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Methyl- and methoxysalicylatocopper complexes with 2-ethylbenzimidazole

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Abstract: Four new compounds of formulae $[Cu(3\text{-Mesal})_2(etbzim)_2]$ (**1**), $[Cu(4\text{-Mesal})_2(etbzim)_2]$ (**2**), $[Cu(4\text{-MeOsal})_2(etbzim)_2]$ (**3**), $[Cu(5\text{-MeOsal})_2(etbzim)_2]$ (**4**) where 3- or 4-Mesal = 3- or 4-methylsalicylate anionic ligand, 4- or 5-MeOsal = 4- or 5-methoxysalicylate anionic ligand, etbzim = 2-ethylbenzimidazole) have been prepared and characterised by elemental analysis and available spectral methods (EPR, UV-vis and IR spectra). EPR spectra of all measured complexes are axial symmetry. Other spectral methods led to conclusion that all prepared complexes probably contain the etbzim ligand coordinated in equatorial plane together with the asymmetrically bonded salicylato anions thus giving $\{CuN_2O_2O'O''\}$ chromophore. The supposed structural motive for all prepared complexes might be simmilar to those benzoate complexes with benzimidazole $[Cu(4\text{-OHbz})_2(bzim)_2]$ and $[Cu(4\text{-Mebz})_2(bzim)_2]$ (4-OHbz = 4-hydroxybenzoate, 4-Mebz = = 4-methylbenzoate), but similarity with polymeric salicylate complex $[Cu(sal)_2(bzim)_2]_n$ cannot be excluded.

Keywords: methyl- and methoxysalicylic acid, benzimidazole, spectral properties

Introduction

Ternary complexes play an important role in biological processes, as exemplified by many instances in which enzymes are known to be activated by metal ions. (Regupathy, 2010) In fact copper(II) chelates have been found to interact with biological systems and to exhibit mimetic (Devereux, 2007a), antineoplastic activity and to interact non-covalently with nucleic acids in DNA molecule. (Dey, 2010) Many of these biologically active compounds containing the benzimidazole moieties as well as their transition metal complexes were reported (Mohamed, 2009). Benzimidazole derivatives represent an important group of pharmacophores in medicinal chemistry. It is well known that different substituted benzimidazoles are associated with biological activity. (Bansal, 2012) For instance, benzimidazole derivatives exhibited antimicrobial (Patel, 2012), antifungal (Garudachari, 2012), analgesic, anti-inflammatory (Achar, 2010), anticancer (El-Nassan, 2012), antihypertensive, antioxidant activity (Neochoritis, 2011; Wu, 2007).

The carboxylatocopper complexes containing this type of nitrogen donor ligand are known to be investigated and promising results giving area. In last decades the number of studies focused to this field is growing. As good example it could be mentioned existence of some salicylato- and acetatocopper complexes $[Cu(sal)_2(bzim)_2]$ and $[Cu(CH_3COO)_2(5,6\text{-DMbzim})_2]$, where sal = monoanion of salicylic acid, bzim = benzimidazole, CH_3COO = anion of acetic acid and 5,6-DMbzim = 5,6-dimethylbenzimidazole (Devereux, 2007b). They have shown interesting SOD mimetic activity and significant cytotoxicity. Further, the DNA binding and nuclease activities, and the anticancer chemotherapeutic potential of similar type of complexes with benzimidazole and phenantroline ligand were investigated. It was found that copper complexes containing phenatroline molecules in structure exhibit better nuclease activity. (O'Connor, 2012)

In relation to that, our interest is targeted to systematic study of the prepared salicylatocopper complexes with benzimidazole derivatives that could model different biological function including the antioxidant properties. In this paper, we describe the synthesis and spectral properties of methyl- and methoxysalicylatocopper complexes with ethylbenzimidazole, of composition $[Cu(3\text{-Mesal})_2(etbzim)_2]$ (**1**), $[Cu(4\text{-Mesal})_2(etbzim)_2]$ (**2**), $[Cu(4\text{-MeOsal})_2(etbzim)_2]$ (**3**), $[Cu(5\text{-MeOsal})_2(etbzim)_2]$ (**4**), (where 3- or 4-Mesal = 3- or 4-methylsalicylate anionic ligand, 4- or 5-MeOsal = 4- or 5-methoxysalicylate anionic ligand, etbzim = 2-ethylbenzimidazole) and assumption concerning their structure are presented.

