

Echavarren Research Group



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Laboratory engineer: Imma Escofet

Visiting students: Gabriela Araceli Fernández (July-Dec.)

Summer fellows: Ofelia Rodríguez

Administrative support: Sònia Gavalrà

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, the understanding of their mechanisms, and the application of these catalytic reactions for the synthesis of biologically active natural products and polyarenes of importance in material science.

We have found that the intermolecular [2+2] cycloaddition of terminal alkynes with alkenes to form cyclobutenes, a reaction that we discovered in 2010, can be performed under mild conditions in higher yields by using $t\text{BuXPhosAu}(\text{MeCN})\text{BAR}_4\text{F}^-$ with a bulky and soft anion (Figure 1). A kinetic study on the [2+2] cycloaddition reaction of alkynes with alkenes is consistent with an scenario in which the rate-determining step is the ligand exchange to generate the $(\eta^2\text{-phenylacetylene})\text{gold}(\text{I})$ complex.).

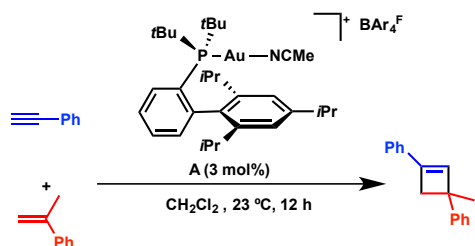


Fig. 1 – Intermolecular [2+2] alkyne/alkene cycloaddition with a new generation of catalysts bearing BAR_4F^- as the anion.

We have studied in detail the mechanism of the retro-Buchner reaction (retro-carbenation) catalyzed by gold(I), a transformation that our group discovered in 2011 and that applied for the development of a new cyclopropanation of alkenes (Figure 2). According to DFT calculations, the gold-catalyzed cleavage of the norcaradienes, which are in equilibrium with the cycloheptatrienes, occurs stepwise, although the two carbon-carbon cleavages occur in a rather flat potential energy surface.

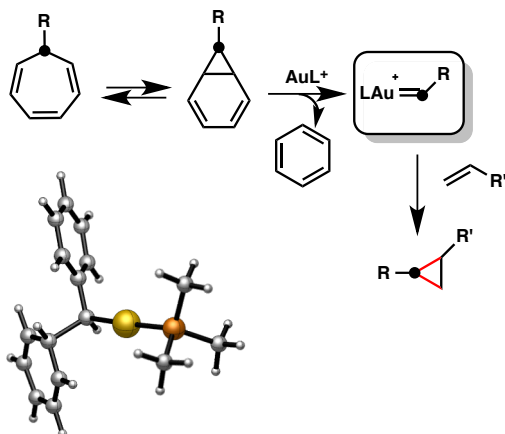


Fig. 2 – Gold(I)-catalyzed retro-Buchner reaction (retro-carbenation).

Gold(I) carbenes generated by the retro-carbenation reaction react intramolecularly with alkenes to form indenenes in a reaction in an electrophilic addition process (Figure 3).

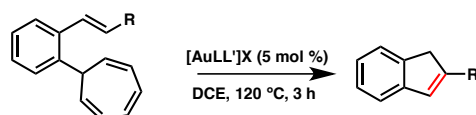


Fig. 3 – Synthesis of indenenes by gold(I)-catalyzed retro-Buchner reaction (retro-carbenation).

Similarly, the intramolecular reaction of the gold(I) carbenes with arenes leads to fluorenes in a general manner (Figure 4).

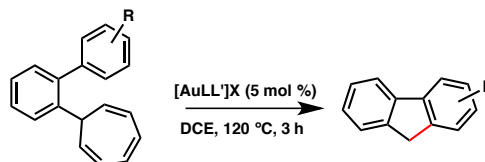


Fig. 4 – Synthesis of fluorenes by gold(I)-catalyzed retro-Buchner reaction (retro-carbenation).

The intermolecular gold(I)-catalyzed reactions of propargyl carboxylates, 1,6-enynes, or 7-substituted 1,3,5-cycloheptatrienes with furans afford cyclopentenones, polyenes or polycyclic compounds by related mechanisms initiated by the electrophilic addition of gold(I) carbenes to furans followed by ring-opening (Figure 5).

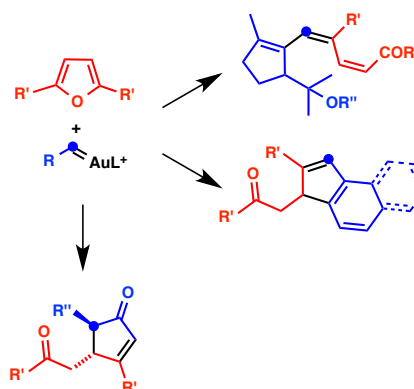


Fig. 5 – Different reactions of gold(I) carbenes with furans.

We also developed a synthesis of substituted cyclopentenones by a formal (4+1) cycloaddition from methylenecyclopropanes or cyclobutenes with gold(I) carbenes generated under catalytic conditions by retro-Buchner reaction of 1,3,5-cycloheptatrienes (Figure 6).



Fig. 6 – Synthesis of cyclopentenones by (4+1) cycloaddition.

As part of a program on the synthesis of natural products by gold(I)-catalyzed cascade processes triggered by the selective activation of alkynes, we completed the highly concise syntheses of three representative aromadendrenes from a single precursor by a stereodivergent gold-catalyzed reaction that establishes four new stereogenic centers from a single one (Figure 7). The three natural sesquiterpenes (-)-epiglobulol, (-)-4 α ,7 α -aromadendranediol, and (-)-4 β ,7 α -aromadendranediol were synthesized in 7 steps in 12, 17 and 15% overall yields, respectively, from commercially available (*E,E*)-farnesol, which constitutes the shortest total syntheses of these natural compounds. This route could be easily extended for the enantioselective synthesis of any enantiomer of other aromadendrenes and non-natural analogues.

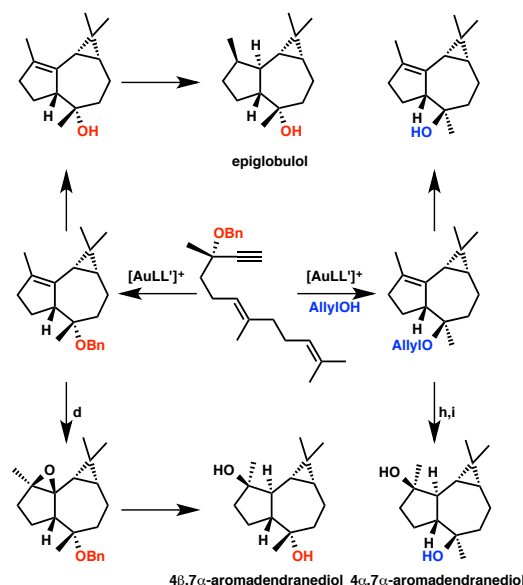


Fig. 7 – Total synthesis of aromadendrene by a stereodivergent gold-catalyzed reaction.

Articles

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“Gold(I) as Artificial Cyclase: Short Stereodivergent Syntheses of (-)-Epiglobulol, (-)-4 β ,7 α , and (-)-4 α ,7 α -Aromadendranediols”

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Book Chapters

“Cycloisomerization Reactions of 1,n-Enynes”
Huguet, N.; Echavarren, A. M.

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“Gold-catalyzed hydroarylation of alkynes”
Muratore, M. N.; Echavarren, A. M.
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edited by Z. Rappoport, J.F. Liebman and I.
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