Equilibrium and kinetic studies of the reactions between [Ru(terpy)(bipy)Cl]Cl complex and biologically important N-donor ligands

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Introduction

The studies in the field of anticancer characteristics of ruthenium(III/II) compounds have caused much attention for several years since some of them such as KP1019 (indazolium-tetrachloridobis(H-indazole)ruthenate(III)) i NAMI-A (imidazolium-*trans*-tetrachlorido(dimethylsulfoxide)indazoleruthenate(III)) reached the level of clinical investigation.[1,2]

Experimental

We studied the kinetics of the substitution reactions of [Ru(terpy)(bipy)Cl]$^+$ complex with biologically important ligands: dimethylsulfoxide, guanosine-5'-monophosphate, thiourea and L-histidine. All reactions were studied by UV-VIS spectrophotometry in 0.1 M $NaClO_4$ with 10 mM NaCl. The excess of ligand concentration was used to observed *pseudo*-first order conditions. The rate constants and activation parameters are calculated using computational program Origin 6.1. Also we investigated the hydrolysis and complexation reactions of Ru(II) complex with guanosine-5'-monophosphate and L-histidine. Potentiometric titrations were carried out at 298 K in inert atmosphere using a glass electrode. For the calculations is used computation program HYPERQUAD2006.[3]

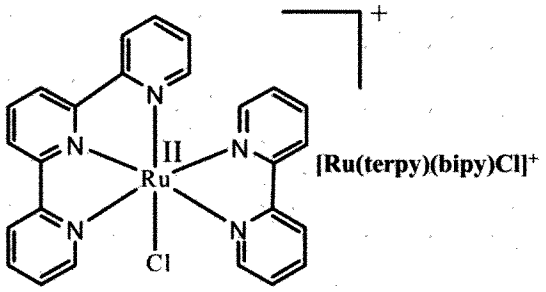

Figure 1. Structures of the investigated complexes

Results

Table 1. Rate constants for the substitution reactions of [Ru(terpy)(bipy)Cl]$^+$ complex with nucleophiles in 0.1 mol $NaClO_4$ and 10 mM NaCl .

	[Ru(terpy)(bipy)Cl]$^+$	
ligandi	k_2 [$M^{-1}s^{-1}$]	k_1 [s^{-1}]
5'-GMP	$(1.30 \pm 0.03) \times 10^{-4}$	$(2.00 \pm 0.07) \times 10^{-5}$
DMSO	$(1.97 \pm 0.20) \times 10^{-2}$	$(1.23 \pm 0.06) \times 10^{-4}$
Tiourea	$(1.89 \pm 0.07) \times 10^{-1}$	$(1.38 \pm 0.20) \times 10^{-4}$
Histidin	$(4.06 \pm 0.20) \times 10^{-1}$	$(1.14 \pm 0.07) \times 10^{-3}$

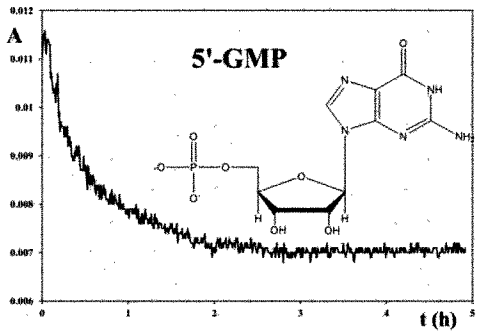

Figure 2. Kinetic traces of the reaction between [Ru(terpy)(bipy)Cl]$^+$ ($2 \cdot 10^{-4}$ M) complex and 5'-GMP ($3.3 \cdot 10^{-3}$ M), T = 310 K, λ = 380 nm

Table 2. Stability constants of $[Ru(terpy)(bipy)H_2O]^{2+}$ – L complexes formed in a 0.1 mol/dm^3 $NaClO_4$ ionic medium, at 298 K.

	$\log \beta_{p,q,r} \pm \sigma$		
Species (p,q,r)[a]		**5'-GMP**	**His**
(1, -1, 0)	**- 7.12(4)**		
(2, -1, 0)	**- 1.34(4)**		
(1, 0, 1)		**-**	**5.06(9)**
(1, 1, 1)		**14.12(2)**	**-**
(2, 1, 1)		**18.26(4)**	**16.51(7)**
Statistics	$\chi^2 = 13.32$ $s = 1.96$	$\chi^2 = 12.99$ $s = 1.51$	$\chi^2 = 14.79$ $s = 2.73$

[a]*p*, *q* and *r* are the stoichiometric coefficients corresponding to $[Ru(terpy)(bipy)H_2O]^{2+}$, H^+ and ligand, respectively

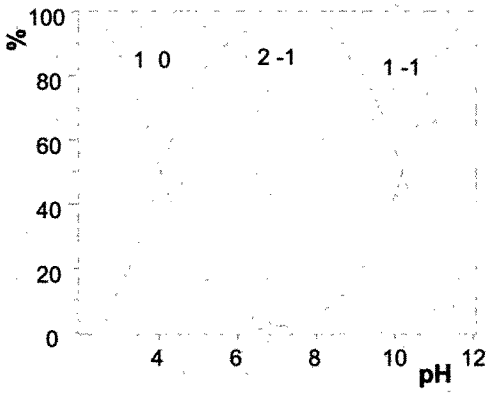

Figure 3. The distribution of $[Ru(terpy)(bipy)H_2O]^{2+}$ hydrolytic species in 0.1 mol dm^{-3} $NaClO_4$ ionic medium at 298 K. $C_{[Ru(terpy)(bipy)H2O]^{2+}} = 2.00$ mmol dm^{-3}

Conclusion

- The reactivity of the used ligands toward monofunctional [Ru(terpy)(bipy)Cl]$^+$ complexes decrease in order: Tiourea>DMSO>His > 5'-GMP.
- As can be seen from Fig. 3, the dominating hydrolytic complex at lower pH values is (2, -1), with maximum a concentration at pH = 7. The formation of the complex (1, -1) starts at about pH=7 and with increasing pH, the concentration of this complex increases.

References

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3. Gans, P., Sabatini, A., Vacca A.,*Talanta*,**1996**, 43, *1739-1753*