Experimental

Synthesis of complexes

2-Ethylbenzimidazole (2 mmol or 1 mmol) was added to water solution of copper(II) acetate

(0.5 mmol) under stirring. Methyl- or methoxysalicylic acid (1 mmol) was added to reaction mixture together with necessary amount of solvent (methanol or ethanol). The reaction mixture was stirred at laboratory temperature until the reaction finished. The precipitates were filtered off, washed with small amount of appropriate solvent and dried in air at ambient temperature. The clear mother liquid solutions were left to crystallize at laboratory temperature. The all samples were characterized by electronic and infrared spectroscopy, elemental analysis and EPR spectroscopy).

Anal Calc for $Cu(3\text{-}Mesal)_2(etbzim)_2$: C, 61.9; H, 5.5; N, 8.5. Found: C, 61.9; H, 5.2; N, 8.4.

Anal Calc for $Cu(4\text{-}Mesal)_2(etbzim)_2$: C, 61.9; H, 5.5; N, 8.5. Found: C, 60.9; H, 5.0; N, 8.0.

Anal Calc for $Cu(4\text{-}MeOsal)_2(etbzim)_2$: C, 59.0; H, 5.2; N, 8.1. Found: C, 59.6; H, 5.0; N, 8.0. Anal Calc for $Cu(5\text{-}MeOsal)_2(etbzim)_2$: C, 59.0; H, 5.2; N, 8.1. Found: C, 58.5; H, 4.8; N, 7.8.

Synthesis of 2-ethylbenzimidazole

A mixture of o-phenylenediamine (0.1 mol) and propionic acid (0.1 mol) were added to 4 N hydrochloric acid (50 mL). The resulting mixture was heated for 4 h under reflux. The solution was cooled and the pH was adjusted to 8 with 26 % amonia solution. The solid was collected by filtration, dissolved in 1 N hydrochloric acid, and tretaed with charcoal. The mixture was filtered and the pH was adjusted to 8 with amonia solution, the solid was collected by filtration. The filter cake was washed with water to get white solid of 2-ethylbenzimidazole in 75 % yield. Purity of refined product was checked by measuring of spectra and data are in good agreement with the published ones. (Bai, 2012)

Apparatus and equipment

Analytical grade chemicals (Sigma-Aldrich) were used without further purification.

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

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

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

The EPR spectra of the polycrystalline samples were measured on a X-band EPR spectrometer (EMX series, Bruker) at room temperature. All EPR spectra were processed using WinEPR (Thiele, 1992) and simulatad by SimFonia (Weber, 1995).

Result and discussion

Changing reaction conditions four new methyl- and methoxysalicylatocopper complexes were prepared. These green-blue products were found by reaction of 2-ethylbenzimidazole with the aqueous solution of copper(II) acetate and salicylic acid derivatives. The elemental analysis has confirmed that all complexes contain two nitrogen donor ligands per copper atom together with two anions, respectively. Their solid-state electronic spectra exhibit broad asymmetric ligand field bands with the *d–d* transition maxima in the range of 544—633 nm, respectively correspond to their colour shade and they are in good agreement with proposed {$CuN_2O_2O'O''$} chromophore. There are also intraligand charge transfer bands (250—300 nm) and charge transfer bands in the range of 300—350 nm.

