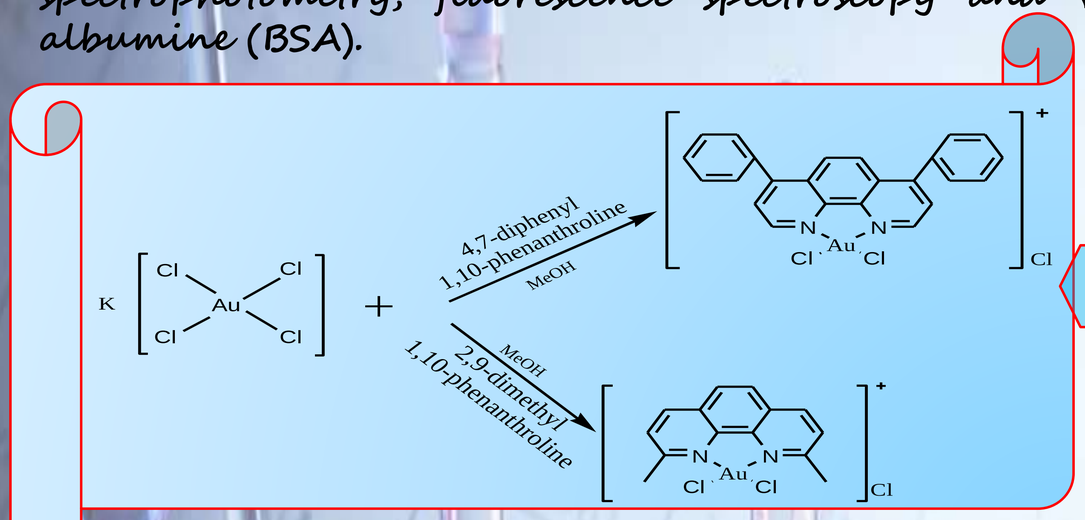
Novi zlato(III) kompleksi: Sinteza, karakterizacija i ispitivanje interakcija sa 5'-GMP, GSH i L-Met

New gold(III) complexes: Synthesis, characterization and study of their interactions with 5'-GMP, GSH and Met

Snežana Radisavljević, Ana Đeković Kesić*, Biljana Petrović
snezana·radisavljevic@pmf·kg·ac·rs
Faculty of Science, University of Kragujevac, R· Domanovića 12, 34000 Kragujevac, Serbia
*Department of Chemical-Technological Sciences, State University of Novi Pazar, Vuka Karadžića bb, 36300 Novi Pazar, Serbia

The pharmacologic properties of gold compounds have been known since the end of 19th century. They have been used for different studies, even though they are usually used for the treatment of rheumatoid arthritis. In the last decade gold complexes have received increased attention due to the variety of their applications. Primary, they have been investigated as potential anticancer and chemotherapeutic agents.[1] It is well known that gold(III) complexes are very similar to platinum(II) compounds, so they could exhibit prospective anticancer, cytotoxic and antitumor properties.[2]

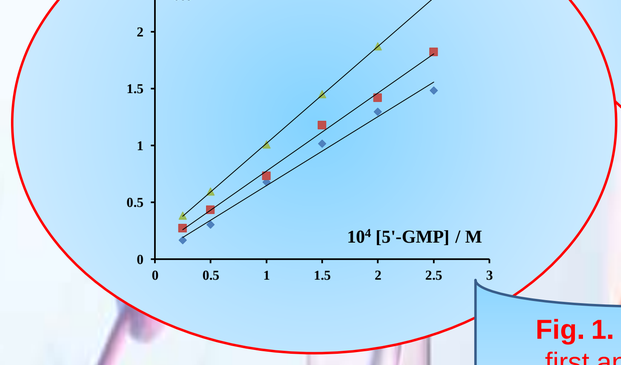
In this study we have synthesized two new gold(III) complexes with general formula $[Au(N-N)Cl_2]$ in which N-N is a bidentate ligand (4,7-diphenyl-1,10-phenanthroline and 2,9-dimethyl-1,10-phenanthroline). These complexes were characterized by spectroscopic techniques (IR, UV-Vis, ^{1}H NMR). Kinetic of the substitution reactions between complexes and biological important molecules, such as guanosine-5'-monophosphate (5'-GMP), glutathione (GSH) and L-methionine (L-Met), were performed by stopped-flow technique. Also, we performed DNA binding studies using UV-Vis spectrophotometry, fluorescence spectroscopy and viscosity measurements, as like as interaction with bovine serum albumine (BSA).



