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Inexpensive and rapid hydrogenation catalyst from $CuSO_4/CoCl_2$ — Chemoselective reduction of alkenes and alkynes in the presence of benzyl protecting groups

Mario Ficker [1], Søren W. Svenningsen [1], Thomas Larribeau, Jørn B. Christensen *

Department of Chemistry, University of Copenhagen, Thorvaldsensvej 40, Frederiksberg, DK-1871 Denmark

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ABSTRACT

The simple reduction of a number of alkenes and alkynes was performed with a typical reaction time of 20 min using a copper-cobalt catalytic system. The reduction did not cleave benzyl protecting groups which are usually vulnerable to catalytic hydrogenation reactions. The catalyst can be prepared *in situ* by reduction of the inexpensive precursor salts $CuSO_4$ and $CoCl_2$ with $NaBH_4$. Sodium borohydride was also used as an easily handled hydrogen source for the catalytic reductions. No pressure, heating or inert atmosphere is required and purification/catalyst removal is achieved using extraction procedures, making this approach simple and efficient.

Introduction

The catalytic reduction of alkenes and alkynes with hydrogen and a transition metal catalyst is a standard reaction in organic synthesis.[1,2] These reactions typically require expensive metals from groups 8 and 10, with platinum metals representing the most active, and a hydrogen source, such as H_2 gas, hydrazine or formates.[3–7] Specialized glassware and inert atmospheres are typically required, and often these reactions are performed under pressure (H_2) or using highly toxic and environmentally harmful reagents (hydrazine, formates),[8,9] which are not practical for a non-industrial laboratory use.

Recently, we described the formation and catalytic activity of bimetallic copper-cobalt nanoparticles that were stabilized by encapsulation in a dendrimer.[10] This procedure gave nanoparticles (1–3 nm) capable of reducing alkenes and alkynes with low catalyst loading and short reaction times using $NaBH_4$ as a solid hydrogen source; however due to cost of the dendrimer this system is expensive, requires a nitrogen atmosphere and is difficult to scale-up. Herein, we describe the development of an inexpensive and simple copper-cobalt catalyst which is prepared *in situ*, and utilises sodium borohydride as a solid and easily manageable hydrogen source. The reaction is fast with an operationally simple extraction work up which could become a viable alternative to Pd/C for standard hydrogenation reactions.

Results and discussion

A promising bi-metallic nano-catalytic system comprising of a 1:1 mixture of cobalt and copper(Cu_6Co_6@G3-PAMAM-Pyr, 1 nm metal particle size) was previously described.[10] These nanoparticles were highly potent in catalytic reductions with low catalyst loading and linear kinetics. However, the system was difficult to transform into an easy and cheap standard laboratory reaction. In this study we investigated the ability of non-stabilized Cu-Co bimetallic particles to reduce alkenes and alkynes without the need of a dendrimer as support.

Gratifyingly, it was found that a mixture of $CuSO_4$ and $CoCl_2$ salts dissolved in methanol formed a metallic catalyst system *in situ* upon the addition of $NaBH_4$. These bimetallic particles were found to promote the decomposition of $NaBH_4$ to hydrogen and could be used as a solid hydrogen source. The reduction of 10-undecen-1-ol was used as test substrate. An initial analysis of different ratios between copper and cobalt revealed that the best ratio for catalytic hydrogenation was a catalyst with the original composition of 91% Cu and 9% Co.

As a general experimental procedure, the precursor salts $CuSO_4 \cdot 6H_2O$ and $CoCl_2 \cdot 5H_2O$ (10:1) were dissolved in methanol, and the unsaturated starting material added directly to the solution. The reaction was initiated by the addition of $NaBH_4$ to the solution, which reduced the copper(II) and cobalt(II) salts to the copper-

* Corresponding author.
E-mail address: jbc@chem.ku.dk (J.B. Christensen).
[1] Authors contributed equally

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cobalt-boride catalyst as finely dispersed particles, similar to the previously employed dendrimer encapsulated nanoparticles. However, the metal catalyst aggregated to form larger particles during the reaction, due to the lack of a stabilizing polymer. The *in situ* generated catalyst immediately started to decompose the excess $NaBH_4$ to hydrogen, which was transferred to the double or triple bond of the starting material. Additional portions of $NaBH_4$ were typically added over 20 min, which was sufficient to quantitatively reduce most double and triple bonds. The operationally simple work-up procedure was achieved by extraction with water/CH_2Cl_2, where the catalyst and the boronic acid salts remained in the water phase, while the product was extracted into the organic layer, which was dried over $MgSO_4$ and evaporated to give isolated yields of typically above 95%.

A systematic study of the catalyst potential was performed with the compounds shown in Scheme 1 and reaction conditions presented in Table 1. α,β-Unsaturated esters were readily reduced, leaving the ester group intact. The lowest reaction time and catalyst loading was observed for dimethyl itaconate **1a** (1 mol% Cu, 0.1 mol% Co, 10 min.), where the conjugated double bond is less hindered than in acrylates (**2a** and **3a**), methyl cinnamate (**4a**) and *cis*,*cis*-dimethyl muconate (**5a**).

