

論文の内容の要旨

論文題目 Study on Highly Functionalized Heterogeneous Catalysts Based on Supported Ruthenium Hydroxides for Green Functional Group Transformations
(環境調和型官能基変換反応のための高機能担持水酸化ルテニウム触媒開発に関する研究)

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1. Introduction

Homogeneous catalysts of inorganic salts and organometallic complexes have been used for many bulk and fine chemicals syntheses until now. They are usually dissolved in reaction solutions making all catalytic sites accessible to substrates and show high catalytic activity and selectivity. Despite these advantages, homogeneous catalysts have a share of only ca. 20–30% in industrial processes because catalyst/product(s) separation (problem of product contamination) and reuse of (expensive) catalysts are very difficult. Therefore, the development of easily recoverable and recyclable heterogeneous catalysts has received a particular research interest and can solve the problems of the homogeneous systems. Furthermore, the design of truly efficient heterogeneous catalysts with the activities and selectivities comparable to or higher than those of the corresponding homogeneous analogues is one of the most important challenges in modern organic synthesis, especially for fine chemicals.

The strategy to design the efficient heterogeneous catalysts for various functional group transformations is a creation of the monomerically (at least mainly if not wholly) dispersed ruthenium hydroxide species on the appropriate supports (Figure 1). Of all elements of the Periodic Table, ruthenium has widest scope of oxidation states ranging from -2 to $+8$ and various coordination geometries in each electron configuration. These properties would lead to the exploitation of efficient and/or novel catalytic transformations. In addition, the monomerically dispersed ruthenium hydroxide species would possess both Lewis acid and Brønsted base sites on the same metal and the various functional group transformations likely be promoted by the “concerted activation” by the Lewis acid and Brønsted base sites.

In this thesis, the highly dispersed ruthenium hydroxide catalysts ($\text{Ru}(\text{OH})_x/\text{support}$) have been prepared with various supports such as Al_2O_3 and TiO_2 . They showed high catalytic performance for liquid-phase hydrogen-transfer reactions such as racemization of chiral secondary alcohols, reduction of carbonyl compounds and allylic alcohols, and aerobic alcohol oxidation. Moreover, they could act as efficient heterogeneous catalysts for the *N*-imine formation and reductive *N*-alkylation of primary alcohols with amines, as well as the oxygenation of primary amines to amides. All these catalyses were truly heterogeneous and the catalysts recovered after the reactions could be reused with keeping their high catalytic performance.

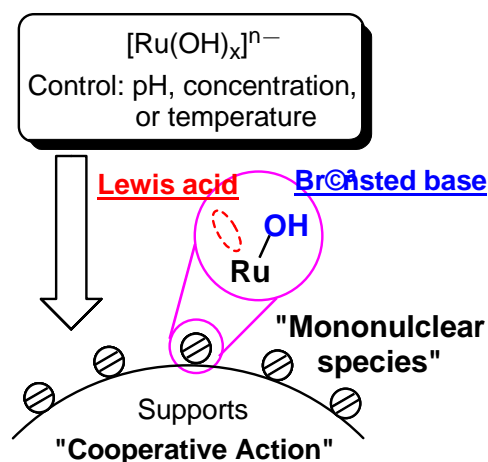


Figure 1. The strategy to design efficient heterogeneous catalysts.

2. Preparation and Characterization of Supported Ruthenium Hydroxide Catalysts

The supported ruthenium hydroxide catalysts were prepared with four different supports, anatase TiO_2 (denoted as $\text{TiO}_2(\text{A})$, Ishihara Sangyo Kaisya Ltd., ST-01, $316 \text{ m}^2\text{g}^{-1}$), anatase TiO_2 ($\text{TiO}_2(\text{B})$, the Catalysis Society of Japan, JRC-TIO-1, $73 \text{ m}^2\text{g}^{-1}$), rutile TiO_2 ($\text{TiO}_2(\text{C})$, Showa Denko K. K., SUPER-TITANIA G-2, $3.2 \text{ m}^2\text{g}^{-1}$), and Al_2O_3 (Sumitomo Chemical Co., Ltd., KHS-24, $160 \text{ m}^2\text{g}^{-1}$). The catalysts were prepared by the reaction of TiO_2 (or Al_2O_3) with RuCl_3 in aqueous medium followed by the treatment with NaOH . A typical procedure is as follows: The powder TiO_2 (or Al_2O_3) (2.0 g) calcined at $550 \text{ }^\circ\text{C}$ for 3 h was vigorously stirred with 60 mL of an aqueous solution of RuCl_3 (8.3 mM, pH ca. 2.0) at room temperature (ca. $22 \text{ }^\circ\text{C}$). After 15 min, the pH of the solution was adjusted to 13.2 by addition of an aqueous solution of NaOH (1 M) and the resulting slurry was stirred for 24 h. The solid was then filtered off, washed with a large amount of water, and dried in vacuo to afford supported ruthenium hydroxide catalysts. The ruthenium contents were 2.1–2.2 wt%.

