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Rhodium-on-carbon catalyzed hydrogen scavenger- and oxidant-free dehydrogenation of alcohols in aqueous media⁺

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The efficient and catalytic dehydrogenation of alcohols is a clean approach for preparing carbonyl compounds accompanied only by the generation of hydrogen gas. We have accomplished the heterogeneous rhodium-on-carbon catalyzed dehydrogenation of secondary, as well as primary, alcohols to the corresponding ketones and carboxylic acids in water under basic conditions.

The oxidation of alcohols is one of the most fundamental organic reactions used to prepare carbonyl compounds.¹ Among the various methods for the oxidation of alcohols, the transition metal-catalyzed dehydrogenation² of hydroxyl groups without an organic hydrogen scavenger (compounds bearing easily reducible functionalities are used to scavenge the hydrogen gas (H_2)), or an oxidant (*e.g.*, molecular oxygen³), is a clean approach to provide the corresponding carbonyl products, due to its safety and the production of less waste, except for hydrogen gas. Additionally, the hydrogen gas generated during the dehydrogenation process as a side-product can be utilized as a valuable energy source. While a variety of homogeneous⁴ and heterogeneous catalysts using Ag,⁵ Au,⁶ Cu,⁷ Co,⁸ Pt⁹ and Ni¹⁰ as a transition metal on a support have been developed for the dehydrogenation of secondary and primary alcohols into the corresponding ketones and aldehydes, only Milstein et al. have pioneered the direct transformation of primary alcohols into carboxylic acids, using a homogeneous Ru catalyst in water.¹¹ Since the reuse of catalysts is eagerly desired from the viewpoint of green chemistry, dehydrogenation reactions using a reusable water soluble Ir catalyst,⁴ⁱ and heterogeneous catalysts,⁵⁻¹⁰ are considered to be the most sustainable processes without any waste, with the exception of H₂. However, all of the previous reactions using heterogeneous catalysts were carried out in organic solvents (e.g. toluene and xylene). Herein, we demonstrate the heterogeneous Rh/C catalyzed dehydrogenation of secondary, as well as primary, alcohols in water as a clean, nontoxic, non-flammable, cheap and environmentally benign solvent, into the corresponding ketones and carboxylic acids.



We have already reported the redox reactions of secondary alcohols under Pd/C catalyzed hydrogenation conditions.¹² A platinum group metal, supported on carbon, generally displays a catalytic activity for hydrogenation.¹³ We have also utilized not only Pd/C, but also Rh/C, Ru/C and Pt/C for the hydrogenation of various substrates, such as arene nuclei, alkyl chlorides and fluorinated arenes.¹⁴ Dehydrogenation using a heterogeneous platinum group metal-on-carbon potentially includes the occurrence of a problematic issue, with the undesirable and inverse reduction of carbonyl products into the corresponding alcohols (substrates) by the in situ-generated H₂ gas (eqn (1)). Nevertheless, we have developed dehydrogenation reactions of alcohols when combined with some platinum group metals on carbon analogs, along with an inorganic base and water as the solvent, during the course of our studies.

We initially examined the catalyst efficiencies for the dehydrogenation of benzhydrol (**1a**) in water at 100 °C for 6 h under an argon atmosphere (Table 1). The 10% Pd/C catalyzed reaction gave a mixture of the desirable ketone (**2a**) and diphenylmethane (**3a**) as a hydrogenolysis product of the *in situ*generated H₂ (entry 1, without base). Furthermore, the reactions using 10% Pt/C, Ru/C and Rh/C produced mixtures of an unreacted or inversely-hydrogenated¹⁵ substrate (**1a**), a ketone product (**2a**), diphenylmethane (**3a**), and bis(diphenylmethyl)ether (**4a**) (entries 3, 5, 7 and 8, without base). The generation ratio of **2a** could be improved by the addition of Na₂CO₃ (1.1 equiv.) (entries 1, 3, 5, and 7, with Na₂CO₃). The incremental increase of Rh/C, from 10 mol% to 20 mol%, gave **2a** in nearly

