Inorganica Chimica Acta 363 (2010) 3887–3896

Contents lists available at ScienceDirect

Inorganica Chimica Acta

journal homepage: www.elsevier.com/locate/ica

Synthesis, spectral (UV–Vis, IR, ESI-MS), magnetic and structural characterizations, and the antimicrobial effect of potassium isothiocyanato-(*N*-salicylidene-amino-acidato)cuprates

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ARTICLE INFO

Article history:
Received 29 March 2010
Received in revised form 9 July 2010
Accepted 15 July 2010
Available online 22 July 2010

The authors would like to dedicate this article to Associate Professor Dr. Ol'ga Švajlenová, Ph.D. on the occasion of her retirement, and for her contribution to the study of transition metal complexes with salicylato and three donor Schiff base ligands.

Keywords:
Copper(II)
Isothiocyanates
Cuprates
Schiff base
Antimicrobial activity

ABSTRACT

A series of potassium isothiocyanato-(*N*-salicylidene-amino acidato)cuprates with the general formulas of $K_2[Cu_2(sal\text{-}aa)_2(\mu\text{-}NCS)_2]\cdot nH_2O$, where $n = 0$ or 4 and (sal-aa) stands for the dianion of *N*-salicylideneamino acid derived from glycine (**I**), DL-α-alanine (**II**), DL-valine (**III**), DL-phenylalanine (**IV**), and $\{K[Cu(sal\text{-}\beta\text{-}ala)(\mu\text{-}NCS)]\}_n$ for β-alanine (**V**), respectively, was synthesized and fully characterized by elemental analysis, UV–Vis and IR spectroscopy, ESI-MS spectrometry, magnetic measurements, and X-ray structural analysis (**II** and **IV**). It has been found that the copper(II) atom adopts a distorted square-pyramidal surrounding in the dimeric complexes **I–IV**, while the geometry in the polymeric complex **V** can be described as distorted square-bipyramidal. The analysis of magnetic properties revealed weak antiferromagnetic exchanges in the dinuclear species **I–IV** and an alternating ferro/antiferromagnetic exchange in the case of 1D-polymeric compound **V**. Moreover, the complexes were tested for their antibacterial activity against the G+ bacteria *Staphylococcus aureus*, G− bacteria *Escherichia coli*, filamentous fungi *Microsporum gypseum*, and yeast *Candida albicans*. The best results were achieved with G+ bacteria *S. aureus* with MIC values in the range of 0.22–0.57 mmol L^{-1}. It may be concluded that both the antimicrobial and antifungal activity decreased within the tested group of cuprates derived from α-amino acids with the increasing lipophility of the complexes, *i.e.* **I** → **IV**.

1. Introduction

Schiff bases, formed by a condensation reaction of 2-hydroxybenzaldehyde (salicylaldehyde) and biogenic amino acids, are documented in virtually all cases of copper(II) complexes as behaving like dianionic three-donor chelate ligands (sal-aa)(2-), thus forming the Cu(sal-aa) coordination units. The remaining coordination sites in the vicinity of the central atom may be occupied by molecular or ionic ligands such as water, urea, derivatives of pyridine or imidazole, thioureas, thiocyanato, or cyanato ligands [1,2]. In such defined systems, the geometry can be described as square-pyramidal [3,4] and square-bipyramidal [5] with the coordination of 4+1 and 4+2, respectively. The apical position of the square-pyramidal polyhedron is very often occupied by donor atoms from a neighbouring coordination unit, thus offering a motive for the formation of dimeric [6,7], oligomeric [8], or polymeric structures [9]. The potassium isothiocyanato-cuprates form a unique group of ionic (*N*-salicylidene-amino acidato)copper(II) complexes, whose syntheses were proposed by the group Krätsmár-Šmogrovič and co-workers in 1989 [10,11]. Unlike simple copper complexes with thiocyanate ions which undergo a reduction to Cu(I) and usually form polymeric chains with different bridging modes [12], the chelated copper(II) atoms resist (usually in mild conditions such as lower temperatures, etc.) the reductive action of thiocyanates and form monomeric [13], dimeric or polymeric structures [14–17]. The isothiocyanato-(*N*-salicylidene-amino acidato)cuprates also overcome the greatest disadvantage of molecular (*N*-salicylidene-amino acidato)copper(II) complexes, which is their limited solubility in polar solvents, especially in water and other biologically applicable media. Moreover, some of them showed interesting biological activities, e.g. the inhibition of a photosynthetic apparatus, or antioxidant activities [18–20]. One of the most frequently studied biological activities of copper(II) complexes derived from the *N*-salicylideneamino acids is their antimicrobial activity, usually targeting the most problematic types of anthropopathogenic microorganisms. There are three different reasons why this method of primary screening is often chosen by investigators. The first reason is usually associated with the same type of coordination polyhedron in the tested compounds with an antimicrobial

