measured with a NICOLET 5700 FT-IR (Nicolet) spectrophotometer at room temperature using the ATR technique.

Electronic spectra (190—1100 nm) of the complexes were measured in a nujol suspension with a SPECORD 250 Plus (Carl Zeiss Jena) spectrophotometer at room temperature.

X-band (≈9.4 GHz) EPR spectra of polycrystalline samples were measured on an EPR spectrometer Bruker (Germany) EMX series at room temperature.

Results and discussion

Three new Cu(II) complexes: $Cu(5\text{-}NSal)_2(2\text{-}ampy)_2$ **(1)**, $Cu(5\text{-}NSal)_2(2\text{-}hmpy)_2$ **(2)** and $Cu(3,5\text{-}DNSal)_2(2\text{-}hmpy)_2$ **(3)** show the favored stoichiometry of Cu : anion : N-donor ligand = 1 : 2 : 2 in spite of the initial stoichiometry of the reactants and the change of reaction conditions (solvents, temperature). Elemental analyses confirmed, that the compounds contain two neutral ligands per one Cu(II) ion, coordinating probably bidentate-chelating, together with two monodentate anions.

Color of complexes corresponds to the d→d transition maxima in electronic spectra at 550.7 cm^{-1} **(1)**, 609 cm^{-1} **(2)** and 605.6 cm^{-1} **(3)** (Table 2.). Absorption bands at 328.6 cm^{-1} **(1)**, 365 cm^{-1} **(2)** and 351.3 cm^{-1} **(3)** are typical for LMCT transitions. Intraligand charge transfer can be observed at the absorption maxima at 254.1 cm^{-1} **(1)**, 268 cm^{-1} **(2)** and 254.1 cm^{-1} **(3)**, respectively.

IR spectra of the complexes contain strong absorption bands at 1591 cm^{-1} **(1)**, 1592 cm^{-1} **(2)** and 1607 cm^{-1} **(3)** corresponding to $\nu_{as}(COO^-)$ and slightly weaker bands at 1429 cm^{-1} **(1)** 1430 cm^{-1} **(2)** and 1422 cm^{-1} **(3)** attributable to $\nu_s(COO^-)$ vibrations. The $\Delta\nu(COO^-)$ difference between the asymmetrical and symmetrical vibration modes is in case of all three complexes higher than that for the ionic form (Nakamoto, 2009) allowing to predict whether the anion ligands coordinate in the monodentate bonding mode to the central atom of Cu(II) (Table 2.). Differences were observed in the range of characteristic group vibrations. In case of $Cu(5\text{-}NSal)_2(2\text{-}ampy)_2$, IR spectrum shows absorption at

Tab. 1. Elemental analyses of complexes (**1**)—(**3**).

Summary formula	N % found calculated	C % found calculated	H % found calculated
$Cu(5\text{-}NSal)_2(2\text{-}ampy)_2$ (1)	13.028 13.049	48.898 48.487	3.788 3.756
$Cu(5\text{-}NSal)_2(2\text{-}hmpy)_2$ (2)	9.304 8.673	48.125 48.340	3.411 3.433
$Cu(3,5\text{-}DNSal)_2(2\text{-}hmpy)_2$ (3)	11.354 11.418	40.541 42.429	2.442 2.739

Tab. 2. Wavenumbers (cm^{-1}) of selected stretches and solid-state electronic spectra (nm) of complexes (**1**)—(**3**).

Complex	$\nu_{as}(NO_2)$	$\nu_{as}(COO^-)$	$\nu_s(COO^-)$	$\Delta\nu(COO^-)$	λ(d→d)
$Cu(5\text{-}NSal)_2(2\text{-}ampy)_2$ (1)	1481	1591	1429	162	550.7
$Cu(5\text{-}NSal)_2(2\text{-}hmpy)_2$ (2)	1474	1592	1430	162	609
$Cu(3,5\text{-}DNSal)_2(2\text{-}hmpy)_2$ (3)	1475	1607	1422	185	605.6

3192 cm^{-1} which is typical for $\nu_{as}(OH)$ vibration and slightly weaker bands at 3105 cm^{-1} and 3074 cm^{-1} attributable to $\nu_{as}(NH_2)$ and $\nu_{sym}(NH_2)$ vibrations. In the IR spectra of $Cu(5\text{-}NSal)_2(2\text{-}hmpy)_2$ and $Cu(3,5\text{-}DNSal)_2(2\text{-}hmpy)_2$, peaks at 3080 cm^{-1} **(1)** and 3086 cm^{-1} **(3)**, respectively, corresponding to $\nu_{as}(OH)$ were observed together with a wide absorption band in the range from 2929 cm^{-1} to 2638 cm^{-1} for **(1)** and 2810—2247 cm^{-1} for **(3)** suggesting the existence of intramolecular hydrogen bonds.

