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Generalized Chemoselective Transfer Hydrogenation/ hydrodeuteration

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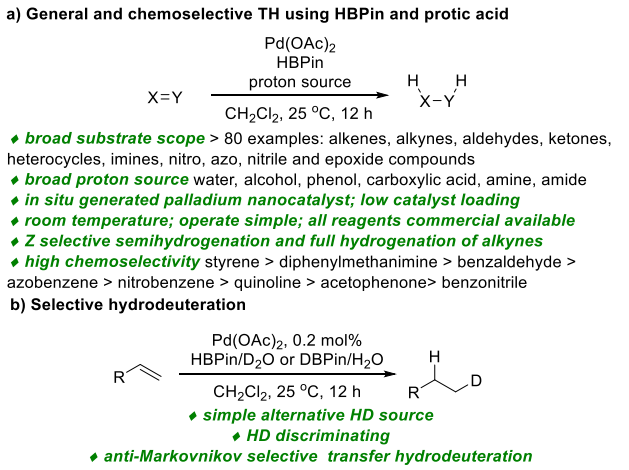
Abstract. A generalized, simple and efficient transfer hydrogenation of unsaturated bonds has been developed using HBPin and various proton reagents as hydrogen sources. The substrates, including alkenes, alkynes, aromatic heterocycles, aldehydes, ketones, imines, azo, nitro, epoxy and nitrile compounds, are all applied to this catalytic system. Various groups, which cannot survive under the Pd/C/H_2 combination, are tolerated. The activity of the reactants was studied and the trends are as follows: *styrene> diphenylmethanimine> benzaldehyde> azobenzene> nitrobenzene> quinoline> acetophenone> benzonitrile.* Substrates bearing two or more different unsaturated bonds were also investigated and transfer hydrogenation occurred with excellent chemoselectivity. Nano-palladium catalyst *in situ* generated from $Pd(OAc)_2$ and HBPin extremely improved the TH efficiency. Furthermore, chemoselective anti-Markovnikov hydrodeuteration of terminal aromatic olefins was achieved using D_2O and HBPin *via in situ* HD generation and discrimination.

Keywords: chemoselective; HBPin; hydrodeuteration; palladium nanocatalyst; transfer hydrogenation

Introduction

Reduction of multiple bonds through transfer hydrogenation (TH) instead of a flammable hydrogen gas has been intensely developed and extensively applied in academic and industrial syntheses.[1] Amine/ammonia-borane adducts [2] as hydrogen storage materials and water/alcohol mediated by diboron [3] have been used as alternative hydrogen sources in recent years. Comparatively stable HBPin as hydride with proton source could generate hydrogen gas,[4] which is rarely used as hydrogen sources mainly because only one equivalent H_2 generated from HBPin and proton source is not enough for fully hydrogenation of alkenes or other unsaturated bonds in the presence of metal catalyst, however, that might be advantageously used in selective reduction of substrates bearing two or more unsaturated bonds in a highly active catalysis system, since the easily reduced unsaturated bond would be hydrogenated and others would remain due to the limited amount of H_2 in the reaction system.

Chemoselective hydrogenation of multiple unsaturated bonds has being of long-standing challenge,[5] for instance, stere- and chemoselective semi- and full hydrogenation of alkynes,[3m, 6] azo compounds,[7] regio- and chemoselective hydrogenation of dienes,[8] chemoselective hydrogenation of alkenes,[9] aldehydes,[10] nitrobenzene derivatives,[11] imines[12] or quinolines.[13] So far, there is no report on the general chemoselective (transfer) hydrogenation. Therefore, we intended to explore a generalized, effective and efficient catalytic system to realize the selective TH of diverse unsaturated bonds using HBPin and protic acids as hydrogen sources. Based on the known nano-palladium particles prepared from the reduction of Pd^{2+} with $NaBH_4$,[11i, 14] we assumed that active nano-metal particles could be formed using HBPin as reductant and exhibit powerful and special performance on (transfer) hydrogenation,[3a, 15] which might increase TH efficiency and avoid hydroboration. Herein, we disclose a palladium catalyzed generalized and diverse transfer hydrogenation of various unsaturated bonds. In this protocol, HBpin and water, alcohols, phenol, carboxylic acids, amines or amides were employed as hydride and proton sources (scheme 1a). Moreover, the activity of diverse unsaturated bonds was investigated systematically by orthogonal experiment method. The trends are *styrene>diphenylmethanimine>benzaldehyde>azobenzene>nitrobenzene> quinoline>acetophenone>benzonitrile*.

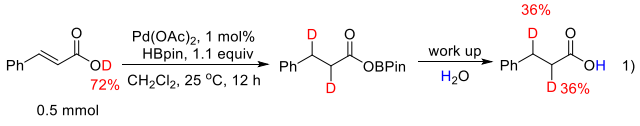


Scheme 1. Generalized and chemoselective transfer hydrogenation/hydrodeuteration using HBPin and diverse proton sources.

On the other hand, selective hydrodeuteration of alkenes was rarely reported mainly because of the difficulty of discriminating two isotopes of HD and selective transference to two atoms of alkenes.[16] Furthermore, the high cost of HD ($223/L, Cambridge Isotope Laboratories) extremely limited the development of hydrodeuteration. Recently, Webster and Macgregor's groups[17] reported a Fe catalyzed transfer hydrodeuteration of alkenes using HBPin and *N*,*N*-d_2-aniline as hydrogen and deuterium sources, respectively. Our protocol also realized the selective hydrodeuteration using HD *in situ* generated from HBPin and commercially available and simple deuterium reagent (D_2O, MeOD or AcOD). The *in situ* generated HD was discriminated by *in situ* generated nano palladium particles *via* oxidative addition and selective migration insertion to terminal alkenes. Deuterium was transferred selectively to terminal carbon of aromatic olefins (Scheme 1b).

