

1 Literature Review

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Anion-Induced Enantioselective Cyclization Catalyzed by Cationic Gold Catalysts
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1.1 Homogeneous gold catalysis

1.1.1 Introduction

Since millennia, mankind has used gold in the activities of daily living. Because of the malleability, ductility, and the tarnish resistance of gold, it has been used for eras as currency as well as in the manufacturing of jewelry. Gold is also correlated to diverse industrial processes thanks to its properties of resisting oxidation from air or moisture. Moreover, gold's excellent chemical resistance and conductivity have made this metal a key component in electronics such as mobile telephones, laptop computers, space travel, and many other high-tech applications.

It is well-known that gold has been used for many years in the field of medicine and dentistry due to its non-allergenic and non-toxic characteristics.^[1] Gold is at the heart of the treatments for rheumatoid arthritis ^[2] and is under investigation as a potential treatment for a number of other diseases such as cancer.^[3] In addition to this, gold is highly resistant to bacteria therefore it can be used for implants.^[4] Gold nanoparticles have been utilized to detect some diseases in an effective and non-invasive technique in which particles of a radioactive gold isotope are implanted into tissues to serve as a radiation source in the treatment of certain forms of cancer.^[5]

Contrarily, employment of gold in the field of organic chemistry arose only in the last few decades. This can be attributed to the fact that chemists used to consider gold as a chemically inert and very expensive metal although rhodium and platinum, which are commonly used in catalysis, were much more expensive than gold. Likewise, the high toxicity associated with mercury catalysis drove the interest of chemists towards gold, its neighbor in the periodic table.

The remarkable growth in the development of homogeneous gold-catalyzed processes in the past decade indicates that chemists have realized the importance of using gold complexes in organic chemistry.^[6] Nevertheless, these recent developments in the field of gold catalysis have heightened the need for gold in organic synthesis transformations due to its excellent functional group tolerance, its low sensitivity to moisture, and its ability to conduct reactions at ambient conditions.

Moreover, in the arena of employing gold catalysts in natural product synthesis, there has been a recent surge in interest and research, since gold is playing a key role in the synthesis of a variety of natural products (*vide infra*).^[7]

1.1.2 Relativistic effects

For a thorough understanding of the reactivity modes in gold complexes, Pyykkö *et al.* studied the relativistic effects in the periodic table's sixth period which not only expounded the contraction of the *s*- and *p*-orbitals of this period's elements but also were more significant for gold than any other metal (**Figure 1**).^[8] In this case the electrons of *s*- and *p*-orbitals are therefore closer to the nucleus and have greater ionization energies leading to an increase in the π -acidity of gold comparing to other metals like silver for example. Consequently, an expansion of the *5d*- and *4f*-orbitals, which are more shielded from the core, is taking place causing the increase of electron delocalization leading to the increase of the backbonding.^[9]

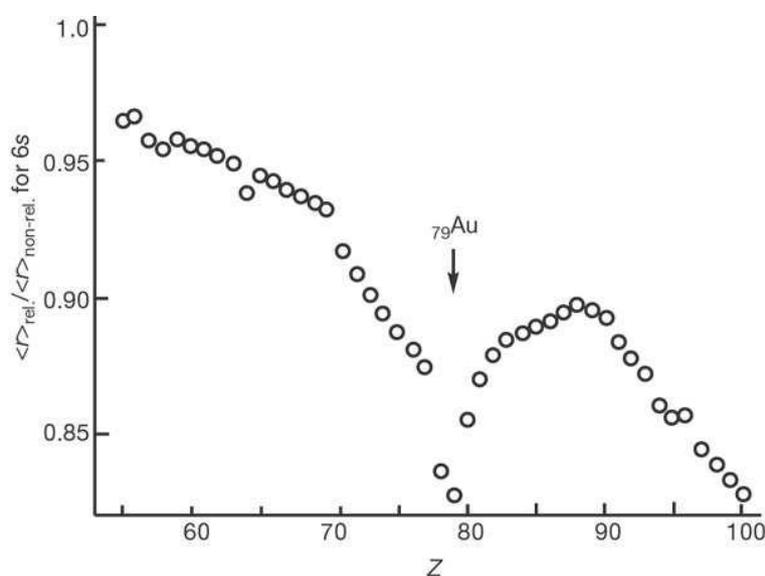


Figure 1:^[8a] Calculated relativistic contraction of the 6s orbital.

Since the 6*s*-orbital is suffering from relativistic contraction, the Au-L (gold-ligand) bond length in gold complexes will be shortened in comparison to its neighboring metals in the sixth period (Pt and Hg).

According to the above-mentioned facts, the relativistic effects should be taken into account during the later discussion of π -acidity and alkynophilicity of gold catalysts.

