Journal of Molecular Catalysis A: Chemical 424 (2016) 323–330

Contents lists available at ScienceDirect

Journal of Molecular Catalysis A: Chemical

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

Au-complex containing phosphino and imidazolyl moieties as a bi-functional catalyst for one-pot synthesis of pyridine derivatives

Da Yang, Huan Liu, Dong-Liang Wang, Yong Lu, Xiao-Li Zhao, Ye Liu*

Shanghai Key Laboratory of Green Chemistry and Chemical Processes, School of Chemistry and Molecular Engineering, East China Normal University, 3663 North Zhongshan Road, Shanghai 200062, P. R. China

ARTICLE INFO

Article history:
Received 1 August 2016
Received in revised form 5 September 2016
Accepted 6 September 2016
Available online 8 September 2016

Keywords:
Bi-functional catalyst
Sequential reactions
Gold complexes
Pyridine derivatives
One-pot synthesis

ABSTRACT

The complex of **Au-L1** containing imidazolyl ring and the phosphine-ligated-Au moiety was synthesized and applied as the efficient bi-functional catalyst for the one-pot sequential condensation/annulation reaction for the synthesis of pyridine derivatives. It was found that, as for **Au-L1**, the involved imidazolyl group acted as a Lewis base to catalyze the condensation of carbonyl compounds with propargylamine to form the imino intermediate, and the involved Au^+-complex species with alkynophilicity corresponded to the subsequent activation of imino-tailed alkynyl to afford dehydropyridine intermediate. The latter proceeded auto-oxidation reaction to afford the pyridine derivatives. The observed sequential catalysis over **Au-L1** proved more efficient than that over the mechanical mixtures of the Au-complex (**Au-L2**) and *N*-methylimidazole, because the free *N*-methylimidazole as an N-containing donor competed with the alkyne substrate to coordinate to Au-center. Moreover, **Au-L1** exhibited good generality to a wide range of the substrates for the synthesis of 2,3-fused pyridine derivatives and 2-aryl(heteroaryl)-substituted pyridines.

1. Introduction

Pyridine derivatives have gained considerable attention due to their central role as the versatile building blocks in the synthesis of natural products, active pharmaceuticals, and functional materials with novel photo-/electrochemical or catalytic properties [1–3]. Historically, many pyridine derivatives syntheses rely on the condensation of amines with carbonyl compounds without involvement of transition metal catalyst [4–8]. For example, ammonia (NH_3) has served as the nitrogen source, including [5 + 1] condensation with 1,5-dicarbonyls (Scheme 1-**A**) [9]. Ammonia is also frequently used in the [2 + 2 + 1 + 1] Hantzsch pyridine synthesis (Scheme 1-**B**) [10,11]. Other pyridine syntheses rely on vinyl amines such as the [3 + 3] condensation of 1,3-dicarbonyl derivative with vinylogous amide (Scheme 1-**C**) [12]. In these condensation methods, auto-oxidation (dehydrogenation) is necessary for aromatization.

On the other hand, the [4 + 2] aza-Diels-Alder cycloaddition reaction basically is another prevalent approach for the construction of pyridine derivatives especially with alkynes as the electron-deficient groups over the transition-metal catalysts [4] (Scheme 2). Specifically, α,β-unsaturated imines and alkynes are the most widely applied substrates for this method [13–16].

Although many synthesis routes to pyridine derivatives have been developed [4], comparatively, the one-pot synthesis of pyridines derivatives with high atom-economy by using easily available starting materials is still challengeable but in great demand [17–21]. Arcadi firstly reported a novel one-pot sequential amination/annulation reaction of carbonyl compounds and propargylamine for the synthesis of pyridine derivatives [22]. It was believed that the applied Au-catalyst not only catalyzed the condensation of carbonyl compounds and primary amines to afford imino- moieties as a Lewis π-acid [22], but also activate alkynes for the subsequent annulation due to its unique alkynophilicity [23–32].

Highlighted by Arcadi's elegant method, herein, a novel Au(I)-complex (**Au-L1**) containing the Lewis basic amino group (imidazolyl) and the phosphine-ligated-Au-complex unit was developed as a bi-functional catalyst for the one-pot sequential reaction of ketones (or aldehydes) and propargylamine for the synthesis of pyridine derivatives. The incorporated imidazolyl group in **Au-L1** was expected to behave as a base to catalyze the condensation reaction and the phosphine-ligated-Au-complex unit was responsible for the subsequent annulation (Scheme 3). For comparison, the similar structured complex of **Au-L2,** in which the basicity of imidazolyl group was quenched via quaternization of N-site, was

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* Corresponding author.
E-mail address: yliu@chem.ecnu.edu.cn (Y. Liu).