Results and Discussion

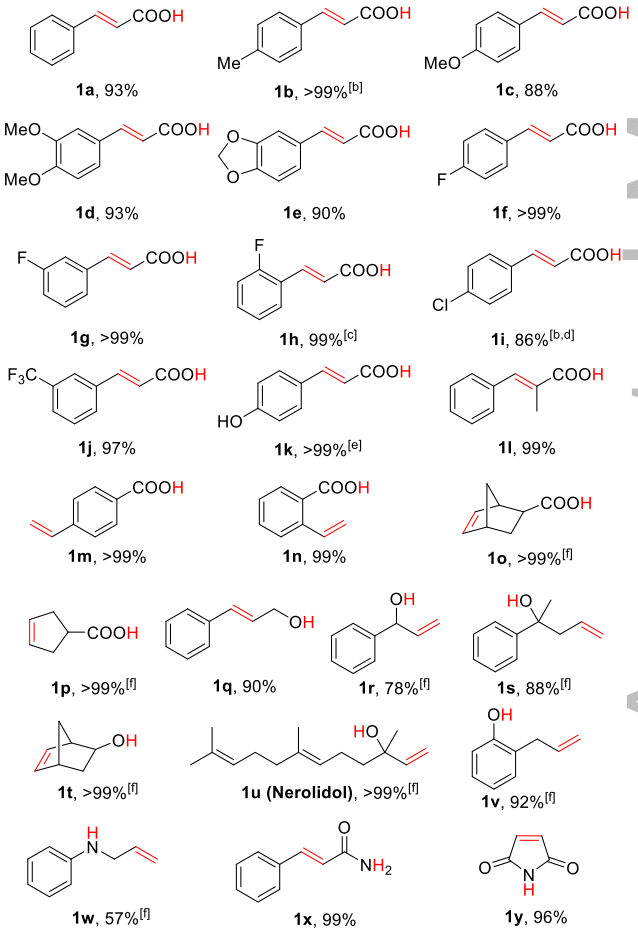
Cinnamic acid **1a** was chosen as a model substrate to initiate our research. According to the optimization of various reaction parameters, 96% isolated yield of hydrocinnamic acid was obtained using 1 mol% $Pd(OAc)_2$ as precatalyst, HBPin as hydride source, CH_2Cl_2 as solvent, at 25 °C in a sealed tube for 12 h (see Supporting Information, Table S1). D was transferred to the C=C bond when O-*d* cinnamic acid was employed as the starting material and the H of carboxyl group was regenerated from H_2O during the work up process (eq 1 and Supporting Information, Scheme S1). This result demonstrated that the protic acid worked as hydrogen source.



Then the scope of cinnamic acids was examined (Table 1). Electron-donating (**1b-1e**), electron-withdrawing (**1j**) groups, halogen (**1f-1i**) and hydroxyl (**1k**) on the phenyl ring were smoothly converted to hydrogenated products in good to excellent yields (79-99%). And, tri-substituted alkene containing a carboxyl group also worked well (**1l**). For nonconjugated olefin acids, proton of carboxyl could be transferred to the remote C=C bond (**1m-1p**). Unsaturated aliphatic acid (**1o** and **1p**) proved to be suitable substrates and the corresponding products were afforded in >99% yields. We further examined alkenes bearing primary, secondary, tertiary alcohol and phenol (**1q-1v**), proton of OH group was also smoothly transferred to the C=C bonds. Terminal C=C bond was selectively reduced when two internal C=C bonds remained, such as Nerolidol (**1u**) with three C=C bonds. Amine and amide were also effective in TH reactions (**1w-1y**).

We turned our attention to alkenes without protic functional group. Methyl cinnamate **3a** was selected as a model substrate to optimize reaction conditions (Table 2). When 1 mol% $Pd(OAc)_2$ was used as

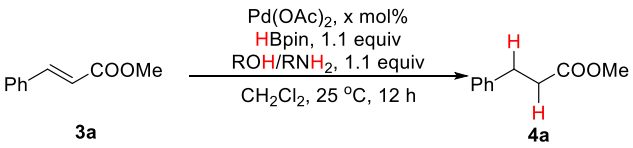
Table 1. TH of alkenes bearing carboxyl, hydroxyl, amino or amide group.[a]



[a] Reaction conditions: **1** (0.25 mmol), $Pd(OAc)_2$ (1 mol%), HBPin (1.1 equiv), CH_2Cl_2 (0.5 mL), 25 °C, sealed tube under N_2 atmosphere for 12 h, isolated yields. [b] $Pd(OAc)_2$ (2 mol%). [c] $Pd(OAc)_2$ (5 mol%). [d] 2 mL EtOAc as solvent. [e] EtOAc as solvent. [f] $Pd(OAc)_2$ (0.5 mol%).

precatalyst, diverse protic reagents including benzoic acid, acetic acid, MeOH, $PhNH_2$ and H_2O could work as effective proton sources in TH under sealed N_2 atmosphere (>99% conversions, entries 1-5). Lower conversion (44%) was obtained in the absence of protic additives (entry 6). To confirm whether the hydrogen gas was generated in the reaction, control experiments were conducted. 54% Conversion was obtained using H_2O as the proton source in an open flask under N_2 atmosphere (entry 7), which revealed that hydrogen gas might be generated *in situ* and escaped from the solution. While sealed tube could inhibit H_2 escaping and substrates were reduced fully. Additional experiment was carried out under H_2 in sealed tube and gave 99% conversion of **3a** using 0.1 equivalent of HBPin as catalyst activator (entry 8). This result suggested that H_2 could also be activated by this catalyst system. No hydrogenation product was detected using $Pd(PPh_3)_4$ instead of $Pd(OAc)_2$ (entry 9). Mercury poison experiment was conducted and only trace amount of product was detected (entry 10). These results indicated that *in situ* generated Pd nanoparticles might be the real catalyst.[15k, 18] However, Pd/C could not work for this reaction (entry 11). Because of strong adsorption of activated carbon toward gas, the limited *in situ* generated hydrogen gas could not be utilized effectively in Pd/C system. That's the main possible reason that the hydrogenation did not occur in the presence of Pd/C. In addition, the *in situ* generated nano-palladium differs from Pd/C in the aspect of size, shape, matrix,

