Novel Pd/C-Catalyzed Redox Reactions between Aliphatic Secondary Alcohols and Ketones under Hydrogenation Conditions: Application to H−D Exchange Reaction and the Mechanistic Study

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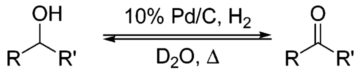

A liquid-phase redox system between secondary alcohols and ketones is described. Deuteration of either secondary alcohols or ketones using the Pd/C−H_2−D_2O system gave a mixture of deuterium-labeled secondary alcohols and ketones. The results indicated that the secondary alcohol was oxidized to the corresponding ketone without oxidants under the hydrogenation conditions and the hydrogenation of the aliphatic ketone to the corresponding secondary alcohol simultaneously proceeded. Detailed mechanistic studies on the redox system as well as the H−D exchange reaction are discussed.

Introduction

Oxidation of alcohols and reduction of ketones are both fundamental organic transformations.[1] Palladium is one of the most active and versatile transition metals employed for the oxidation of alcohols[2,3] including the Wacker process.[4] Traditionally, palladium-catalyzed oxidation of alcohols required a stoichiometric amount of an oxidant, such as benzoquinone or $CuCl_2$,[2,3] but these oxidants usually complicate the reaction progress and product isolation, reduce the atom economy, and/or are accompanied with formation of a large quantity of metal sludge. From both the economic and environmental points of view, numerous effective palladium-catalyzed systems have been developed for the oxidation of alcohols using molecular oxygen as a stoichiometric oxidant.[5] For example, Peterson and Larock reported a $Pd(OAc)_2$−DMSO system for oxidation for a wide range of benzylic and allylic alcohols.[5g,h] Uemura and coworkers also developed an efficient and versatile oxidation method for primary and secondary alcohols using a $Pd(OAc)_2$−pyridine system.[5i−k] Stoltz[5n,r,s] and Sigman[5o−q,t−v] independently reported the oxidative kinetic resolution of secondary alcohols using a modification of Uemura's method. They showed that

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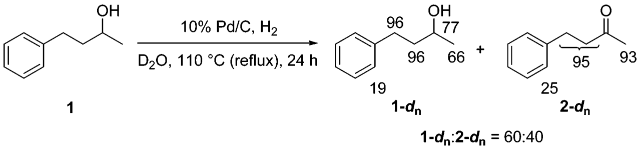
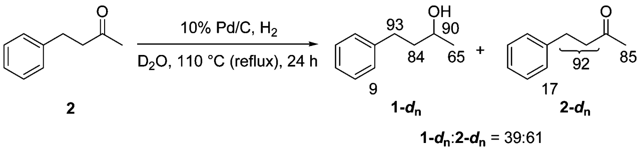
the addition of (−)-sparteine achieved highly enantioselective oxidation of secondary alcohols. Additionally, Sheldon and coworkers developed an efficient aerobic oxidation of alcohols in aqueous solvent catalyzed by a water-soluble palladium complex,[5l,w] which meets the needs of green chemistry. While many excellent palladium-catalyzed oxidation methods of alcohols have been reported, comparatively few examples for palladium-catalyzed hydrogenation of ketones have been developed. One notable exception is the heterogeneous Pd/C-catalyzed hydrogenation of aromatic ketones (ArCOR, R = alkyl or aryl) although aromatic ketones are easily susceptible to hydrogenolysis to the corresponding methylene compounds ($ArCH_2R$).[6] It is commonly considered that heterogeneous palladium catalysts have almost no activity for the hydrogenation of aliphatic ketones except for some steroidal ketones.[7−9]

We have recently reported that an efficient Pd/C-catalyzed H−D exchange reaction at the aliphatic positions of aromatic derivatives readily proceeded in D_2O under a hydrogen atmosphere.[10,11] The procedure was general and efficient for a wide variety of substrates such as nucleic acids,[12] amino acids,[13] and heterocyclic compounds.[14] We have also reported that the use of Pt/C accomplished an effective deuterium incorporation into the aromatic nuclei.[15] During the course of our further study to explore the scope of H−D exchange reaction using the $Pd/C-H_2-D_2O$ system, we have found that the use of either secondary alcohols or ketones as substrates led to formation of a mixture of secondary alcohols and ketones together with effective deuterium incorporation into both of the products. The results indicated that dehydrogenation of secondary alcohols proceeds even under the hydrogenation conditions without oxidants and that palladium-catalyzed hydrogenation of aliphatic ketones to the corresponding secondary alcohols took place without difficulty. Although alcohol−ketone pair interchange is well-known as the Meerwein−Ponndorf−Verley reduction or Oppenauer oxidation,[16] only a few examples of transformation of secondary alcohols and ketones into the corresponding oxidized or reduced forms under transition-metal-catalyzed hydrogenation conditions have been reported before.[17] Herein we report a liquid-phase and interactive redox system between secondary alcohols and ketones using the $Pd/C-H_2-D_2O$ system and provide a detailed discussion regarding the mechanistic studies of the H−D exchange reaction of secondary alcohols and ketones based upon the redox reaction.

