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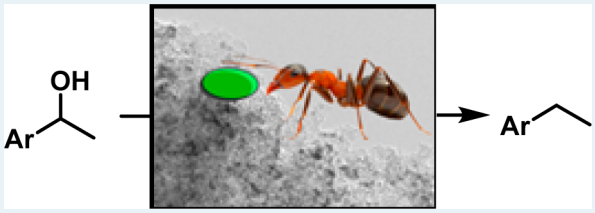
Pd-Catalyzed Transfer Hydrogenolysis of Primary, Secondary, and Tertiary Benzylic Alcohols by Formic Acid: A Mechanistic Study

Supaporn Sawadjoon, Anna Lundstedt, and Joseph S. M. Samec*

Department of Chemistry, BMC, Uppsala University, Box 576, 751 23 Uppsala, Sweden

Supporting Information

ABSTRACT: A palladium-catalyzed transfer hydrogenolysis of primary, secondary, and tertiary benzylic alcohols by formic acid has been developed and studied. The product hydrocarbons were obtained in excellent yields from both secondary and tertiary benzylic alcohols and in good yields for primary benzylic alcohols. The rate of disappearance of 1-phenylethanol (**1**) follows zero-order dependence in **1** and first-order dependence in formic acid and palladium. Catalytic amounts of base inhibit a competing disproportionation reaction of alcohol to alkane and ketone, and an optimum was obtained when 5 equiv of base to palladium was used. Deuterium kinetic isotope studies for the transfer hydrogenolysis reveal individual isotope effects for the hydridic position (k_{CHOH}/k_{CDOH} = 2.26 ± 0.24) and the protic position (k_{CHOH}/k_{CHOD} = 0.62 ± 0.06) of the formic acid. Simultaneous deuteration in both positions of formic acid gave a combined isotope effect of (k_{CHOH}/k_{CDOD} = 1.41 ± 0.11). We propose a mechanism involving the following steps: a competitive inhibition of the open palladium site by adsorption of the formate anion to generate formato-palladium species, followed by a reversible protonation and a rate-limiting hydride transfer to obtain the active palladium with chemisorbed hydrogen that performs the hydrogenolysis of the alcohol in a fast reaction step.



KEYWORDS: *heterogeneous catalysis, transfer hydrogenolysis, alcohols, kinetic isotope effect*

INTRODUCTION

The reduction of C−O bonds to the corresponding C−H bond is a fundamental transformation in organic synthesis.[1−3] While the reduction of benzylic ethers is a common reaction, the corresponding reaction of benzylic alcohols is studied to a lesser extent. There is an ambition to utilize lignocellulose as a carbon feed-stock for organic synthesis and biofuels.[4,5] Taking into account that benzylic alcohols are abundant functional group in lignin,[6] efficient methodologies to reduce the C−O bond in benzylic alcohols are highly desired. Traditionally, either Clemmensen[7] or Wolff−Kishner[8] reductions are performed on ketones, or Barton−McCombie deoxygenation[9] is performed on manipulated alcohols. A drawback of the traditional methodologies is the use of a stoichiometric amount of hazardous reagents.

An alternative methodology for transforming benzylic alcohols is the catalytic hydrogenolysis of nonmanipulated hydroxyl groups, in which the C−O bond is cleaved and substituted for a hydride.[10,11] Most studies have used catalysts based on palladium,[12−15] but ruthenium[16] and rhodium[17] have also been explored. Traditionally, hydrogen gas has been used in catalytic hydrogenolysis to generate the alkane and water as side product.[14,15] More recently, formic acid has been employed as the source of hydrogen, and the ensuing reaction has been termed "transfer hydrogenolysis" (eq 1).[12,13] Formic acid as a hydrogen source has many advantages with regards to handling, transport, and storage[18] and can easily be generated from hydrogen gas and carbon dioxide.[19] Because carbon dioxide can be recycled into formic acid with the addition of hydrogen gas, the overall process is atom efficient[20,21] and only water is formed as a byproduct. Another advantage of formic acid over hydrogen gas is that the latter can lead to over-reduction of aromatic substrates, thus resulting in lower chemoselectivity.[22]

$$\mathrm{R{-}OH + HCOOH \xrightarrow{[M]} R{-}H + CO_2 + H_2O} \quad (1)$$

Different reaction mechanisms have been proposed for catalytic hydrogenolysis. Van Bekkum et al. have performed detailed mechanistic studies in which they demonstrated by isotopic labeling that the acidic carbon support facilitates an initial elimination to generate the corresponding styrene, which is then attacked by a hydride to produce the alkane product.[16] Kwak et al. even referred to this effect as part of a bifunctional catalysis.[23] The corresponding study of transfer hydrogenolysis has been lagging behind. When formic acid was used as the hydrogen donor in the transfer hydrogenolysis of alcohols, a competing disproportionation of the alcohol was observed (Scheme 1, pathway a).[12] Formic acid may result in esterification of the alcohol (Scheme 1, pathway b).[24] It has been proposed that the esterification may precede the hydrogenolysis by converting the hydroxyl group into a better leaving group.[25] There are also reports where the formate ester intermediate decomposes into the alkane[26] or undergoes