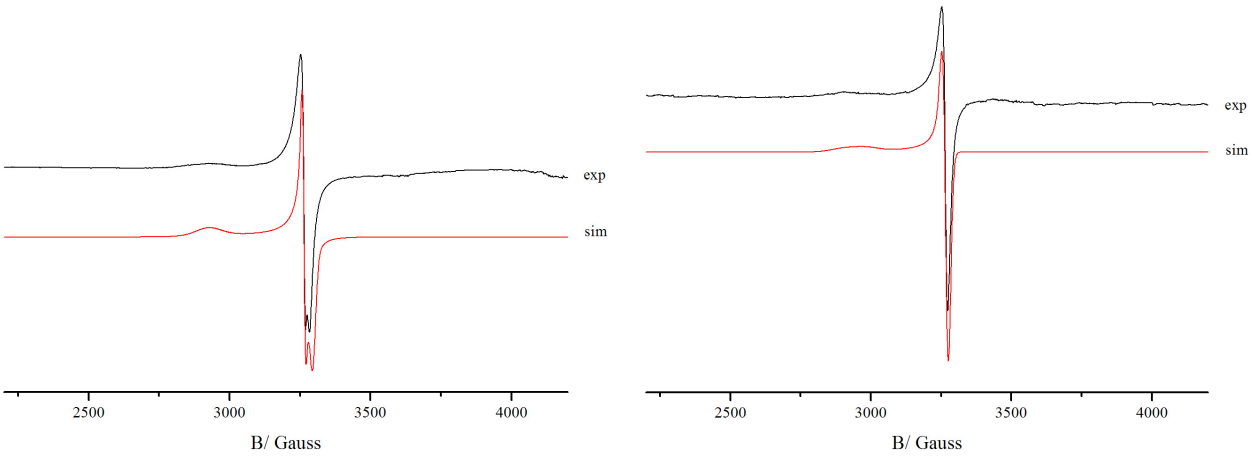

Fig. 1. Cu(II) EPR spectra of a) $Cu(3\text{-}Mesal)_2(etbzim)_2$ (**1**) and b) $Cu(4\text{-}Mesal)_2(etbzim)_2$ (**2**).

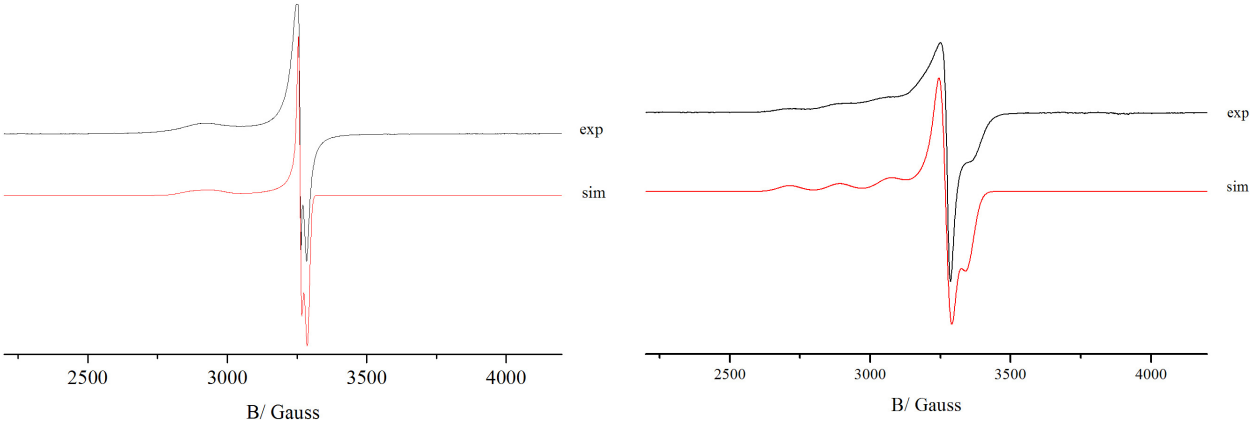

Fig. 2. Cu(II) EPR spectra of a) Cu(4-MeOsal)$_2$(etbzim)$_2$ (**3**), b) Cu(5-MeOsal)$_2$(etbzim)$_2$ (**4**).

Experimental and simulated Cu(II) EPR spectra of complexes (1-4) are shown in Fig. 1 and Fig. 2. The hyperfine splitting is good resolved only for the compounds (**2**) and (**4**). The spin Hamiltonian parameters (which were obtained from experimental EPR spectra and further refined by computer simulation) are collected in the Table 1.

Tab. 1. Spin Hamiltonian parameters of Cu(II) EPR spectra of compounds (1-4).