SCHEME 1



SCHEME 2



Results and Discussion

To investigate the scope of our H−D exchange method, we initiated the studies using secondary alcohols and ketones as substrates. When 4-phenyl-2-butanol (**1**; 300 mg, 2 mmol) was heated with 10% Pd/C (30 mg, 10 wt % **1**, ca. 0.03 mmol of Pd metal) in D_2O (4 mL) under a H_2 atmosphere for 24 h, a 60:40 mixture of the expected deuterium-labeled substrate, 4-phenyl-2-butanol-d_n (**1-d_n**), and an unexpected ketone, 4-phenyl-2-butanone-d_n (**2-d_n**) was obtained (Scheme 1). The alkyl chain of the ketone **2-d_n** was nearly quantitatively deuterated.

On the other hand, when 4-phenyl-2-butanone (**2**) was used as a substrate for the deuteration, a 39:61 mixture of **1-d_n** and **2-d_n** was obtained with progress of an efficient H−D exchange on both alkyl chains of **1-d_n** and **2-d_n** (Scheme 2).

These results suggested the simultaneous progress of dehydrogenation of a secondary alcohol and hydrogenation of a ketone under the heterogeneous Pd/C-catalyzed hydrogenation conditions. To confirm the generality of these palladium-catalyzed redox reactions in a hydrogen atmosphere, we investigated the H−D exchange reactions of a variety of secondary alcohols and the corresponding ketones, and the results are summarized in Table 1.

All of the reactions (160 °C, 24 h) except for entry 8 led to formation of a mixture of a deuterium-labeled secondary alcohol and a ketone (Table 1). It is noteworthy that nonactivated secondary alcohol and ketone derivatives which lack a benzene ring are deuterated effectively (entries 1−9).[11] Whereas a cyclic alcohol, cyclooctanol, was also deuterated to give a mixture of secondary alcohols and ketones (entry 7), the deuterium-labeled substrate cyclooctanone-d_n was exclusively obtained when cyclooctanone was used for the H−D exchange reaction (entry 8). When secondary alcohols were employed as substrates, the deuterium efficiency of the deuterated alcohols was lower than that of the ketone which formed from the substrate (entries 1, 3, 5, 7, 9, and 10). On the other hand, the H−D exchange of

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TABLE 1. Pd/C (10%)-Catalyzed Redox Reactions between Secondary Alcohols and Ketones and the H−D Exchange Results in D_2O^a

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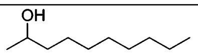
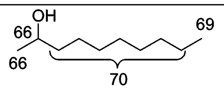
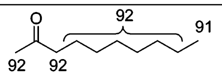
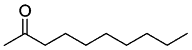
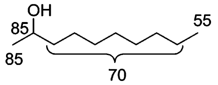
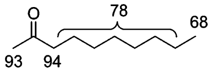
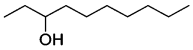
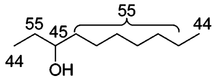
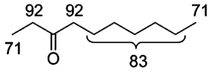
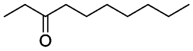
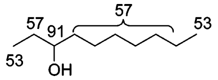
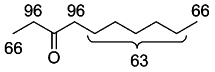
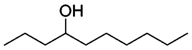
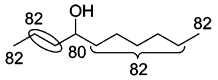
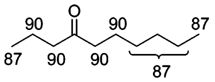
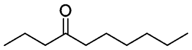
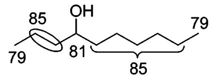
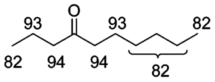
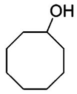
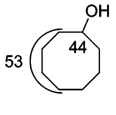
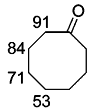
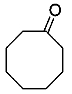
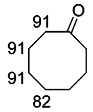
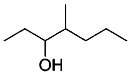
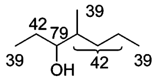
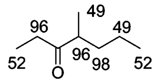
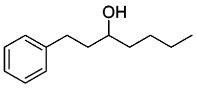
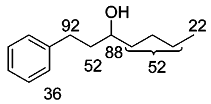
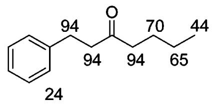
		sec-alcohol	ketone	*sec*-alcohol	ketone
1				19	55
2				12	64
3				36	37
4				8	70
5				38	49
6				13	70
7[c]				27	39
8[c]		–		–[d]	65
9[c]				23	38
10				7	75