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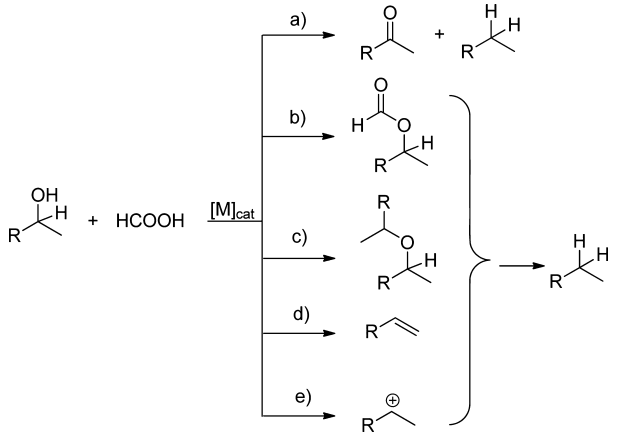
Scheme 1. Intermediates Observed (a–d) and Proposed (e) for the Transfer Hydrogenolysis of Alcohols



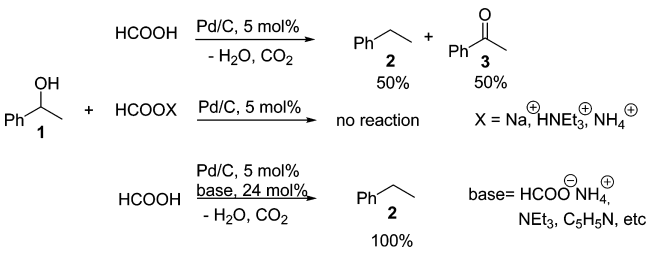
elimination to form the alkene.[24] The alcohol may also undergo etherification to generate the symmetrical ether as the first step,[27] followed by hydrogenolysis (Scheme 1, pathway c).[28] Formic acid may promote initial elimination to generate the alkene, followed by hydrogenation in line with van Bekkum's study on the catalytic hydrogenolysis of benzylic alcohols (Scheme 1, pathway d).[23] Alternatively, the acidity may promote activation of the hydroxyl group by generating a carbenium ion followed by a hydride addition (Scheme 1, pathway e).[12−15]

In the present work, we have studied the transfer hydrogenolysis of different benzylic alcohols, using palladium on carbon as the catalyst. A remarkable effect of added base was observed whereby the competing disproportionation reaction (Scheme 1, pathway a) was inhibited, allowing an efficient and general transfer hydrogenolysis to be demonstrated. A detailed mechanistic study of the transfer hydrogenolysis has been performed. On this basis, we propose that the significant element to the reaction is the generation of the formato-palladium intermediates that inhibit the competing disproportionation. This is followed by a reversible protonation and a rate-limiting hydride transfer to generate palladium with chemisorbed hydrogen, which is responsible for the hydrogenolysis of the alcohol.

RESULTS AND DISCUSSION

(A). Transfer Hydrogenolysis of Alcohols. *Effect of Hydrogen Donor and Base.* When attempts were made to perform the Pd-catalyzed transfer hydrogenolysis of phenylethanol (**1**) in ethanol–water mixture (4:1) using formic acid as hydrogen donor at 80 °C, a rapid disproportionation was observed to yield a 1:1 mixture of ethylbenzene (**2**) and acetophenone (**3**) after 2 min (Scheme 2). After the initial disproportionation, a slow transfer hydrogenation of **3** to **1** and subsequent formation of **2** was observed. After 1 h, 60% conversion to **2** was observed. Palladium on carbon (5 mol %) was used as catalyst, since it has previously been reported to be most active in both catalytic hydrogenolysis and catalytic transfer hydrogenolysis.[12−15] The disproportionation was also observed in the absence of formic acid albeit at a lower reaction rate. Attempts to activate the palladium by vacuum and heat prior to the reaction did not affect the outcome. Attempts to activate the palladium by exposure to hydrogen gas prior to catalysis or running the transfer hydrogenolysis under an atmosphere of hydrogen gas gave marginal improvement; a 70% conversion to ethylbenzene was observed after 30 min. Even though the mechanism of the disproportionation of alcohols has not been elucidated, a pathway proceeding through a palladium with chemisorbed hydrogen, in analogy to a hydrogenolysis,[14,15] would be expected. Both previous studies describing the use of formic acid as a hydrogen donor for the catalytic transfer hydrogenolysis of benzylic alcohols reported that the addition of base gave a lower yield of the product.[12,13] This is in contrast to the transfer hydrogenolysis of esters[25] and halides,[29] in which formic acid was found to be inactive in the reaction. Instead, formate salts of either Group 1A or ammonium were used for a successful catalytic transfer hydrogenolysis. Trials using pure formate salts in the transfer hydrogenolysis of **1** did not lead to any reactivity and only the original material was observed in the reaction mixture. Ammonium formate is known to generate Pd–H^- species, and transfer hydrogenolysis of both benzylic esters and halides are promoted using formate salts.[25,29] The greater leaving group ability for these substrates would not require proton transfer as in the case of benzylic alcohols.

Scheme 2. Effect of Base in the Transfer Hydrogenolysis of 1



We found that the addition of a catalytic amount of base generated a powerful reduction medium for the catalytic transfer hydrogenolysis of **1**. Within 30 min, full conversion to **2** was observed (Scheme 2). Triethylamine, pyridine, ammonium formate, and sodium carbonate were tested as bases, and all gave similar performance in the catalytic transfer hydrogenolysis of **1**. The order of addition was important. Successful transfer hydrogenolysis was achieved when the palladium on carbon was activated by the base in a solvent–water mixture for at least 2 min before the addition of formic acid and substrate. The amount of base affected the amount of **3** formed and also how efficiently **2** was generated. With a 5:1 molar ratio of base to palladium, 70% conversion of **1** was observed after 5 min, and the concentration of disproportionation product **3** was below 10%. Using a 10:1 ratio of base to palladium gave a 45% conversion of **1** and only traces of **3** were observed in the reaction medium. At higher concentration of base, the transfer hydrogenolysis reaction was inhibited.

