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International Symposium on Metal Complexes
Florence, June 3-7, 2018

Acta of the International Symposia on Metal Complexes

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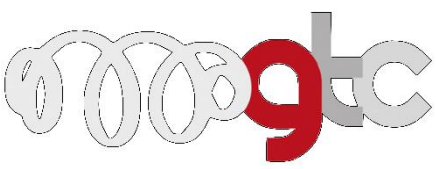

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Edited by:

Antonio Bianchi

University of Florence (Italy)
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Foreword

On behalf of the International Scientific Committee and of the Local Organization Committee, it is my great pleasure to welcome you in Florence for the 2018 edition of the **International Symposium on Metal Complexes** (**ISMEC 2018**). ISMEC 2018 is the 45th edition of a series of meetings that begun in Florence in 1974 as the annual congress of the Italian group of "Thermodynamics of Metal Complexes". In 1988 it became an Italian-Spanish, or Spanish-Italian congress with annual meetings alternating between Italy and Spain. From 2010, participation was widened at an international level and the meeting took the name of International Symposium on Metal Complexes. The participation in ISMEC 2018 of scientists from all over the world confirms the international vocation of these meetings and the worldwide interest for their core subject which focuses on the thermodynamic and the kinetic properties of metal complexes and related applications in the fields of Analytical, Biomedical, Environmental, Inorganic and Physical Chemistry. Main topics include, but are not limited to:

- Complexation thermodynamics and kinetics
- Solution equilibria and coordination chemistry
- Complexation processes in supramolecular chemistry
- Metal-based reactivity and catalysis
- Metal-complex interactions with biomolecules
- Metals in diseases: transport, homeostasis and toxicity
- Metal-based drugs: diagnosis and therapy
- Metal complexes of environmental and biological interest
- Nanostructured metal complexes
- Analytical methods and sensors based on complexation equilibria
- Computer methods for equilibrium analysis

The "Acta of ISMEC Symposia" has been published since 2011, immediately after each symposium, to highlight the ongoing interest in the covered topics and to provide an overview of the most recent progresses in the field.

I like to express my highest appreciation for the work done by the members of the local organizing committee. Without them, this symposium would not have been possible.

Antonio Bianchi

Chairman of ISMEC 2018
President of the ISMEC Group

June 2018

Interaction of gold N-heterocyclic carbenes with nucleic acids

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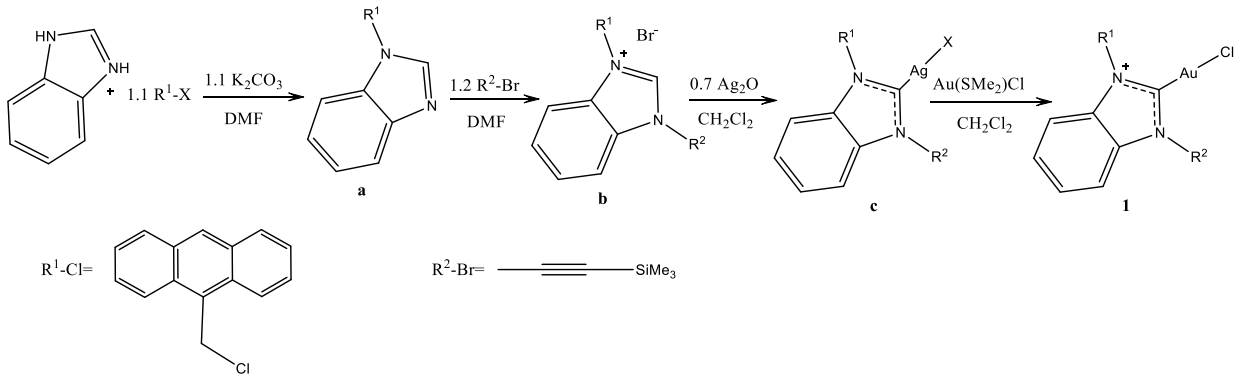
Metal complexes with N-heterocyclic carbenic ligands (NHCs) have found applications not only in catalysis but also as anticancer agents [1]. In particular, gold-NHCs turned out to be particular promising. First of all, they are stable complexes whose synthesis is relatively simple. Moreover, their biological and targeting properties can be tuned by modifying substituents on the carbenic ligand. Preclinical studies showed antiproliferative properties both *in vitro* and *in vivo* and encouraging results on selectivity [2,3]. These compounds target mitochondria and proteins, among which of paramount importance is the selenoenzyme Thioredoxin reductase. However, more recent studies also consider their interaction with dsDNA or G-quadruplexes [4,5]. Indeed, some of the latest approaches on anticancer metallodrug design include the synthesis of multitargeting platforms [6], cancer being such a complex series of genetic diseases that a single target therapy may not be effective enough.

Within this frame, we synthesized and chemically characterized a gold monocarbene with a planar aromatic moiety (Scheme 1) able to interact with dsDNA.



Scheme 1. Synthesis of 1-(9-anthracenylmethyl)3-(1-trimethylsilyl-3-propynil)-benzimidazol-2-ylidene gold chloride

Binding with natural DNA has been characterized by means of different spectroscopic methods such as spectrofluorimetric titrations and thermal denaturation spectrophotometric studies. Moreover, inhibition of purified Thioredoxin reductase has been measured. Preliminary *in vitro* cytotoxicity experiments show moderate antiproliferative activity.

In addition, single crystals of bis-(1-buthyl-3-methyl)imidazol-2-ylidene-gold hexafluorophosphate ([$BMIm_2Au$][PF_6]) with the human telomere Tel-23 have been obtained. The adduct has been also characterized in solution by means of ESI-MS, circular dichroism and melting experiments.

As for dsDNA binding, the results show that the synthesized gold-NHC does indeed bind the nucleic acid in a complex manner that includes both intercalation and interaction with the groove. Great stabilization of the helix is observed at compound/DNA molar ratio of 1. As for TrxR inhibition, IC_{50} values in the micromolar range comparable with the *in vitro* cytotoxicity suggest that the enzyme may play an important role for the biological action.

As for the telomere, solution studies on the [$BMIm_2Au$][PF_6]/Tel 23 adduct confirm the features already pointed out by the crystal structure. The gold compound binds the G-quadruplex externally with a 1:1 stoichiometry. CD spectra and melting studies show that the interaction exists but is rather weak.

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