Figure 2 shows the radial distribution functions (RDFs) from the Fourier transform of the k^3 -weighted EXAFS for $\text{Ru}(\text{OH})_x/\text{support}$, $\text{Ru}(\text{OH})_x$, and anhydrous RuO_2 . The first Ru–O shell parameters for $\text{Ru}(\text{OH})_x$ and $\text{Ru}(\text{OH})_x/\text{support}$ were similar to those for anhydrous RuO_2 . On the other hand, the RDFs exhibited significant differences for the longer range Ru–Ru environments. The intensities of the Ru–Ru shell signal at $r = 2.8 \text{ \AA}$ for $\text{Ru}(\text{OH})_x$ and $\text{Ru}(\text{OH})_x/\text{support}$ were considerably damped in comparison with that for anhydrous RuO_2 and the signals at $r = 3.3 \text{ \AA}$ due to the Ru–O–Ru shells were hardly observed for $\text{Ru}(\text{OH})_x$ and $\text{Ru}(\text{OH})_x/\text{support}$. The CNs (coordination numbers) of nearest-neighbor Ru atoms suggest the presence of different sizes in the supported hydroxide catalysts. These supported catalysts likely consist of the mixture of the monomeric ruthenium hydroxide species and polymeric one. Judging from the CNs of the Ru–Ru shell signals, the sizes of the $\text{Ru}(\text{OH})_x$ decreased in the order of $\text{Ru}(\text{OH})_x > \text{Ru}(\text{OH})_x/\text{TiO}_2(\text{C}) > \text{Ru}(\text{OH})_x/\text{Al}_2\text{O}_3 > \text{Ru}(\text{OH})_x/\text{TiO}_2(\text{B}) > \text{Ru}(\text{OH})_x/\text{TiO}_2(\text{A})$. In the ESR measurements, the signal intensity due to Ru^{3+} species with low spin d^5 electron configuration also increased with the decrease in the size of the supported ruthenium hydroxide species.

3. Size-dependent Catalytic Activity of Supported Ruthenium Hydroxides for Hydrogen Transfer Reactions and Aerobic Alcohol Oxidation

The catalytic activities of a series of the supported ruthenium hydroxide catalysts for the racemization of (*R*)-1-phenylethanol (>99% *ee*) were examined. No reaction proceeded in the absence of the catalyst, or in the presence of Al_2O_3 , TiO_2 , or $\text{Ru}(\text{OH})_x$. Among the supported ruthenium hydroxide catalysts tested, the reaction rates decreased in the order of $\text{Ru}(\text{OH})_x/\text{TiO}_2(\text{A})$ ($\text{TOF} = 380 \text{ h}^{-1}$) > $\text{Ru}(\text{OH})_x/\text{TiO}_2(\text{B})$ (120 h^{-1}) > $\text{Ru}(\text{OH})_x/\text{TiO}_2(\text{C})$ (3 h^{-1}), while the selectivities to the racemization were 88–95% and did not much change. The TOF_{obs} (observed turnover frequencies) monotonically increased with the decrease in CNs (sizes of ruthenium hydroxide species) as shown in Figure 3(a), suggesting that the present hydrogen transfer reactions depend on the sizes of supported $\text{Ru}(\text{OH})_x$ species. In the presence of the most active $\text{Ru}(\text{OH})_x/\text{TiO}_2(\text{A})$ catalyst, the scope of the present system towards various kinds of structurally diverse chiral secondary alcohols was examined (Table 1). $\text{Ru}(\text{OH})_x/\text{TiO}_2(\text{A})$ showed high catalytic activities for the racemization of activated chiral secondary alcohols as well as non-activated ones. A major advantage of using $\text{Ru}(\text{OH})_x/\text{TiO}_2(\text{A})$ is the heterogeneous nature, which was confirmed by the fact that the reaction did not proceed after removal of the catalyst at the reaction temperature and no leaching of the ruthenium species was observed. It was confirmed by XANES and EXAFS spectra that the local structure of the ruthenium species in the used $\text{Ru}(\text{OH})_x/\text{TiO}_2(\text{A})$ catalyst was the same as that in the fresh catalyst. In addition, the $\text{Ru}(\text{OH})_x/\text{TiO}_2(\text{A})$ catalyst could be reused for the racemization of (*R*)-1-phenylethanol at least three times with retention of its high catalytic performance (<1% *ee*, 86% select. for the 3rd reuse experiment). The $\text{Ru}(\text{OH})_x/\text{TiO}_2(\text{A})$ catalyst could also act as an effective heterogeneous catalyst for the reduction of carbonyl