Table 2. Screening reaction conditions for TH using HBpin and ROH/RNH_2 as proton source.[a]



3a **4a**

Entry	x	ROH/RNH_2	Conv. (%)[b]
1	1	PhCOOH	>99
2	1	AcOH	>99
3	1	MeOH	>99
4	1	$PhNH_2$	>99
5	1	H_2O	>99
6	1	-	44
7[c]	1	H_2O	54
8[d]	1	H_2O	99
9[e]	1	H_2O	0
10[f]	1	H_2O	trace
11[g]	1	H_2O	0
12	0.2	H_2O	>99
13	0.1	H_2O	trace

[a] Reaction conditions: **3a** (0.25 mmol), $Pd(OAc)_2$ (x mol%), HBPin (1.1 equiv), ROH/RNH_2 (1.1 equiv), CH_2Cl_2 (0.5 ml), 25 °C, sealed tube under N_2 atmosphere for 12 h. [b] Detected by NMR using CH_2Br_2 as an internal standard. [c] Open to N_2. [d] Under H_2 in sealed tube, HBPin (0.1 equiv). [e] $Pd(PPh_3)_4$. [f] 13 equiv Hg was added. [g] Pd/C.

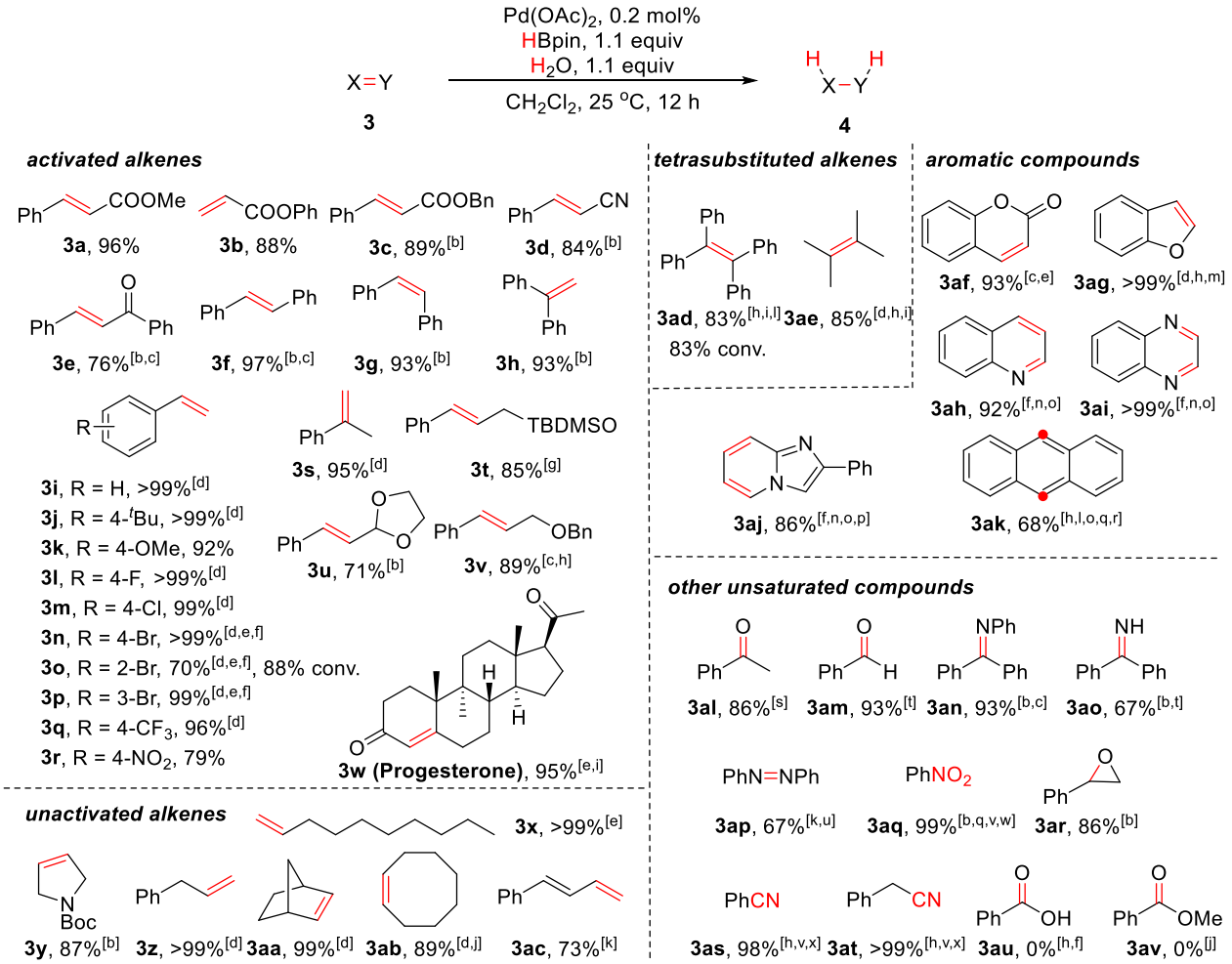
surface and catalytic activation. Further screening of precatalyst loading showed that 0.2 mol% of $Pd(OAc)_2$ was enough to convert the starting material completely (entry 12).