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doi:10.1016/j.ica.2010.07.041

highly effective complex of $[Cu_2(quin)_4]$, where quin = quinoline-8-olato(1−) [21], while the second one is based on the fact that the ligands, forming these complexes, show a significant intrinsic antimicrobial activity themselves [22]. The third reason is connected with pragmatic rules, *i.e.* the method can be considered to be fast and relatively accessible, and it can provide significant information regarding the practical applications of the tested compounds. Moreover, this method fully respects the principles of the three R's (Replacement, Reduction, and Refinement) [23].

In this article, we wish to add to the information on the magnetic properties, structural aspects and antimicrobial activity of potassium isothiocyanato-(*N*-salicylidene-amino acidato)cuprates with the general formulas $K_2[Cu_2(sal\text{-}aa)_2(\mu\text{-}NCS)_2]\cdot nH_2O$, $n = 0$ or 4, and $\{K[Cu(sal\text{-}\beta\text{-}ala)(\mu\text{-}NCS)]\}_n$, derived from amino acids such as glycine, DL-α-alanine, DL-valine and DL-phenylalanine, and β-alanine, respectively.

2. Experimental

2.1. Materials and methods

All chemicals were purchased from commercial sources (Sigma–Aldrich Co., Fluka Co.) and used as received without any further purification.

2.2. Preparation of the potassium isothiocyanato-(*N*-salicylideneaminoalkanoato)cuprates (**I–V**)

The studied potassium isothiocyanato-(*N*-salicylideneamino-alkanoato)cuprates, $K_2[Cu_2(sal\text{-}aa)_2(\mu\text{-}NCS)_2]\cdot nH_2O$, $n = 0$ or 4 and $\{K[Cu(sal\text{-}\beta\text{-}ala)(\mu\text{-}NCS)]\}_n$, were prepared according to the methods and procedures published previously [5,10,11]. In general, the cuprates were prepared by the reaction of an aquacomplex, having the $[Cu(sal\text{-}aa)(H_2O)_x]$ basic unit {sal-aa stands for the dianion of *N*-salicylideneamino acid derived from glycine (**I**), DL-α-alanine (**II**), DL-valine (**III**), DL-phenylalanine (**IV**), and β-alanine (**V**)} with KSCN in a water/ethanol solution. Crystals suitable for single crystal X-ray analysis were obtained directly from the reaction mixtures by the evaporation of the solvents used.

2.2.1. Dipotassium di-μ-isothiocyanato-κ^4N:S-bis[(*N*-salicylideneglycinato-κ^3O,N,O′)cuprate(II)] tetrahydrate (**I**)

Green crystals of $K_2[Cu_2(sal\text{-}gly)_2(\mu\text{-}SCN)_2]\cdot 4H_2O$; Yield: 75%; *Anal.* Calc. for $C_{20}H_{22}N_4O_{10}K_2S_2Cu_2$ (M_r = 747.80): C, 32.12; H, 2.97; N, 7.49. Found: C, 32.42; H, 2.89; N, 7.45%. λ_{max}/nm (Nujol mull): 363 (*LMCT*), 638 (*d–d*). λ_{max}/nm (ε/M^{-1} cm^{-1}, DMSO): 369 (5011), 661 (13). IR (*ν*, cm^{-1}; KBr; w, weak; m, medium; s, strong intensity): 3470 m (ν_{O-H}), 2101 s (ν_{SC-N}), 1633 m ($\nu_{C\equiv N}$), 1538 m ($\nu_{as\ COO}$), 1347 m ($\nu_{s\ COO}$), $\Delta\nu_{COO}$ = 191 cm^{-1}, 1312 m (ν_{Ph-O}), 765 m, 801 m (ν_{C-S}). ESI-MS (MeOH, *m/z*$^-$): 254.9 (relative abundance 3.32%) $[Cu(sal\text{-}gly)+OCH_3]^-$; 299.0 (100%) $[KCu(sal\text{-}gly)(SCN)]^-$; 396.0 (29.38%) $[Cu_2(sal\text{-}gly)(SCN)+H_2O+OCH_3]^-$; 635.6 (75.05%) $[KCu_2(sal\text{-}gly)_2(SCN)_2]^-$; 732.0 (14.84%) $[K_2Cu_2(sal\text{-}gly)_2(SCN)_3]^-$.