Effect of Solvent Mixture. Water is necessary for efficient catalytic transfer hydrogenolysis, as is the presence of a cosolvent, without which only poor results were obtained. However, a variety of cosolvents, ranging in polarity from benzene to methanol, worked well in the Pd-catalyzed transfer hydrogenolysis of **1**. In the absence of water, a disproportionation reaction was observed. The water is expected to promote the solubility of the formate ion and thereby the generation of the formato-palladium species that inhibit the disproportionation reaction.[12,13]

Transfer Hydrogenolysis of Benzylic Alcohols. The optimized reaction conditions, using a 5:1 molar ratio of base to palladium, and formic acid (3 molar equiv. to alcohol) in an

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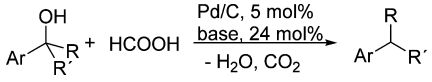
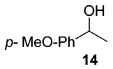
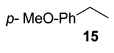
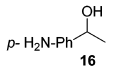
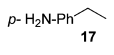
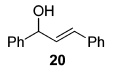
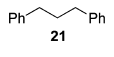
ethanol/water mixture, were employed for the transfer hydrogenolysis of different benzylic alcohols. The reactions were run at 80 °C and performed in a 0.42 mmol scale. The yield was determined by isolation or quantitative NMR spectroscopy using mesitylene as an internal standard. Alcohol **1** was reduced to **2** in 98% conversion within 40 min using 5 mol % palladium (Table 1, entry 1). We were curious whether a tertiary alcohol would work, since the dehydrogenation pathway would not be possible. 2-Phenyl-propan-2-ol (**4**) was reduced to the isopropylbenzene (**5**) in 87% conversion using 5 mol % Pd. We were also curious as to whether a primary alcohol would work in spite of its presumed reluctance to generate a carbenium ion intermediate. Gratifyingly, benzyl alcohol (**6**) was reduced to toluene (**7**) in a 61% conversion within 40 min. These substrates demonstrate a broad scope in which primary, secondary, and tertiary benzylic alcohols were reduced to their corresponding hydrocarbons (Table 1, entries 1−3).

Table 1. Transfer Hydrogenolysis of Different Benzylic Alcohols to the Corresponding Hydrocarbon[a]



Entry	Alcohol	Product	Yield[b]
1	 **1**	 **2**	98
2	 **4**	 **5**	87
3	 **6**	 **7**	61
4	 **8**	 **9**	95[c]
5	 **10**	 **11**	94[c]
6	 **12**	 **13**	56[c,d]
7	 **14**	 **15**	98
8	 **16**	 **17**	96
9	 **18**	 **19**	50[d]
10	 **20**	 **21**	67[c]
11	 **22**	 **23**	78
12	 **24**	 **25**	99[c]

[a]Conditions: Alcohol (0.4 mmol), 5% Pd/C (42 mg), $HCOONH_4$ (0.095 mmol), HCOOH (1.3 mmol), MeOH (2.4 mL), water (0.6 mL), temperature 80 °C. [b]Yields were calculated using ^1H NMR with mesitylene as an internal standard. [c]Isolated yield. [d]10 mol % of Pd was used.

1,1-Diphenylethanol (**8**) was reduced to generate 1,1-diphenylethane (**9**) in a 95% yield within 40 min. Diphenylmethanol (**10**) was reduced to diphenylmethane (**11**) in a 94% yield within 40 min. 1-Phenylethane-1,2-diol (**12**) was selectively reduced in the benzylic position to generate 1-phenyl-2-propanol (**13**) (Table 1, entry 6). Substitution of the phenyl group in the *para*-position by electron donating groups gave the corresponding hydrocarbons in excellent yields (Table 1, entries 7 and 8). Substitution of the phenyl group in the *para*-position by an electron withdrawing group gave the corresponding hydrocarbons in lower yields (Table 1, entry 9). The allylic alcohol **20** was reduced to saturated **21** in a good yield, in which both the hydroxyl group and the alkene were reduced (Table 1, entry 10). Naphthyl ethanol (**22**) was reduced to generate naphtyl ethane (**23**) in a good yield (Table 1, entry 11). Triphenyl methanol (**24**) was reduced to triphenylmethane (**25**) in a quantitative yield (Table 1, entry 12).

(B). Mechanistic Studies. While the mechanism of palladium-catalyzed alkyne transfer hydrogenation by formic acid has been well studied, the corresponding study on the transfer hydrogenolysis of alcohol has not.[30] The importance of developing atom efficient reductions of alcohols in general and for biomass related compounds in particular,[4,5] in addition to our interest in the mechanism of C−O activation,[31−33] motivated us to perform a mechanistic study.

Nature of the Catalyst. The catalyst was characterized by Transmission Electron Microscope (TEM) and Brunauer−Emmett−Teller (BET) techniques. The mean particle size was 2−3 nm and the BET surface area 813 m^2/g. At stirring rates below 300 rounds per minute, diffusion control was operating, whereas at higher stirring rates, kinetic control was operating (Supporting Information). High reproducibility in the kinetic experiments (relative standard deviation of 3.9%, $n = 6$) supported the observation that kinetic control, rather than diffusion control, was operating under our reaction conditions (Supporting Information). The reactions showed good reproducibility between different batches of Pd/C and were also unaffected by using inert and purified reagents and solvent. Inhibition experiments were performed to determine the heterogeneous nature of the catalyst where the addition of triphenylphosphine inhibited the reaction and polymer bound triphenylphosphine did not affect the rate of the transfer hydrogenolysis (Supporting Information).[34]

Initial Rates for the Transformation of Postulated Intermediates to Ethylbenzene. Different intermediates for the catalytic hydrogenolysis and transfer hydrogenolysis of alcohols have previously been proposed.[12,13] During the optimization of the reaction conditions, we observed a few of these intermediates (**3**, **27**, **28**, **29**) by ^1H NMR spectroscopy. To be able to exclude the observed intermediates as intermediates in the mechanism of **1** to **2**, we compared the initial rates of conversion of these possible intermediates.

