Tetrahedron Letters 50 (2009) 5951–5953

Contents lists available at ScienceDirect

Tetrahedron Letters

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

Glycerol as solvent and hydrogen donor in transfer hydrogenation–dehydrogenation reactions

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ARTICLE INFO

Article history:
Received 26 June 2009
Revised 22 July 2009
Accepted 17 August 2009
Available online 20 August 2009

Keywords:
Transfer hydrogenation–dehydrogenation
Catalysis
Glycerol
Green solvent

ABSTRACT

Glycerol is employed successfully as a green solvent and hydrogen donor in catalytic transfer hydrogenation–dehydrogenation reactions. The glycerol donates hydrogen to various unsaturated organic compounds under mild reaction conditions and as a solvent, allows easy separation of products and catalyst recycling.

Redox reactions are a family of reactions that deal with the transfer of electrons between species.[1] Several routes, using different reducing agents and oxidants, are available for reduction and oxidation, respectively, of organic compounds. In general, three techniques exist for the reduction of unsaturated organic compounds, which include the use of metal hydrides, employing molecular hydrogen, or via transfer hydrogenation. Likewise, organics can be oxidized by three main routes: (i) oxidation with toxic inorganic oxidants, which usually generate high levels of pollution; (ii) catalytic dehydrogenation or catalytic oxidative dehydrogenation, in which oxygen or peroxides are used as oxidants; and (iii) catalytic transfer dehydrogenation, in which an organic oxidant adsorbs the hydride and proton.

Transfer hydrogenation–dehydrogenation reaction, in which hydrogen is transferred from an alcohol to an unsaturated bond, is an environmentally benign method for reducing unsaturated compounds or oxidizing alcohols.[2–5] One of the advantages of this pathway is that it is performed in the absence of gaseous hydrogen or oxygen, which requires precautions and special high pressure equipment. Although transfer hydrogenation–dehydrogenation is not as highly developed as catalytic hydrogenation or oxidation, it is recognized as an attractive technology with a high potential for wide industrial applicability.

A variety of homogeneous and heterogeneous catalysts can be used in transfer hydrogenation–dehydrogenation reactions, such as salts and complexes of Pd, Pt, Ru, Ir, Rh, Fe, Ni, and Co in addition to their supported heterogeneous analogs.[6] In many systems, the addition of catalytic amounts of an organic or inorganic base is also required to activate the metal complex and/or to assist in proton dissociation from the hydroxy group of the alcohol. Transfer hydrogenation–dehydrogenation coupled reactions with heterogeneous bases are also common. These reactions are proposed to operate through the Meerwein–Ponndorf–Verley–Oppenauer mechanism, which entails direct hydrogen transfer from a C–H of the alcohol to a carbonyl carbon via a cyclic mechanism. A common solid base catalyst is MgO, which catalyzes transfer hydrogenation in either gas or liquid phase.[5,7] Recently it was reported that insoluble solid alkaline metal hydroxides by themselves can also be used as catalysts for transfer hydrogenation–dehydrogenation reactions in organic solvents.[8]

Several organic compounds, such as 2-propanol and tetralin, have been used as solvents and as hydrogen donors in the transfer hydrogenation of unsaturated organic compounds.[5] We recently reported that glycerol can also be successfully employed as a versatile and alternative green solvent in a variety of organic reactions and synthetic methodologies, all of which achieve high product conversions and selectivities.[9–12] We therefore explored the possibility of using glycerol, as with other alcohols, as an environmentally friendly 'donor solvent' in transfer hydrogenation–dehydrogenation reactions.[13] A polar, non-toxic, biodegradable, and recyclable liquid manufactured from renewable sources, glycerol has promising physical and chemical properties that facilitate the dissolution of inorganic salts, acids, and bases and of enzymes and transition metal complexes. Furthermore, it also dissolves organic compounds that are poorly miscible in water and it is considered non-hazardous. Hydrophobic solvents such as ethers and hydrocarbons, which are immiscible in glycerol, enable the products to be removed by simple

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doi:10.1016/j.tetlet.2009.08.035

