

Echavarren Research Group



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Laboratory Engineer: Imma Escofet

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Summer Fellows: Elena de Orbe

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Abstract

Our research group works in the “OMCOS” (*organometallic chemistry directed towards organic synthesis*) arena, with a focus on the discovery of new catalytic transformations and the understanding of their mechanisms. In the

last few years, we have developed new gold catalyzed reactions for the activation of alkynes. Some of these new reactions have been applied for the synthesis of complex, biologically active natural products. We are also interested in the synthesis of nanographenes and other related molecules of importance in material science.

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1,n-Enynes give rise to a series of fascinating cycloisomerizations in the presence of gold(I) catalysts (Figure 1). The development of intermolecular reactions of alkynes with functionalized has been more challenging.

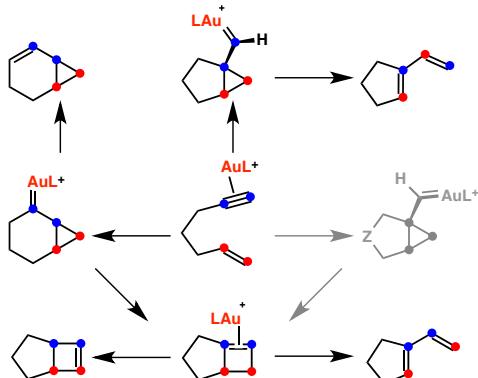


Fig. 1 – Gold(I)-catalyzed cycloisomerization manifold of 1,6-enynes.

Following our report on the first example of a gold(I)-catalyzed reaction of terminal alkynes with alkenes to form cyclobutenes in 2010, we examined the intermolecular gold(I)-catalyzed reaction of terminal alkynes with oxoalkenes to form 8-oxabicyclo[3.2.1]oct-3-enes by [2+2+2] cycloaddition process that proceeds through cyclopropyl-gold(I) intermediates (Figure 2).

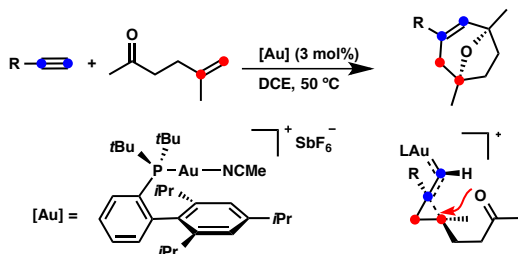


Fig. 2 – Intermolecular [2+2+2] alkyne/alkene/carbonyl cycloaddition of alkynes with oxoalkenes.

The [2+2] cycloaddition reaction has also been applied for the first time for the synthesis of large macrocycles by using the same cationic gold(I) catalyst we used for the preparation of oxabicyclo[3.2.1]oct-3-enes (Figure 3).

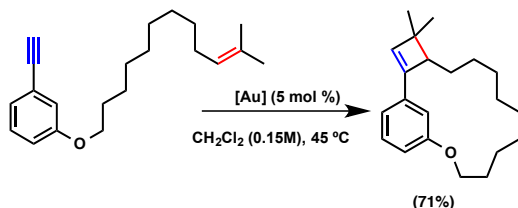


Fig. 3 – Macrocyclization via [2+2] cycloaddition of alkynes with alkenes.

In another intermolecular process, phenols were obtained by the reaction of furans with terminal alkynes using cationic IPr gold catalysts (Figure 4). Products of hydroarylation are not formed in significant amounts. Furthermore, 1,3-diphenylisobenzofuran reacted with terminal alkynes via a cyclopropyl gold-carbene to form selectively 2,3-disubstituted indenenes via a Friedel-Crafts type annulation.