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Laboratory of Organic Chemistry, Gifu Pharmaceutical University, 1-25-4 Daigakunishi, Gifu 501-1196, Japan. E-mail: sajiki@gifu-pu.ac.jp; Fax: +81-58-230-8109 †Electronic supplementary information (ESI) available: The typical procedure, the reusability tests of the catalyst, the ICP-OES results of metal leaching and the spectroscopic data of the products are depicted. See DOI: 10.1039/c4gc00434e

Table 1 The catalyst efficiencies towards the dehydrogenation of benzhydrol (1a) as a sec-alcohol

Ph´ 1a (0	OH catalyst → Ph H ₂ O (1 mL) P .25 mmol) Ar, 100 °C, 6 h	O h [⊥] Ph + Ph [^] Ph · 2a 3a	Ph Ph + →O→ Ph 4a Ph	
		Ratio of 1a/2a/3a/4a <i>^a</i>		
Entry	Catalyst	Without base	With Na ₂ CO ₃ ^b	
1	10% Pd/C (10 mol%)	0/68/32/0	0/70/30/0	
2	10% Pd/C (20 mol%)	—	29/71/0/0	
3	10% Pt/C (10 mol%)	29/46/1/24	9/82/9/0	
4	10% Pt/C (20 mol%)	_	1/87/7/0	
5	10% Ru/C (10 mol%)	67/28/1/4	22/77/1/0	
6	10% Ru/C (20 mol%)	_	59/49/0/0	
7	10% Rh/C (10 mol%)	32/56/11/1	16/78/6/0	
8	10% Rh/C (20 mol%)	20/66/4/10	$0/98(92)^{c}/2/0$	

Na₂CO₃ were used. ^c Isolated yield.

Table 2 Base efficiencies

OH Ph Ph 1a (0.25 mmol	10% Rh/C (20 mo base (1.1 equiv) H ₂ O (1 mL) Ar, 100 °C	^{l%)} 0 Ph Ph + Ph 2a	$\frac{Ph}{3a} \xrightarrow{Ph} - O \xrightarrow{Ph} \frac{Ph}{4a}$
Entry	Base	Time (h)	Ratio of 1a/2a/3a/4a <i>^a</i>
1	Na ₂ CO ₃	3	35/63/2/0
2	Na_2CO_3	6	$0/98(92)^{b}/2/0$
3	NaOH	3	45/53/2/0
4	NaHCO ₃	3	35/65/0/0
5	NaHCO ₃	6	5/92/2/1
6	Et ₃ N	3	74/26/0/0
7	K_2CO_3	3	21/78/1/0
8	K_2CO_3	6	$2/97(91)^b/1/0$
^{<i>a</i>} The ratios v	vere determined	by ¹ H NMR sr	pectroscopy. ^b Isolated

yields.

^a The ratios were determined by ¹H NMR spectroscopy. ^b 1.1 equiv. of

Table 3 Solvent effects



^a The ratios were determined by ¹H NMR spectroscopy.

Table 4 Double dehydrogenations of pri-alcohol (6a) into the corresponding carboxylic acid (8a)

10% Rh/C (20 mol%) base (2.2 equiv) H_2O (1 mL) Ar, 100 °C, 24 h then acidic quench	$\begin{array}{cccc} & & & & & & \\ & & & & & \\ & & & & & \\ & & & & $
Solvent	Ratio of 6a/7a/8a <i>^a</i>
Na ₂ CO ₃	$0/0/100(32)^{b}$
K ₂ CO ₃	$12/44/44(22)^{c}$
Li_2CO_3	8/39/53 (24) ^c
NaHCO ₃	$45/3/52(30)^{c}$
NaOH	$0/0/100(53)^{b}$
Et_3N	$0/0/100(37)^{c}$
	$\frac{10\% \text{ Rh/C (20 mol%)}}{\text{base (2.2 equiv)}}$ $\frac{10\% \text{ Rh/C (20 mol%)}}{\text{H}_2\text{O (1 mL)}}$ Ar, 100 °C, 24 h then acidic quench $\frac{\text{Solvent}}{\text{Solvent}}$ $\frac{\text{Na}_2\text{CO}_3}{\text{K}_2\text{CO}_3}$ $\frac{\text{Li}_2\text{CO}_3}{\text{Na}\text{HCO}_3}$ NaOH Et_3N

^{*a*} The ratios were determined by ¹H NMR spectroscopy. Other products, which could not be identified, were also obtained. ^{*b*} Isolated yields of 8a. ^c The yields of 8a were determined by ¹H NMR spectroscopy using 1,2-methylenedioxybenzene as the internal standard.

quantitative isolated yields (92%, entry 8, with Na₂CO₃). The role of the Na₂CO₃ is unclear and is under investigation.