[a] Unless otherwise noted, 2 mmol of the substrate was stirred with 10% Pd/C (10 wt % substrate) in D_2O (4 mL) under a H_2 atmosphere at 160 °C for 24 h. All reactions were carried out in a sealed tube. [b] Determined by ^{1}H NMR. [c] A 4 mmol amount of the substrate was used. [d] A trace amount of cyclohexanol-d_n was detected by TLC.

ketones led to high deuterium efficiency of both the starting ketone and the corresponding alcohol (Table 1, entries 2, 4, 6, and 8). In addition, a comparison of the product ratio showed that a ketone was the major product from either the alcohol or ketone in all cases. Furthermore, the H−D exchange reaction of 4-methyl-3-heptanol, which possesses a blanched methyl substituent, also proceeded smoothly (entry 9). When 1-phenyl-3-heptanol was used as a substrate for the H−D exchange reaction, effective deuterium incorporation into the benzylic position took place (entry 10).

Not only palladium but also other transition metals were active for the redox reactions between secondary alcohols and ketones (Tables 2 and 3). When 2-decanol (**3**) was used as a substrate, the use of Pd/C led to relatively high deuterium efficiency (Table 2, entry 1). All heterogeneous transition-metal catalysts worked well for the oxidation of **3** under the reaction conditions, and the highest proportion of **4-d_n** was observed when 10% Pd/C was used (entry 1).

The H−D exchange reaction of 2-decanone (**4**) using a variety of heterogeneous catalysts was also investigated (Table 3). In each case, efficient incorporation of deuterium atoms into **4** was observed and simultaneous hydrogenation of **4** occurred to give the corresponding alcohol **3-d_n**. On the other hand, significant hydrogenation of **4** did not proceed when 10% Pt/C was used as a catalyst (entry 3).[18]

To investigate the mechanism of our unique H−D exchange reaction accompanied by dehydrogenation of secondary alcohols and hydrogenation of aliphatic ketones, we initially examined

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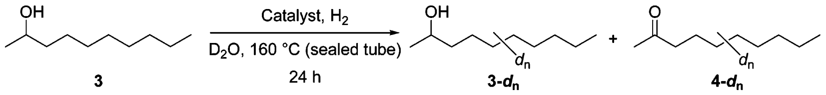
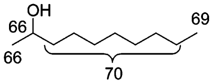
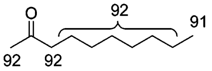
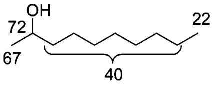
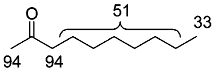
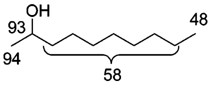
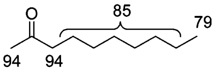
(18) Although suspicions are raised about the effect of the contaminated acid in the catalyst[21] toward the reduction of 2-decanone (**4**), the acidity of the catalyst (Pd/C, Rh/C, or Pt/C) did not correlate with the present redox reaction (see the Supporting Information).

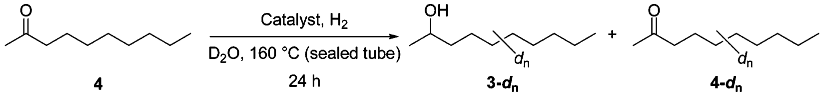
TABLE 2. H−D Exchange of 3 with a Variety of Heterogeneous Catalysts[a]

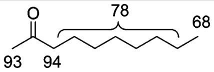
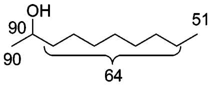
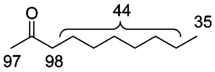
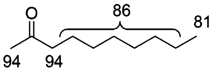


entry	catalyst	D content (%)[b]		isolated yield (%)	
		3-*d*$_n$	**4-*d*$_n$**	**3-*d*$_n$**	**4-*d*$_n$**
1	10% Pd/C			19	55
2	10% Rh/C			39	29
3	10% Pt/C			53	23

[a] A 2 mmol amount of the substrate was used in D_2O (4 mL) under a H_2 atmosphere at 160 ˚C for 24 h. Reactions were carried out in a sealed tube. [b] Determined by ^{1}H NMR.

