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Xanthine-based gold(I) N-heterocyclic carbene complexes: synthesis and anticancer evaluation

Benoit Bertrand, Geny M M Groothuis, Angela Casini, Loïc Stefan, Ewen Bodio,
Richard Philippe, Pierre Legendre, David Monchaud, Michel Picquet

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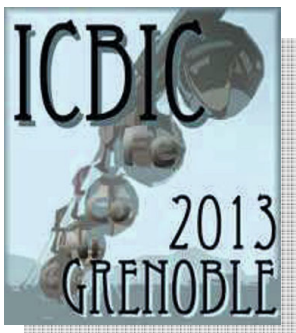
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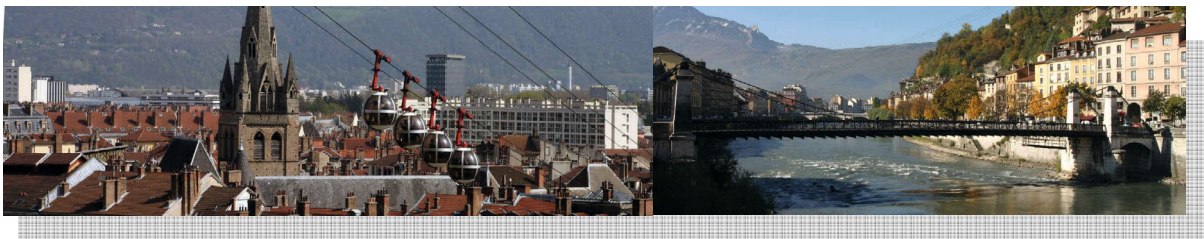


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TITLE: Xanthine-based gold(I) N-Heterocyclic Carbene complexes: synthesis and anticancer evaluation.

AUTHORS/INSTITUTIONS: B. Bertrand, G.M. Groothuis, A. Casini, Research institute of Pharmacy, Rijksuniversiteit Groningen, Groningen, NETHERLANDS|L. Stefan, E. Bodio, P. Richard, P. Le Gendre, D. Monchaud, M. Picquet, Institut de Chimie Moléculaire de l'Université de Bourgogne, Université de Bourgogne, Dijon, FRANCE|

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ABSTRACT BODY:

Abstract Body: Gold compounds have been used in medicine for many years, the earliest use dating back to ancient China. In more modern times, gold complexes have been investigated for their activity against tuberculosis, and several gold containing anti-arthritis drugs have subsequently entered the market and remain in clinical use today. Gold complexes, both in oxidation state (I) and (III), have also appeared in the last years as promising candidates as new possible anticancer agents [1].

Within this frame, N-heterocyclic carbene (NHC) metal complexes have recently evolved from laboratory curiosities to compounds with unique properties for applications in catalysis and medicine [2]. Purines present an imidazole ring making them natural substrates for NHC precursors. Thus, we report here the synthesis of a series of N-7 substituted bis-NHC gold(I) complexes with xanthine scaffolds (Scheme 1). It is worth mentioning that xanthines molecules belonging to the purine family- are known to possess very interesting biological properties. For example, caffeine (1,3,7-trimethylxanthine) has shown promising antimetastatic properties in vivo [3]. The new compounds' possible anticancer effects have been tested on various cancer cell lines in comparison to healthy cells in vitro and their toxicity against healthy rat precised-cut liver and colon slices have been evaluated ex vivo.

Initial mechanistic studies have highlighted the properties of some of the new compounds as DNA G-quadruplex stabilizers by FRET-melting analysis and circular dichroism spectroscopy (Figure 1).

References

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- [2] Ott, I. Coord. Chem. Rev. 2009, 253, 1670-1681.
- [3] Yang H. et al., Clin. Exp. Metastasis 2004, 21,719-735