Compound	g_1	g_2	g_3
Cu(3-Mesal)$_2$(etbzim)$_2$ (**1**)	2.0523	2.0723	2.3132
Cu(4-MeOsal)$_2$(etbzim)$_2$ (**3**)	2.055	2.0723	2.322
	$g_\perp$	$g_\parallel$	$A_\parallel$-[Gauss]
Cu(4-Mesal)$_2$(etbzim)$_2$ (**2**)	2.132	2.37	80
Cu(5-MeOsal)$_2$(etbzim)$_2$ (**4**)	2.067	2.279	175

Infrared spectra of the compounds (**1**)—(**4**) comprise bands confirming the presence of all characteristic functional groups. Spectra of all complexes are characteristic of broad envelope of probably two or three overlapping medium intensity bands with maxima in the region from 3250 to 3400 cm^{-1} assignable to OH stretches and single medium intensity band assignable to NH vibration at about 3169 cm^{-1} for (**1**), 3170 cm^{-1} for (**2**), 3200 cm^{-1} for (**3**), 3210 cm^{-1} for (**4**), respectively. Weak bands between 3000 and 2850 cm^{-1} could be assigned to the H-bond system. The finger print part of spectra clearly distinguishing of complexes. The absorption bands of ethylbenzimidazole are found at 960 cm^{-1}, 630 cm^{-1}. The bands corresponding to ν_{as}(COO$^-$) and ν_s(COO$^-$) are about 1620—1604 cm^{-1} and 1437—1425 cm^{-1} respectively (Table 2). The differences between antisymmetric and symmetric stretch ($\Delta\nu = \nu_{as} - \nu_s$) are greater than $\Delta\nu$ for the ionic form. The $\Delta\nu$ values for the complexes (**1**)—(**4**) are consistent with the asymmetric bidentate bonding mode of carboxylate group (Nakamoto 2009). The absence of C=O vibrations (around 1650 cm^{-1}) and the presence of OCO vibration bands, proved that carboxylate groups are in all complexes probably bonded in bidentate bonding mode.

Another evidence of the presence of benzimidazole type ligand we can found in FAR IR spectra where nitrogen atom of benzimidazole molecule could be found in the copper(II) coordination sphere where the bands close to 300 cm^{-1} (Tab. 3) could be attributed to ν_{as}(Cu—N) vibration of the equatorial plane of bonded benzimidazole groups and asymmetric deformation vibration δ_{as}(Cu—N) could be found about 270 cm^{-1}. (Goodgame, 1966; Melson, 1967—68; Nakamoto. 2009).

Tab. 2. Infrared spectra data (cm^{-1}) and solid-state electronic spectra (nm).

Compound	ν_{as}(COO$^-$)	ν_s(COO$^-$)	$\Delta\nu$(COO$^-$)	λ/nm
Cu(3-Mesal)$_2$(etbzim)$_2$ (**1**)	1606	1429	177	629
Cu(4-Mesal)$_2$(etbzim)$_2$ (**2**)	1613	1435	178	622
Cu(4-MeOsal)$_2$(etbzim)$_2$ (**3**)	1620	1437	183	633
Cu(5-MeOsal)$_2$(etbzim)$_2$ (**4**)	1604	1425	179	544, 720sh

