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Short communication

SHORT COMMUNICATION

Stereospecific ligands and their complexes. Synthesis and characterization of the *s-cis*-K[Ru(*S,S*-eddp)Cl_2]·$3H_2O$

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Abstract: In the reaction of ruthenium(III) chloride and an edda-like ligand ethylenediamine-*N,N'*-di-*S,S*-2-propionic acid (*S,S*-eddp) in aqueous solution led to the formation of only one of the three possible geometrical isomers potassium-*s-cis*-dichlorido-(ethylenediamine-*N,N'*-di-*S,S*-2-propionato)-ruthenate(III)-trihydrate, *s-cis*-K[Ru(*S,S*-eddp)Cl_2]·$3H_2O$. The assumed geometry of the complex was based on its electronic absorption and infrared spectra.

Keywords: ruthenium(III) complex; *S,S*-ethylenediamine-*N,N'*-di-*S,S*-propionate ligand; electronic absorption and infrared spectra.

INTRODUCTION

The synthesis and pharmacological evaluation of new compounds bearing metal ions other than platinum is a field of growing interest.[1,2] Complexes based on ruthenium, one of the platinum group metals, have been proposed as potential antitumour substances,[3–8] demonstrating remarkable antitumour activity and antimetastatic behaviour, as well as lower systematic toxicity than platinum compounds.[9–12] Recent biochemical studies demonstrated that the new ruthenium compounds bind proteins in a tight covalent manner.[9]

Today, ruthenium complexes with polyaminopolycarboxylic chelating agents constitute a new group of potential anticancer compounds.[2,3,13] The most representative example, *cis*-H[Ru(H_2-pdta)Cl_2], (H_4-pdta = 1,3-propanediamine-tetraacetic acid), binds rapidly to serum proteins through surface histidines, damages nuclear DNA, inhibits DNA recognition and DNA lysis by restriction enzymes, alters the conformation of pHV14 DNA, stimulates NADPH oxidase and a respiratory burst in phagocytic neutrophils and elicits phosphorylation of tyrosine residues.[2,9,14,15]

In an effort to improve the antitumour properties of ruthenium compounds, a series of new Ru(III) complexes was prepared with stereospecific ligands similar

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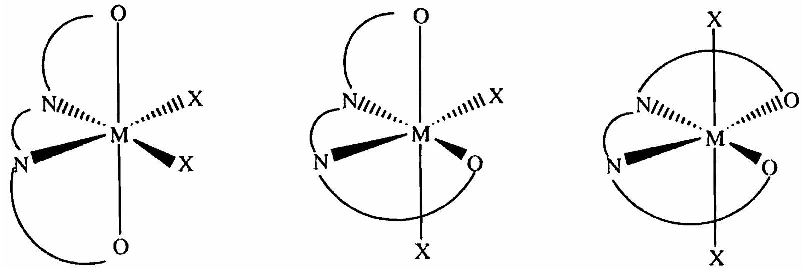
to the linear quadridentate edda ligand (edda = ethylenediamine-*N,N'*-acetic acid ion), such as the *S,S*-eddp ligand (*S,S*-eddp = ethylenediamine-*N,N'*-di-*S,S*-2-propionic acid ion), by changing the substituent on the chiral carbon atom.

The *S,S*-eddp (*S,S*-eddp = *S,S*-ethylenediamine-*N,N'*-di-2-propionate ion) is similar to the edda ligand and it can form three possible geometrical isomers, *s-cis, uns-cis* and *trans* (Fig. 1), when it is coordinated as a tetradentate agent together with two additional monodentate ligands in octahedral Ru(III) complexes. With a known absolute configuration, on coordination to a Ru(III) ion, the *S,S*-eddp ligand forms complexes maintaining the *S* configuration of both carbon atoms, yielding complexes with a ΔΔΔ (net Δ) absolute configuration.[16,17] However, the orientation of the methyl groups of the *S,S*-eddp ligand, in complexes can be different after coordination to a metal ion and two diastereoisomers can theoretically be formed for every geometric isomer.



s-cis *uns-cis* *trans*

Fig. 1. Possible geometric isomers of the $[Ru(S,S\text{-eddp})Cl_2]^-$ complex.

As part of continuing studies on this important class of complexes, the synthesis and characterization of the new Ru(III) complex, *s-cis*-$K[Ru(S,S\text{-eddp})Cl_2]\cdot 3H_2O$, in which the chelating agent ethylenediamine-*N,N'*-di-*S,S*-2-propionic acid acts as tetradentate ligand is presented here.

EXPERIMENTAL

Materials

Ethylenediamine-*N,N'*-di-*S,S*-2-propionic acid (*S,S*-eddp) was prepared using a previously described procedure.[18] Commercial hydrated ruthenium(III) chloride was dissolved in concentrated HCl and refluxed for 30 min. After concentration to dryness, the compound was stored under $CaCl_2$.