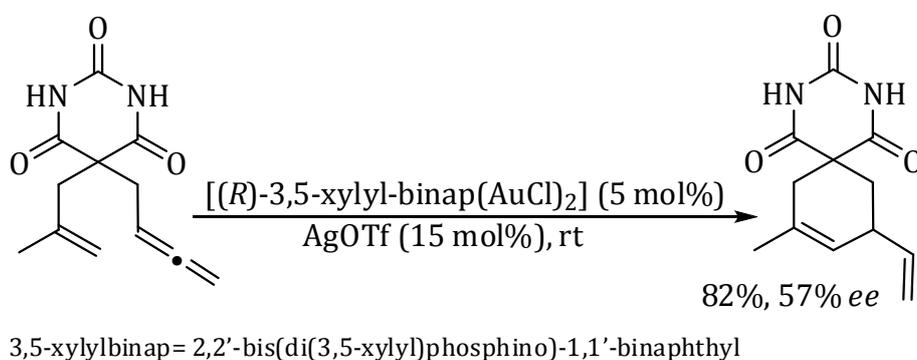
1.1.3 Gold catalysis: π -acidity

The π -acidity of gold(I) species is considered to be one of the most important implications related to the relativistic effects. Despite the fact that Pearson's HSAB principle suffers from profound limitations,^[10] a vast number of studies considered

cationic gold(I) a “soft” Lewis acid^[6i, 11] due to its large and diffuse *d*-orbitals. Therefore, cationic gold(I) species prefer to bind to phosphine ligands or any other soft ligands.^[12]

Additionally, the relativistic contraction of the valence *s*- and *p*-orbitals in cationic gold(I) complexes led to high electronegativity of Au (2.54) compared to Ag (1.9). Therefore, it revealed strong Lewis acidity character and a coordination site will be available for accepting an electron pair. Accordingly, cationic gold(I) species will have relatively low-lying LUMO and the binding in cationic R₃PAuL will be achieved through the low-lying *s*-orbital.^[13]

Thus, gold catalysts predominantly activate “soft” nucleophilic π -systems such as alkynes, alkenes, and allenes, and this is also the main reason for the functional groups tolerance gold catalysis exhibits (**Scheme 1**).^[14]



Scheme 1: Gold(I)-catalyzed cycloisomerization

As it is shown in **Scheme 1** for example, gold (I) catalyst exhibit pronounced functional group tolerance and the pyrimidinetrione did not decompose.

1.1.4 Bonding in gold(I) complexes

1.1.4.1 Bonding geometry to phosphine

Turning now to gold(I) complex geometry, experimental evidence reveals that although three- and four-coordinate gold(I) complexes are known, they are much less common.^[15] Gold(I) has a pronounced tendency to coordinate in a linear geometry with two ligands yielding bond angle of 171-179° (**Figure 2**).^[16] Consequently, due to this bond angle the binding site of the metal will be far away from a chirality-inducing ligand environment rendering asymmetric catalysis using gold(I) complexes employing optically active ligands to be very challenging.

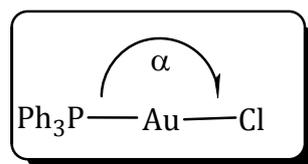
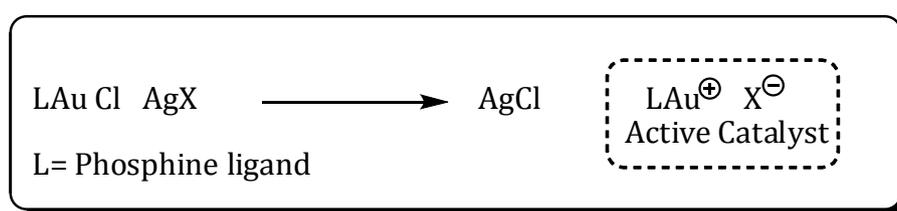


Figure 2:^[14] Structure of $[(PPh_3)AuCl]$ in the solid state; $\alpha=179.68^\circ$, $r_{Au-P}= 2.235 \text{ \AA}$, $r_{Au-Cl}= 2.279 \text{ \AA}$

Furthermore, in order to obtain an active gold species (LAu^+) bearing an empty coordination site, one of the ligands should be abstracted. Therefore, silver salts are commonly used in an *in situ* ligand substitution step to replace chloride by a weakly coordinating counterion (**Scheme 2**)

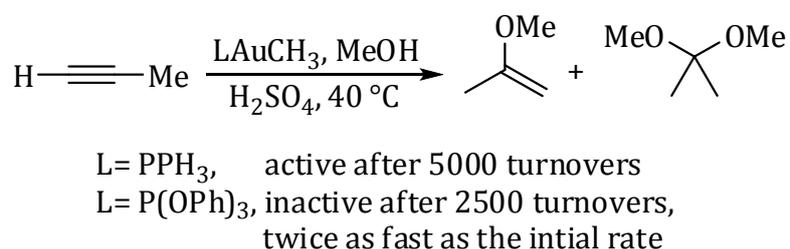


Scheme 2: Formation of gold active species

1.1.4.2 Bonding geometry to alkynes and π -system activation

Owing to its propensity to decompose to metallic gold after few turnovers, gold(I) was considered “catalytically dead”.^[17] Nowadays, a diverse range of transformations have been developed based on the activation of alkynes by gold salts and complexes.