The observed initial rate for the disappearance of **1** was 3.3×10^{-3} mol L^{-1} s^{-1} (Table 2, entry 1). Styrene (**26**) underwent a fast transfer hydrogenation with a higher initial rate than **1**

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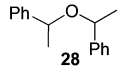
Table 2. Transfer Hydrogenolysis of Different Intermediates Found in Catalysis[a]

Entry	Substrate	Initial rate ($\times 10^{-3}$ mol $L^{-1}s^{-1}$)
1	 **1**	3.3
2	 **26**	19.1
3	 **3**	4.6
4	 **27**	2.4
5	 **28**	0.9
6	 **29**	1.2

[a]Conditions: The optimized reaction conditions were used [substrates (0.4 mmol), Pd/C (4.9 mol %), $HCOONH_4$ (0.095 mmol), HCOOH (1.3 mmol), MeOH (2.4 mL), water (0.6 mL), temperature 25 °C, stirring speed 350 rpm]. Initial rate was determined as an average of two runs (Supporting Information).

(Table 2, entry 2). The disappearance of acetophenone **3** also gave a high initial rate of starting material (Table 2, entry 3). Thereby these two intermediates, especially **26** would be difficult to observe as such during the transfer hydrogenolysis of **1**. 1-Phenylethyl formate (**27**) was transformed into **2** at a lower rate relative to **1** (Table 2, entry 4). Intermediate **27** was observed under acidic conditions, but not in the presence of the formate/formic acid mixture used in the successful hydrogenolysis. Also, the diphenylethyl ether (**28**) and 1-methoxy-1-phenylethane (**29**) were reduced at a lower rate than **1** (Table 2, entries 5−6).

Reaction Order Determination. Initial rates were determined for the Pd/C catalyzed transfer hydrogenolyis of **1** by formic acid at 25 °C. Concentrations of **1** were varied between 0.06 and 2.6 M, and initial rates were determined at a conversion of **1** below 10%. The initial rates for the transfer hydrogenolysis of **1** was performed in a thermostatted oil bath where aliquots were withdrawn from the reaction mixture at the different time intervals and the conversions were determined by ^{1}H NMR spectroscopy. As seen in Figure 1, the initial rate for transfer hydrogenolysis of **1** using Pd/C and formic acid and formate was independent of the substrate concentration in the examined range.

This zero-order dependence of **1** is in accordance with a mechanism where the hydrogen transfer to the substrate or C−O bond cleavage is not the rate-determining step. It should be noted that intermediates **27**−**29** were not observed during the course of the reaction, and would have been if they were intermediates in the mechanism from **1** to **2**. This is in agreement with the lower relative rates observed for the transfer hydrogenolysis of **27**−**29** compared to **1** and **3** (Table 2).

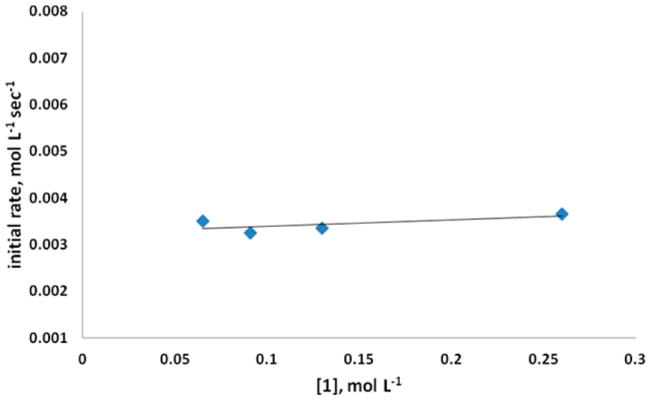


Figure 1. Dependence of initial rate on concentration of substrate **1** in the Pd/C catalyzed transfer hydrogenolysis of **1** by formic acid. Reaction conditions: **1** (0.065−0.26 M), Pd/C (4.9 mol %), $HCOONH_4$ (0.095 mmol), HCOOH (1.3 mmol), MeOH (2.4 mL), water (0.6 mL), temperature 25 °C, stirring speed 350 rpm.

The plot of initial rate of reaction versus the concentration of hydrogen donor is shown in Figure 2. The reaction rate followed a linear relationship with the concentration of formic acid over the range 0.1−0.45 M. The first-order dependence of the hydrogen donor supports a reaction mechanism in which the proton and/or hydride transfer is involved in, or precede, the rate-limiting step.

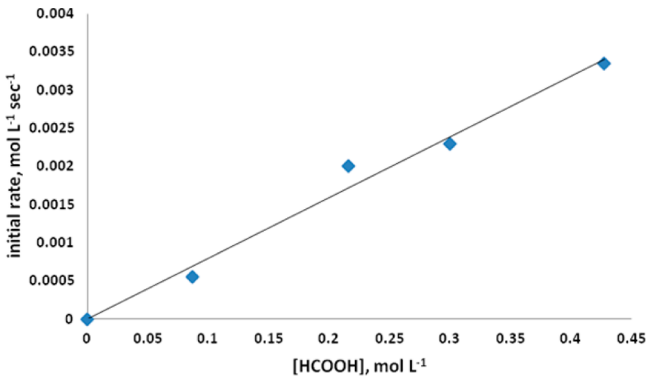


Figure 2. Dependence of initial rate on concentration of formic acid in the Pd/C catalyzed transfer hydrogenolysis of **1** by formic acid. Reaction conditions: **1** (0.4 mmol), Pd/C (4.9 mol %), $HCOONH_4$ (0.095 mmol), HCOOH (0.087−0.427 M), MeOH (2.4 mL), water (0.6 mL), temperature 25 °C, stirring speed 350 rpm.

