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Environmentally Friendly One-Pot Synthesis of α-Alkylated Nitriles Using Hydrotalcite-Supported Metal Species as Multifunctional Solid Catalysts

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Abstract: A ruthenium-grafted hydrotalcite (Ru/HT) and hydrotalcite-supported palladium nanoparticles (Pd_{nano}/HT) are easily prepared by treating basic layered double hydroxide, hydrotalcite (HT, $Mg_6Al_2(OH)_{16}CO_3$) with aqueous $RuCl_3\cdot n H_2O$ and $K_2[PdCl_4]$ solutions, respectively, using surface impregnation methods. Analysis by means of X-ray diffraction, and energy-dispersive X-ray, electron paramagnetic resonance, and X-ray absorption fine structure spectroscopies proves that a monomeric Ru^{IV} species is grafted onto the surface of the HT. Meanwhile, after reduction of a surface-isolated Pd^{II} species, highly dispersed Pd nanoclusters with a mean diameter of about 70 Å is observed on the Pd_{nano}/HT surface by transmission electron microscopy analysis. These hydrotalcite-supported metal catalysts can effectively promote α-alkylation reactions of various nitriles with primary alcohols or carbonyl compounds through tandem reactions consisting of metal-catalyzed oxidation and reduction, and an aldol reaction promoted by the base sites of the HT. In these catalytic α-alkylations, homogeneous bases are unnecessary and the only by-product is water. Additionally, these catalyst systems are applicable to one-pot syntheses of glutaronitrile derivatives.

Keywords: alkylation · heterogeneous catalysis · hydrotalcite · nitriles · palladium · ruthenium

Introduction

α-Alkylated nitriles are important building blocks for synthesizing amides, carboxylic acids, ketones, and a variety of biologically active agents.[1] The main method for the synthesis of α-alkylated nitriles has been stoichiometric reaction of nitriles with alkyl halides using homogeneous inorganic bases such as NaH and $NaNH_2$ (Scheme 1 A). These traditional α-alkylations have serious drawbacks: toxicity of halogenated substrates, the use of homogeneous strong bases, and production of large amounts of waste (low atom efficiency). With ever-increasing environmental concerns, catalytic α-alkylation of nitriles using alcohols or carbonyl compounds instead of halides is a desirable protocol for both laboratory and industrial synthetic chemistry.[2] Grigg and co-workers demonstrated the α-alkylation of phenylacetonitriles with primary alcohols using homogeneous Ru and Rh complexes in the presence of bases.[3] However, these reported reaction systems suffer from low catalytic activity, significant limitation of substrate scope, and the necessity of using stoichiometric amounts of inorganic bases as additives. In addition, the use of homogeneous metal catalysts on an industrial scale leads to practical problems owing to the difficulties involved in recovering the expensive metals and ligands from the reaction mixture and in separation of products. There is a strong need for development of an environmentally friendly heterogeneous catalyst system for α-alkylation of nitriles.

Hydrotalcites, referred to as HTs, are layered, mixed hydroxides of Mg and Al. The HTs have received much attention as advanced materials because of their unique properties, such as the cation exchange ability of the Brucite layer, anion exchange ability of the interlayer, surface tunable basicity, and adsorption capacity.[4,5] The development of highly functionalized HT catalysts for a variety of organic

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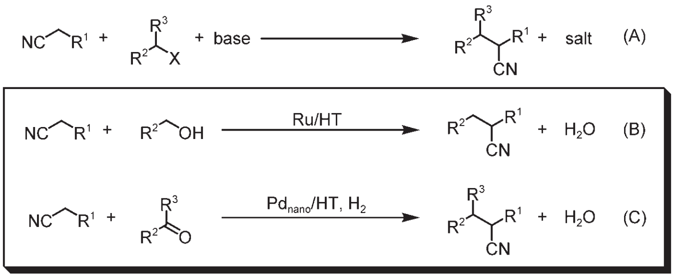


Scheme 1.

transformations has already been reported by our group and others.[6,7] For example, the surface basicities of the HTs result in high catalytic activities for the epoxidation of olefins,[6a,b] *N*-oxidation of pyridines,[6c] and carbon–carbon bond-forming reactions.[6d–g] Additionally, the introduction of transition-metal species, such as Ru,[7a–c] Mn,[7c] Pd,[7d–g] W,[7h,i] Os,[7j] Ni,[7k,l] or Cu,[7m,n] into the Brucite layer or solid surface of the HTs could afford high-performance supported metal catalysts. From these results, HT-supported metal compounds have potential as excellent multifunctional catalysts containing both surface base sites and transition-metal species as active centers for one-pot sequential reactions.[7d,8,9,10] In this context, we present the synthesis and characterization of a ruthenium-grafted hydrotalcite (Ru/HT) and hydrotalcite-supported palladium nanoparticles (Pd_{nano}/HT) for efficient α-alkylation of nitriles with primary alcohols (Scheme 1 B) and carbonyl compounds (Scheme 1 C). Since these catalysts possess both strong surface basicities and oxidation/reduction abilities based on the surface metal species, one-pot formation of α-alkylated nitriles could be achieved through several tandem reactions. This report also includes the further transformation of α-alkylated nitriles to glutaronitrile derivatives in a single reactor.[1b,e]

Results and Discussion

Catalyst preparation and characterization: Surface impregnation is one of the most simple and efficient protocols for the introduction of active species onto solid supports.[11] Because of the high adsorption capacity of the HT, a variety of catalytically active metals can easily be created on the HT surface.