Scheme 1. Synthetic pathways for the preparation of complexes **1 – 2**

1	k_1 [M^{-1} s^{-1}]	k_{-2} [M^{-1} s^{-1}]	$\Delta H^{\neq}$ [kJ mol^{-1}]	$\Delta S^{\neq}$ [J^{-1}k mol^{-1}]
5'-GMP 288K	6.44×10^3	6.08×10^3	10±1	-154±2
298K	7.46×10^3	6.87×10^3	9±2	-156±5
308K	9.14×10^3	8.53×10^3		
Glutathione 288K	9.24×10^3	7.33×10^3	3±1	-176±1
298K	9.81×10^3	7.81×10^3	8±3	-160±10
308K	1.07×10^4	9.79×10^3		
Methionine 288K	1.13×10^4	1.03×10^4	3±0	-172±1
298K	1.23×10^4	1.06×10^4	1±0	-181±3
308K	1.32×10^4	1.13×10^4		
2				
5'-GMP 288K	1.12×10^4	1.03×10^4	7±2	-159±6
298K	1.21×10^4	1.14×10^4	4±1	-169±1
308K	1.47×10^4	1.24×10^4		
Glutathione 288K	1.20×10^4	1.08×10^4	6±2	-161±7
298K	1.28×10^4	1.17×10^4	3±1	-172±1
308K	1.54×10^4	1.27×10^4		
Methionine 288K	1.38×10^4	1.17×10^4	2±1	-174±6
298K	1.41×10^4	1.20×10^4	1±0	-179±2
308K	1.57×10^4	1.28×10^4		

Table 1. Rate constants and activation parameters for the substitution reactions between complexes with **5'-GMP**, **Glutathione** or **Methionine**



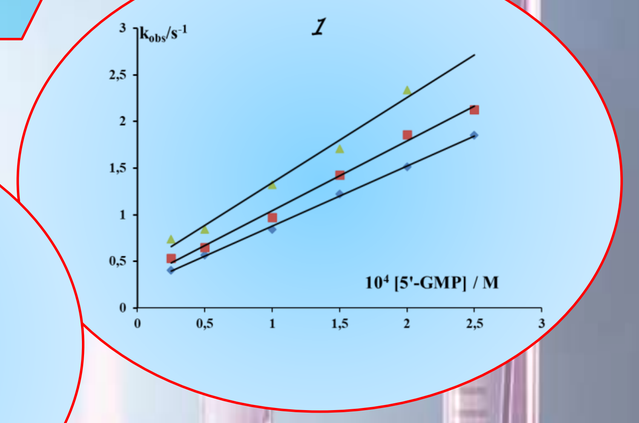


Fig. 1. Pseudo-first order rate constants for first and second step, k_{obs} as a function of nucleophile concentration for the substitution reaction between complex **1** and **5'-GMP** in HEPES buffer.

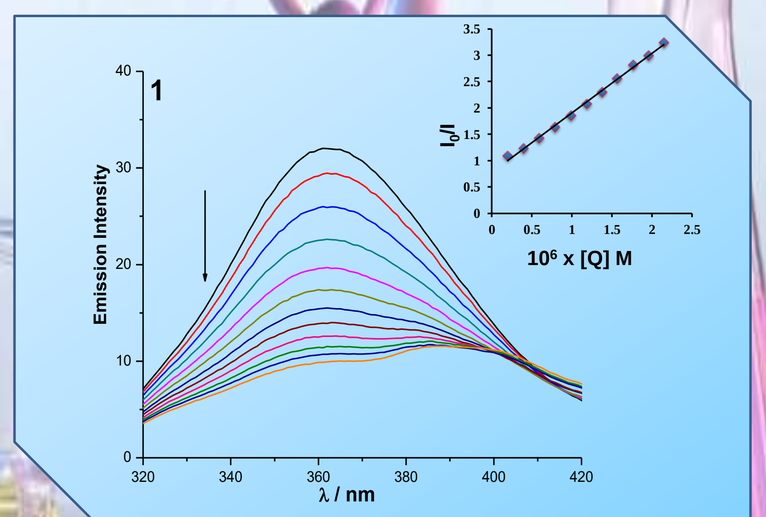


Fig. 2. Emission spectra of BSA in the presence of complex 1. [BSA] = 2 μM, [complex] = (0.199 – 2,91) x 10^{-6} M. Arrow shows the absorbance changing upon increasing DNA concentrations. Insert plots of $[DNA]/(\varepsilon_A - \varepsilon_f)$ *versus* [DNA] for complex 1.