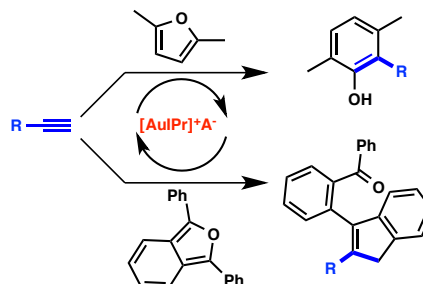


Fig. 4 – Gold(I)-catalyzed intermolecular reaction of furans with alkynes.

We also developed a synthesis of tetrazoles by gold(I)-catalyzed reaction of terminal alkynes with TMSN₃ by a C-C cleavage (Figure 5).

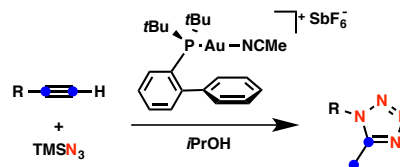


Fig. 5 – Gold(I)-catalyzed synthesis of tetrazoles.

We have prepared a robust hexanuclear (Au)₆ cluster with two of the Au(I) centers bound only to two carbons and four other Au(I) centers by 3c-2e bonds (Figure 6). This gold cluster is active in a variety of gold-catalyzed reactions.

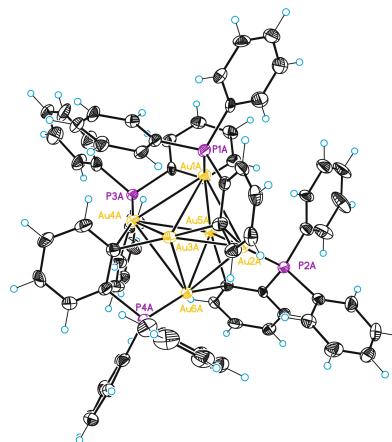


Fig. 6 – A hexanuclear gold(I) cluster.

We have demonstrated that the incomplete removal of chloride ligand in the formation of

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cationic gold(I) catalysts could lead to false negative results when using silver-promoted chloride abstraction. This is due to the formation of chloride-bridged dinuclear gold(I) species.

Continuing with our interest in applying gold chemistry for the synthesis of diverse biologically relevant natural products, we have completed the first enantioselective synthesis of (+)-schisanwilsonene A (Figure 7). The hexahydroazulene skeleton was built by a gold(I)-catalyzed reaction, followed by a divinyl cyclopropane rearrangement. In this total synthesis, gold(I) orchestrates one of the most complex transformations that has been applied thus far in total synthesis.

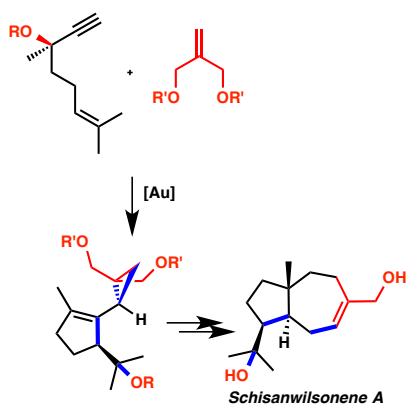


Fig. 7 – Total synthesis of the antiviral sesquiterpene (+)-schisanwilsonene A.

A gold(I)-catalyzed allene-vinylcyclopropane cycloisomerization led to the tricyclic framework of the protoilludanes in a single step by a reaction that involves a cyclopropane ring expansion and a Prins cyclization (Figure 8).

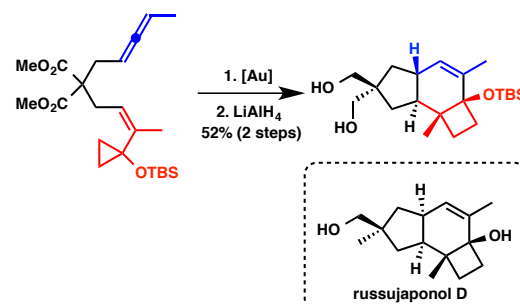


Fig. 8 – Approach for the synthesis of the protoilludanes by a gold(I)-catalyzed allene-vinylcyclopropane cycloisomerization.

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