Ru/HT: In our previous work on hydrotalcite-supported Ru catalysts for aerobic oxidation of alcohols, Ru species placed on the solid HT surface showed higher activity than those in the inner HT framework owing to the ease of accessibility of substrates to the metal centers.[9a–c] Preparation of the catalyst by introducing active Ru species onto the hydrotalcite surface takes place as follows: Treatment of the HT with an aqueous solution of $RuCl_3 \cdot nH_2O$ at room temperature afforded the Ru/HT as a gray powder (Ru content 0.05 mmolg^{-1}). Retention of the original HT interlayer distance (3.0 Å), as shown by X-ray diffraction (XRD), confirmed that the Ru species were deposited onto the HT surface. The K-edge X-ray absorption near-edge structure (XANES) spectrum of the Ru species on the Ru/HT was similar to that of $[RuO_2]$ but different from that of $[Ru(acac)_3]$, and the Ru/HT was EPR silent (EPR = electron paramagnetic resonance). These results show that the Ru species of the Ru/HT is in the +4 oxidation state.[12] The absence of chlorine on the Ru/HT was confirmed by X-ray photoelectron spectroscopy (XPS) and energy-dispersive X-ray (EDX) analysis. In Fourier transform (FT) of the k^3-weighted Ru K-edge X-ray absorption fine structure (EXAFS) spectrum of the Ru/HT, a peak near 3.5 Å corresponding to Ru–Ru bonds was barely observed (Figure 1).

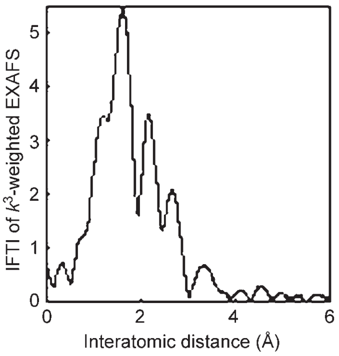


Figure 1. Fourier-transform (FT) of k^3-weighted Ru K-edge EXAFS of the Ru/HT.

The coordination number (*CN*), bond length (*R*), and Debye–Waller factor (Δσ) of the Ru–O and Ru–Mg bonds were estimated by a curve-fitting analysis (Table 1). The length of the shortest Ru–O bond (1.82 Å) was comparable to that of a Ru^{IV}–OH moiety (1.79 Å) observed in $[Ru^{IV}(OH)_2(TDCPP)]$.[13] The Ru–O distance of 2.04 Å is close to the bond length between a Ru cation and an oxygen atom in an aqua ligand.[14] Conclusively, a monomeric Ru^{IV} species with one hydroxy and two aqua ligands was grafted onto a triad of oxygen atoms on the HT surface, as illustrated in Figure 2.[15]

Table 1. Curve-fitting results of Ru K-edge EXAFS of the Ru/HT.

Shell	*CN*[a]	*R*[b] [Å]	Δ*σ*[c] [Å^2]
Ru–O(1)	3.0	1.97	0.0022
Ru–O(2)	2.3	2.04	0.0006
Ru–O(3)	0.9	1.82	0.0064
Ru–Mg	1.5	3.18	0.0060

[a] Coordination number. [b] Interatomic distance. [c] Δ*σ* is the difference between the Debye–Waller factor of the samples and that of the reference sample.

Pd/HTs: The hydrotalcite-supported palladium nanoparticles (Pd_{nano}/HT) can be synthesized by simple surface impregnation followed by reduction.[16] A mixture of the solid

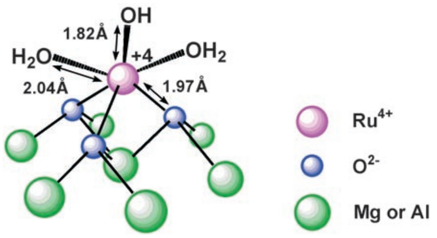


Figure 2. A proposed surface structure around Ru^{IV} of the Ru/HT.

HT and an aqueous solution of $K_2[PdCl_4]$ was stirred at room temperature under air to form a pale yellow powder (Pd^{II}/HT), which was then successively reduced in the presence of 1 atm H_2 at 100 °C to afford the Pd_{nano}/HT as a black powder (Pd content: 0.1 mmol g^{-1}). The retention of the HT interlayer distance (3.0 Å) in the Pd^{II}/HT and Pd_{nano}/HT were confirmed by XRD. In UV/Vis/DRS measurement, the peak corresponding to Pd^{II} species at 280 nm disappeared after reduction of the Pd^{II}/HT. The shapes of Pd K-edge XANES spectra of the Pd^{II}/HT and Pd_{nano}/HT were similar to those of $Pd(OAc)_2$ and Pd foil, respectively (Figure 3).