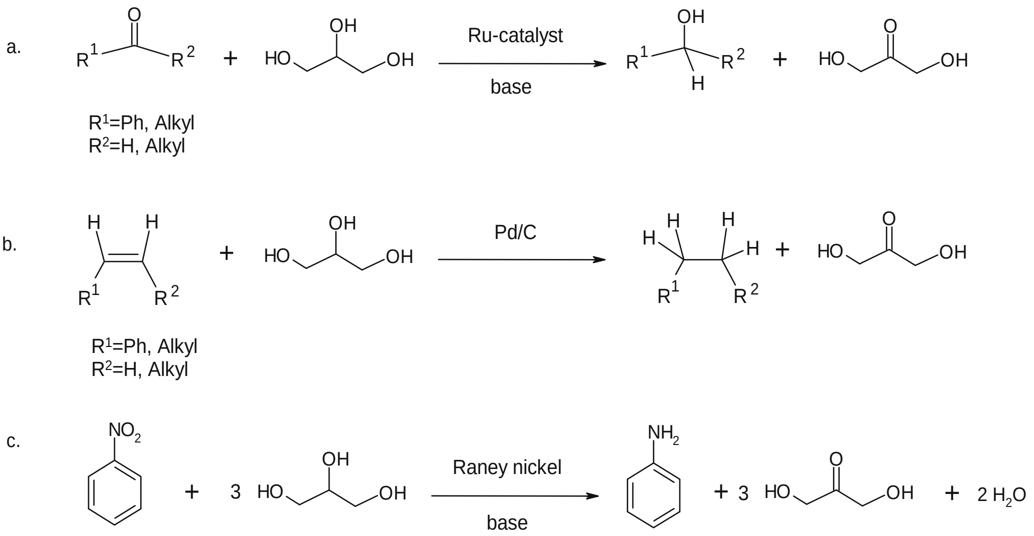

Figure 1. Transfer hydrogenations of unsaturated organic compounds in glycerol: (a) carbonyl compounds; (b) alkenes; and (c) nitrobenzene.

extraction. Additionally, the high boiling point of glycerol makes distillation of the products an attractive, efficient separation technique. In addition to the favorable solubilities of both the reactants and the catalysts and the easy separation of the product in reactions with glycerol, transition metal complex recycling is also facilitated by glycerol.

The production of many important organic intermediates can be accomplished using glycerol as the raw material.[14,15] Aerobic oxidation of glycerol over supported metal and bimetallic catalysts resulted in a variety of products such as dihydroxyacetone, glyceraldehyde, glyceric acid, glycolic acid, hydroxypyruvic acid, oxalic acid, and tartronic acid. Dihydroxyacetone, glyceraldehyde, and derivatives of the two are valuable precursors for target products in an assortment of applications. For example, dihydroxyacetone and its derivatives are used extensively in the cosmetics industry. In addition, both these chemicals are used as starting materials for the synthesis of many other important chemical compounds.

In this study, glycerol was used for the first time as both solvent and hydrogen donor in the transfer hydrogenation of various representative unsaturated organic compounds while itself being dehydrogenated to dihydroxyacetone (Fig. 1). Different homogeneous and heterogeneous catalysts were tested.

Catalytic transfer hydrogenations of representative unsaturated organic compounds were studied in reactions that typically utilized homogeneous and heterogeneous metal catalysts and a base as co-catalyst. The results are summarized in Table 1. In a typical procedure, the reaction was performed as follows: in a 10 mL vial, the appropriate amounts of metal catalyst together with base were added to 4 g of glycerol. Then, 0.20–0.55 g of substrate was added to the vial with stirring and the mixture was heated to 70 °C in an

Table 1
Transfer hydrogenations using glycerol as solvent and hydrogen donor[a]