Room temperature EPR spectra of complexes (**1**) and (**2**) are shown in Fig. 1. Fig 2. presents EPR spectra of complex (**3**). All Cu(II) EPR spectra are axially symmetric with unresolved hyperfine splitting. The spin Hamiltonian parameter values evaluated from the experimental Cu(II) EPR spectra and further refined by computer simulation using the original program SimFonia (Weber, 1995) are summarized in Table 3. The g-factor values hit the interval of $g_{\perp}$ = 2.074—2.081 and $g_{||}$ = 2.190—2.280.

All axially symmetric Cu(II) EPR spectra meet the usual relation $g_{||} > g_{\perp} > 2.0023$, which is consistent with the $d_{x^2-y^2}$ ground electronic state. To obtain more information, the geometric parameter, $G = (g_{||} - 2)/(g_{\perp} - 2)$, was calculated for each EPR spectrum. Obtained G-values (see Table 3.) are in good agreement with the proposed elongated tetragonal-bipyramidal coordination sphere with deflected local tetrahedral axes. The relation G > 4 indicates the negligible exchange interaction between the Cu(II) centers (Hathaway et al., 1970a; 1970b).

Based on these results and on previous studies (Crawford et al., 1994; Bertlich et al. 2014; Moncol' et al., 2006) it can be predicted that in all three complexes the neutral ligand can coordinate in the bidentate-chelating mode via the nitrogen of pyridine ring together with the —NH_2 (2-ampy) or —OH (2-hmpy) group. In case of anionic ligands $5\text{-}NSal^-$ and $3,5\text{-}DNSal^-$ the unidentate bonding

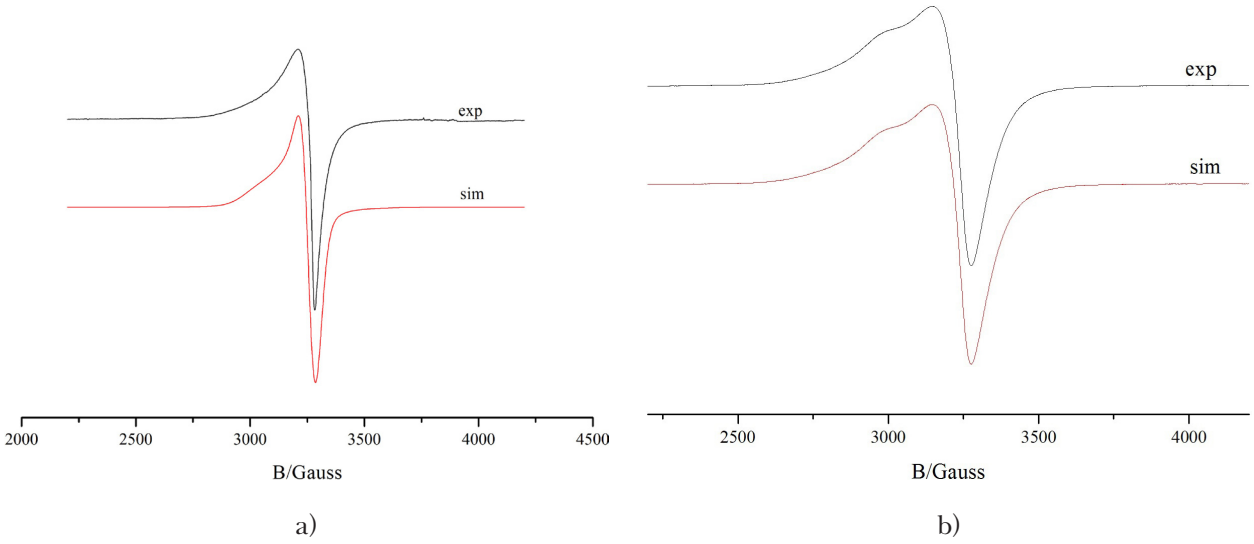

Fig. 1. Experimental and calculated EPR spectra of complexes: a) (**1**) and b) (**2**).

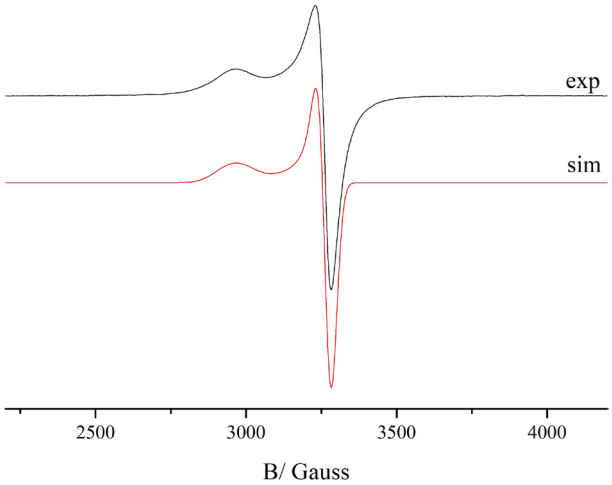

Fig. 2. Experimental and calculated EPR spectra of complex (**3**).