The dehydrogenation efficiency of 1a, using various bases, was estimated using 10% Rh/C as the catalyst for 3 h (Table 2, entries 1, 3, 4, 6 and 7). Na₂CO₃, NaHCO₃, and K₂CO₃ were found to be more effective than NaOH and Et₃N. An organic base was less efficient due to the catalytic poison effect by the coordination ability of Et₃N towards Rh metal. For comparison, the generation ratios of 2a using Na₂CO₃, NaHCO₃, and K₂CO₃ for 6 h (entries 2, 5 and 8) were investigated. Na₂CO₃ was chosen as the appropriate base for the Rh/C catalyzed dehydrogenation.

While the present dehydrogenation in organic solvents [MeOH, toluene, cyclopentyl methyl ether (CPME) and 1,4-dioxane] led to low conversion yields (Table 3, entries 2-5), the desired ketone (2a) was nearly quantitatively obtained in water (entry 1).

Water as a solvent can also play a crucial role in the transformation of primary alcohols into carboxylic acids (Table 4).

Namely, the first dehydrogenation stage of decanol (6a), as a primary alcohol, can give the corresponding decanal (7a), which is subsequently transformed into the hydrate intermediate (A) in water, and the following second dehydrogenation (A) produces the corresponding carboxylic acid (8a).^{11,16} NaOH was found to be the most effective base for the double dehydrogenation of decanol (6a) to provide decanoic acid (8a) with a yield of 53% (entry 5 in comparison with entries 1-4 and 6), since the hydroxyl ion of NaOH synergistically facilitated the formation of the hydrate (A). Decanal (7a) as the starting material was also efficiently converted into decanoic acid (8a) under the same reaction conditions with a yield of 52% (eqn (2)), which clearly indicates that the presented double dehydrogenation of 6a into 8a proceeded via the formation of 7a as an intermediate. The reaction of 6-phenylhexanol (6b) also gave the desired carboxylic acid (8b) with a yield of 50%, accompanied by trace amounts of pentylbenzene (9b) and 1-phenyl-1-pentene (10b) as byproducts (eqn (3)). Undesirable decarbonylations of the terminal aldehyde and the carboxylic

Table 5 Scope of the substrates^a

		10% Rh/C (20 mol%) Na ₂ CO ₃ or NaOH		
	Substrate - 1 or 6 (0.25 mmol)	H ₂ O (1 mL) Ar, 100 °C, 6 h	Product	
Entry	Substrate	Product	Time (h)	Yield (%)
1 ^{<i>b</i>}	OH Ph	Ph 2b	6	74
2	OH Ph 1c	Ph 2c	6	81
3	OH Ph 1d	Ph 2d	48	76
4	OH Ph	Ph	6	76
	1e 🗸	2ea O Ph 2eb		7
5	OH If	2f	6	64
6	OH 1g	2g	6	89
7	OMe HeO 1h	MeO 2h	6	89
8	СІ	CI CI	24	89
9		CI ⁻ 2i	6	63 ^{<i>d</i>}
	F 1j	F 2ja		29 ^d
		F 2jb		

	Substrate - 1 or 6 (0.25 mmol)	10% Rh/C (20 mol%) Na ₂ CO ₃ or NaOH H ₂ O (1 mL) Ar, 100 °C, 6 h	Product	
Entry	Substrate	Product	Time (h)	Yield (%)
10	OH 1k		6	82
11	но-	0=	24	38 (42) ^e
12	OH Ph 1m	Ph 2m	6	51
13	OH BnO	BnO ₁₁₉	24	74
14	OH BnO ₍₎₉ Ph 1o	BnO ₍₎₉ Ph 20	12	$62 (10)^e$
15 ^c	ОН 6с	CO ₂ H	24	54
16 ^{<i>c</i>}	n-C ₄ H ₉ OH	n-C ₄ H ₉ 8d	H ₂₄	44
17 ^c	MeO 6e	MeO Se CO ₂ H	24	38

Table 5 (Contd.)