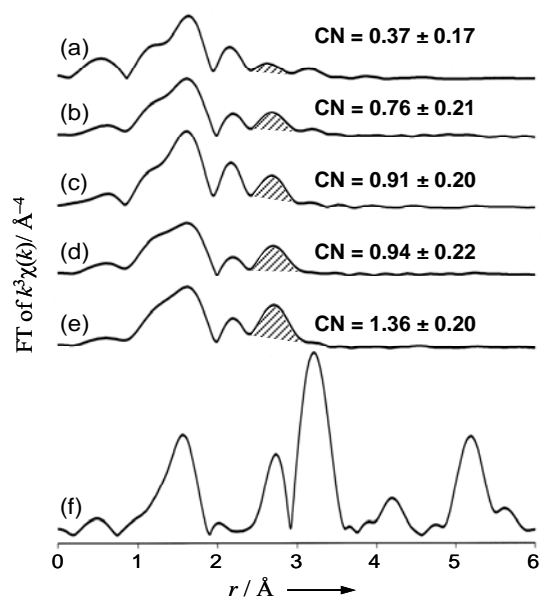


Figure 2. The RDFs from the Fourier transformation of the k^3 -weighted EXAFS for (a) $\text{Ru}(\text{OH})_x/\text{TiO}_2(\text{A})$, (b) $\text{Ru}(\text{OH})_x/\text{TiO}_2(\text{B})$, (c) $\text{Ru}(\text{OH})_x/\text{Al}_2\text{O}_3$, (d) $\text{Ru}(\text{OH})_x/\text{TiO}_2(\text{C})$, (e) $\text{Ru}(\text{OH})_x$, and (f) anhydrous RuO_2 . The phase shift was not corrected.

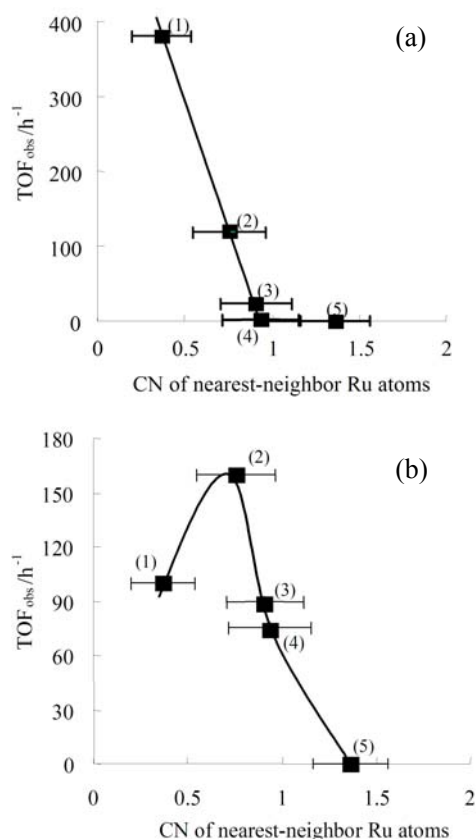
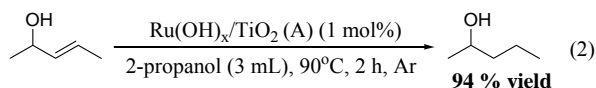
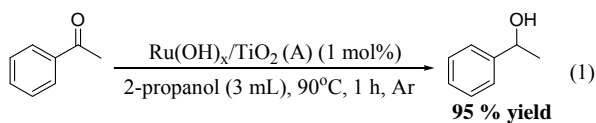


Figure 3. Relationship between TOF_{obs} and CNs of nearest-neighbor Ru atoms for (a) the racemization of (*R*)-1-phenylethanol and (b) the aerobic oxidation of 1-phenylethanol by various ruthenium hydroxide catalysts. (1): $\text{Ru}(\text{OH})_x/\text{TiO}_2(\text{A})$, (2): $\text{Ru}(\text{OH})_x/\text{TiO}_2(\text{B})$, (3): $\text{Ru}(\text{OH})_x/\text{Al}_2\text{O}_3$, (4): $\text{Ru}(\text{OH})_x/\text{TiO}_2(\text{C})$, and (5): $\text{Ru}(\text{OH})_x$.

compounds to alcohols [Eq. (1)] and allylic alcohols to saturated alcohols [Eq. (2)] in the presence of 2-propanol as a hydrogen source.