Table 3. Spin Hamiltonian parameters of Cu(II) complexes (**1**)—(**3**), which were refined by computer simulation of experimental EPR spectra.

Complex	$g_{\perp}$	$g_{\parallel}$	G
$Cu(5\text{-}NSal)_2(2\text{-}ampy)_2$ (1)	2.074	2.190	2.56
$Cu(5\text{-}NSal)_2(2\text{-}hmpy)_2$ (2)	2.081	2.280	3.45
$Cu(3,5\text{-}DNSal)_2(2\text{-}hmpy)_2$ (3)	2.069	2.287	4.15

mode through the O^- anion of the carboxylate group was designed in the three prepared compounds (Fig. 3.).

Reaction of the Cu(II) ion with 3,5-dinitrosalicalic acid and (2-aminomethyl)pyridine showed unusual bonding of $(3,5\text{-}DNSal)^-$ in compound $[Cu(3,5\text{-}DNSal)_2(2\text{-}ampy)_2]$, where the anion was coordinated preferentially through the phenolate group. The changes of reaction conditions did not have any impact on the formation of coordination compounds and their bonding mode. The expected coordination mode of the anion in complex (**3**) was similar to that of the previous structure of $[Cu(3,5\text{-}DNSal)_2(2\text{-}ampy)_2]$ (Puchoňová et al., 2015). However, the IR spectrum of $[Cu(3,5\text{-}DNSal)_2(2\text{-}ampy)_2]$ contains clear evidence of a free localized carboxyl group: $\nu_{as}(C{=}O) = 1697\ cm^{-1}$, in case of $Cu(3,5\text{-}DNSal)_2(2\text{-}hmpy)_2$, the spectrum does not show the presence of free C═O group, contrariwise, it contains vibrations typical for monodentate bonding $(COO)^-$ creating intramolecular hydrogen bonds.

Considering $(5\text{-}NSal)^-$, $(3,5\text{-}DNSal)^-$ prefer monodentate bonding mode via phenolate oxygen in $[Cu(3,5\text{-}DNSal)_2(2\text{-}ampy)_2]$; however, in case of $(5\text{-}NSal)^-$, this tendency was not observed in any complex. One of the explanations is related to the hydrogen bond system of $[Cu(3,5\text{-}DNSal)_2(2\text{-}ampy)_2]$, in which both —$NO_2$ groups play an important role. Deficit of —NO_2 groups at the *meta* position can cause that conditions of stable supramolecular system in 5-nitrosalicilatocopper(II) complexes are not fulfilled.

Conclusion

It can be summarized that all three nitrosalicylatocopper(II) complexes are obtained by reaction condition changes. These complexes were characterized by elemental analyses, infrared, UV-VIS and EPR spectroscopy. The expected structure motives of $Cu(5\text{-}NSal)_2(2\text{-}hmpy)_2$, $Cu(5\text{-}NSal)_2(2\text{-}ampy)_2$, and $Cu(3,5\text{-}DNSal)_2(2\text{-}hmpy)_2$ coordinate in the similar bidentate-chelating mode of N-donor ligands and two monodentate bonding anions thus resulting in $\{CuN_2O_2O_2'\}$ or $\{CuN_2N_2'O_2\}$ chromophores. In the IR spectra of complexes $Cu(5\text{-}NSal)_2(2\text{-}hmpy)_2$ and $Cu(3,5\text{-}DNSal)_2(2\text{-}hmpy)2$, intramolecular hydrogen bonds were observed. EPR spectra showed axial symmetry with unresolved hyperfine splitting. G-values indicated slightly elongated tetragonal-bipyramidal geometry of the coordination sphere.

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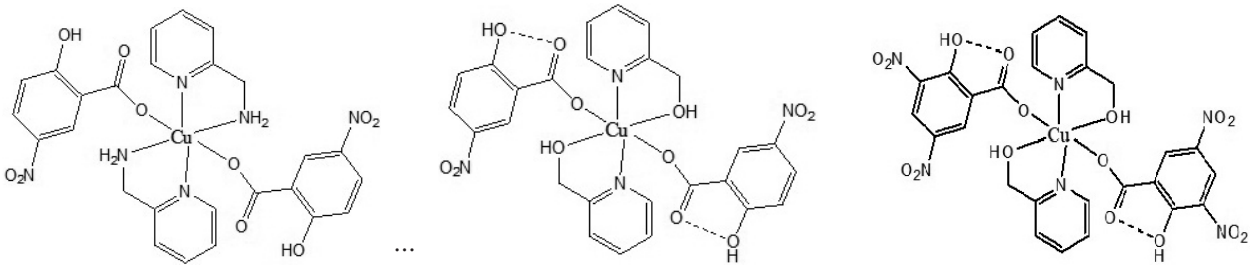

Fig. 3. Predicted structures of nitrosalicylatocopper(II) complexes.

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