With the optimal conditions in hand, we investigated the scope of alkenes. Electron-deficient alkenes **3a**-**3e** were hydrogenated cleanly in good to excellent yields with 0.2 or 0.5 mol% $Pd(OAc)_2$ loading. Among them, ester (**3a**-**3c**), nitrile (**3d**) and carbonyl (**3e**) were tolerated and C=C bond were selectively reduced. *Trans*- and *cis*-stilbene (**3f** and **3g**) was hydrogenated smoothly in 97% and 93% yields, respectively. Subsequently, various substituted styrenes were examined (**3h**-**3s**). Styrenes with alkyl, electron-donating (**3k**) and electron-withdrawing (**3q** and **3r**) groups worked well. Especially, **3r** with nitro group was selectively reduced to 1-ethyl-4-nitrobenzene in good yield. Furthermore, halogen (F, Cl and Br) groups could survive well (**3l**-**3p**). In particular, bromo-substituted styrenes at *ortho*, *meta* and *para* positions were not observed to affect significantly this transformation, affording hydrogenated products in good to excellent yields (**3n**-**3p**) and avoiding hydrogenolysis side reaction. Protected alcohol and carboxyl groups remained intact after hydrogenation of C=C bonds, which were subject to C−O[19] or Si−O[20] cleavage under Pd/C catalysis and H_2 atmosphere (**3c**, **3t** and **3v**). Glycol protected cinnamaldehyde (**3u**) led to C=C bond hydrogenated product in good yield. Steroids play important role in natural product, synthetic pharmaceuticals and biologically active compounds. In order to demonstrate the utility of this TH system, progesterone **3w** was selectively hydrogenated smoothly while carbonyl preserved.

Then unactivated alkenes **3x**-**3ab** were surveyed. Increasing the loading of $Pd(OAc)_2$ to 5 mol% was required for the TH of *cis*-cyclooctene (COE, **3ab**). To our delight, terminal C=C bond of conjugated diene **3ac** was hydrogenated with high selectivity.[8a] Tetrasubstituted olefin is one of most difficult and least active substrate for hydrogenation.[21] In this protocol, tetraphenyl- and tetramethyl- ethylene (**3ad** and **3ae**) were hydrogenated in 83% and 85% yields, respectively, and high activity of this TH system was exhibited.

The hydrogenation of aromatic compounds is challenging due to their resonance stabilization[22] and heterocycles' potential poison to metal catalysts. Aromatic lactone coumarin **3af** was fully hydrogenated in the presence of 1 mol% $Pd(OAc)_2$, yielding 93% isolated product. Turn to more inactive substrate benzofuran **3ag**, increasing $Pd(OAc)_2$ loading to 10 mol%, 55.0 equiv MeOH as proton source, 2,3-dihydrobenzofuran was obtained in >99% yield. With 8 mol% $Pd(OAc)_2$, 2.2 equiv HBPin and 11.0 equiv MeOH as proton source, quinoline (**3ah**) and quinoxaline (**3ai**) were hydrogenated in 92% and 99% isolated yields, respectively. Additionally, two cyclic conjugation C=C bond of heterocycle **3aj** was hydrogenated in CH_2Cl_2 (2 mL). Polycyclic aromatic hydrocarbon anthracene **3ak** was selectively

Table 3. Examination of TH using HBpin and H_2O/MeOH/AcOH as hydrogen source.[a]



[a] Reaction conditions: **3** (0.25 mmol), $Pd(OAc)_2$ (0.2 mol%), HBPin (1.1 equiv), H_2O (1.1 equiv), CH_2Cl_2 (0.5 mL), 25 °C, sealed tube under N_2 atmosphere for 12 h, isolated yields are reported and starting material was consumed in full, unless otherwise noted. [b] $Pd(OAc)_2$ (0.5 mol%). [c] MeOH instead of H_2O. [d] NMR yields using CH_2Br_2 as an internal standard. [e] $Pd(OAc)_2$ (1 mol%). [f] MeOH (11.0 equiv). [g] TBDMSO = *tert*-butyldimetylsilyloxy. [h] $Pd(OAc)_2$ (10 mol%). [i] H_2O (11.0 equiv). [j] $Pd(OAc)_2$ (5 mol%). [k] HBPin (1.0 equiv). [l] 2 mL EtOAc as solvent. [m] MeOH (55.0 equiv). [n] $Pd(OAc)_2$ (8 mol%). [o] HBPin (2.2 equiv). [p] 2 mL CH_2Cl_2. [q] H_2O (2.2 equiv). [r] 9,10-Dihydroanthracene and 1,2,3,4-tetrahydroanthracene was obtained in 86% and 11% yield, respectively. [s] $Pd(OAc)_2$ (3 mol%). [t] No H_2O. [u] $Pd(OAc)_2$ (0.1 mol%). [v] HBPin (3.3 equiv). [w] $PhNH_2$ was product. [x] Conc. HCl (50 μL), amine hydrochloride was product.

hydrogenated to 9,10-dihydroanthracene in 68% yield as main product.