The plot of initial rate versus concentration of the catalyst is displayed in Figure 3. The first-order dependence of the catalyst is clear from the plot. The high reproducibility of the kinetic runs with the catalyst implies that kinetic-, rather than diffusion control, is operating (Supporting Information).[34] Noteworthy, no sigmoidal kinetic curve was observed during these experiments. This supports that palladium on carbon and not leaked colloidal metal is reactive in the transfer hydrogenolysis of alcohols.[34]

The rate order of the base was studied (Figure 4). Without base, a disproportionation reaction occurs, in which the substrate also acts as a hydrogen donor, generating a 1:1 ratio of **2** and **3**. The rate of the disproportionation reaction is proportionally inhibited by the base ($HCOONH_4$ concen-

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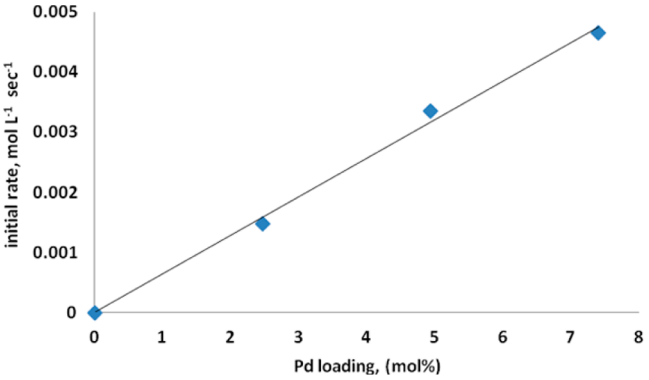


Figure 3. Dependence of initial rate on catalyst loading in the Pd/C catalyzed transfer hydrogenolysis of **1** by formic acid. Reaction conditions: **1** (0.4 mmol), Pd/C (2.47−7.40 mol %), $HCOONH_4$ (0.095 mmol), HCOOH (1.3 mmol), MeOH (2.4 mL), water (0.6 mL), temperature 25 °C, stirring speed 350 rpm.

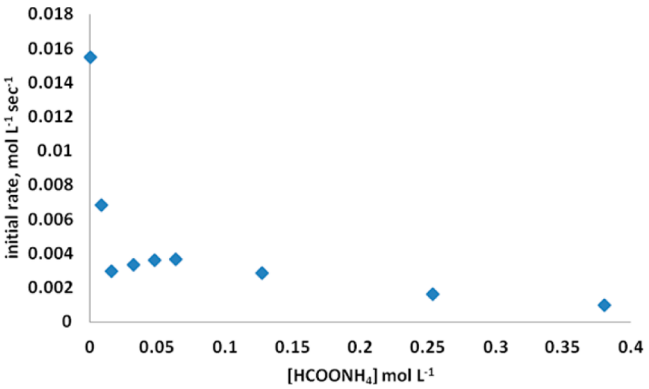


Figure 4. Dependence of initial rate on concentration of ammonium formate in the Pd/C catalyzed transfer hydrogenolysis of **1** by formic acid. Reaction conditions: **1** (0.4 mmol), Pd/C (4.9 mol %), $HCOONH_4$ (0.0079−0.3806 M), HCOOH (1.3 mmol), MeOH (2.4 mL), water (0.6 mL), temperature 25 °C, stirring speed 350 rpm.

trations 0−15.9 mM). Between 15.9 and 63 mM of the ammonium formate, the rate is independent of the base. At these concentrations, negligible concentration of **3** was observed, and a transfer hydrogenolysis is operating, in which the formic acid acts as a hydrogen donor. At base concentrations above 63 mM, the transfer hydrogenolysis is negatively affected by the concentration of base, and with only formate, no reaction occurs.

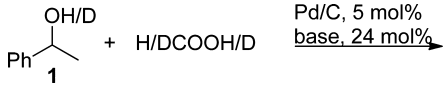
This gives a rate equation for the transfer hydrogenolysis in which the reaction rate is dependent on Pd and formic acid, depicted in eq 2. At lower concentration of the base, a fast disproportionation reaction occurs. At higher concentrations of the base, the transfer hydrogenolysis is inhibited and another mechanism is operating, involving a formato-palladium or palladium monohydride species not active in the transfer hydrogenolysis of alcohols.

$$-\frac{d[\mathbf{1}]}{dt} = k[\mathrm{Pd}][\mathrm{HCOOH}] \quad (2)$$

The rate equation implies that the hydrogen transfer between the formic acid and palladium is involved in the rate-determining step, and that C−O bond cleavage is not. Therefore, we decided to study the hydrogen transfer in detail.

