Tetrahedron Letters 58 (2017) 4420–4426

Contents lists available at ScienceDirect

Tetrahedron Letters

journal homepage: www.elsevier.com/locate/tetlet

Digest paper

Recent applications of gold-catalyzed cascade reactions in total synthesis of natural product

Kenji Sugimoto *, Yuji Matsuya

Graduate School of Medicine and Pharmaceutical Sciences, University of Toyama, Toyama 930-0194, Japan

ARTICLE INFO

Article history:
Received 22 September 2017
Revised 10 October 2017
Accepted 11 October 2017
Available online 13 October 2017

Keywords:
Gold catalysis
Cascade reaction
Total synthesis

ABSTRACT

From the point of the view of the synthetic efficiency, the concept 'step economy' was required in total synthesis of natural product. Recently, versatile gold-catalyzed cascade reactions have been developed, and relating reports on practical applications in total synthesis has increased. This digest focuses and summarizes the gold-catalyzed reaction cascades in natural product synthesis during last five years with brief discussion on the reaction mechanism of the key gold-catalyzed cascade transformations.

Contents

Introduction

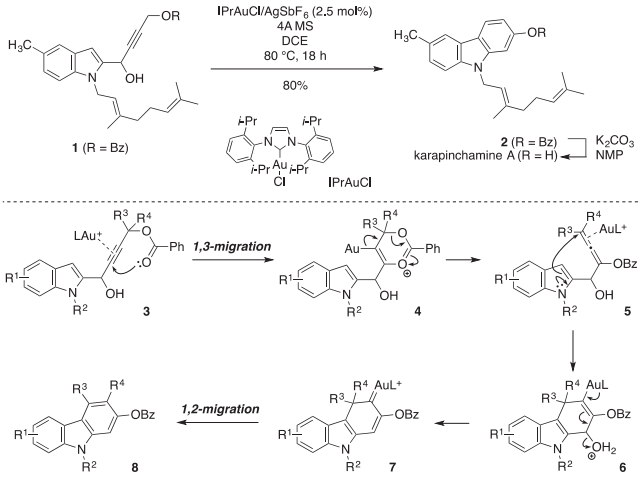
To date, total syntheses of natural products have played important roles in the field of organic chemistry. For example, classically, total synthesis has been a powerful tool to confirm a structure of natural product,[1] and recently some structural revisions have been reported indeed based on total syntheses of previously proposed structures.[2] Furthermore, the natural products have been believed as a storehouse of various biologically active substances and have fascinated not only biologists but synthetic organic chemists.[1] Actually, with the know-hows matured in total synthesis, the some natural products or their synthetic derivatives on the market have been manufactured. However, beyond the total syntheses, ideal synthesis has come to be required from the point of view of the efficiency. The one of the several concepts which meets the demand would be step economy minimizing the total number of steps for the target molecule.[3] At this point, cascade reactions, which can provide quantum structural modifications on the organic molecules forming several chemical bonds in one-pot process, potentially open up novel synthetic strategies to complex natural products.[4] Recently, because of their high alkynophilicity and functional group tolerance, the gold catalysts have been widely utilized in the field of natural product synthesis,[5] and especially paid attentions as an activator of cascade reaction to accord with step economy. In this digest, we will pick up and showcase the outstanding works of gold-catalyzed cascade reaction leading to carbocyclic framework, oxygen heterocycles, and nitrogen heterocycles in total syntheses of natural products during last five years.

Cascade reactions for carbocycles

Carbazole **2**, which was precursor of natural product karapinchamine A, could be prepared by gold-catalyzed cascade cyclization of indole **1** (Scheme 1).[6] The reaction would commence with

* Corresponding author.
E-mail address: ksugimo@pha.u-toyama.ac.jp (K. Sugimoto).

https://doi.org/10.1016/j.tetlet.2017.10.029
0040-4039/

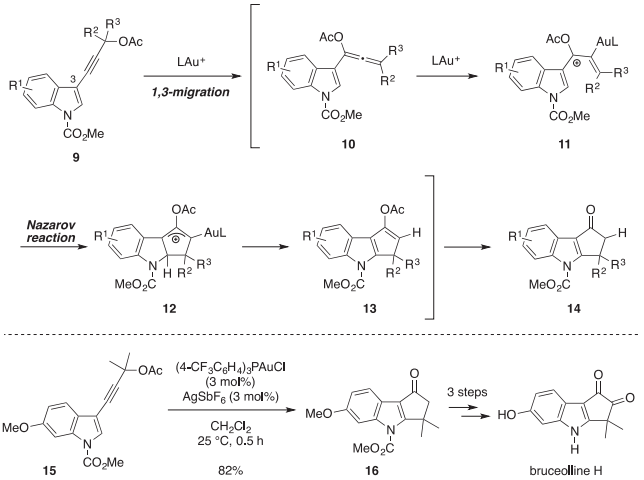


Scheme 1. Total synthesis of karapinchamine A.

