One-pot Synthesis of Amides by Aerobic Oxidative Coupling of Alcohols and Amines using Supported Gold and Base as Catalysts

Jerrik Mielby, Søren Kegnæs and Anders Riisager*
Centre for Catalysis and Sustainable Chemistry, Department of Chemistry, Technical University of Denmark, Building 207, DK-2800 Kgs. Lyngby, Denmark
*ar@kemi.dtu.dk

Introduction

In the past years, the interest for efficient production of fine and bulk chemicals by selective heterogeneously catalysed oxidation reactions has increased [1]. In particular, considerable effort has been devoted to the development of aerobic oxidation methods, as oxygen is a cheap and readily available oxidant that produces water as the only by-product.

Gold-catalysed aerobic oxidation of alcohols [2] and amines [3,4] is an emerging field in organic chemistry and represents a green and highly atom-efficient alternative to current industrial methods. By applying the right reaction conditions a broad variety of products can be formed, including carbonyls [5], carboxylic acids [6], esters [7], amides [4] and imines [8].

Here, we present a new and highly selective one-pot, two-step reaction protocol for the formation of amides by aerobic oxidative coupling of alcohols and amines using supported gold nanoparticles and base as catalysts.

Experimental

All chemicals and reagents were purchased from commercial sources and used without further purification. The employed catalysts consisted of Au nanoparticles (typically 2-4 nm in diameter) supported on different composite materials, such as TiO_2, Al_2O_3, and ZnO. The employed base was different metal methoxides, including LiOMe, NaOMe, and KOMe.

In a general oxidation experiment, the substrates were charged to a reaction flask and connected to a reaction station providing stirring, heating and O_2 for the oxidation (atmospheric pressure). The system was then flushed with O_2 before the catalyst was added. During the reaction samples were periodically collected, filtered and analysed by GC-FID and GC-MS using a HP-5 column from Agilent Technologies Inc. The amounts of substrates and reaction products were quantified using an internal standard.

Results and Discussion

The combination of supported gold nanoparticles and base was shown to compose an active and highly selective (>90%) catalytic system for the one-pot, two-step synthesis of amides depicted in Figure 1. The oxidising agent was pure molecular oxygen and the reactions were conducted at mild conditions (25 to 65°C and atmospheric pressure). Initially, phenylmethanol and hexan-1-amine was used as model substrates, but the reaction protocol was also applied to a number of other alcohols and amines, demonstrating the procedure to be versatile and applicable to a broad range of substrates.

Furthermore, a Hammett study was performed in order to investigate the effect of different substituents at the para-position of phenylmethanol. As expected from theoretical calculations, the study showed that electron withdrawing groups generally increase the reaction rate in the second step of the reaction while electron-donating groups generally decrease the reaction rate.

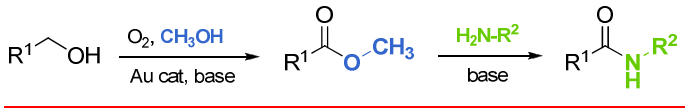

Figure 1. Synthesis of amides using supported gold nanoparticles and base as catalysts. R^1 = alkyl or benzyl, R^2 = H, alkyl, benzyl

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