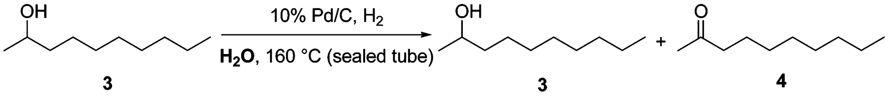
TABLE 3. H−D Exchange of 4 with a Variety of Heterogeneous Catalysts[a]



entry	catalyst	D content (%)[b]		isolated yield (%)	
		3-*d*$_n$	**4-*d*$_n$**	**3-*d*$_n$**	**4-*d*$_n$**
1	10% Pd/C			12	64
2	10% Rh/C			50	21
3	10% Pt/C	–		–[c]	54

[a] A 2 mmol amount of the substrate was used in D_2O (4 mL) under a H_2 atmosphere at 160 °C for 24 h. Reactions were carried out in a sealed tube. [b] Determined by ^{1}H NMR. [c] **3-*d*$_n$** was hardly detected. **3-*d*$_n$**:**4-*d*$_n$** = 36:44 was obtained when 5% Pt/C (Aldrich) was used as a catalyst.

TABLE 4. Dehydrogenation of 3 Catalyzed by Pd/C in H_2O under a Hydrogen Atmosphere



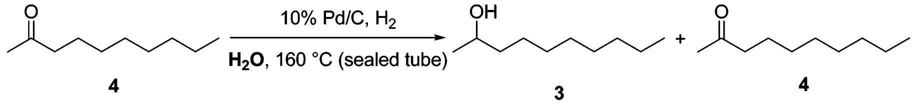
entry	time (h)	**3**:**4**[a]
1	24	67:33
2[b]	24 × 3	24:69

[a] Determined by ^{1}H NMR or GC. [b] A trace amount of decane was detected.

whether the redox reaction would reach an equilibrium between secondary alcohols and ketones. When **3** was heated with Pd/C in H_2O at 160 °C for 24 h, a 67:33 mixture of **3** and **4** was obtained (Table 4), and the reaction of **4** for 24 h led to formation of a mixture of **3** and **4** in a ratio of 16:84, respectively (Table 5). Although the distribution of the products was completely opposite, the **3**:**4** ratios were reached closely after 24 h of stirring was repeated three times using the resulting reaction mixture (Tables 4 and 5, entries 2), indicating the redox reaction between the dehydrogenation of a secondary alcohol and hydrogenation of a ketone is in equilibrium under the reaction conditions.

Furthermore, the reaction using optically active (*R*)-(−)-2-decanol [(*R*)-(−)-**3**] as a substrate gave the partially racemized alcohol after 24 h (Scheme 3). A longer reaction time of up to 7 days resulted in complete racemization of (*R*)-(−)-**3** together

TABLE 5. Hydrogenation of 4 Catalyzed by Pd/C in H_2O under a Hydrogen Atmosphere



entry	time (h)	**3**:**4**[a]
1	24	16:84
2[b]	24 × 3	27:65

[a] Determined by ^1H NMR or GC. [b] A trace amount of decane was detected.

SCHEME 3. Racemization and H−D Exchange Reaction of Optically Active (*R*)-(−)-2-Decanol

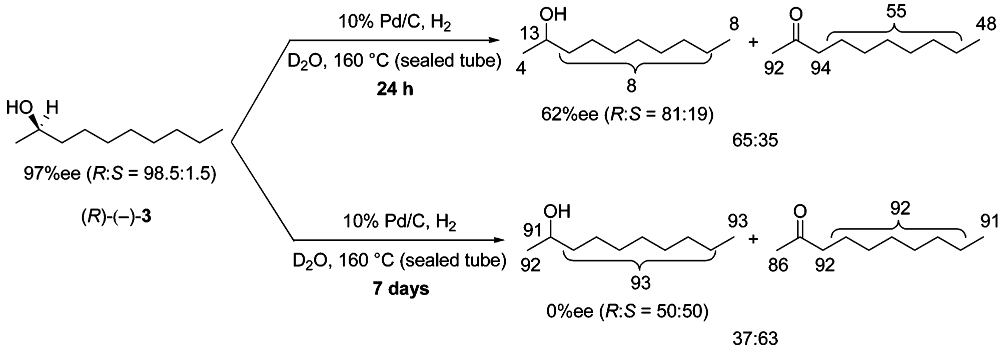
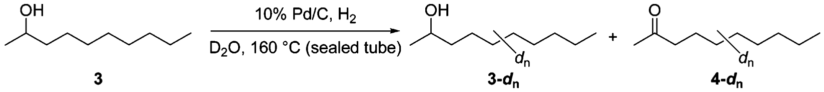
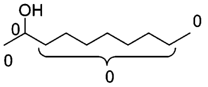
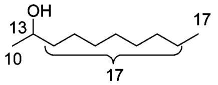
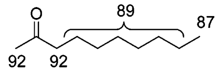
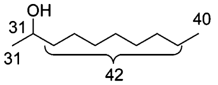
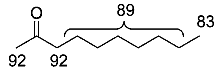
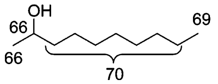
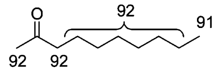


