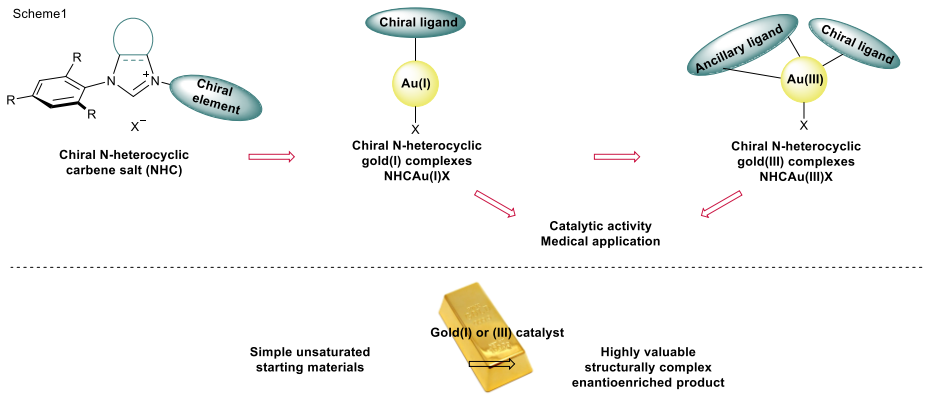
New N-heterocyclic carbene gold complexes: from catalytic activity to medical application

For many centuries, metallic gold has been considered a precious metal which has become the primary means of payment, and a sign of social and economic status. Besides this obvious role of gold, humanity was fascinated by gold due to its unique hue (from latin. *aurum*) and the highest malleability and ductility among metals. For those reasons, metallic gold is used as a decorative element in jewellery and architecture. Its extensive applications also result from its chemical resistance, comparable to the noble gases. Metallic gold does not undergo oxidation in air and reacts only with *aqua regia* ("royal water"). Low reactivity became the reason for the lack of its practical applications in chemistry, in particular in catalysis, in comparison to other metals such as palladium, ruthenium, or copper. For many years, gold has been regarded as a chemical curiosity, completely extraneous in the chemical laboratory. Along with the progress of knowledge, this statement proved untrue, and the first decade of the 21st century has witnessed a "gold rush" in organic chemistry, in particular in catalysis. Gold complexes with their intrinsic π-acidic properties, that is the ability to interact with π-electrons of unsaturated bonds, allow to perform many useful transformations of alkenes, alkynes and allenes (non-viable with other metals) in an efficient manner due to the lack of by-products (the so-called *atom economy*). The design of new chiral gold catalysts for the development of effective enantioselective processes constitutes a key challenge of modern catalysis. Moreover, it is poorly documented in the case of gold-catalyzed transformations and carries significant cognitive value. Selective formation of one enantiomer (chemical compound which is not identical with its mirror image) is the fundamental basis of the functioning of living organisms consisting of proteins, carbohydrates, and nucleic acids, as well as modern drug design (where only one enantiomer exhibits biological activity and the second can be ballast or a poison). The synthesis of a specific enantiomer in highly selective and economical fashion leading to a structurally complex product is the Holy Grail of modern catalysis. The main objective of this proposal is the possibility to get closer to this goal, applying new stable gold complexes which are poorly documented in the literature.



The innovative approach of the project entails the development of a new class of chiral gold complexes and their subsequent application in the transformations of simple substrates leading to structurally complex products. The key solution is to apply N-heterocyclic carbenes as the ligands, which would enable the development of organometallic chemistry of other metals by the synthesis of stable complexes. The use of well-defined metal complexes derived from amino alcohols provides a creative solution for the development of novel or difficult enantioselective chemical transformations leading to complex structural motifs present in natural products or drugs. The synthesis of stable gold complexes would also provide an opportunity to gain knowledge of poorly understood mechanistic aspects of gold catalysis, both from the experimental and the theoretical angle.

Stable gold complexes also open the opportunity to evaluate their biological activity. Gold compounds are often used in medicinal chemistry due to their low toxicity in comparison to other metals. Rather surprisingly, the application of chiral gold compounds is marginally recognized which is bound to affect the development of this research field.

In conclusion, the proposed original approach towards the synthesis of stable gold complexes and their use in challenging transformations will greatly contribute to the development of modern gold catalysis, offering simultaneously a chance for mechanistic studies and applicability in medicinal chemistry.