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Catalytic Transfer Hydrogenation Using Biomass as Hydrogen Source

Srimanta Manna[a,b] and Andrey P. Antonchick[a,b,c]*

Abstract: We developed an operationally simple method for the direct use of biomass derived chemical entities in a fundamentally important process such as hydrogenation. Various carbohydrates, starch and lignin were used in for stereoselective hydrogenation. Employing a transition metal catalyst and a novel catalytic system, the reduction of alkynes, alkenes and carbonyl groups with high yields was demonstrated. The regioselective hydrogenation to access different stereoisomers was established by simple variations in the reaction conditions. Our discovery is based on an unprecedented catalytic system and represents a straightforward application of biomass as reducing reagent in chemical reaction.

Hydrogenation of chemical compounds is a fundamental process which found wide application.[1] Application of biomass as renewable carbon source for high added-value chemicals received great attention.[2] Biomass encompasses contemporary carbon and its application does not alter the carbon balance of ecosystems. The conversion of renewable biomass to fuel or hydrogen gas has become a very important topic and provides an alternative option for the limited fossil energy sources.[2c, 2e] Biomass derived hydrocarbons such as sugars, cellulose and starch are potentially important feedstock obtained by photosynthesis in plants from carbon dioxide. Biomass was utilized in large scale production of fuels and simple chemicals (Figure 1).[3] Interestingly, several methods for hydrogen production were developed using enzymes as catalysts.[4, 5] However, all modern methods coproduce carbon dioxide together with hydrogen and further gas separation is needed. The direct application of biomass in hydrogenation reactions is advantageous due to renewability, low cost and the unnecessity of purification of the hydrogen or application of any additional chemical reactions. The established hydrogenation is beneficial to prevent global warming and climate changes, since biomass is a product of utilization of water and CO_2 in Nature. Here we describe a rhodium catalyzed selective transfer hydrogenation of chemical compounds using biomass as renewable reagent for a fundamental chemical transformation. The simple reaction conditions provide a straightforward selective hydrogenation of unsaturated compounds. The regioselective hydrogenation to access different stereoisomers is demonstrated by variation of reaction conditions and its selectivity can be controlled. Our discovery provides a new method for the usage of biomass as a renewable reducing reagent in chemical reactions (Figure 1).

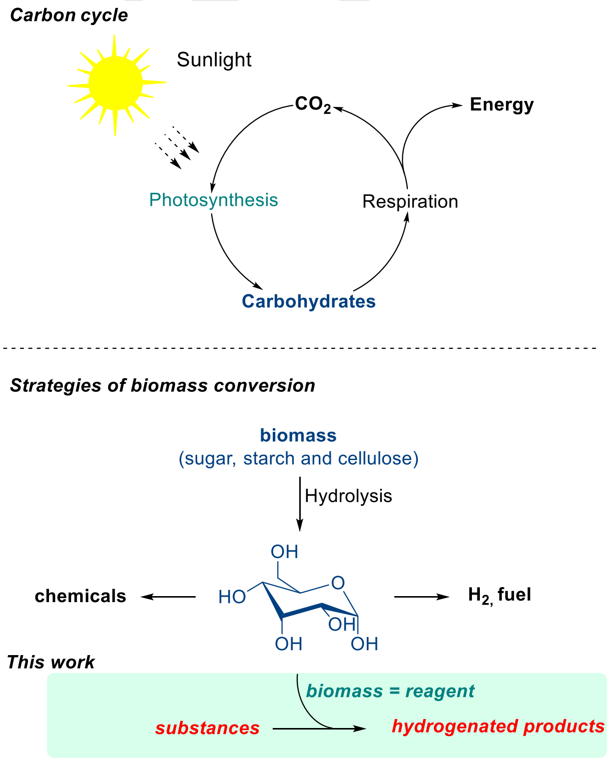

Figure 1. Overview of Biomass Application.

Having interest in the development of sustainable methods for chemical transformations,[3] we anticipated the application of biomass in transfer hydrogenation. In the past decades, several transition-metal catalysts such as ruthenium and rhodium were used as catalysts for hydrogen atom transfer from alcohol.[7] A catalytic transfer hydrogenation of glucose-fructose syrups in alkaline media using Pt or Rh-catalysts was reported by van Bekkum´s group.[8] The reported method is applicable only for the reduction of carbohydrates. Initially, we investigated the reduction of alkynes in the presence of $[Cp^*RhCl_2]_2$ as catalyst at 120°C under air using simple sugars such as glucose as renewable biomass (Table 1). To our delight, stilbene (**2a**) was formed with 56% yield as a mixture of *cis*/*trans* isomers from diphenylacetylene (**1a**). Upon variation of additives and bases, we observed an improvement in yield (Table S1). The yield of **2a** and the stereoselectivity of the reduction was improved with decreasing the amount of NaOAc (Table 1, entries 2, 3). Using