TABLE 6. Time-Course Study of the H−D Exchange Reaction of 3 under the Pd/C−H_2−D_2O System[a]



entry	time (h)	D content (%)[b]		ratio (**3-*d*$_n$**:**4-*d*$_n$**)[c]
		3-*d*$_n$	**4-*d*$_n$**	
1	3		–	>99:<1[d]
2	6			84:16
3	12			56:44
4	24			26:74

[a] A 2 mmol amount of the substrate was used with 10% Pd/C (10 wt % substrate) in D_2O (4 mL) under a H_2 atmosphere at 160 °C. Reactions were carried out in a sealed tube. [b] Determined by ^1H NMR. [c] Indicated on the basis of the isolated yields. [d] **4-*d*$_n$** was hardly detected.

with quite high deuterium efficiency.[19] The racemization of (*R*)-(−)-**3** is more evidence of the presence of equilibrium between dehydrogenation of a secondary alcohol and hydrogenation of a ketone during the deuteration reaction under the Pd/C−H_2−D_2O system.

Next, we examined the time-course study of the H−D exchange reactions of both **3** and **4** to compare the deuterium efficiency and component ratio of products at each reaction time (Tables 6 and 7). When **3** was used as a substrate, the deuterium efficiency of the alkyl chain of **3-*d*$_n$** was slowly increased, whereas the deuterium efficiency of **4-*d*$_n$** rapidly improved even after 6 h (Table 6). It is noteworthy that **4-*d*$_n$** was hardly detected after 3 h and the deuterium efficiency of the corresponding alcohol (**3-*d*$_n$**) was practically nil. However, the ratio of **4** to **3** varied significantly within 24 h and led to an excess percentage of **4-*d*$_n$** against **3-*d*$_n$** (26:74) after 24 h (entry 4).

On the other hand, when **4** was used as a substrate, not only the deuterium efficiency of **4-*d*$_n$** but also that of **3-*d*$_n$** was high even at a short reaction time (Table 7). The proportion of **4-*d*$_n$**

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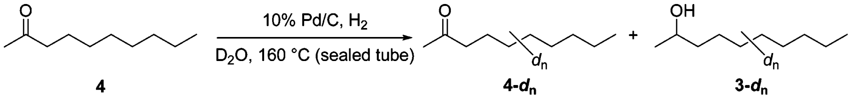
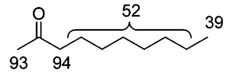
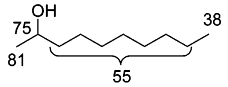
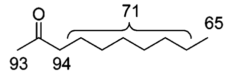
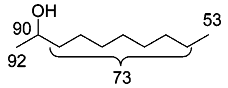
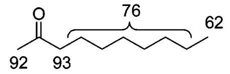
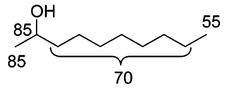
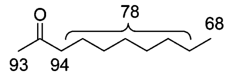
[19] Derdau and Atzrodt reported the deuteration at the benzylic position of the optically active 1-phenylbutan-1-ols using the Pd/C−$NaBD_4$−D_2O system was accompanied by racemization; see: Derdau, V.; Atzrodt, J. *Synlett* **2006**, 1918−1922. We also observed racemization during the deuteration of L-phenylalanine; please see ref 13.