Deuterium Kinetic Isotope Effect. The kinetic deuterium isotope effect of the transfer hydrogenolysis of **1** was studied at room temperature using the optimized reaction conditions monitored by removing aliquots at regular intervals and measuring the disappearance of **1** by ^1H NMR spectroscopy. The water (H_2O or D_2O) and methanol (CH_3OH or CD_3OD) present in the reaction medium determined whether deuterium or hydrogen was present at the protic position of formic acid. In the transfer hydrogenolysis of **1** using HCOOH and H_2O, we found k_{obs} = 3.27 (±0.12) × 10^{-3} mol L^{-1} s^{-1}. When running the reaction in deuterated formic acid and deuterated solvents, k_{obs} = 2.33 (±0.25) × 10^{-3} mol L^{-1} $s^{-1}$was determined. The observed deuterium kinetic isotope effect (k_H/k_D) was therefore 1.41 (±0.11) (Table 3). When running the reaction

Table 3. Kinetic Deuterium Isotope Effect for Transfer Hydrogenolysis of 1



k_{CHOH}/k_{CDOH}	2.26 ± 0.24
k_{CHOH}/k_{CHOD}	0.62 ± 0.06
k_{CHOH}/k_{CDOD}	1.41 ± 0.11

with selective deuterium incorporation at the OD position, we measured k_{obs} = 5.33 (±0.34) × 10^{-3} mol L^{-1} s^{-1}, giving a deuterium kinetic isotope effect of 0.62 (±0.06) (Table 3). When running the reaction with formic acid selectively deuterated at the hydridic position, we determined a value of k_{obs} = 1.47 (±0.21) 10^{-3} mol L^{-1} s^{-1}, giving a deuterium kinetic isotope effect of 2.26 (±0.24) (Table 3).[35,36] These kinetic isotope effect values are consistent with a reversible proton transfer and a rate-determining hydride transfer from formic acid to palladium.

Attempts to perform a labeling study using selectively deuterated formic acid (DCOOH or HCOOD) to distinguish whether the proton or hydride of formic acid can be discriminated in the product were unsuccessful. The proton source determined the label of both the α- and the β-position of the product, even at a 10% conversion. In a competitive experiment, we observed that the deuterium incorporation in toluene by HCOOD was faster than the transfer hydrogenolysis of benzylic alcohol by HCOOD. The inverse kinetic isotope effect for the proton transfer is consistent with a scrambling of the proton and may explain why the labeling studies were unsuccessful.

MECHANISTIC DISCUSSION

Disproportionation and Transfer Hydrogenation Pathway. Palladium on carbon catalyzes the disproportionation of **1** in the presence or absence of formic acid to generate a 1:1 mixture of **2** and **3** (Scheme 2).[13] The reaction is fast and within 2 min, a 90% conversion of **1** is observed. A possibility is that a fast disproportionation of the alcohol is followed by a slower transfer hydrogenation of the ketone to regenerate the alcohol. In this case, the formic acid would operate as a hydrogen donor to regenerate **1** from **3** (Scheme 3). Because the conversion of **3** to **1** is faster than the conversion of **1**, this may be a possible reaction mechanism. However, the transfer hydrogenolysis was successful even with tertiary alcohols (which cannot undergo β-hydride elimination); this is inconsistent with a disproportionation pathway, as is the rate

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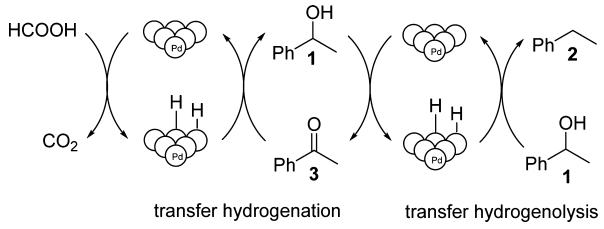
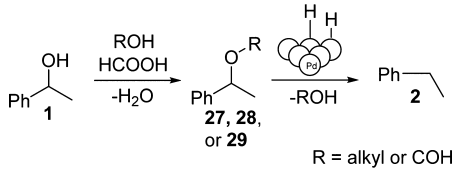
Scheme 3. Disproportionation and Transfer Hydrogenation Pathway



expression in which the substrate is absent (zero-order dependence in **1**). The fact that the initial rate was independent of **1** is inconsistent with a disproportionation pathway, where a rate-determining transfer dehydrogenation is expected to be operating during the initial turnovers (>10% conversion, measured in Figure 1).

Ester and Ether Pathways. Both the ether and ester have been observed by other research groups as well as by our group during the optimization studies with low catalyst loadings under acidic conditions (Scheme 4). However, under our optimized

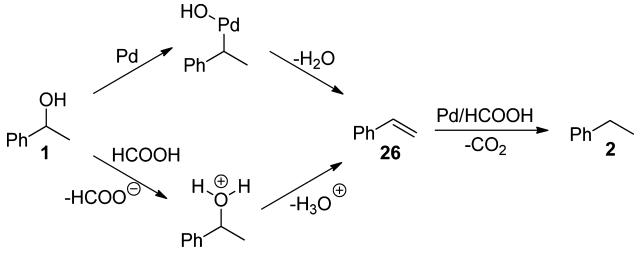
Scheme 4. Transfer Hydrogenolysis via Ether or Ester Intermediates



reaction conditions, these intermediates were not observed. Since the transfer hydrogenolysis rates for both the ester and the two ethers were much slower (20% and 35% conversion after 20 min, respectively) than the rate of transfer hydrogenolysis of **1** (a 90% conversion after 20 min), one would expect them to be detectable by ^{1}H NMR spectroscopy if they were true intermediates. However, we were unable to observe **27**−**29** under the reaction conditions.