http://dx.doi.org/10.1016/j.molcata.2016.09.008
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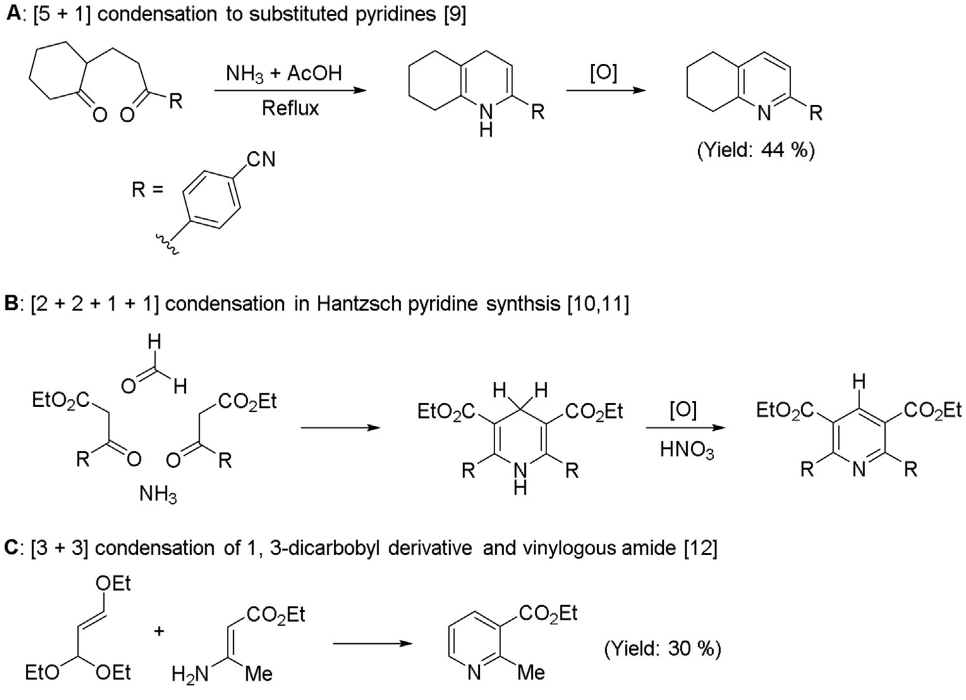
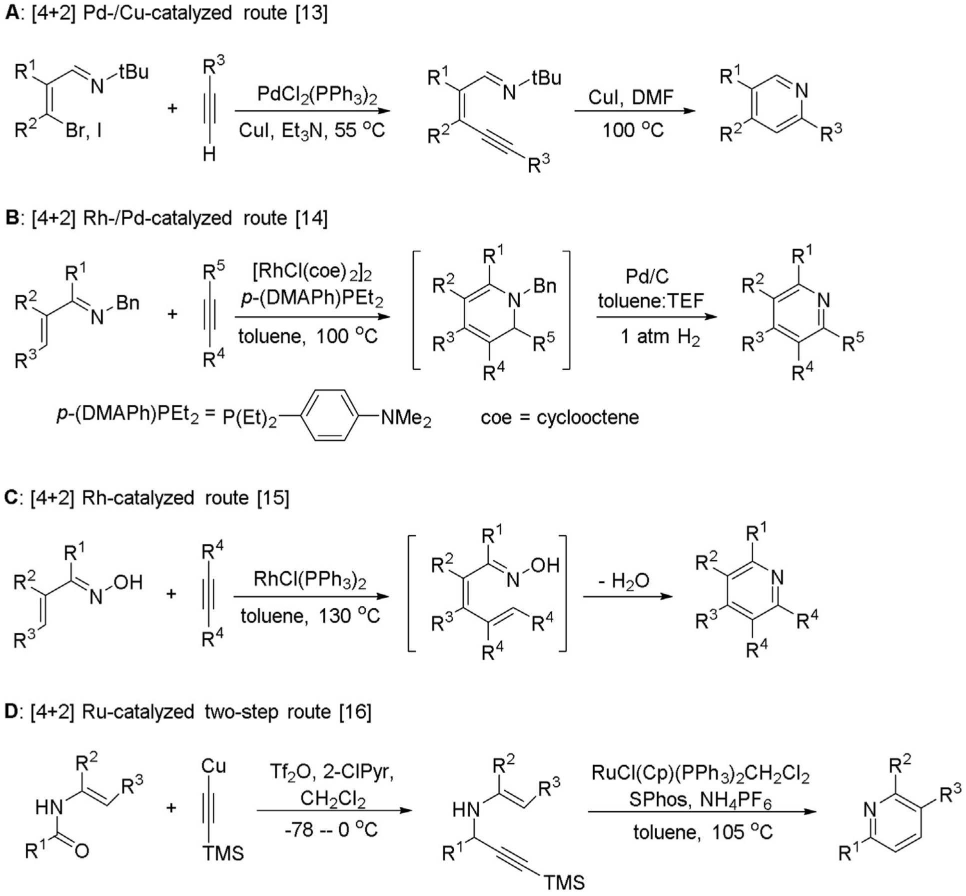


Scheme 1. Pyridine derivative synthesis via condensation of carbonyl compounds with amines.



Scheme 2. Pyridine derivative synthesis via [4 + 2] aza-Diels-Alder cycloaddition of α,β-unsaturated imines with alkynes.