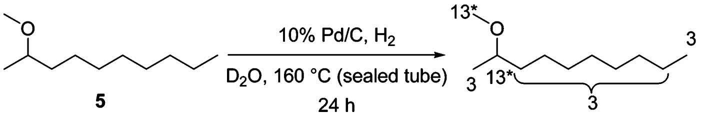
TABLE 7. Time-Course Study of the H−D Exchange Reaction of 4 under the Pd/C−H_2−D_2O System[a]



entry	time (h)	D content (%)[b]		ratio (**3-d_n**:**4-d_n**)[c]
		3-d_n	**4-d_n**	
1	3	–		<1:>99[d]
2	6			4:96
3	12			27:73
4	24			16:84

[a] A 2 mmol amount of the substrate was used with 10% Pd/C (10 wt % substrate) under a H_2 atmosphere in D_2O (4 mL) at 160 °C. Reactions were carried out in a sealed tube. [b] Determined by ^1H NMR. [c] Indicated on the basis of the isolated yields. [d] **3-d_n** was hardly detected.

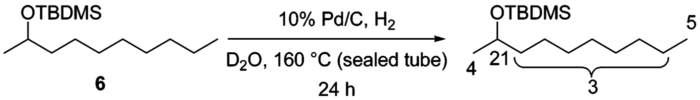
SCHEME 4. H−D Exchange Reaction of 5



Isolated yield: 78%

* Indiacte as the average D content.

SCHEME 5. H−D Exchange Reaction of 6



Isolated yield: 8%

was always higher than that of **3-d_n** at each reaction time. While **3-d_n** was hardly detected within 3 h, the corresponding ketone (**4-d_n**) indicated a comparatively high level of deuterium efficiency (entry 1). It is quite interesting to compare the results of Table 6, entry 1.

Compared with the results of Tables 6 and 7, the H−D exchange reaction of a ketone is much faster and more efficient than that of a secondary alcohol. In addition, considering the significant change of the ratio of **3-d_n** to **4-d_n** in Table 6 and the constant high proportion of **4-d_n** in Table 7, the transformation of secondary alcohols into ketones seems to be faster than the reverse reaction. Taking into account the equilibrium between secondary alcohols and ketones, we presumed that the high deuterium efficiency of the secondary alcohol starting from the ketone as a substrate was attributed to the hydrogenation of the deuterated ketone rather than direct deuterium incorporation into the secondary alcohol; that is to say, the H−D exchange reaction of secondary alcohols would exclusively proceed via deuteration of the corresponding ketones and reduction to the deuterated secondary alcohols.

If our presumption is correct, the use of the methyl and TBDMS ethers **5** and **6** derived from **3** would lead to a decrease of deuterium efficiency, since they cannot be transformed into a ketone. As a result, almost no deuterium incorporation into either 2-methoxydecane (**5**) or 2-[(*tert*-butyldimethylsilyl)oxy]decane (**6**) was observed (Schemes 4 and 5). The low isolated yield of **6** was due to the exclusive cleavage of the TBDMS group in the course of the reaction.[20]

Furthermore, the deuteration of tertiary alcohol **7**, which cannot also be transformed into the ketone, resulted in a nearly no deuteration level (Scheme 6). These results strongly support our presumption that the H−D exchange of the alkyl chain of the secondary alcohol **3** proceeds through the corresponding ketone derivative **4**.

Reaction Pathway. When the reaction was carried out in D_2O under a hydrogen atmosphere in the absence of a Pd catalyst, the conversion of secondary alcohols into ketones or ketones into secondary alcohols was not observed and no H−D exchange reaction proceeded (Table 8, entries 1 and 4). While oxidation of **3** took place even under an argon atmosphere, H−D exchange proceeded only on **4** formed via oxidation of **3** (entry 2). On the other hand, no detectable amount of reduced product **3** was observed in the same investigation using **4** as a

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[20] (a) Hattori, K.; Sajiki, H.; Hirota, K. *Tetrahedron Lett.* **2000**, *41*, 5711−5714. (b) Hattori, K.; Sajiki, H.; Hirota, K. *Tetrahedron* **2001**, *57*, 2109−2114. (c) Sajiki, H.; Ikawa, T.; Hattori, K.; Hirota, K. *Chem. Commun.* **2003**, 654−655.

[21] Ikawa, T.; Sajiki, H.; Hirota, K. *Tetrahedron* **2004**, *60*, 6189−6195.