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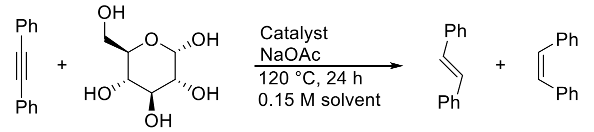
1.5 equivalents of NaOAc led to the formation of a single isomer with quantitative yield. Afterwards, various solvents were examined and we found that several solvents are suitable for this transformation (Table 1, entries 4-9 and Table S2). We observed that 1,2-dichloroethane (DCE) is the best solvent with respect to yield and selectivity. It is notable that the stereoselectivity of the reduction can be switched changing the solvent to dimethylformamide or dimethylacetamide. In dimethylformamide, **2a** was obtained in 77% yield with *E*/*Z*=1/9. Afterwards, we tested different catalysts for the hydrogenation reaction. The application of traditional catalysts for hydrogenation did not provide any improvements (Table 1, entries 10-14 and Table S3). Afterwards, we screened different bases and to our pleasure, we found that LiOAc and NaOAc were the best bases promoting the synthesis of **2a** with 99% yield and good selectivity (95-99%) (Table S4).

Table 1. Screening of Reaction Conditions[a]



1a 3 equiv **2a**

Entry	NaOAc (x equiv)	Catalyst (x mol%)	Solvent	Yield (%) (*E*:*Z*)[b]
1	3	$[Cp^*RhCl_2]_2$ (3)	DCE	56 (1.7:1)
2	1.5	$[Cp^*RhCl_2]_2$ (3)	DCE	99 (*E*) (96)[c]
3	1	$[Cp^*RhCl_2]_2$ (3)	DCE	99 (*E*) (95)[c]
4	1	$[Cp^*RhCl_2]_2$ (3)	H_2O	n.d.
5	1	$[Cp^*RhCl_2]_2$ (3)	DMSO	n.d.
6	1	$[Cp^*RhCl_2]_2$ (3)	DMF	77 (1:9)
7	1	$[Cp^*RhCl_2]_2$ (3)	DMA	50 (1:9)
8	1	$[Cp^*RhCl_2]_2$ (3)	TCE	83 (4:1)
9	1	$[Cp^*RhCl_2]_2$ (3)	DMC	37 (3:1)
10	1	$RhCl_3 \cdot H_2O$ (3)	DCE	trace
11	1	$Rh(PPh_3)_3Cl$ (3)	DCE	12 (6:1)
12	1	Pd/C (5)	DCE	trace
13	1	$[Cp^*IrCl_2]_2$ (3)	DCE	34 (1:2.3)
14	1	$[Ru(p\text{-}cymene)Cl_2]_2$ (3)	DCE	39 (1.2:1)

[a] Reaction conditions: **1a** (0.15 mmol), glucose (0.45 mmol), catalyst (x mol%), NaOAc (x equiv), in 0.15 M solvent at 120 °C for 24 h under air. [b] Yields and *E*:*Z* ratios were determined by GC analysis. [c] Isolated yield after column chromatography. [c] Reaction carried out at 100 °C. DCE = 1,2-dichloroethane, TCE = 1,1,2,2-tetrachloroethane, DMSO = dimethylsulfoxide, DMF = dimethylformamide, DMA = dimethylacetamide, DMC = dimethylcarbonate.

To identify the best hydrogen sources derived from biomass, we tested various carbohydrates for the transfer hydrogenation of **1a** (Table 2). In general, a variety of monosaccharides was successfully used in the transfer hydrogenation providing selectively *trans*-**2a** with high yield (Entries 1-4). The application of a disaccharide – sucrose – was not efficient due to low solubility (Entry 5). Carbonyl group-free carbohydrates such as mannitol led to product **2a** with low yield (Entry 6). Furthermore, oxidized carbohydrates could not be used for hydrogenation (Entry 7). Afterwards, we tested polysaccharides. To our delight, starch from wheat and homemade starch from potatoes provided **2a** in moderate yield (Entries 8-9). The use of dimethylformamide as solvent for the hydrogenation with polysaccharides was needed due to the saccharides' low solubility in DCE. Protected polysaccharides such as cellulose acetate cannot be used as reagent (Entry 10). Ascorbic acid, which is biosynthetically derived from monosaccharides, gave the product in trace amounts (Entry 11). Finally, we tried biopolymers such as lignin as reagent for the transfer hydrogenation. Initial attempts were not successful using the optimized reaction conditions. Only after modification of the reaction conditions, we obtained **2a** in moderate yield as a mixture of isomers. Therefore, for further experiments we decided to use glucose as reagent.[9]