2.2.2. Dipotassium di-μ-isothiocyanato-κ^4N:S-bis[(*N*-salicylidene-DL-alaninato-κ^3O,N,O′)cuprate(II)] (**II**)

Dark green crystals of $K_2[Cu_2(sal\text{-}DL\text{-}ala)_2(\mu\text{-}SCN)_2]$; Yield: 70%; *Anal.* Calc. for $C_{22}H_{18}N_4O_6K_2S_2Cu_2$ (M_r = 703.80): C, 37.54; H, 2.58; N, 7.96. Found: C, 37.25; H, 2.64; N, 8.03%. λ_{max}/nm (Nujol mull): 375 (*LMCT*), 614 (*d–d*). λ_{max}/nm (ε/M^{-1} cm^{-1}, DMSO): 369 (5370), 654 (13). IR (*ν*, cm^{-1}; KBr; w, weak; m, medium; s, strong intensity): 2067 s (ν_{SC-N}), 1634 s ($\nu_{C\equiv N}$), 1534 m ($\nu_{as\ COO}$), 1345 m ($\nu_{s\ COO}$), $\Delta\nu_{COO}$ = 189 cm^{-1}, 1318 m (ν_{Ph-O}), 762 s, 798 m, 812w (ν_{C-S}). ESI-MS (MeOH, *m/z*$^-$): 270.5 (relative abundance 0.68%) $[Cu(sal\text{-}ala)+OCH_3)]^-$; 312.9 (51.82%) $[KCu(sal\text{-}ala)(SCN)]^-$; 410.4 (4.73%) $[Cu_2(sal\text{-}ala)(SCN)+H_2O+OCH_3]^-$; 663.9 (100%) $[KCu_2(sal\text{-}ala)_2(SCN)_2]^-$; 760.0 (7.04%) $[K_2Cu_2(sal\text{-}ala)_2(SCN)_3]^-$.

2.2.3. Dipotassium di-μ-isothiocyanato-κ^4N:S-bis[(*N*-salicylidene-DL-valinato-κ^3O,N,O′)cuprate(II)] (**III**)

Dark green crystals of $K_2[Cu_2(sal\text{-}DL\text{-}val)_2(\mu\text{-}SCN)_2]$; Yield: 70%; *Anal.* Calc. for $C_{26}H_{26}N_4O_6K_2S_2Cu_2$ (M_r = 759.92): C, 41.09; H, 3.45; N, 7.37. Found: C, 40.71; H, 3.40; N, 7.38%. λ_{max}/nm (Nujol mull): 366 (*LMCT*), 599 (*d–d*). λ_{max}/nm (ε/M^{-1} cm^{-1}, DMSO): 369 (5370), 654 (14). IR (*ν*, cm^{-1}; KBr; w, weak; m, medium; s, strong intensity): 2070 s (ν_{SC-N}), 1635 m ($\nu_{C\equiv N}$), 1538 m ($\nu_{as\ COO}$), 1345 m ($\nu_{s\ COO}$), $\Delta\nu_{COO}$ = 193 cm^{-1}, 1317 s (ν_{Ph-O}), 755 s, 803 m (ν_{C-S}). ESI-MS (MeOH, *m/z*$^-$): 297.6 (relative abundance 0.72%) $[Cu(sal\text{-}val)+OCH_3]^-$; 341.0 (100%) $[KCu(sal\text{-}val)(SCN)]^-$; 437.6 (6.98%) $[Cu_2(sal\text{-}val)(SCN)+H_2O+OCH_3]^-$; 719.8 (100%) $[KCu_2(sal\text{-}val)_2(SCN)_2]^-$.