SCHEME 6. H−D Exchange Reaction of 2,5-Dimethyl-2,5-hexanediol (7)

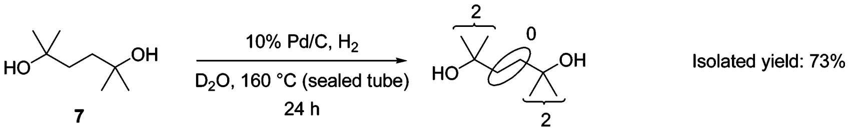
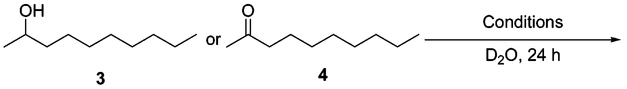
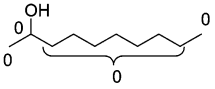
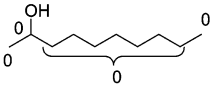
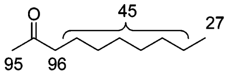
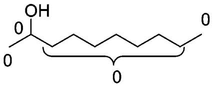
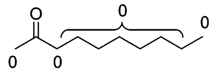
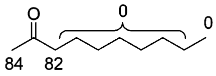
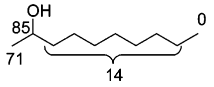
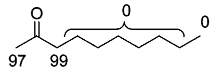


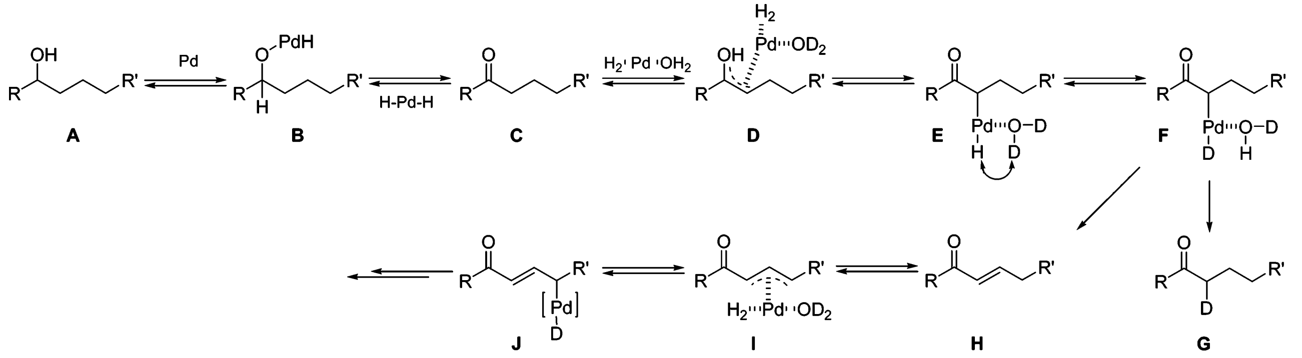
TABLE 8. Investigation of the Role of Pd/C and H_2 Gas[a]



entry	substrate	conditions	D content (%)[b]		isolated yield (%)	
			3-*d*$_n$	**4-*d*$_n$**	**3-*d*$_n$**	**4-*d*$_n$**
1	**3**	H_2, 160 °C		–	87	–[c]
2	**3**	10% Pd/C, **Ar**, 160 °C			76	9
3	**3**	10% Pd/C, H_2, **rt**		–	90	–[c]
4	**4**	H_2, 160 °C				87
5	**4**	10% Pd/C, **Ar**, 160 °C				94
6	**4**	10% Pd/C, H_2, **rt**			5	79

[a] A 2 mmol amount of the substrate was used with 10% Pd/C (10 wt % substrate) in D_2O (4 mL) at 160 °C. Reactions were carried out in a sealed tube. [b] Determined by ^1H NMR. [c] A trace amount of **4-*d*$_n$** was detected by TLC.

SCHEME 7. Plausible Mechanism for the H−D Exchange Reaction



substrate under an argon atmosphere, and the high deuterium efficiency of only both α-positions of the ketone was observed (entry 5). These experimental results indicate the following facts: (1) both Pd/C and hydrogen gas are necessary to effect the redox reactions and deuteration at the nonactivated carbons; (2) whereas dehydrogenation of secondary alcohols to ketones is feasible under an inert atmosphere, no hydrogenation of ketones is available without hydrogen gas conditions (entries 2 and 5); (3) application of heat is also necessary to effect the oxidation of alcohols to ketones (entry 3); (4) the direct deuterium incorporation into secondary alcohols may not proceed (entry 2). Consequently, the H−D exchange of ketones which formed from the starting secondary alcohols and subsequent reduction are necessary to produce deuterated secondary alcohols.