Table 2. Screening of Biomass Derived Reagents[a]

Entry	Reagents	Yield (%) of **2a**	*E*:*Z* ratio of **2a**
1	*D*-(+)-glucose	99	Only *E*
2	*D*-(+)-xylose	77	8:1
3	*D*-(+)-mannose	91	Only *E*
4	*D*-(-)-ribose	97	Only *E*
5	sucrose	15	1:1
6	*D*-mannitol	21	1:2
7	δ-gluconolactone	8	1:3.5
8[b]	wheat's starch	53	1:4
9[b]	potato starch (homemade)	51	1:4
10[b]	cellulose acetate	traces	-
11	*L*-ascorbic acid	10	1:1
12[c]	lignin (dealkaline)	40	1:1

[a] For reaction conditions see Table 1, entry 3 using 3 equiv of reagent. [b] Reaction was carried in DMF [c] $[Cp^*RhCl_2]_2$ (5 mol%), 50 µL H_2O, $Cu(OAc)_2$ (0.5 equiv) in dioxane (1.0 mL) at 130°C for 24 h under air.

Having optimized reaction conditions in hand, we applied the hydrogen atom transfer reaction to a wide range of alkynes. As shown in Figure 2a, we were pleased to find that the application of this method allowed selective formation of the desired alkene as single isomer. Substrates containing various functional groups at para-position of the aryl part such as methyl-, tert-butyl-, methoxy- and fluoro- were well tolerated (**2b**-**2e**) and the products were isolated in 90-98% yield as single isomers. To our delight, *meta*- and *ortho*-substituted alkynes were employed and afforded in 85-97% yield (**2f**-**2g**). Having successfully applied the hydrogen atom transfer to symmetrical alkynes, later on unsymmetrical alkynes were investigated. An electron-rich unsymmetrical alkyne could be efficiently converted into the corresponding product within 12 h in 95% yield. Electron-deficient unsymmetrical alkynes could also be efficiently and stereoselectively reduced using higher loading of catalyst (**2i**-**2l**). Alkynes were reduced selectively to alkenes in the presence of carbonyl groups such as ketones and esters (**2k**-**2l**). An alkyl substituted alkyne led to product **2m** in 87% yield with *E*/*Z* = 9/1 under optimized reaction conditions. During the optimization of the reaction conditions, we demonstrated that the selectivity of reduction can be switched from *trans*- to *cis*- by changing the solvent (Table 1, entries 3 and 6). Therefore, we tested some alkynes using DMF as solvent. Alkynes bearing electron-donating and electron-withdrawing groups are compatible, and gave predominantly the corresponding (*Z*)-alkenes in 74-86% yield (**2n**-**2p**).