In 1998, Teles published a paper in which he reported for the first time the utility of cationic phosphine gold(I) complexes in catalyzing the addition of alcohols to alkynes representing the first highly active and long-lasting gold(I) catalyst (**Scheme 3**).^[18]



Scheme 3: Gold(I)-catalyzed alcohol addition to propyne

Also, applying the Dewar-Chatt-Duncanson (DCD) model, which presents the bonding situation for alkenes or alkynes as π -ligands bound to gold(I) complexes indicates that a charge-transfer will take place from the π -system of the ligand through σ -bonding from its p -orbital to an empty metal d -orbital of suitable symmetry.^[19] Concomitantly, π -

interaction will take place through back-donation from a filled d -orbital of the metal into the empty π^* -orbital of the ligand. Two more π and δ interactions are also involved in the interaction between the metal and alkyne ligand, the δ interaction contributing only very weakly to the bonding because of the poor overlapping (**Figure 3**).

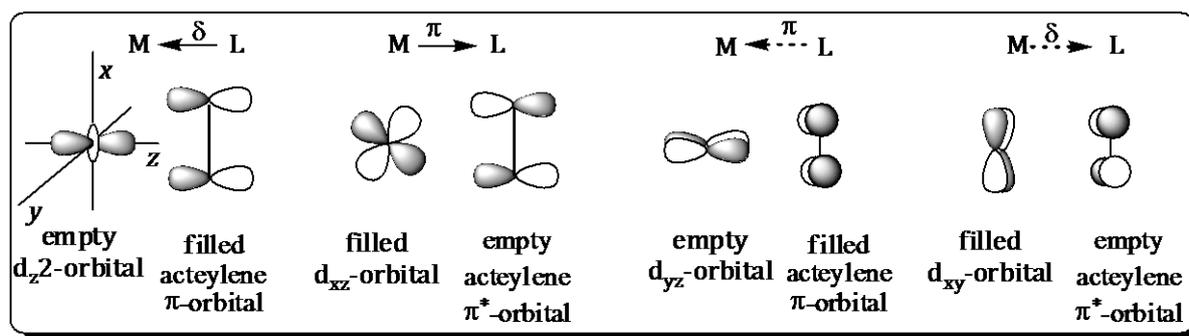


Figure 3: Qualitative orbital diagram illustrating interaction between gold and alkyne ligand

As gold complexes follow this DCD mode of interaction, the geometry of the carbon atoms will be changed from trigonal planar (alkene) and linear (alkyne) to a bent geometry and this would attribute to the lengthening of the resulting activated C-C multiple bond in alkynes and also alkenes. This change in geometry was confirmed *via* spectroscopic data and isolation of such complexes (**Figure 4**).^[20]

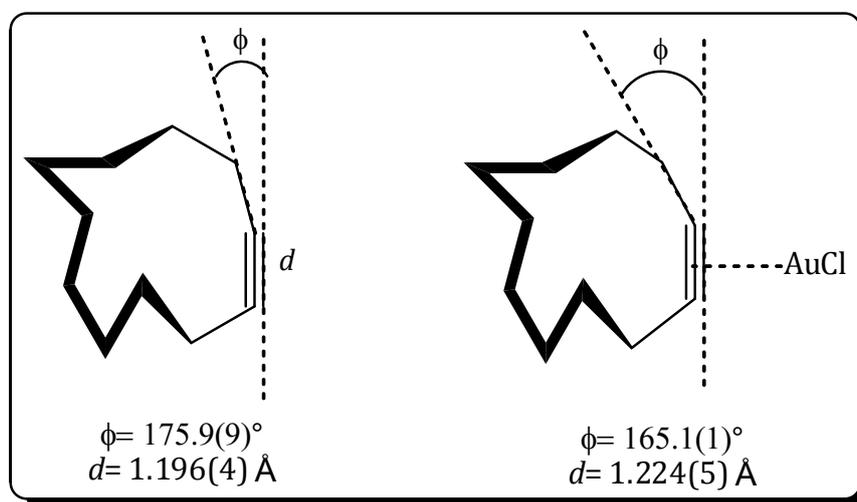


Figure 4: Effect of coordination of gold(I) to cyclododecyne on the geometry

Nevertheless, calculations suggested that the metal center will exhibit a significant reluctance to back-donate electrons to the π -system.^[21] In particular, 64% of the interaction with the acetylene ligand model $[\text{Au}^+(\text{C}_2\text{H}_2)]$ would be due to the filled p -orbital of the C-C multiple bond while the back-donation from the metal would