Elimination and Transfer Hydrogenation Pathway. An elimination to form an alkene intermediate either via an acid-catalyzed E_1-mechanism or by an insertion of palladium into the C−O bond, followed by a β-hydride elimination has been suggested as the pathway for the hydrogenolysis of alcohols by hydrogen gas (Scheme 5).[14] The acid-catalyzed elimination reaction would generate styrene in the absence of palladium, but this was not observed in subsequent studies. Moreover, if this were the case, tertiary alcohols would be expected to undergo faster transfer hydrogenolysis than secondary alcohols,

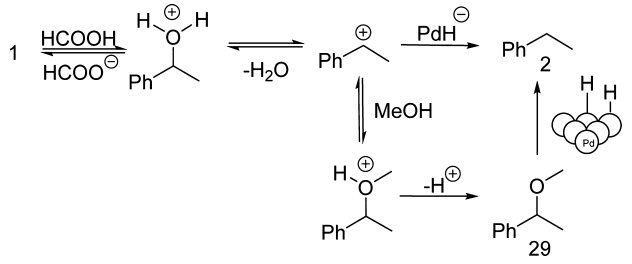
Scheme 5. Mechanism Proceeding through Elimination and a Transfer Hydrogenation



but this was not observed. Furthermore, primary alcohols that were successfully transformed to the corresponding hydrocarbons are not susceptible toward an elimination pathway. Also, secondary alcohols without β-hydrogens, such as **10**, were successfully transformed, which would not be expected if the transformation proceeded through an elimination pathway.

Protonation and Carbocation Formation. The formic acid may facilitate protonation to convert the hydroxyl group of **1** into a better leaving group, which is subsequently eliminated to leave behind a carbenium ion (Scheme 6). That *para*-

Scheme 6. Reaction Mechanism for the Transfer Hydrogenolysis Involving a Carbenium Intermediate



substitution by electron-donating substituents facilitates transfer hydrogenolysis, while electron-withdrawing substituents impede the reaction and supports the elimination hypothesis (Table 1, entries 7−9). In addition, the primary benzylic alcohols showed lower reactivity than the secondary and tertiary benzylic alcohols (Table 1, entries 1−3). If the carbenium ion was generated, the excess methanol in the reaction medium would be expected to trap the carbenium ion and form 1-methoxy-1-phenylethane (**29**), via an S_N1 reaction mechanism (MeOH/Pd is 2650:1). If the ether was an intermediate in the reaction, it would have been observed because the rate of reduction of the ether is lower compared to the transfer hydrogenolysis of **1**, and this is not the case. Furthermore, the reaction rate for a tertiary benzylic alcohol would be expected to be faster than a secondary alcohol if the reaction proceeded through a carbenium ion intermediate. The fact that the transfer hydrogenolysis works on unactivated primary benzylic alcohols that are highly unlikely to generate a carbenium ion counts heavily against this proposed pathway.

Proposed Mechanism. In the proposed reaction mechanism, a formate anion adsorbs with palladium to generate formato-palladium intermediate **A** (Scheme 7). This adsorption inhibits the disproportionation pathway by blocking the open coordination site of palladium for **1** ($K_2 > k_1$). This is consistent with the negative rate dependence for the base between 0 and 16 mM (Figure 4), where the mechanism changes from a fast disproportionation to a slower transfer hydrogenolysis. Complex **A** or a generated monohydride palladium species is not active in the transfer hydrogenolysis of benzylic alcohols, because of the poor leaving group ability of the hydroxyl group (Scheme 2). In the presence of formic acid a proton equilibrates with complex **A** and complex **B**. This is consistent with the inverse kinetic isotope effect for the proton transfer ($k_{CHOH/CHOD}$ = 0.62 ± 0.06) observed when using formic acid deuterated in the protic position. The proton transfer is followed by a rate-limiting hydride transfer to generate palladium with chemisorbed hydrogen (**C**). This is consistent with the primary kinetic isotope effect ($k_{CHOH/CDOH}$ = 2.26 ± 0.24) observed for the hydride transfer.[30,37,38] The transfer of

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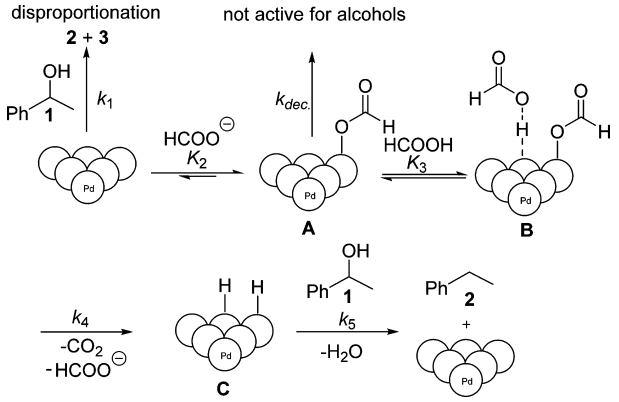
Scheme 7. Proposed Reaction Mechanism of the Transfer Hydrogenolysis of 1 by Formic Acid



the proton and the hydride from the formic acid to palladium may occur in a concerted process. The product of the two individual isotope effects (0.62 × 2.26 = 1.40), falls within experimental error of the combined D isotope effect measured for ($k_{CHOH/CDOD}$ = 1.41 ± 0.11), in accordance to Casey's methodology to determine concerted hydrogen transfers in transition metal catalysis.[39] Complex **C** reduces the benzylic alcohol in a fast reaction step. The fact that palladium on carbon alone catalyzes the disproportionation, which is known to proceed through a palladium with chemisorbed hydrogen intermediate, counts in support of this mechanistic proposal.[40] The observation that the transfer hydrogenolysis showed zero-order dependence in benzylic alcohol is consistent with a reaction mechanism in which both the adsorption of the alcohol to **C** and the reduction step, and thus also C−O bond cleavage, is not rate-limiting. The formic acid may promote the C−O bond cleavage by protonation, however not in a rate-determining step.