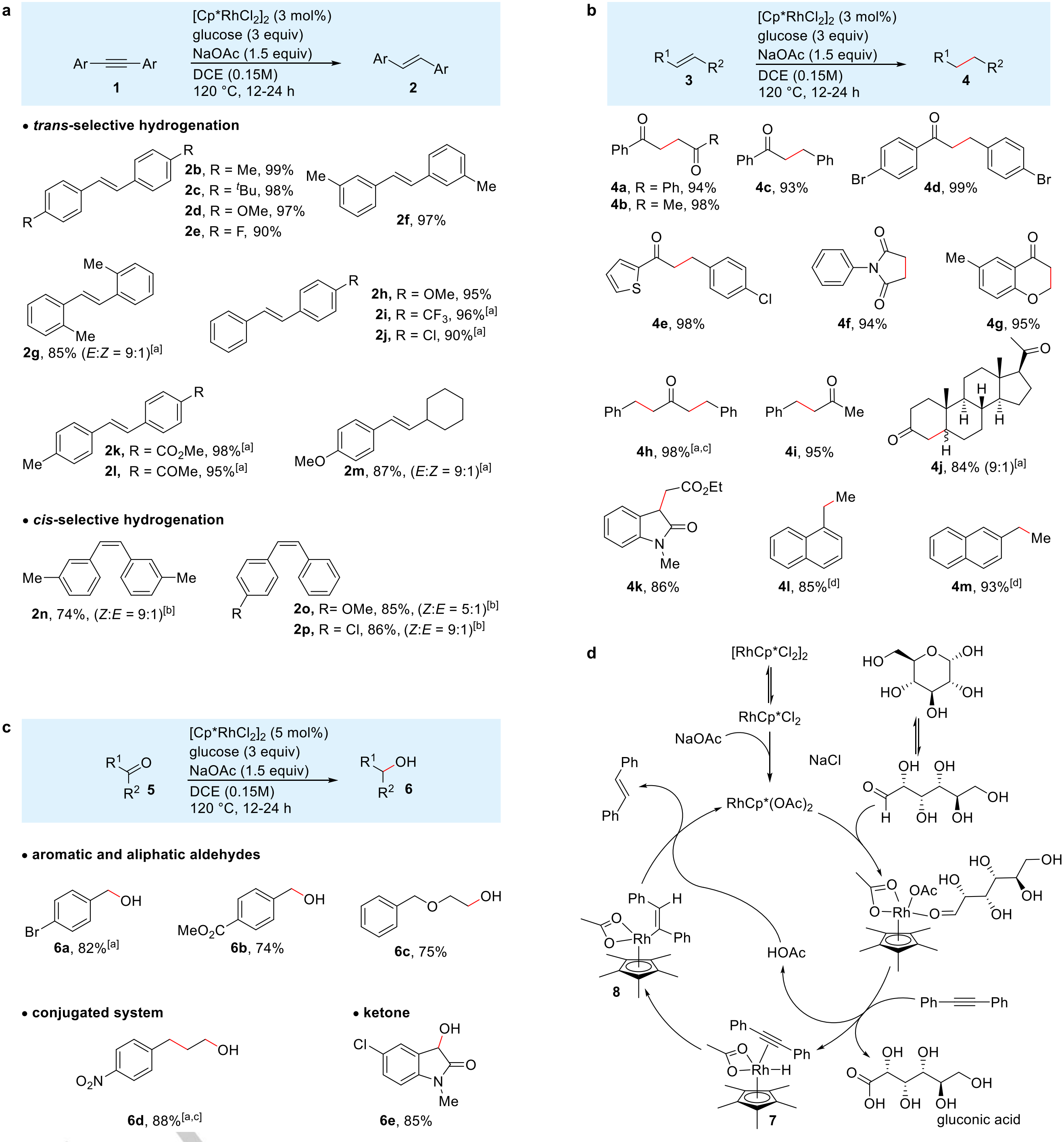


Figure 2. Transfer hydrogenation with biomass. Reaction conditions: **1** or **3** or **5** (0.15 mmol), glucose (0.45 mmol), [Cp*RhCl$_2$]$_2$ (3 mol%, 4.5 μmol), NaOAc (1.5 equiv), in DCE (0.15 M) at 120°C for 24 h under air. **a**, Hydrogenation of alkynes. **b**, Hydrogenation of alkenes. **c**, Hydrogenation of carbonyl compounds. **d**, Proposed reaction mechanism. [a] Catalyst (6 mol%, 9.0 μmol) was used. [b] Catalyst (5 mol%, 7.5 μmol) catalyst was used in DMF (0.15 M) for 12 h. [c] Glucose (6 equiv) was used. [d] Catalyst (5 mol%, 7.5 μmol) catalyst was used. *E*:*Z* ratios determined by ^{1}H-NMR analysis.

Having established the substrate scope of different alkynes, various alkenes and carbonyl-containing compounds were tested under optimal conditions. We were pleased to find that chemoselective reduction of alkene derivatives to the corresponding alkanes could be achieved in 84-99% yields. We found that a wide range of electron-deficient alkenes with various functional groups was well tolerated under optimized conditions (Figure 2b, **3a**-**3k**). Several electron-withdrawing alkenes were compatible and even with low catalyst loading affording the desired products smoothly. 1,4-Dicarbonyl alkene derivatives and chalcone derivatives led to products (**4a**-**4i**). Chemoselective reduction of chromone was observed in good yield without disturbing the carbonyl group (**4g**). The hydrogenation of two double bonds led to ketone **4h** in 98% yield using an excess of glucose. Pleasingly, a 2-oxindole derivative and progesterone with trisubstituted double bond were reduced selectively to **4k** and **4j**. Afterwards, we explored the scope of the reaction with terminal alkenes under the developed reaction conditions. The corresponding ethyl arenes **4l** and **4m** were isolated with 85-93% yields. Having described the reduction of alkenes, we examined various carbonyl containing compounds under standard reaction conditions (Figure 2c). The desired products were observed for the reduction of benzaldehyde derivatives to their corresponding benzyl alcohols (**6a**, **6b**). The aliphatic 2-(benzyloxy)acetaldehyde was selectively reduced to alcohol (**6c**) in 75% yield without cleavage of the benzyl group. A cinnamaldehyde derivative underwent a cascade reduction leading to the formation of **6d** in 88% yield. Finally, the keto group in isatin (**5e**) can be selectively reduced to give 3-hydroxyoxindole (**6e**) with 85% yield.