Entry	Substrate (g)	Catalyst (g)	Base (g)	Time (h)	Yield (%)
1	Benzaldehyde (0.22)	Ru(*p*-cumene)Cl$_2$-dimer (0.16)	KOH (0.02)	5	25
2	Benzaldehyde (0.22)	Ru(*p*-cumene)Cl$_2$-dimer (0.16)	KOH (0.02)	24	99
3	Benzaldehyde (0.22)	Ru(*p*-cumene)Cl$_2$-dimer (0.16)	NaOH (0.024)	1	20
4	Benzaldehyde (0.22)	Ru(*p*-cumene)Cl$_2$-dimer (0.16)	Et$_3$N (0.1)	1	17
5	Benzaldehyde (0.22)	RuCl$_2$(TPPS)$_3$[b] (0.18)	KOH (0.02)	5	18
6	Benzaldehyde (0.22)	5% Ru/C (0.3)	KOH (0.02)	5	12
7	2-Octanone (0.22)	Ru(*p*-cumene)Cl$_2$-dimer	KOH (0.02)	20	21
8	Cyclohexene (0.5)	5 wt % Pd/C (0.03)	—	5	81
9	Cyclohexene (0.)5	5 wt % Pd/C (0.03)	—	9	100
10	Styrene (0.5)	5 wt % Pd/C (0.03)	—	5	100
11	Nitrobenzene (0.25)	Raney-nickel (0.1)	NaOH (0.2)	5	11
12	Nitrobenzene (0.25)	Raney-nickel (0.1)	NaOH (0.2)	24	43

[a] Reaction conditions: glycerol (4 g), 70 °C.

[b] TPPS: tris-(3-sulfophenyl)phosphine trisodium salt.

oil bath. The reactions were run for 5–24 h and were then allowed to cool. The products were separated by extraction with diethyl ether (3 × 5 mL). The combined organic phase was concentrated under reduced pressure, and the resulting crude residue was analyzed by gas chromatography (GC) using a HP-1 column to determine the extent of conversion.

As illustrated in Table 1, glycerol can be used as a solvent and hydrogen donor in the transfer hydrogenation of various unsaturated compounds. When carbonyl and nitro-compounds were reduced (entries 1–7, 11 and 12, respectively), the addition of a base as co-catalyst was essential, and performing the reaction with a metal catalyst in the absence of a base did not yield any product. However, performing the reaction with only KOH, under similar reaction conditions, yielded the corresponding products in limited amounts, and the conversions were lower than 15% even after 24 h. It was found that both organic and inorganic bases could be used as co-catalysts (entries 3 and 4). On the other hand, the transfer hydrogenation of cyclohexene and styrene (entries 8–10) was run only in the presence of Pd/C, while the addition of KOH deactivated the catalyst, resulting in negligible amounts of cyclohexane and ethylbenzene. In general, increasing the reaction temperature, reaction time, or catalyst loading increased the conversions in all the tested reactions. Finally, it was found that glycerol was dehydrogenated to dihydroxyacetone as expected from the higher oxidation potential of the secondary alcohols, however, mass balance calculations showed that under the reaction conditions, some of the dihydroxyacetone decomposed.

The use of glycerol as a solvent also allowed easy product separation and catalyst recovery. For the first reaction cycle, benzaldehyde (2 g), Ru(*p*-cumene)Cl_2-dimer (0.12 g), and KOH (0.17 g) were dissolved in 25 g of glycerol and the reaction mixture was heated in an oil bath to 70 °C. At the end of the reaction, after 18 hours, the conversion of benzaldehyde was 62%. A catalyst recycling test was performed after extraction of the product and the remaining substrates over three cycles with diethyl ether (25 mL), after which fresh substrate was added and the reaction was run under conditions similar to the first trial. Benzaldehyde conversions after the second and third reaction cycles were found to be 56%, and 48%, respectively. The lower conversion may be attributed to partial deactivation of the catalyst. However, since hydrogenation–dehydrogenation transfers are equilibrium reactions, the conversion of benzaldehyde in the second cycle may has been affected by the partial dehydrogenation of glycerol, the hydrogen donor, during the first reaction cycle.

In conclusion, we have demonstrated that glycerol can be successfully utilized as an environmentally friendly solvent and as the hydrogen donor in the transfer hydrogenation of representative unsaturated organic compounds. Dehydrogenation of glycerol resulted in the formation of dihydroxyacetone.

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