Next, the catalytic activities of a series of the supported ruthenium hydroxide catalysts for the aerobic oxidation of 1-phenylethanol were examined. The TOFs_{obs} were also dependent on the sizes of the ruthenium hydroxide species and increased with the decrease in CNs. However, they reached maximum with Ru(OH)_x/TiO₂(B), and then decreased (Figure 3(b)). A reaction mechanism involving the Ru alcoholate formation/ β -elimination has been proposed for the present catalytic oxidations. Both of them are reversible reactions. The kinetic isotope effects ($k_H/k_D = 5.3$) indicate that the C-H bond breaking is included in the rate-determining step. Intrinsically, the catalytic activities of Ru(OH)_x for both the hydride abstraction and hydride re-addition increased with the decrease in the CNs. The size effect on the hydride re-addition was larger than that on the hydride abstraction in the CNs from 0.76 to 0.37. As a result, the Ru(OH)_x/TiO₂(B) catalyst with the suitable size showed the highest catalytic activity for the aerobic alcohol oxidation.

Table 2 shows the results of the aerobic oxidation of various alcohols with the most active Ru(OH)_x/TiO₂(B) catalyst. All primary and secondary benzylic alcohols were converted into the corresponding carbonyl compounds, respectively, in almost quantitative yields. The α,β -unsaturated alcohol afforded the corresponding enal without the intramolecular hydrogen transfer. The present system could also oxidize secondary aliphatic and heteroatom-containing alcohols in high yields. The oxidation of radical clock substrate of cyclopropylphenyl carbinol exclusively produced cyclopropylphenyl ketone without the ring-opened products, suggesting that free-radical intermediates are not involved in the present alcohol oxidation. The present alcohol oxidation was also heterogeneously catalyzed and the Ru(OH)_x/TiO₂(B) catalyst could be reused for the oxidation of benzyl alcohol with retention of its high catalytic performance (>99% yield for the 3rd reuse experiment).

4. Catalytic Tandem One-pot Syntheses of Aldimines and Secondary Amines from Primary Alcohols and Amines

The tandem one-pot synthesis of aldimines from primary alcohols and amines could be efficiently promoted by supported ruthenium hydroxide catalysts, in particular Ru(OH)_x/TiO₂(B). The various combinations of substrates (seven alcohols and six amines) with the most active catalyst, Ru(OH)_x/TiO₂(B), have been investigated and all reactions efficiently proceeded to afford the corresponding aldimines in high yields. The catalyst (B) could be applied to the large-scale production and the TOF remarkably reached up to 182 h⁻¹, showing the highest value among the heterogeneous systems to this day. Furthermore, the tandem syntheses of benzylidenealdehyde and 2-phenylbenzimidazole could be realized with good yields in the presence of supported ruthenium hydroxide catalysts.

Table 1. Ru(OH)_x/TiO₂(A)-catalyzed racemization of various chiral secondary alcohols.^[a]

entry	substrate	product	time [h]	ee [%]	select. [%]
1			3	<1	83
2			3	<1	83
3 ^[b]			4	6	76
4			8	<1	76
5 ^[b]			4	4	84
6 ^[b]			4	2	85

[a] Reaction conditions: Substrate (1 mmol), Ru(OH)_x/TiO₂(A) (Ru: 1 mol%), toluene (3 mL), 80°C, in 1 atm of Ar. The enantiomeric excess (ee[%]) and selectivity to racemization (select. [%]) were determined by GC or HPLC using an internal standard. The main by-products were ketones. [b] Ru: 2 mol%.

Table 2. Ru(OH)_x/TiO₂(B)-catalyzed aerobic oxidation of various alcohols.^[a]

entry	substrate	product	time [h]	yield [%]
1			2	>99
2			1	>99
3			1	>99
4			7	>99
5 ^[b]			3	84
6			3	76
7 ^[c]			3	>99

[a] Reaction conditions: Substrate (1 mmol), Ru(OH)_x/TiO₂(B) (Ru: 1 mol%), toluene (3 mL), 80°C, in 1 atm of O₂. Yields were determined by GC using an internal standard. [b] Ru: 2 mol%. [c] Ru: 5 mol%.

The selective *N*-alkylation of aromatic and heteroaromatic amines with alcohols was described. A variety of aromatic and heteroaromatic amines in the presence of Ru(OH)_x/Al₂O₃ were selectively converted into the corresponding secondary amines in high to excellent yields without any co-catalysts such as bases and ligands. The present *N*-alkylation likely proceeds via the following three sequential reactions; the oxidative dehydrogenation of an alcohol to a carbonyl compound occurred to form the corresponding imine followed by the hydrogen transfer reaction of the imine to afford the corresponding secondary amine.

