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Sodium hydroxide-catalyzed transfer hydrogenation of carbonyl compounds and nitroarenes using ethanol or isopropanol as both solvent and hydrogen donor

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ABSTRACT

The development of a clean and renewable energy carrier has become a subject of high priority, and new catalytic system that involves both abundant and cheap catalysts and green solvents is highly desirable in terms of practical and sustainable chemistry. In this spirit, sodium hydroxide-catalyzed transfer hydrogenation of carbonyl compounds using ethanol as both hydrogen source and solvent is developed in this report. The process is successfully utilized in the hydrogenation of various ketones and aldehydes, and the corresponding primary and secondary alcohols are synthesized with excellent conversions. Furthermore, sodium hydroxide also smoothly promotes the transfer hydrogenation of nitroarenes providing anilines and azobenzenes. For both carbonyl compounds and nitroarenes, results in ethanol and isopropanol are compared, and a remarkable change of selectivity between these two solvents is disclosed for the NaOH-catalyzed transfer hydrogenation to nitroarenes.

1. Introduction

Economic, regulatory and environmental concerns have prompted a remarkably increasing demand for sustainable, practical and “green” catalytic processes [1]. This demand pushes industry and academia to shift their focus toward improvement of catalyst recovery, restriction of catalyst leaching, development of abundant, cheap and less toxic catalysts, as well as the use of green solvents [1a,2].

Reduction of carbonyl compounds yielding alcohols is a very important transformation in organic synthesis, its industrial application span, fine chemical conversions to pharmaceuticals synthesis. Direct hydrogenation with pressures of H_2 gas [3] and transfer hydrogenation from a hydrogen donor molecule [4] are two often employed strategies (Chart 1). As a key example of green catalysis, transfer hydrogenation methodology has become in recent years a center of attraction because it does not require pressurized hydrogen gas and elaborate experimental setups, the hydrogen donors are readily available, inexpensive, easy to handle, and the major side product (such as acetone) can be recycled.

Transition metal-catalyzed transfer hydrogenation of carbonyls, involving first-, second- and third-row transition metals of groups 8–10, has attracted growing interest owing to their high efficiency and selectivity [4,5]. However, the noble metals (such as Ru, Rh, Pd, Ir, Os and Pt) among them are very expensive, in addition, regulatory organizations limit the metal residual levels in pharmaceutical products to ppm or less levels because of their inherent toxicity. Although more abundant and biocompatible iron seems an excellent candidate for an economic and “greener” alternative, most of the reactions do not proceed in the absence of uneasy-to-get and environmentally-unfriendly ligands [6]. Furthermore, organocatalytic [7] and base-catalyzed transfer hydrogenation [8] have also emerged recently, and received considerable attention. The importance of the hydroxide bases [8] has been first illustrated in 2009 by the reports of the groups of Polshettiwar and Varma with KOH [8a] and Ouali et al., with NaOH [8b] without any transition metal complex for the hydrogenation of carbonyls by 2-propanol. In this context, we have further investigated base-catalyzed transfer hydrogenation.

In all cases of transfer hydrogenation, 2-propanol and formate are the mainly used “sacrificial” reducing sources and solvents. The use of a green solvent is one of the 12 principles of green chemistry [1a]. A green solvent must therefore, possess specific features including low toxicity, non-mutagenicity, widespread availability, and reproducibility. These common green solvents used in organic

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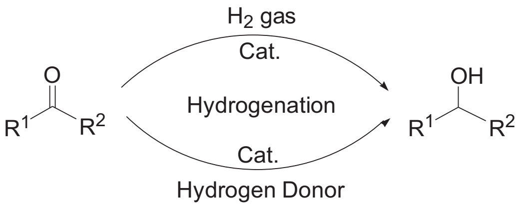


Chart 1. Hydrogenation of carbonyl compounds yielding alcohols.

synthesis include in particular H_2O, glycerine, EtOH, some ionic liquids, and supercritical CO_2. As one of renewable and cheapest reagents, ethanol, usually produced by fermenting starch, has the potential to be ideal an alternative to 2-propanol and formate in transfer hydrogenation [9]. However, the successful application of ethanol as hydrogen source was rarely reported [10], mainly due to its ability to produce stable transition metal complexes containing carbonyl with the catalysts that are used for the transfer hydrogenation process.

