Gold(I)/(III)-catalyzed synthesis of 2-substituted piperidines; valency-controlled cyclization modes

Nobuyoshi Morita
Showa Pharmaceutical University, Japan

Gold catalysts were initially recognized as π-acidic catalysts that activate unsaturated bond (alkynes, allenes and alkenes) for nucleophilic attack to form C-C, C-O, C-N, and C-S bonds. Later, some groups reported the oxophilic character of gold (III) catalysts, which efficiently activated oxygen functionalities even in the presence of an unsaturated bond. We rationalized these observations in terms of the hard and soft acids and bases (HSAB) principle, which states that metal ions in low valence states soft character, whereas metal ions in high positive oxidation states show hard character. Thus, gold(I) catalysts may behave as soft acids and gold (III) catalysts as hard acids. On the basis of this working hypothesis, we developed a synthetic method to obtain two types of cyclic ethers from the same propargylic alcohols by means of valency-controlled gold-catalyzed regiodivergent activation. In order to extend our strategy, we turned our attention to the use of nitrogen nucleophile in place of oxygen nucleophile and explored the synthesis of piperidines from propargylic alcohols bearing nitrogen functionality at the terminal position. Thus, use of hard gold (III) catalyst which resulted in cyclization to furnish piperidines having an acetylenic moiety, due to coordination of hard gold (III) to the oxygen atom at propargylic position. On the other hand, treatment of propargylic alcohols with soft gold (I) catalyst induces Meyer-Schuster rearrangement to afford α,β-unsaturated ketones, which undergo intra-molecular aza-Michael addition to give piperidines bearing carbonyl gorup, due to the activation of the triple bond by coordination of soft gold(I).

Biography

Nobuyoshi Morita has completed his PhD from Osaka University in the year 2003 and then trained as a Post-doctoral fellow at Dortmund University of Technology in Germany (Prof. Norbert Krause). He was then recruited as an Assistant Professor of Organic Chemistry in Showa Pharmaceutical University (SPU) in 2006 and became an Associate Professor of Organic Chemistry in SPU in the year 2016. His researches focus on gold catalyzed reactions.

morita@ac.shoyaku.ac.jp

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