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Crystal Structures of Two Potential Tumor Imaging Agents and Therapeutic Agents—Copper(II) Ternary Complexes with Salicylidene-tyrosinato Schiff Base and Nitrogen-donor Chelating Lewis Base

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Abstract: The crystal structures of two potential tumor imaging agents and therapeutic agents —copper(II) complexes with salicylidene-tyrosinato Schiff base and nitrogen-donor chelating Lewis base, [Cu(sal-tyr)(bipy)] 1 and [Cu(sal-tyr)(phen)]·2CH_3OH 2, are presented. Our work is helpful to get deep understanding of novel ^{64}Cu tumor imaging agents and therapeutic agents.

Keywords: Copper, salicylidene-tyrosinato Schiff base, phen, bipy, crystal structure.

Schiff bases-metal complexes have attracted many attentions for their biological activity and perspective for pharmaceuticals[1], but less effort has been devoted to N-salicylidene-aminoacidato Schiff bases metal complexes. As a part of our radiopharmaceutical investigation work[2], here we present the crystal structures of two novel ternary complexes, [Cu(sal-tyr)(bipy)] **1** and [Cu(sal-tyr)(phen)]·2CH_3OH **2** (sal-tyr: N-salicylidene-tyrosinato; bipy: 2,2′-bipyridine; phen: 1,10-phenathroline) synthesized by means of *in situ* coordination. In our knowledge it is the first report about the crystal structure of copper(II) complex with salicylidene-α-aminoacidato Schiff base and nitrogen-donor chelating Lewis base.

The crystal structure determination reveals that the Cu^{2+} ion is five coordinated in both complexes by one oxygen atom of carboxylate, the imine nitrogen atom and the phenol oxygen atom of the salicylidene as well as two nitrogen atoms of the nitrogen-donor-containing chelating Lewis base, resulting in the distorted square pyramid coordination polyhedron. The hydroxyl hydrogen atom hydrogen bonds with the uncoordinated oxygen atom of the carboxylate from the neighboring molecule in the

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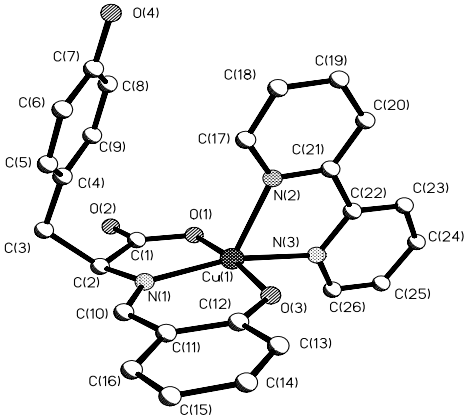
complex **1**, while in the complex **2** this kind hydrogen bond pairs of two centrosymmetrical molecules form a cycle that is almost vertical to the two Schiff base chelating planes. Besides, one methanol molecule in the complex **2** forms hydrogen bonds, using its oxygen atom O5 to the hydroxyl hydrogen atom H6 of another methanol molecule and utilizing its hydroxyl hydrogen atom H5 to the coordinated phenol oxygen atom O3 of adjacent complex molecule. It is especially worth mention that the chiral carbon atom C2 of tyrosine changes its configuration from S to R during the synthesis of **2**, while it maintains the S configuration in **1**. The preliminary antitumor experiments of both complexes upon ICR mice (18~22 g, female) implanted with S-180 sarcoma, giving T/C of 0.435 and 0.675, respectively, showing that they will be potentials for utilization as tumor PET imaging and therapeutic agent. The further animal experiments of the complexes and that of ^{64}Cu labeled compounds as well as theoretic calculation are underway.

Figure 1 Molecular structures of **1** and **2**
(hydrogen atoms omitted for clarity)



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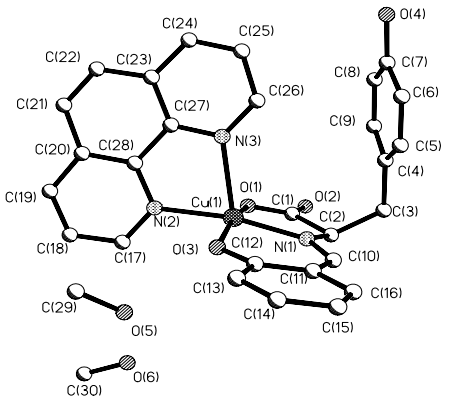

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3 *Crystal data*: $C_{26}H_{21}N_3O_4Cu$ **1**, M = 503.00, orthorhombic, a = 9.0356(18), b = 11.992(2), c = 20.618(4) Å, V = 2234.1(8) Å^3, T = 293 K, space group $P2_12_12_1$(#19), Z = 4, μ(MoKα) = 10.17 cm^{-1}, 21373 reflections measured, 8292 unique (R_{int} = 0.043) all included in the refinement; R = 0.0558 [for 5477 reflections with $I \geq 2.00\sigma(I)$]; R_w = 0.0944 (all data).
$C_{30}H_{29}N_3O_6Cu$ **2**, M = 591.10, triclinic, a = 10.343(2), b = 12.099(2), c = 13.036(4) Å, α = 67.00(3), β = 75.06(3), γ = 67.22(3) ° , V = 1373.6(5) Å^3, T = 293 K, space group Pī(#2), Z = 2, μ(MoKα) = 8.44 cm^{-1}, 12711 reflections measured, 9342 unique (R_{int} = 0.027) all included in the refinement; R = 0.0473 [for 6219 reflections with $I \geq 2.00\sigma(I)$]; R_w = 0.0777 (all data).

4 Crystallographic parameters have been deposited in the editorial office of CCL.

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