Synthesis of the complex s-cis-*K[Ru(*S,S-*eddp)Cl₂]·3H₂O*

The new ruthenium(III) complex, *s-cis*-$K[Ru(S,S\text{-eddp})Cl_2]\cdot 3H_2O$, was synthesized by heating, on a steam bath (2 h), an aqueous solution of *S,S*-eddp with $RuCl_3$ obtained as described above (molar ratio = 1:1). After this process, the pH of the system was adjusted to 3.0 and the mixture refluxed for 3 h, evaporated to a small volume and left overnight. After adding acetone, a black powder of the complex formed. The complex is stable on air and soluble in water. An aqueous solution (0.10 %) gave $[\alpha]_D = -142°$ ($[M]_D = -663$). Anal. Calcd. (%) for *s-cis*-$K[Ru(S,S\text{-eddp})Cl_2]\cdot 3H_2O \equiv KRuC_8H_{20}N_2O_7Cl_2$ (M_r = 467.33 g mol^{-1}): C, 20.56; H, 4.31; N, 6.00. Found: C, 20.69; H, 4.65; N, 6.16.

Physical measurements

Electronic absorption spectra were recorded on a Perkin–Elmer Lambda 35 double-beam UV-Vis spectrophotometer. An aqueous 1×10^{-3} mol dm^{-3} solution of the complex was used for this measurement. The infrared spectra were recorded on a Perkin–Elmer FTIR 31725-X spectrophotometer using the KBr pellet technique. The $[\alpha]_\lambda$ value was measured in a 1.0 dm tube at 20 °C using a Perkin–Elmer SP polarimeter. Elemental microanalyses for C, H, and N were performed by standard methods.

RESULTS AND DISCUSSION

Electronic absorption spectrum

The absorption maxima in the corresponding electronic absorption spectrum of the isolated *s-cis*-[Ru(S,S-eddp)Cl_2]$^-$ complex are summarized in Table I. The corresponding data for the similar [Ru(edda-type)L]$^-$ complexes are given for comparison.

TABLE I. Electronic absorption spectra of Ru(III) complexes with some tetradentate ligands

Complex	λ_{max} / nm	ε_{max} / m^2 mol^{-1}	Ref.
[Ru(edta)H_2O]$^-$	350	68.0	19
	280	280.0	
s-cis-[Ru(eddp)Cl_2]$^-$	470	60.0	8
	300	214.0	
s-cis-[Ru(H_2edta)Cl_2]$^-$	470	70.0	20
	300	190.0	
[Ru(S,S-eddp)Cl_2]$^-$	464	69.4	This work
	307	232.4	

The electronic absorption spectra of the ruthenium(III) complexes polyaminopolycarboxylic chelating agents contain bands that in most cases can be interpreted as arising from one or more of the following types of transitions: d–d, interligand, metal to ligand charge transfer, ligand to metal charge transfer and ligand field. The electronic spectrum of an aqueous solution of the prepared *s-cis*-K[Ru(S,S-eddp)Cl_2]·$3H_2O$ complex shows bands at 307 nm (ε = 69.4 m^2 mol^{-1}) and 464 nm (ε = 232.4 m^2 mol^{-1}). The registered absorptions may be attributed to the ligand to metal charge transfer band ($\pi_{Cl} \rightarrow \pi^*_{Ru}$) and the d–d transition, respectively.

The two symmetrical absorption bands suggest that the isolated [Ru(S,S-eddp)Cl_2]$^-$ complex has pseudo-octahedral symmetry (Table I). Based on a comparison of the positions of its absorption band maxima and the molar absorbances, it can be concluded that the isolated K[Ru(S,S-eddp)Cl_2]·$3H_2O$ complex has *s-cis* geometry (Fig. 1).

Infrared spectrum

The isolated complex shows a rather broad absorption band near 1600 cm^{-1} (a strong band at 1580 cm^{-1} and a shoulder at about 1630 cm^{-1}) of the asymmetric stretching frequencies of the coordinated carboxylate groups of the S,S-

-eddp ligand. The lack of absorption between 1700–1750 cm^{-1} indicates that the carboxyl groups of *S,S*-eddp are coordinated to the central Ru(III) ion and are not present as free acid groups. The strong asymmetric stretching band of the coordinated carboxylate groups, which is less influenced by the coordination effects, lies in the expected region at 1399 cm^{-1}. The N–H stretching band of the *s-cis*-K[Ru(*S,S*-eddp)Cl$_2$]·3H$_2$O complex appears at 3434 cm^{-1}.

CONCLUSIONS

Based on the electronic absorption and infrared spectra of potassium-dichlorido-(ethylenediamine-*N,N'*-di-*S,S*-2-propionato) ruthenate(III) trihydrate, K[Ru(*S,S*-eddp)Cl$_2$]·3H$_2$O, prepared by the direct synthesis from RuCl$_3$ and *S,S*-eddp in aqueous solution, the *s-cis* geometrical configuration is proposed.

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ИЗВОД

СТЕРЕОСПЕЦИФИЧНИ ЛИГАНДИ И ЊИХОВИ КОМПЛЕКСИ. II. СИНТЕЗА И КАРАКТЕРИЗАЦИЈА *s-cis*-K[R*u*(*S,S*-eddp)Cl$_2$]·3H$_2$O

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У реакцији између рутенијум(III)-хлорида и една-типа лиганда, етилендиамин-*N,N'*-ди-*S,S*-2-пропионска киселина (*S,S*-еддп) у воденом раствору настао је само један од могућа три геометријска изомера калијум-*s-cis*-дихлоридо-(етилендиамин-*N,N'*-ди-*S,S*-2-пропионато) рутенат(III)-трихидрат, *s-cis*-K[Ru(*S,S*-eddp)Cl$_2$]·3H$_2$O. Геометрија насталог комплекса је претпостављена на основу електронских апсорпционих и инфрацрвених спектара.

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