Nitro derivatives are a major family of pollutants. Their reduction products of nitroarenes, functionalized anilines are important precursors and intermediates for the manufacture of pharmaceuticals, agrochemicals, pigments, dyes, rubbers, polymers, rubbers, corrosion inhibitors and photographic developers [11,12]. Reduction of poisonous nitroarenes [13] based on catalytic hydrogenation, metal mediated reductions and electrolytic reduction is the traditional synthesis methods for anilines [14]. Recently, catalytic transfer hydrogenation has emerged as a green and efficient route for the formation of anilines, however, the uses of expensive transition metals and/or ligands are necessary in the transformation [15], in addition, the product contamination by these noble metals restricts the application of such systems in several fields, and especially in biomedicine. Thus, it is highly desirable to develop more economic and pharmaceutically safe methodologies for synthesis of anilines, as well as degradation of nitroarenes.

Herein, we report that abundant and cheap NaOH promotes transfer hydrogenation of carbonyls including ketones and aldehydes compounds forming primary and secondary alcohols, respectively, using EtOH as both hydrogen source and solvent under relatively mild conditions. Additionally, nitroarenes are hydrogenated to form anilines and azobenzenes based on the NaOH-catalyzed transfer hydrogenation protocol with 2-PrOH as both hydrogen donor and solvent.

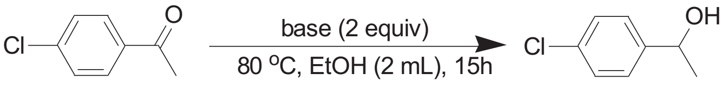
2. Results and discussion

2.1. *Investigation of the optimal reaction conditions for transfer hydrogenation of carbonyl compounds*

In a preliminary experiment, 4-chloroacetophenone **1a** was chosen as a test substrate to identify the optimal reaction conditions. The transfer hydrogenation was initially carried out using EtOH (2 mL) as hydrogen source and solvent, in the presence of 2 equiv of NaOH at 80 °C. The conversion increased with increased reaction time in the range of 1–15 h, providing 95% conversion (Fig. 1a). It was further found that the amount of NaOH is one of the most crucial factors for the formation. Within 15 h, fleetly decreased conversion was detected with the reduction of NaOH; 0.5 equiv of NaOH promoted transfer hydrogenation producing only 23% conversion (Fig. 1b). When 0.25 equiv of NaOH was used in the reaction, 78% conversion was obtained within 60 h, which revealed that NaOH played the role of catalyst in this transfer hydrogenation. Furthermore, the decreased conversion caused by the temperature reduction, was demonstrated (Fig. 1c). The secondary alcohol **2a** was obtained with conversions of 13%, 31%, and 52%, at temperatures of 50 °C, 60 °C, and 70 °C, respectively.

Then we examined the influence of different bases and hydrogen sources on the transfer hydrogenation of 4-chloroacetophenone **1a**. As shown in Table 1, the reaction did not proceed at all when K_2CO_3 and Na_2CO_3 were employed at 80 °C in EtOH (Table 1, entries 1 and 2). K_3PO_4 was able to promote the same reaction, albeit in poor conversion (9%) within 15 h. The transfer hydrogenation by EtOH also took place in the presence of other alkali hydroxides such as KOH and CsOH, the same cation effect being revealed: both KOH (33%) and CsOH (57%) being farther less active than NaOH (95%). The organic base Et_3N was not efficient at all for this transformation (entry 6). These results are in agreement with those reported by the groups of Ouali et al. [8] using 2-PrOH as solvent and hydrogen donor. The model reaction was further carried out in various alcoholic solvents (hydrogen sources), with NaOH as catalyst at 80 °C for 15 h. It was found that the reaction did not occur in H_2O nor in MeOH (entries 7 and 8). On the contrary, the transfer hydrogenation proceeded perfectly in EtOH or 2-PrOH, and the latter is more active than the former. From the point of view of the goal of an economic and environmentally friendly reaction solvent, renewable and cheap EtOH is clearly more favorable than 2-PrOH. In addition, the use of another primary alcohol, *n*-BuOH, produced the desired product **2a** with the conversion of 16%.

Table 1
Screening of bases and solvents (hydrogen sources) for the transfer hydrogenation of 4-chloroacetophenone promoted by NaOH.[a]



1a (1 mmol) **2a**

Entry	Base (2 equiv)	Solvent (1 mL)	Conversion (%)[b]
1	K_2CO_3	EtOH	0
2	Na_2CO_3	EtOH	0
3	K_3PO_4	EtOH	9
4	CsOH	EtOH	56
5	KOH	EtOH	33
6	Et_3N	EtOH	0
7	NaOH	H_2O	0
8	NaOH	MeOH	0
9	NaOH	EtOH	95
10	NaOH	*i*-PrOH	>99
11	NaOH	*n*-BuOH	16

[a] The reaction was carried out with 4-chloroacetophenone (1 mmol) in the presence of bases (2 mmol) in alcohols (2 mL) at 80 °C under a nitrogen atmosphere for 15 h.
[b] Conversion was determined by NMR.