Inspirited by the efficient results for such broad C=C bonds, we went ahead to the substrates bearing polar unsaturated bonds, such as C=O, C=N, N=N and N=O. C=O bond of acetophenone (**3al**) was hydrogenated in 86% yield using 3 mol% $Pd(OAc)_2$. D from D_2O was transferred to the C atom of C=O, which proved TH process (Supporting Information, Scheme S2). No matter H_2O was added or not, hydrogenated product (benzyl alcohol) of benzaldehyde **3am** was obtained in excellent yield. Both hydroboration and TH might exist in the reaction process. Imine **3an** was hydrogenated using MeOH instead of H_2O as proton source due to possible hydrolysis. Diphenylmethanimine **3ao** could be reduced and diphenylmethanamine was obtained in 67% yield, because of existing N-H group in substrate and avoiding external proton source. N=N bond of azobenzene **3ap** was selectively hydrogenated into NH-NH and 1,2-diphenylhydrazine was afforded in 67% isolated yield.[7a-c, 23] Nitrobenzene **3aq** was hydrogenated into aniline with 0.5 mol% $Pd(OAc)_2$, 3.3 equiv HBPin and 2.2 equiv H_2O. Styrene oxide **3ar** was hydrogenated and ring opened chemo- and regio-selectively, giving anti-Markovnikov 2-phenylethanol in 86% yield. In this reaction, Markovnikov product 1-phenylethanol or styrene were not detected, suggesting regioselectivity mainly depend on electronic effect.[24] D from D_2O was transferred to β-C, which indicated TH occurring (Supporting Information, Scheme S3). Reduced benzonitrile **3as** was failed to obtain in the presence of 3 mol%

$Pd(OAc)_2$, 3.3 equiv H_2O and HBPin. However, TH of benzonitrile **3as** and phenylacetonitrile **3at** worked well when conc. HCl was added and amine hydrochlorides were obtained in quantitative yields. Benzoic acid **3au** and methyl benzoate **3av** were ineffective under the current conditions and these function groups could remain in transformation of effective unsaturated groups.

Chemoselective transfer hydrodeuteration

The chemoselective hydrodeuteration using D_2O was carried out (Table 4). D from D_2O was mainly selectively transferred to terminal C atom of alkenes. When MeOD or AcOD were used as D source, the same selective product **5a** was obtained in the ratio 75:25 of anti-Markovnikov and Markovnikov product. The selectivity was influenced by electronic effect. The selectivity of styrenes with electron-withdrawing groups was better than electron-donating groups (**5a-5f**). **5g** was obtained with better anti-Markovnikov selectivity than **5a**, perhaps because of steric hindrance of -OMe on the ortho-position of benzene. Likewise, D from DBPin was also mainly selectively transferred to terminal C atom of alkenes. The same selectivity (anti-Markovnikov product) of different D source (D_2O, MeOD, AcOD and DBPin) illustrated HD might be generated.

Chemoselective transfer hydrogenation

The scope of alkynes was also explored (Table 5). Internal alkynes bearing carboxyl or hydroxyl group were reduced to *cis*-alkenes in good stereoselectivity and yields employing 1.0 equiv HBPin as hydride source (**8a** and **8c**). 2.1 equiv HBpin led to full hydrogenation of alkynes (**8b** and **8d**) when additional 1.1 equiv H_2O or MeOH was added as proton source. Diphenylethyne could be semihydrognated into *cis* product **8e** in excellent stereoselectivity. Terminal alkynes were semi- and full hydrogenated in moderate to good yields (**8g-8l**).

Table 4. Chemoselective hydrodeuteration of terminal alkenes with D_2O or DBPin.

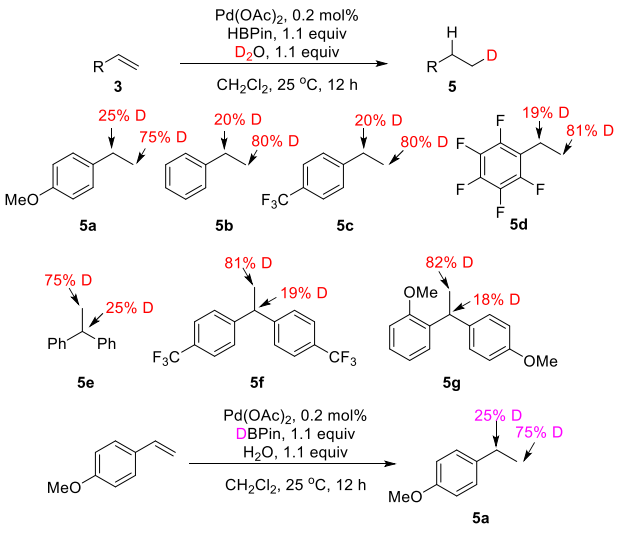
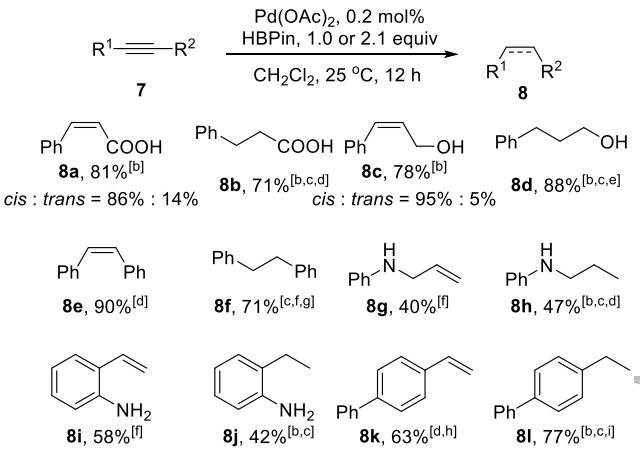