2.2.4. Dipotassium di-μ-isothiocyanato-κ^4N:S-bis[(*N*-salicylidene-DL-phenylalaninato-κ^3O,N,O′)cuprate(II)] (**IV**)

Dark green crystals of $K_2[Cu_2(sal\text{-}DL\text{-}phe)_2(\mu\text{-}SCN)_2]$; Yield: 74%; *Anal.* Calc. for $C_{34}H_{26}N_4O_6K_2S_2Cu_2$ (M_r = 856.01): C, 47.71; H, 3.06; N, 6.54. Found: C, 47.51; H, 3.05; N, 6.55%. λ_{max}/nm (Nujol mull): 373 (*LMCT*), 613 (*d–d*). λ_{max}/nm (ε/M^{-1} cm^{-1}, DMSO): 370 (5754), 654 (13). IR (*ν*, cm^{-1}; KBr; w, weak; m, medium; s, strong intensity): 2070 s (ν_{SC-N}), 1634 s ($\nu_{C\equiv N}$), 1527 m ($\nu_{as\ COO}$), 1346 m ($\nu_{s\ COO}$), $\Delta\nu_{COO}$ = 181 cm^{-1}, 1317 s (ν_{Ph-O}), 757 m, 795 m (ν_{C-S}). ESI-MS (MeOH, *m/z*$^-$): 389.5 (100%) $[KCu(sal\text{-}phe)(SCN)]^-$; 486.8 (8.85%) $[Cu_2(sal\text{-}phe)(SCN)+H_2O+OCH_3]^-$.

2.2.5. Catena-poly[potassium[copper(II)-μ-isothiocyanato-μ-*N*-salicylidene-β-alaninato(2−)]] (**V**)

Dark green crystals of $\{K[Cu(sal\text{-}\beta\text{-}ala)(\mu\text{-}NCS)]\}_n$; Yield: 85%; *Anal.* Calc. for $C_{11}H_9N_2O_3KSCu$ (monomeric unit, M_r = 351.90): C, 37.54; H, 2.58; N, 7.96. Found: C, 37.70; H, 2.64; N, 7.93%. λ_{max}/nm (Nujol mull): 363 (*LMCT*), 675 (*d–d*). λ_{max}/nm (ε/M^{-1} cm^{-1}, DMSO): 366 (5371), 672 (11). IR (*ν*, cm^{-1}; KBr; w, weak; m, medium; s, strong intensity): 2083 s (ν_{SC-N}), 1632 m ($\nu_{C\equiv N}$), 1545 m ($\nu_{as\ COO}$), 1395 m ($\nu_{s\ COO}$), $\Delta\nu_{COO}$ = 150 cm^{-1}, 1318 m (ν_{Ph-O}), 765 s, 792w, 805w (ν_{C-S}). ESI-MS (MeOH, *m/z*$^-$): 270.5 (0.78%) $[Cu(sal\text{-}\beta\text{-}ala+OCH_3)]^-$; 313.0 (53.53%) $[KCu(sal\text{-}\beta\text{-}ala)(SCN)]^-$; 410.4 (6.47%) $[Cu_2(sal\text{-}\beta\text{-}ala)(SCN)+H_2O+OCH_3]^-$; 663.9 (100%) $[KCu_2(sal\text{-}\beta\text{-}ala)_2(SCN)_2]^-$; 760.0 (6.90%) $[K_2Cu_2(sal\text{-}\beta\text{-}ala)_2(SCN)_3]^-$.

2.3. Physical measurements

Elemental analyses (CHN) were obtained with a Thermo-Finnigan Flash EA-1108 CHN Elemental Analyzer. UV–Vis spectra were obtained with an HP 8453 spectrometer (Agilent Technologies, Germany) in DMSO solutions at a concentration of 10^{-3} mol dm^{-3}, and diffuse-reflectance spectra were recorded with a Lambda 40 spectrometer (Perkin Elmer Instruments) in the range of 200–900 nm in Nujol mulls. Infrared spectra (4000–400 cm^{-1}) were recorded with a Nicolet Impact 400D FT-IR spectrometer (Thermo Electron Co.) using the KBr technique and the single-reflection ATR technique on the ZnSe crystal, and with a Nexus 670 FT-IR spectrometer (Thermo-Nicolet) using the Nujol technique in the region of 600–150 cm^{-1}. Electrospray mass spectra (ESI-MS) were recorded in a negative ionisation mode using an HP 1100 LC/MSD Trap VL system with a direct injection of a measured solution in MeOH with a flow rate of 300 μL h^{-1}, and the monitoring mass interval of 100–800 *m/z*. The ESI-MS spectra were recorded under the following conditions: nitrogen was used as a drying and nebulising gas, a nebulizer pressure of 80 psi, a drying gas flow of 10 L min^{-1}, the dry gas temperature of 350 °C, the capillary voltage was set to ±3500 V versus the end plate voltage of ±500 V (negative/positive mode), the scan range was 100–800 *m/z* with the target ion count set to 30 000, with