5. Oxygenation of Primary Amines to Amides by Supported Ruthenium Hydroxide Catalysts

Amides are very important class of compounds in chemistry and biology that have been used as intermediates in peptide and protein synthesis, intensifiers of perfume, color pigments for inks, detergents, and lubricants. Traditionally, amides have been synthesized by the reaction of activated carboxylic acid derivatives with amines including ammonia or by the acid-catalyzed rearrangements of ketoximes. However, these traditional methods often produce vast amounts of toxic chemical wastes. Therefore, the development of efficient procedures for the synthesis of amides that avoids wasteful use of stoichiometric reagents and/or acidic and basic media is highly desirable and still a great challenge in modern organic synthesis. In general, it is very difficult to oxygenate the α -methylene groups of amines to the corresponding amides and a stoichiometric oxidant of RuO₄ have been used with the protection of amino groups, for example. To date, efficient catalytic oxygenations of primary amines to amides including homogeneous as well as heterogeneous ones have never been reported. In the presence of supported ruthenium hydroxide catalysts, the oxygenation of primary amines to amides with molecular oxygen (air) in water could be realized. This is the first example of catalytic oxygenation of amines to amides with molecular oxygen.

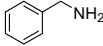
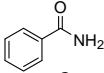
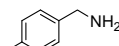
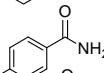
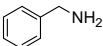
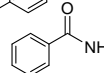
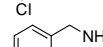
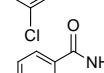
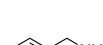
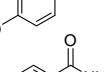
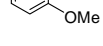
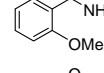
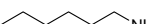
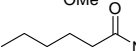
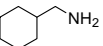
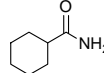

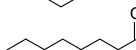
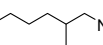
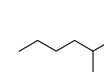
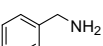
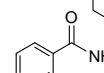
In this transformation, the Ru(OH)_x/Al₂O₃ catalyst showed the highest selectivity to the desired amides because the hydrolytic decomposition of amides (and/or nitrile intermediates) to carboxylic amides proceeded to some extent in the presence of supported ruthenium hydroxide catalysts on TiO₂. In the presence of Ru(OH)_x/Al₂O₃, various primary amines including aromatic, aliphatic, and heterocyclic could be converted into the corresponding amides in high yields (Table 3). After the reaction was completed, the Ru(OH)_x/Al₂O₃ catalyst could be easily retrieved from the reaction mixture and reused without significant loss of its catalytic performance.

The Ru(OH)_x/Al₂O₃-catalyzed transformation of benzylamine in ¹⁸O-labeled water (¹⁸O content: $\geq 98\%$) led to the selective formation of ¹⁸O labeled benzamide in almost quantitative yield, suggesting that the oxygen atom incorporated into benzamide originates from water. The reaction profile for the oxygenation of benzylamine showed that benzonitrile was initially formed, followed by the formation of benzamide, indicating that the Ru(OH)_x/Al₂O₃-catalyzed transformation possibly proceeds by a tandem process of the oxidative dehydrogenation of amines to nitriles followed by hydration to produce the corresponding amides.

6. Conclusion

The supported ruthenium hydroxide catalysts showed high catalytic activities and selectivities for hydrogen transfer reactions, aerobic alcohol oxidation, *N*-imine formation and reductive *N*-alkylation, and oxygenation. The present transformations were intrinsically heterogeneous and the supported ruthenium hydroxide catalysts could be reused with retention of their high catalytic performance.

Table 3. Ru(OH)_x/Al₂O₃-catalyzed transformation of various primary amines to amides.^[a]

entry	substrate	product	time [h]	yield [%] ^[b]
1			10	92
2			10	82
3			10	92
4			10	89
5			24	86
6			10	87
7			24	87
8 ^[c]			24	86
9			24	83
10 ^[d]			24	77
11			24	90

[a] Reaction conditions for benzylamines and picolylamine (entries 1–6 and 11): Substrate (0.25 mmol), Ru(OH)_x/Al₂O₃ (Ru: 5 mol%), water (1 mL), 140°C, in 5 atm of air; for alkylamines (entries 7–10): Substrate (0.5 mmol), Ru(OH)_x/Al₂O₃ (Ru: 5 mol%), water (2 mL), 130°C, in 5 atm of air. [b] Isolated yield. [c] 140°C. [d] 160°C.