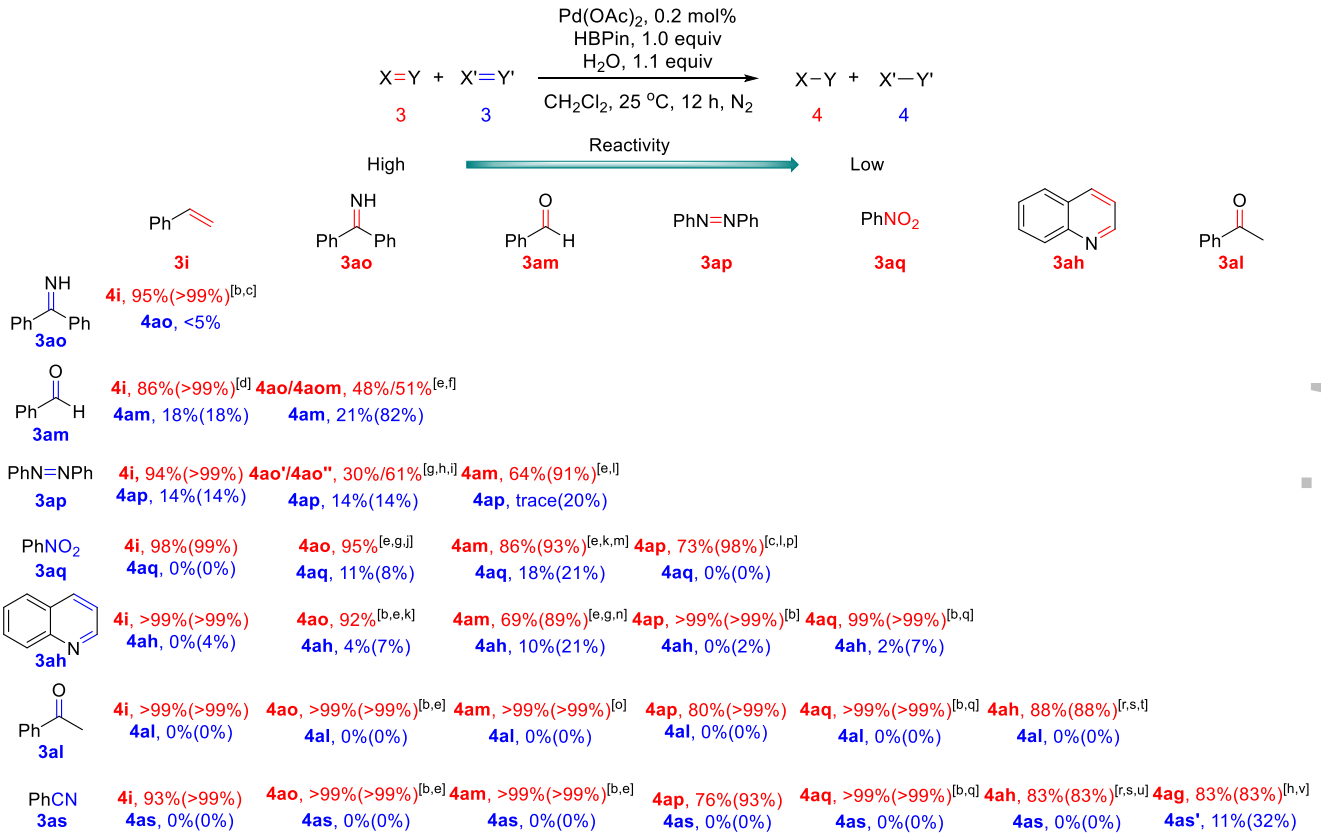
Table 5. Stereo-, chemoselective semi- and full TH of alkynes.[a]



[a] Reaction conditions: **7** (0.25 mmol), $Pd(OAc)_2$ (0.2 mol%), HBPin (1.0 equiv), CH_2Cl_2 (0.5 ml), 25 °C, sealed tube under N_2 atmosphere for 12 h. [b] $Pd(OAc)_2$ (1 mol%). [c] HBPin (2.1 equiv). [d] H_2O (1.1 equiv) was added. [e] MeOH (1.1 equiv) was added. [f] $Pd(OAc)_2$ (0.5 mol%). [g] H_2O (3.3 equiv). [h] $Pd(OAc)_2$ (0.8 mol%). [i] H_2O (2.2 equiv).

Encouraged by the good chemo- and regioselectivity TH of alkenes and alkenes, we embarked on chemoselective TH of different unsaturated groups, such as styrene, diphenylmethanimine, benzaldehyde, azobenzene, quinoline, nitrobenzene, acetophenone and benzonitrile as substrates. Through orthogonal experiment the TH chemoselectivity of every two reducible groups were examined (Table 6 and Supporting Information). After a series of simple conditions screening, the order of TH activity was obtained as follows: *styrene* > *diphenylmethanimine* > *benzaldehyde* > *azobenzene* > *nitrobenzene* > *quinoline* > *acetophenone*> *benzonitrile*. Styrene **3i** was hydrogenated smoothly when azobenzene, nitrobenzene, quinoline, acetophenone or benzonitrile was added as competitive substrates, which were fully recovered. With regard to styrene (**3i**) and diphenylmethanimine (**3ao**), H_2O was replaced by MeOH as proton source due to potential hydrolysis of imine. With 5.5 equiv MeOH, styrene was mainly reduced (**4i**, 87%). Diphenylmethanimine (**3ao**) was fully reduced to amine, partial of which further reacted with benzaldehyde, providing *N*-benzylidene-1,1-diphenylmethanamine (**4aom**) in 51% yield. Diphenylmethanimine (**3ao**) was reduced in excellent yield (**4ao**, 92->99%) when nitrobenzene, quinoline, acetophenone or benzonitrile as competitive substrates which were mostly recovered (92->99%). For benzaldehyde **3am**, hydrogenation and hydroboration products were produced in 69-86% yields while azobenzene, nitrobenzene and quinoline as competitive substrates. Aldehyde **3am** was reduced in excellent yield competing with carbonyl group. Azobenzene **3ap** was hydrogenated to 1,2-