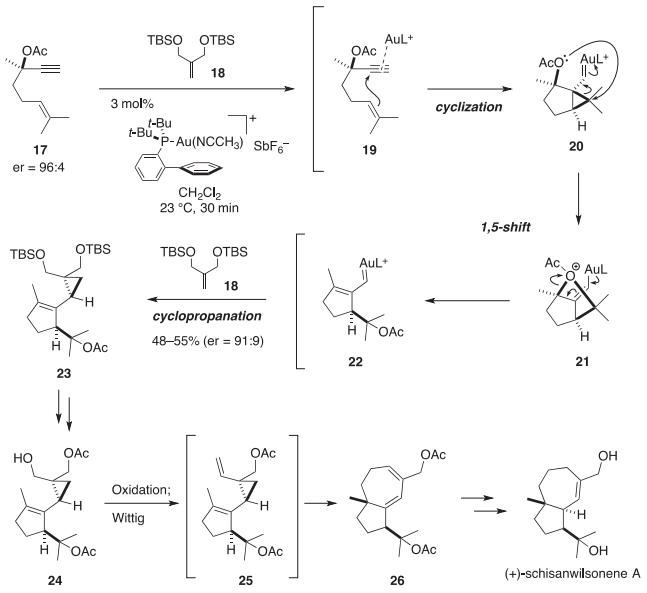
1,3-migration of benzoyloxy group of **3** followed by nucleophilic attack of indolyl C3 on the resultant allene unit (**5** to **6**). After elimination of water, 1,2-migration of gold carbenoid **7** afforded the carbazole **8**. The reaction was scalable and finally melanogenesis inhibitor karapinchamine A could be firstly synthesized in 5 g scale.

For a construction of cyclopenta[*b*]indol-1-ones, a cascade gold-catalyzed 1,3-migration/Nazarov reaction was found to be effective (Scheme 2).[7] Exposure of 1-(3-indolyl)-propargyl acetate **9** to $(4\text{-}CF_3C_6H_4)_3PAuCl/AgSbF_6$ system immediately afforded **14** through the 1,3-migration of acetoxy group on **9** followed by 4π-electrocyclization of **11** and hydrolysis of resultant vinyl acetate **13**. The advanced substrate **15** could be uneventfully applied for a first synthesis of bruceolline H.

1,6-Enynes were proved to be splendid precursors for highly functionalized cyclopentenes via gold-catalyzed cascade reaction by Echavarren and co-workers in 2009.[8] They recently applied the useful method for the syntheses of some terpenes. (+)-Schisanwilsonene A, antiviral sesquiterpenoid, could be effectively synthesized via a cyclization/1,5-migration/cyclopropanation sequence by gold catalysis (Scheme 3).[9] In the presence of Au(I) catalyst, 1,6-enyne **17** (er = 96:4) could be transformed into the bicyclic intermediate **20**. A 1,5-shift of acetoxy group of **20** through **21** would afford an α,β-unsaturated gold carbene **22**. The cyclopentene **23** (er = 91:9) could be generated by a cyclopropanation reaction between the carbene **22** and the olefin



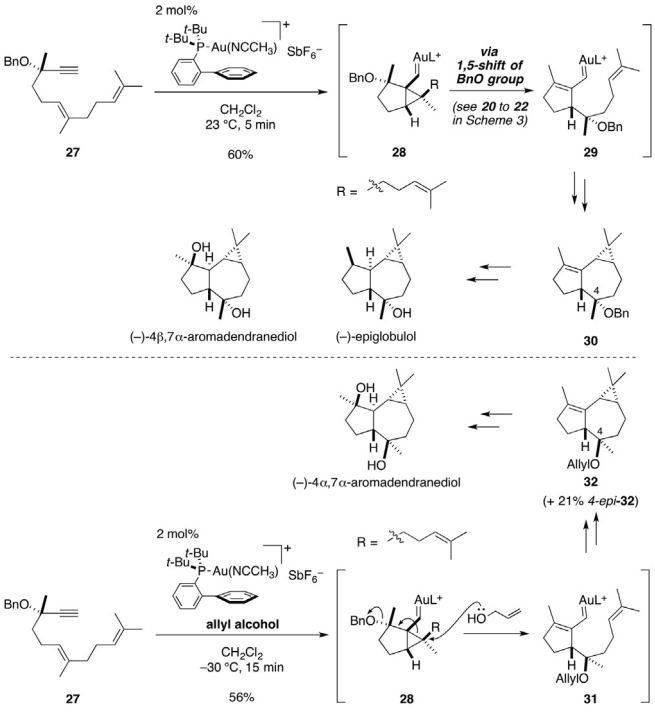
Scheme 2. Total synthesis of bruceolline H.



Scheme 3. Total synthesis of (+)-schisanwilsonene A.

18. The vinyl cyclopropane functionality in **24** was further utilized for [3,3] sigmatropic rearrangement of divinylcyclopropane **25** to furnish a fused seven-membered ring in **26** effectively.

This strategy worked well via intramolecular fashion and unique 5-7-3 tricyclic skeleton in natural sesquiterpenes could be constructed in one-pot process (Scheme 4).[10] Interestingly, starting with the common dienyne (*S*,*E*)-**27** (prepared from (*E*,*E*)-farnesol), stereodivergent synthesis was accomplished. Whereas the reaction conducted with gold(I) catalyst afforded the tricyclic **30**, the reaction in the presence of gold(I)-catalyst with allyl alcohol under lower temperature gave the **32** (equivalent of 4-*epi*-**30**), which should be synthesized from commercially unavailable (*E*,*Z*)-farnesol. Thus, the gold(I) acts as an artificial cyclase and enables a



Scheme 4. Total syntheses of (−)-epiglobulol and its derivatives.