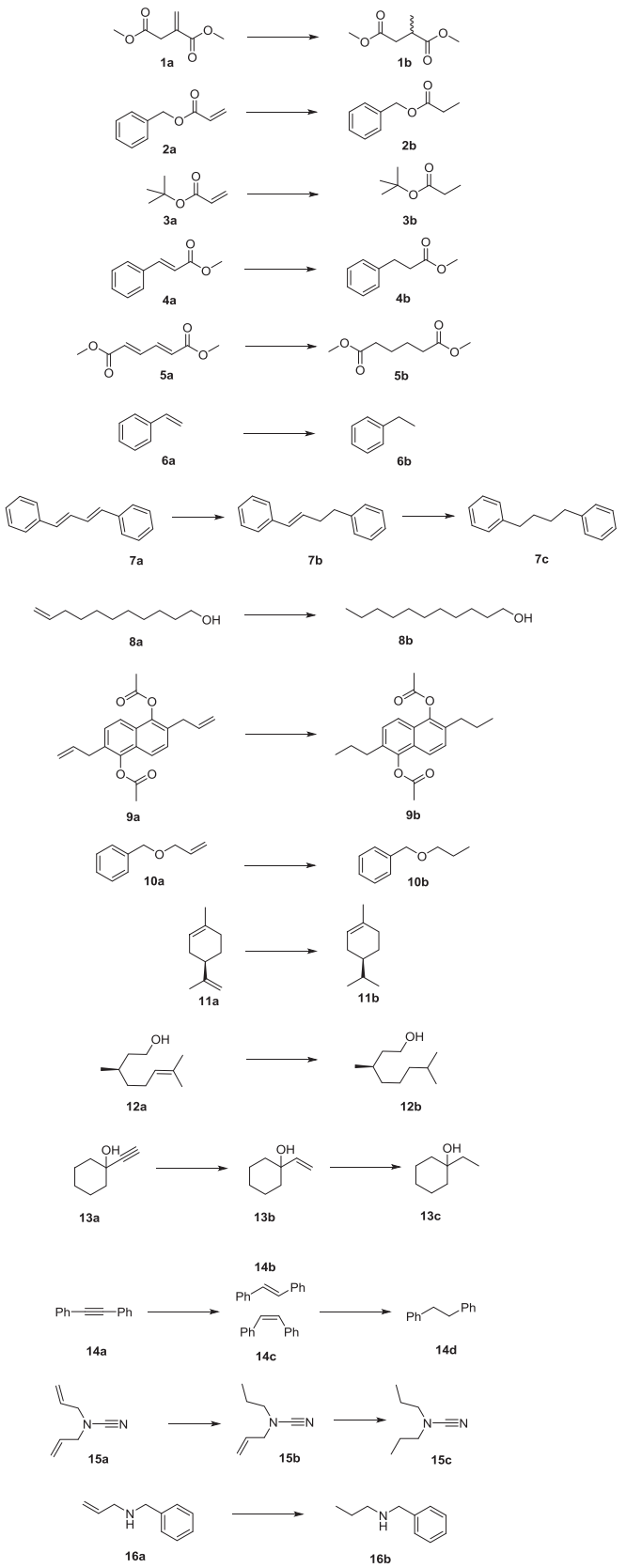
Reduction of a terminal double bond conjugated to an aromatic ring system (styrene **6a**) was rapid with low catalyst loading (3mol % Cu and 0.3 mol% Co), while internal double bonds (**7a**) were harder to reduce (10 mol% Cu and 1 mol% Co), which could also be explained by the *trans–trans* structure of the compound, which is difficult to reduce *via* the *syn*-addition of hydrogen. In all aromatic compounds the conjugated ring system remained intact during the reaction. Typical ester protection groups such as benzyl ester (**2a**) and *tert*-butyl ester (**3a**) were unaffected by the catalytic system. The stability of the benzyl ester is notable, since this group is usually removed by hydrogenation reactions;[11–13] this could open new pathways for reducing unsaturated carbon systems in the presence of benzyl protecting groups. The chemoselective hydrogenation of olefins is usually achieved by selective poisoning of Pd/C or other expensive rare metal catalysts, which is time consuming due to catalyst preparation and long reaction times of the deactivated catalyst.[14–16]

Terminal double bonds not conjugated to another π-system were readily reduced as demonstrated with compounds **8a**, **9a** and **10a**. The acetyl ester in compound **9a** and the benzyl ether (**10a**), a group potentially vulnerable to hydrogenation reactions,[13,17] remained intact during the reaction.

The preference for terminal double bonds was demonstrated with (+)-limonene (**11a**) where the terminal alkene was selectively hydrogenated, leaving the more hindered double-bond virtually untouched; only 2% of the fully reduced compound was observed by GC–MS. However, the catalyst loading for **11a** was almost ten times higher than for the other compounds (25 mol% Cu and 2.5 mol% Co). This suggests that hydrogenation under these conditions is sensitive to the substitution pattern of the double-bond. The internal double bond in β-citronellol (**12a**) could be almost quantitatively reduced; this could be due to the less sterically hindered nature of the double bond compared to the aliphatic ring system in (+)-limonene where the double bond can hardly be accessed by the catalyst.

Furthermore, alkynes could also be successfully reduced to the alkene and further to the corresponding alkane. The reduction of compounds **13a** was quantitative with a fully saturated product, whereas compound **14a** was chosen for a mechanism study with low catalyst loading (2 mol% Cu and 0.2 mol% Co) and short reaction time (15 min) in order to isolate intermediate products (*vide infra*).

Amine containing compounds (**15a** and **16a**) showed incomplete reaction (36% **15c**, 64% **16b**) under the applied catalytic conditions. Furthermore, the copper salts from the catalyst seemed to form stable complexes with the amines which interfered with



Scheme 1. Test substrates and products of the catalytic hydrogenation reaction using the copper-cobalt-boride catalyst. Reaction conditions and conversions are listed in Table 1.