Table 6. Chemoselective and competitive TH of different unsaturated compounds.[a]



[a] Reaction conditions: **3** (0.25 mmol), **3** (0.25 mmol), $Pd(OAc)_2$ (0.2 mol%), HBPin (1.0 equiv), H_2O (1.1 equiv), CH_2Cl_2 (0.5 mL), 25 °C, sealed tube under N_2 atmosphere for 12 h, yields and conversions (in parentheses) were determined by NMR analysis using CH_2Br_2 or mesitylene as internal standard. [b] $Pd(OAc)_2$ (0.5 mol%). [c] MeOH (1.1 equiv). [d] MeOH (5.5 equiv). [e] No H_2O was added. [f] **4aom** = *N*-benzylidene-1,1-diphenylmethanamine. [g] $Pd(OAc)_2$ (0.1 mol%). [h] HOAc (1.1 equiv). [i] **4ao'** = *N*-benzhydryl-4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-amine, **4ao''** = *N*-benzhydrylacetamide. [j] HBPin (2.7 equiv). [k] HBPin (1.3 equiv). [l] $Pd(OAc)_2$ (1 mol%). [m] $Pd(OAc)_2$ (0.4 mol%). [n] HBPin (2.5 equiv). [o] $Pd(OAc)_2$ (0.3 mol%). [p] 4-Nitrotoluene as substrate. [q] HBPin (3.3 equiv), H_2O (2.2 equiv). [r] $Pd(OAc)_2$ (10 mol%). [s] HBPin (2.2 equiv). [t] MeOH (11.0 equiv). [u] AcOH (2.2 equiv). [v] $Pd(OAc)_2$ (7 mol%), **4as'** = *N*-benzylacetamide.

diphenylhydrazine (yields 73->99%) when nitrobenzene, quinoline or acetophenone as competitive substrates. It was worth noting that none of aniline was detected as byproduct when quinoline was added. Nitrobenzene **3aq** was chemoselectively reduced smoothly in >99% yield with quinoline, acetophenone or benzonitrile competitor. Quinoline's selective TH took place in 88% and 83% yield with acetophenone or benzonitrile. C=O was selectively reduced preferentially when aceto-phenone and benzonitrile were both substrates.

To examine the utility of this chemoselective TH in Table 6, we selected some compounds with two or more reducible groups as substrates (Scheme 2). 4-Nitrobenzaldehyde **9** was reduced to 4-nitrobenzyl alcohol **10** in 81% yield and nitro group was intact. Nitro group was also intact when **11** was substrate in which N=N was hydrogenated selectively. Nitro group was reduced while carboxyl and quinoline remained in substrate **13** and **15**. 3-Acetylquinoline **17** with three different double bonds (C=C, C=N and C=O bond), TH only occurred at C=N bond and **18** was obtained in 57% yield. Carboxyl was hydrogenated selectively and nitrile intact when 4-acetylbenzonitrile **19** was substrate. Predictably, the selective TH reaction might be potential to be applied to more compounds bearing different unsaturated bonds.

In situ generated Pd nano-particle characterization

As showed in Table 2 (entries 9 and 10), when mercury or PPh_3 was added at the start of reaction, only trace amount of **3a** was reduced, which suggested a possible nanoparticle catalysis. To further verify the *in situ* generated palladium nanoparticle was the active catalyst, the reaction solution (Table 2, entry 5) at 20 min was conducted by Transmission Electron Microscopy (TEM) analysis. Dispersed Pd nanoparticle with an average size of 2.6 nm was observed (Figure 1). Kinetic experiment exhibited typical sigmoidal curve, which indicated an active nanoparticle induction period followed by a rapid increase in catalytic activity (Figure 2). In addition, visible heterogeneous catalysis phenomenon of black

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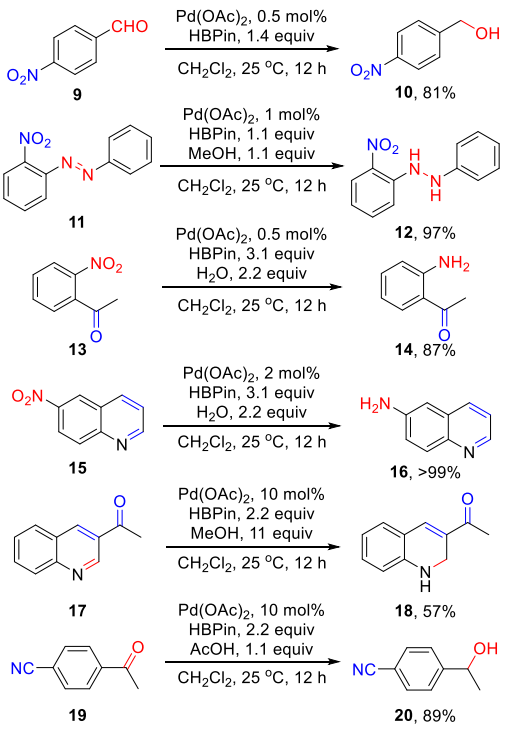


Scheme 2. Chemoselective TH of substrates bearing two or more reducible groups.