Having established the substrate scope of the transfer hydrogenation reaction, we conducted a series of control experiments to gain more mechanistic details. When the reaction was carried out without catalyst or glucose, we did not observe any desired product formation. When we carried out the reaction with δ-gluconolactone under standard reaction conditions, we observed trace amounts of the desired product (see Supporting information for the details). It is clear, that the reaction undergoes through abstraction of hydrogen from the carbonyl group of monosaccharides. Afterwards, we performed the transfer hydrogenation of **1a** using DMF as solvent. Again, in absence of catalyst or glucose, product formation was not detected. This indicates that rhodium is essential for the transfer hydrogenation. Furthermore, DMF cannot be utilized as source of hydrogen. Afterwards, we performed the hydrogenation using hydrogen, formic acid and *iso*-propanol instead of glucose. Using hydrogen, we obtained **2a** in 55% yield with an *E*/*Z* ratio of 2:1. Transfer hydrogenation using formic acid gave **2a** in 74% with *E*/*Z* ratio 4:1. The highest yield of 80% of **2a** was observed using *iso*-propanol as hydrogen source. However, the stereoselectivity of the reaction was lower (*E*/*Z* ratio is 2:1) and the formation of over-reduced product (1,2-diphenylethane) was detected. *This indicates that the developed transfer hydrogenation conditions using glucose as a renewable reagent are superior to commonly used conditions for transfer hydrogenation.*

Based on preliminary investigations and control experiments, a plausible mechanism has been proposed in Figure 2d. Initially, active cationic Cp*Rh(OAc)$_2$ is formed by ligand exchange. Afterwards, the rhodium complex is coordinated with the acyclic form of the monosaccharide via the carbonyl group. In the next step, a rhodium hydride complex is formed via oxidation of the aldehyde of the carbohydrate. This complex is coordinated to the substrate to form intermediate **7**. The following transfer of hydrogen from rhodium to the substrate gave complex **8**. Protonation of complex **8** by acetic acid led to the product of hydrogenation and regeneration of the active catalyst. Using DMF or DMA as solvent, we obtained *cis*-isomers as major products. This selectivity was probably raised by the coordination of the solvent to the rhodium in complex **8**. The introduction of bulkier ligands such as DMF or DMA instead of acetate induced cis-configuration of the alkenes. The transfer hydrogenation led to oxidation of glucose to gluconic acid, which is an important commercial product with wide application.

In conclusion, we have developed a catalytic transfer hydrogenation using biomass derived carbohydrates as reagent. Stereoselective and chemoselective hydrogenation of alkynes, alkenes and carbonyl compounds was demonstrated. Various functional groups were tolerated and hydrogenated products were obtained with up to 99% yield and notable stereoselectivity. The synthesis of stereoisomers by variation of reaction conditions was demonstrated. Developed method allows the application of various renewable carbohydrates and lignin in the hydrogenation. Our discovery provides an operationally simple method for transfer hydrogenation.

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Keywords: Biomass • Hydrogenation• Green chemistry • Carbohydrates • Rhodium

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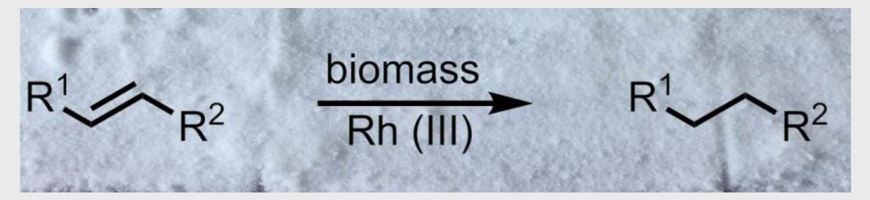
[9] The usage of biomass emmits carbon dioxide, but has been classed as a renewable energy source in the EU, USA and UN legal frameworks, because plant stocks can be replaced with new growth.

COMMUNICATION



Sweet chemistry. A catalytic transfer hydrogenation using biomass derived carbohydrates as reagent was developed. Stereoselective and chemoselective hydrogenation of alkynes, alkenes and carbonyl compounds was demonstrated. Our discovery provides an operationally simple method for transfer hydrogenation and represent a new concept for the application of renewable biomass

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