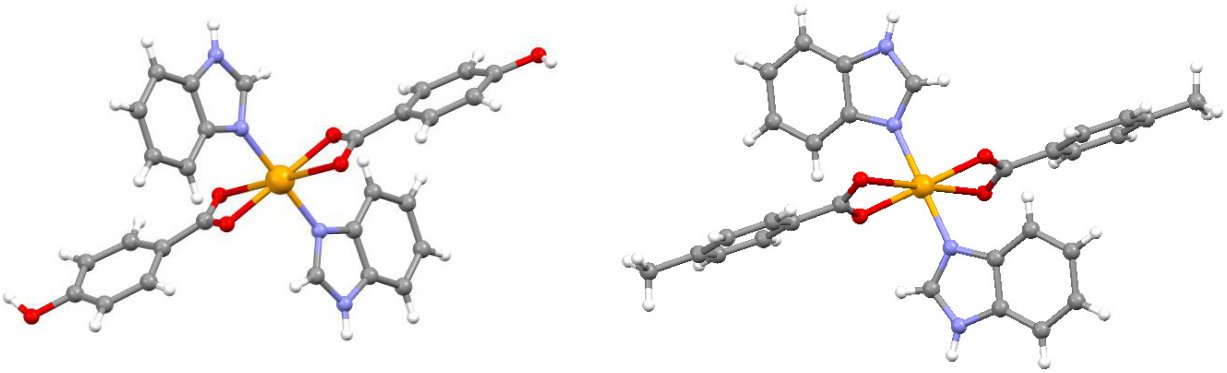

Fig. 3. Molecular structure of complex of $[Cu(4\text{-}OHbz)_2(bzim)_2]$ (Su, 2005) and $[Cu(4\text{-}Mebz)_2(bzim)_2]$ (Song, 2008).

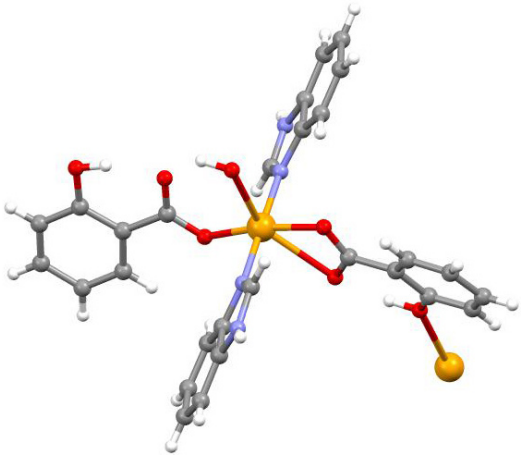

Fig. 4. Molecular structure of complex $[Cu(sal)_2(bzim)_2]_n$ (Devereux, 2007b).

Tab. 3. FAR Infrared spectra data (cm^{-1}).

Compound	ν(Cu—N)	δ_{as}(Cu—N)
$Cu(3\text{-}Mesal)_2(etbzim)_2$ (**1**)	303	278
$Cu(4\text{-}Mesal)_2(etbzim)_2$ (**2**)	306	276
$Cu(4\text{-}MeOsal)_2(etbzim)_2$ (**3**)	300	270
$Cu(5\text{-}MeOsal)_2(etbzim)_2$ (**4**)	305	271

The Cambridge Crystallographic Database contains over 77 copper compounds with benzimidazole and about a one third of all structures of copper(II) complexes containing the bzim ligand, where the Cu : bzim molar ratio is 1 : 1, and there are three "extreme" ratios – four examples of 1 : 4 ratio, five examples of 1 : 3 ratio and the other one exhibits 2 : 1 stoichiometry. The benzimidazole molecules are in six compounds of all 77 located in secondary coordination sphere as cation. Remaining 38 examples exhibit the largest representation of all compounds, which are of 1 : 2 stoichiometry, but only 7 of them are in the presence of benzoate or salicylate anion in coordination sphere. Two complexes with benzoate anion $[Cu(4\text{-}OHbz)_2(bzim)_2]$, $[Cu(4\text{-}Mebz)_2(bzim)_2]$ (Fig. 3) are coordinated bidentate chelating mode to copper atom. Similarly bonding mode is supposed in our products. (Su, 2005; Song, 2008)

On the other hand, chelato-bridging mode of coordination salicylate anion can not be excluded similarly as well as observed in polymeric complex $[Cu(sal)_2(bzim)_2]_n$ (Fig. 4) with this anion (Devereux 2007b).

In conclusion we can say, that the obtained data allow us to suggest that the stoichiometrically complexes of composition $Cu(Xsal)_2(etbzim)_2$ probably contain the etbzim ligand coordinated in equatorial plane together with the asymmetrically bonded salicylato anions thus giving {$CuN_2O_2O'O''$} chromophores.

Acknowledgement

This work was supported by courtesy of the Slovak Grant Agency (VEGA 1/0388/14 and VEGA 1/0765/14).

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