Echavarren Research Group

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Abstract

The major focus of our research efforts is in the area of "OMCOS" (*organometallic chemistry directed towards organic synthesis*). We aim at discovering new catalytic transformations, the understanding of their mechanisms, and the application of these new catalytic reactions for the synthesis of biologically active natural products and polyarenes of importance in material science.

In 2010, we discovered the first [2+2] gold-catalyzed cycloaddition for the synthesis of cyclobutenes. We have now studied the mechanism, which shows that the reaction proceeds in a stepwise manner via cyclopropyl gold(I) carbenes (Figure 1). In addition, 1,3-butadienes are also formed in the case of *ortho*-substituted aryl alkynes by a metathesis-type process.

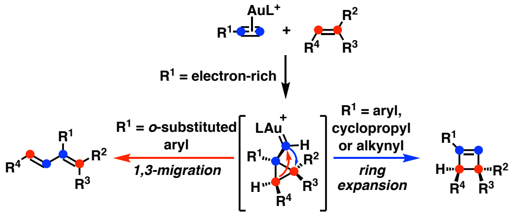


Fig. 1 – Gold(I)-catalyzed [2+2] cycloaddition vs. rearrangement.

The first enantioselective intermolecular gold(I)-catalyzed [2+2] cycloaddition of terminal alkynes and alkenes was achieved using non C2-chiral Josiphos digold(I) complexes as catalysts, by the formation of the monocationic complex. This new approach was applied to the enantioselective total synthesis of rumphellaone A (Figure 2).

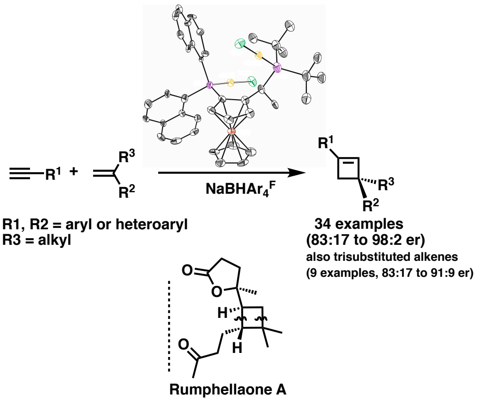


Fig. 2 – Enantioselective gold(I)-catalyzed [2+2] cycloaddition.

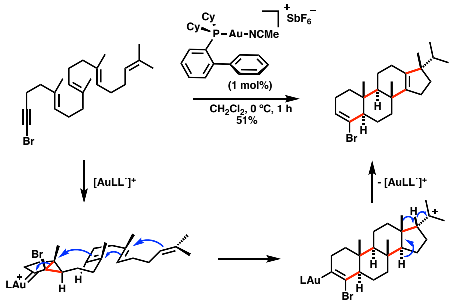


Fig. 3 – Gold(I)-catalyzed [2+2+2] cycloaddition of oxo-1,5-enynes

We reported the cyclization of functionalized 1,5-enynes to form polycyclic compounds that was achieved under mild conditions and with low catalyst loadings. The polycyclization was extended to the bioinspired formation of up to four carbon-carbon bonds in a single transformation (to form steroid-like compounds (Figure 3).

A highly stereoselective gold(I)-catalyzed cis-vinylcyclopropanation of alkenes has been developed via allylic gold carbenes, generated at 75 ºC via retro-Buchner reaction of 7-alkenyl-1,3,5-cycloheptatrienes, which react with alkenes to form vinylcyclopropanes (Figure 4).

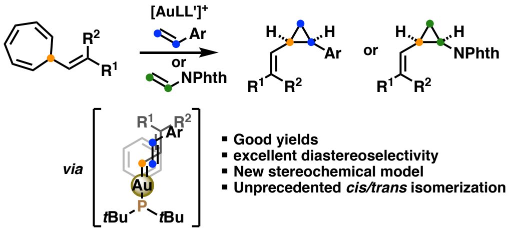


Fig. 4 – Vinylcyclopropanation via retro-Buchner reaction.

The formal (3 + 2) cycloaddition between terminal allenes with aryl or styryl gold(I) carbenes generated by retro-Buchner reaction of 7-substituted 1,3,5-cycloheptatrienes leads to indenes and cyclopentadienes, respectively (Figure 5). These cycloadditions have been applied to the construction of the carbon skeleton of the cycloaurenones and the dysiherbols as well as to the total synthesis of (±)-laurokamurene B.

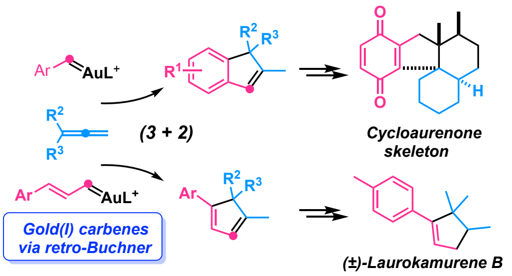


Fig. 5 – Annulation of gold(I) carbenes with allenes.

We have also prepared well-characterized chloromethylgold(I) complexes by reaction of trimethylsilyldiazomethane with the corresponding gold chloride precursors (Figure 66). Activation of these gold(I) carbenoids with a variety of chloride scavengers promotes reactivity typical of metallocarbenes in solution

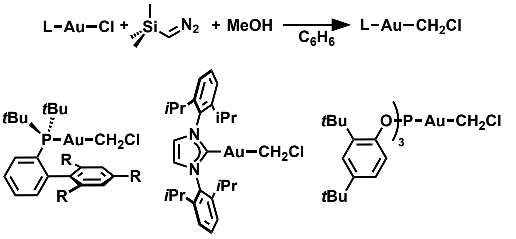
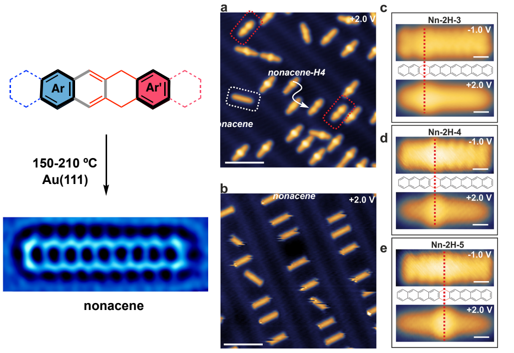


Fig. 6 – Gold(I) carbenoids.

We have also developed the regioselective alkynylation of naphthols at the *peri* position of the hydroxyl group in the presence of $[RuCl_2(p\text{-cymene})]_2$ as the catalyst and highly chemoselective *N*-amidation of tertiary amines under catalytic conditions using Ag(I) to form aminimides by nitrene transfer from PhI=NTs.

Finally, we have also succeeded in developing the first on-surface synthesis of nonacene by dehydrogenation of an air-stable partially saturated precursor, which was prepared by using gold(I)-catalysis. This precursor was aromatized by using a combined scanning tunnelling and atomic force microscope (STM/AFM) tip as well as by on-surface annealing (Figure 4). This transformation allowed the in-detail analysis of the electronic properties of nonacene molecules physisorbed on Au(111) by scanning tunnelling spectroscopy (STS) measurements, which were corroborated by density theory functional (DFT) calculations thus confirming the spatial mapping of its molecular orbitals.



a: nonacene-H4 after annealing to 150 °C; ***b:*** at 210 °C
c-e: filled- and empty-state images of **nonacene-H2** isomers

Fig. 7 – Synthesis of nonacene

Articles

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