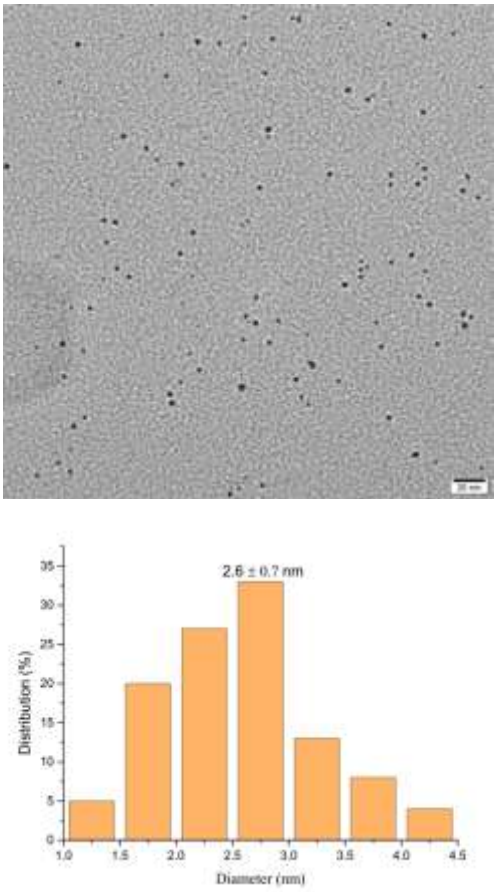


Figure 1. TEM images and particle size distribution of *in situ* generated nano-palladium in the TH reaction of **3a**.

palladium was also observed during the process of the reaction.[15j, 18]

Plausible mechanism

A possible reaction mechanism was proposed (Scheme 3). HD was formed from the combination of D_2O/HBPin or H_2O/DBPin. The double peak of HBPin at 28.2 ppm (J = 176.0 Hz) disappeared in 5 min. During the first 1-3 hours, $Pd(OAc)_2$ was reduced to active nano-palladium.[18] Initially oxidative addition of H-D bond to nano-palladium could afford H-Pd-D. Then H-Pd-D coordinated with alkene **3** and gave intermediate **B** through migratory insertion. The selective Pd-H insertion depended on the steric effect. Intermediate **B** could undergo reductive elimination and anti-Markovnikov hydrodeuteration product **5** was obtained.

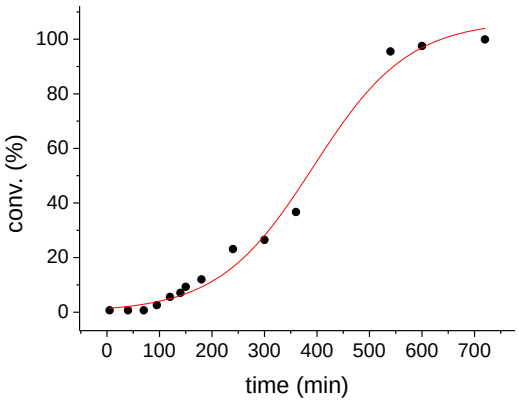
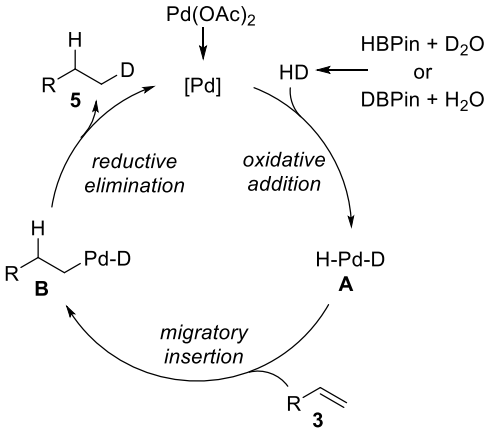


Figure 2. Kinetic profile of the **3a** TH reaction.



Scheme 3. Plausible reaction mechanism.

Conclusion

In summary, we have developed a palladium catalyzed generalized, effective, mild and practical diverse transfer hydrogenation/hydrodeuteration of various unsaturated compounds. In this protocol,

HBpin, water, alcohols, phenol, carboxylic acids, amines or amides were employed as hydride and proton sources. Broad substrates of alkenes were applied to this catalytic system, including activated, unactivated and tetrasubstituted alkenes. Diverse functional groups, which could not survive under the $Pd/C/H_2$ combination, were tolerated, for instance, halogen, nitro, carbonyl, benzyl and O-Si protecting groups. Alkynes could be selectively reduced to *cis*-alkenes or alkanes. In addition, aromatic heterocycles, aldehydes, ketones, imines, azo, nitro, epoxy and nitrile compounds could also be reduced to the corresponding products. The activity of the different substrates was studied and the trends are as follows: *styrene* > *diphenylmethanimine* > *benzaldehyde* > *azobenzene* > *nitrobenzene* > *quinoline* > *acetophenone* > *benzonitrile.* TH occurred with excellent chemoselectivity for the substrates with two or more unsaturated bonds. This is the first general chemoselective TH protocol and tolerates diverse unsaturated compounds. Furthermore, the selective hydrodeuteration occurred when D_2O/HBPin or H_2O/DBPin was used for terminal aromatic alkenes, affording the anti-Markovnikov products. A plausible mechanism involving HD *in situ* generation and discrimination was proposed. The *in situ* generated nano-palladium was proved via TEM analysis. Typical sigmoidal curve of kinetic experiment further demonstrated nano-catalysis process.

Experimental Section

An oven-dried 50 mL Teflon-lined screw cap-sealed tube (with a suction port) equipped with a stir bar was charged with substrate (0.25 mmol), $Pd(OAc)_2$, solvent and proton source (if necessary) under a nitrogen atmosphere, followed by HBPin was added. The reaction mixture was stirred at 25 ºC for 12 h. Work up: A. The reaction mixture was diluted with 10 ml of EtOAc, and extracted with saturated $NaHCO_3$ and EtOAc (x3), then the aqueous phase was acidized with conc. HCl (*CAUTAIN: make sure complete CO_2 emission before extract*) and extracted with EtOAc (x3), organic layer was dried with Na_2SO_4 and concentrated under reduced pressure to provide the corresponding product. B. The reaction mixture was directly purified by flash chromatography on silica gel to provide the corresponding product.

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