CONCLUSION

Pd/C catalyzes the disproportionation of benzylic alcohols to generate a 1:1 ratio of ketone and hydrocarbon. In the presence of formic acid and a catalytic amount of base, this ratio is changed in favor of the hydrocarbon. The base can be an organic or an inorganic base. The transfer hydrogenolysis works equally well for secondary and tertiary alcohols to generate the corresponding hydrocarbons in excellent yields. Primary benzylic alcohols are transformed to the corresponding hydrocarbons in moderate yields. We have found an inverse kinetic isotope effect for the protic position (k_{CHOH}/k_{CHOD} = 0.62 ± 0.06) and a primary kinetic isotope effect for the hydridic position of formic acid (k_{CHOH}/k_{CHOD} = 2.26 ± 0.24). The product of the two individual isotope effects (0.62 × 2.26 = 1.40) is within experimental error of the combined deuterium kinetic isotope effect measured for the transfer hydrogenolysis ($k_{CHOH/CDOD}$ = 1.41 ± 0.11).

We propose a mechanism in which the formate anion adsorbs to the palladium. The role of the base is to inhibit the disproportionation pathway by blocking the vacant coordination sites on Pd, preventing the undesired disproportionation reaction of **1**. A proton from formic acid equilibrates with the formato-palladium complex **A**. The hydride transfer from formic acid to Pd occurs in a rate-determining step. The proton and hydride transfer from formic acid to palladium may occur in a concerted step. The transfer of the hydrogens from Pd, that is, the hydrogenolysis of the benzylic alcohol, occurs in a fast reaction step.

EXPERIMENTAL SECTION

NMR spectra were recorded on a Varian UNITY (^{1}H at 400 MHz, ^{13}C at 100 MHz) or a Varian INOVA (^{1}H at 500 MHz, ^{13}C at 125 MHz) spectrometer. The chemical shifts are reported using the residual solvent signal as an indirect reference to TMS ^{1}H ($CHCl_3$): 7.26 ppm, ^{13}C ($CDCl_3$): 77.16 ppm. The Transmission Electron Microscope (TEM) studies were done in a JEM 2100F (Jeol, Japan) operating at 200 kV and equipped with an Energy Dispersive X-ray Spectrometer (EDS). For the BET measurements, the uptake of N_2 was measured at the temperature of liquid nitrogen (−196 °C or 77 K) using a Micromeritics ASAP2020 volumetric adsorption analyzer. Column chromatography was performed with Merck silica gel (0.04−0.06 mm). Thin layer chromatography (TLC) was performed using Fluka precoated silica gel (0.2 mm) 60-F254 plates. All reactions were performed in heavy-walled glass Emrys process vials (2−5 mL) sealed with aluminum crimp caps fitted with a septum. All yields were determined by isolation or by using qNMR where a ^{1}H NMR spectrum was recorded on a Varian UNITY at 400 MHz with d1 = 30 and using mesitylene as an internal standard. All chemicals including Pd/C were purchased from Sigma-Aldrich. No further purification was needed to obtain reproducible kinetic data (Supporting Information). Controls using purified reagents and solvents were performed, without change in performance or reproducibility.

Reduction of 1-Phenylethanol (1) with Pd/C. 5% Pd/C (42 mg, 0.021 mmol) and $HCOONH_4$ (6 mg, 0.095 mmol) were added to a predried vial. The vial was capped and flushed with argon, and EtOH (2.4 mL) and H_2O (0.6 mL) were added via syringe. The mixture was placed into a preheated oil-bath at 80 °C. Formic acid (50 μL, 1.05 mmol) was added after 3 min and after an additional 2 min, **1** (50 μL, 0.42 mmol) was added. The mixture was stirred at 80 °C for 30 min. NMR samples were prepared by removing 0.05 mL aliquots from the reaction mixture and filtration through Celite using $CDCl_3$ (1.3 mL) containing mesitylene (1 μL) as eluent. The filtrate was dried over Na_2SO_4 and added to an NMR tube. The ^{1}H NMR spectrum of **1** shows a characteristic multiplet at δ 7.20 and a doublet at δ 1.46 ppm, **2** shows a characteristic multiplet at δ 7.36 and a triplet at δ 1.26, and **3** a characteristic multiplet at δ 7.50 and at singlet at δ 2.62 and compared to mesitylene signal at δ 6.76.

General Procedure for Kinetics of Reduction of 1-Phenylethanol (1) with Pd/C. 5% Pd/C (42 mg, 0.021 mmol) and $HCOONH_4$ (6 mg, 0.095 mmol) were added to a predried vial. The vial was capped and flushed with argon, and MeOH (2.4 mL) and H_2O (0.6 mL) were added via syringe. Formic acid (50 μL, 1.05 mmol) was added after 3 min and after 2 min **1** (50 μL, 0.42 mmol) was added. The mixture was stirred at 25 °C. NMR samples were prepared by removing 0.05 mL aliquots from the reaction mixture, filtration through Celite using $CDCl_3$ (1.3 mL) as eluent, followed by the addition of mesitylene (1 μL) as an internal standard. The filtrate was dried over Na_2SO_4 and added to an NMR tube. The disappearance of substrate **1** was monitored by comparison of the signal for a proton in **1** resonating at δ 4.85 with the mesitylene signal at δ 6.76.

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■ ASSOCIATED CONTENT

Supporting Information

The heterogeneous nature of the catalyst have been studied by kinetics and also TEM and BET measurements. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: joseph.samec@kemi.uu.se.

Notes

The authors declare no competing financial interest.

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