^a Na₂CO₃ (2.2 equiv.) was used for the dehydrogenation of the secondary alcohols and NaOH (2.2 equiv.) was used for the double dehydrogenation of the primary alcohols as the bases, unless otherwise noted. b Na₂CO₃ (1.1 equiv.) was used as the base. c After the reaction, the reaction mixture was neutralized with diluted H_2SO_4 , and then filtered and extracted. ^{*d*} The yields were determined by ¹H NMR spectroscopy because the generated products were inseparable. ^e Isolated yields of the starting materials.

acid under the transition metal-catalyzed hydrogenation conditions¹⁷ could not be completely suppressed.



Table 6 Reusability tests^a



 a 10% Rh/C was reused after simple filtration, washing with H₂O and MeOH, and drying *in vacuo*. In each run, 91–99% of the Rh/C could be recovered.

The scope of application of the substrates was next investigated, using Na₂CO₃ for the secondary alcohols and NaOH for the primary alcohols as the bases (Table 5). Various secondary benzylic and aliphatic alcohols, bearing linear and cyclic substructures, efficiently underwent dehydrogenation to give the corresponding carbonyl products (entries 1-14). As mentioned in the introduction, a platinum group metal-on-carbon potentially possesses a hydrogenation activity.¹³ Therefore, the H₂ gas generated under the dehydrogenation conditions may cause the hydrogenation of the coexisting reducible functionalities. The alkene was completely hydrogenated (entry 12), while the cyclopropane, the aromatic fluoride¹⁸ and the benzyl ether functionalities were partially reduced (entries 4, 9, 13 and 14). Meanwhile, the aromatic chloride was perfectly tolerated under the Rh/C catalyzed conditions (entry 8).¹⁸ Primary benzylic alcohols also underwent double dehydrogenation in water to give the corresponding carboxylic acids in moderate vields (entries 15-17).

Since reuse is one of the key components for heterogeneous transition metal-catalyzed reactions, from the view point of green chemistry and cost performance, the reuse of 10% Rh/C was attempted during the dehydrogenation of 1a.¹⁹ While Rh/C was reusable up to four times without any loss of the catalytic activity, after simple filtration and washes with H₂O and MeOH, a gradual decrease in the catalytic activity was observed in the fifth and sixth runs. Since analysis using Inductively Coupled Plasma-Optical Emission Spectroscopy (ICP-OES) indicated no metal leaching into the reaction mixture,²⁰ the modest decrease in the catalytic activity might have been due to the chemical or mechanical damage caused by the basic conditions and/or the stirring (Table 6).

Conclusions

We have accomplished the Rh/C catalyzed, hydrogen scavenger- and oxidant-free, dehydrogenation of secondary and primary alcohols in water, under basic conditions, to provide the corresponding ketone and carboxylic acid derivatives. The heterogeneous Rh/C could be recovered by a simple procedure and reused up to four times. The presented dehydrogenation is the first successful case using water as the solvent for this heterogeneous catalytic system, and carboxylic acids were obtained from primary alcohols using water as part of the oxygen source.

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- 15 Rh/C has the hydrogenation activity as shown below. The reaction of 2a under a hydrogen atmosphere in H₂O at 100 °C in the presence of Na₂CO₃ provided 1a as the main reduced product.



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- 18 Aromatic fluorides were effectively hydrogenated in comparison with aromatic chlorides under the Pt/C catalyzed hydrogenation conditions using isopropanol as the hydrogen source. A similar tendency was observed in the present reactions. See details in our previous report shown as ref. 14*c*.
- 19 The reactions in Tables 1–5 were carried out in a test-tube under argon (balloon), and stirred using the Chemist Plaza personal organic synthesizer (Shibata Scientific Technology, Ltd, Tokyo). Meanwhile, the reusability tests listed in Table 6 were carried out in a two-necked flask attached to a reflux condenser. Although control of the accumulation of the generated hydrogen gas can effectively revise the dehydrogenation activity, the reproducibility of the reaction can be easily obtained. Actually, the reaction of **1a** in test-tube (Table 2, entry 2) could be investigated several times to give similar yields of **2a**. See details in the ESI.†

20 The results of metal leaching are described in the ESI.†