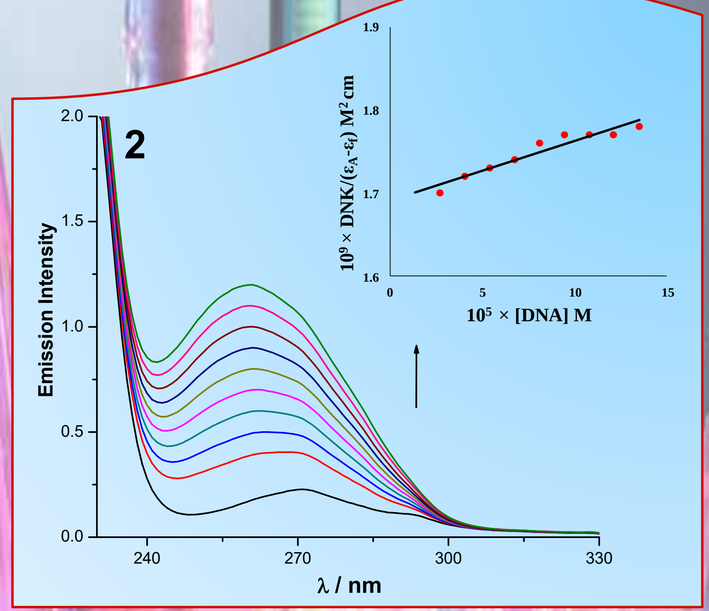


Fig. 4.. Absorption spectra of the complex **2** in buffer (HEPES) upon addition of CT DNA. [Au] = 1.35 x 10^{-5} M, [DNA] = (0.135-1.35) x 10^{-4} M. Arrow shows the absorbance changing upon increasing DNA concentrations. Insert plots of $[DNA]/(\varepsilon_A - \varepsilon_f)$ *versus* [DNA] for complexes **2.**

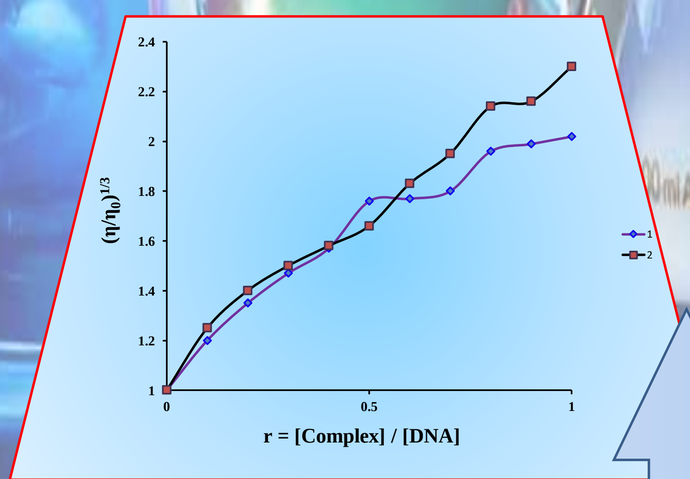


Fig. 3. Relative viscosity $(\eta/\eta_0)^{1/3}$ of CT DNA (0.011mM) in buffer (HEPES) in the presence of the complexes **1** – **2** at increasing amounts (r).

Conclusion

❑The new gold complexes were synthesized and characterized by different experimental methods.

❑ Kinetic experiments were performed with small bio-molecules and new synthesized complexes have a good affinity toward studied biomolecules

❑The studied complexes exhibited good DNA and BSA interaction ability.

1. Patanjali P, Kumar R, Sourabh, Kumar A, Chaudhary P, Singh R, *Main Group Chemistry* 17 (2018) 35-52.
2. Baron M, Tiezza MD, Carlotto A, Tubaro C, Graiff C, Orian L *J Organomet Chem* 866 (2018) 144-152.