A plausible mechanism for the redox reaction and H−D exchange reaction of secondary alcohols and ketones using the Pd/C−H_2−D_2O system is outlined in Scheme 7. Dehydrogenation of secondary alcohols would proceed via oxidative addition of Pd to the O−H bond of **A** (**A** to **B**) followed by β-hydride elimination (**B** to **C**), and hydrogenation of ketones could occur through the reverse mechanism (**C** to **A**). These mechanisms are reasonable to explain why oxidation of secondary alcohols did not proceed in the absence of palladium catalyst (Table 8, entry 1) and the necessity of both Pd/C and hydrogen gas for the reduction of ketones (Table 8, entries 4 and 5).

As described in Scheme 7, an oxidative insertion of palladium, which is coordinated and activated by the H_2 gas and D_2O, to the C−H bond would take place via the formation of the corresponding Pd−π-allyl complex (**C** to **E**). Then, intramolecular H−D exchange reaction and subsequent reductive elimination could give the deuterium-labeled compound **G** through **F**. **G** submits to further deuteration as well as **C** to **G** until the formation of an α fully deuterated carbonyl product. Deuterium incorporation into another nonactivated C−H bond would proceed via β-hydride elimination of **F** to give olefin **H**. The subsequent formation of a palladium complex (**H** to **I**) and continuous isomerization of the olefin via the corresponding Pd−π-allyl complex would cause further deuteration.

Conclusion

In conclusion, we have demonstrated that the efficient H−D exchange reaction of secondary alcohols and ketones using the Pd/C−H_2−D_2O system was accompanied with a simultaneous redox reaction: the oxidation of alcohols and reduction of the corresponding ketones under the hydrogenation conditions. The H−D exchange reaction of both secondary alcohols and ketones might take place only in ketone form via a Pd−π-allyl complex.

Experimental Section

General Procedures. ^1H, ^2H, and ^{13}C NMR spectra were recorded (^1H, 400 MHz; ^2H, 61 MHz; ^{13}C, 100 MHz). Chemical shifts (δ) are given in parts per million relative to the peak for the residual solvent. The deuterium content was determined using *p*-anisic acid as an internal standard. EI and FAB mass spectra, GC spectra, and optical rotations were obtained. 10% Pd/C (Aldrich), other catalyst (N.E.ChemCat Cop.) and deuterium oxide (99.9% isotopic purity) were obtained from commercial supplier.

Typical Procedure for the H−D Exchange Reaction of 2-Decanone (4) using the Pd/C−H_2−D_2O System (Table 1, Entry 2). A mixture of 2-decanone (313 mg, 2 mmol) and 10% Pd/C (31.3 mg, 10 wt % substrate) in D_2O (4 mL) in a sealed tube was stirred at 160 °C under a H_2 atmosphere. After 24 h the mixture was cooled to rt, diluted with diethyl ether (10 mL), and passed through a membrane filter (0.45 μm) to remove the catalyst. The filtered catalyst was washed with diethyl ether (2 × 10 mL). The combined filtrates were washed with H_2O (2 × 30 mL) and brine (30 mL), dried over $MgSO_4$, and evaporated under reduced pressure. The residue was purified by flash column chromatography (hexane: ether = 40:1 to 10:1) on silica gel to afford 2-decanol-d_n (**3-d_n**; 37.7 mg) and 2-decanone-d_n (**4-d_n**; 199 mg).

Data for 3-d_n: ^1H NMR (CD_3OD, *p*-anisic acid as an internal standard) δ 3.59 (s, 0.15H), 1.32−1.17 (m, 4.23H), 1.05−1.01 (m, 0.46H), 0.83−0.76 (m, 1.36H); ^2H NMR (CH_3OH) δ 3.65 (br s), 1.31−1.22 (m), 1.07 (br s), 0.82 (br s).

Data for 4-d_n: ^1H NMR (CD_3OD, *p*-anisic acid as an internal standard) δ 2.41 (s, 0.13H), 2.09−2.08 (m, 0.21H), 1.48 (s, 0.27H), 1.27−1.17 (m, 2.28H), 0.90−0.83 (m, 0.96H); ^2H NMR (CH_3OH) δ 2.36 (br s), 2.03 (br s), 1.43 (br s), 1.17 (br s), 0.78 (br s).

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Supporting Information Available: Experimental procedures and ^1H and/or ^2H NMR data of each compound in Table 1. This material is available free of charge via the Internet at http://pubs.acs.org.

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