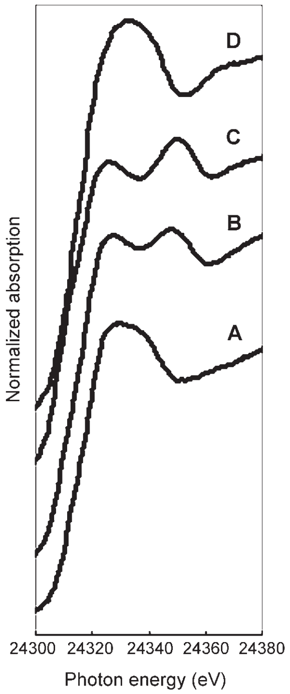


Figure 3. Pd K-edge XANES spectra of A) Pd^{II}/HT, B) Pd_{nano}/HT, C) Pd foil, and D) $[Pd(OAc)_2]$.

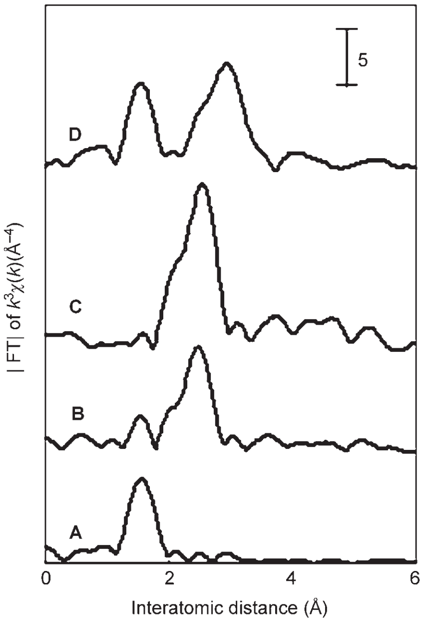


Figure 4. Fourier transforms of k^3-weighted Pd K-edge EXAFS experimental data for A) Pd^{II}/HT, B) Pd_{nano}/HT, C) Pd foil, and D) Pd oxide. Phase shift was not corrected.

The FTs of k^3-weighted EXAFS data are depicted in Figure 4. Peaks due to Pd–Pd bonds in the second coordination sphere, detectable in those of Pd foil at around 2.5 Å, were observed for the Pd_{nano}/HT but not for the Pd^{II}/HT. These results suggest that the Pd^{II} species on the HT surface were reduced to Pd^0. In EDX analysis, neither chlorine nor potassium was detected in the Pd^{II}/HT or Pd_{nano}/HT. The inverse FT of the peaks at around 1–2 Å for the Pd^{II}/HT was well fitted with two types of oxygen atoms at Pd–O distances of 1.98 and 2.10 Å (Table 2). The slightly longer Pd–O bond (2.10 Å) was similar to the Pd–OH_2 bond (2.095 Å) in $[Pd^{II}(NO_3)_2(H_2O)_2]$.[17] On the basis of these facts, the most reasonable surface structure for the Pd^{II}/HT is shown in Figure 5. The inverse FT of the single peak at 2.5 Å due to the Pd–Pd bond in the Pd_{nano}/HT revealed a metallic form, with an *R* of 2.75 Å and a *CN* of 8.75, respectively, as listed in Table 2. The smaller *CN* value relative to that of Pd foil

Table 2. Curve-fitting analysis for the Pd/HT catalysts.[a]

Sample	Shell	*CN* [b]	*R*[c] [Å]	$\Delta\sigma$[d] [$Å^2$]
Pd^{II}/HT	Pd–O(1)	2.03	1.98	0.005
	Pd–O(2)	2.00	2.10	0.002
Pd_{nano}/HT	Pd–Pd	8.75	2.75	0.072

[a] Inverse Fourier transformations were performed for the regions of 1.2–2.0 Å in Pd^{II}/HT and 2.0-2.9 Å in Pd_{nano}/HT. [b] Coordination number. [c] Interatomic distance. [d] Difference between Debye–Waller factor of Pd/HTs.

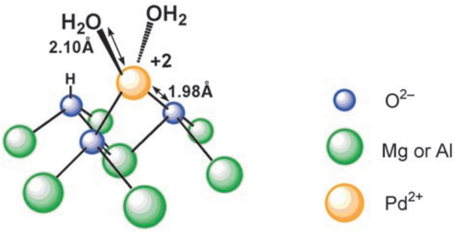
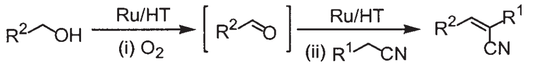


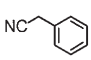
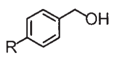
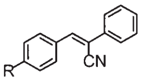
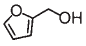
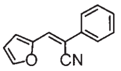
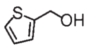
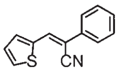
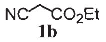
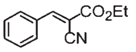
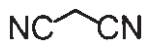
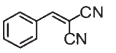
Figure 5. A proposed structure around Pd^{II} species of the Pd^{II}/HT.

(12) demonstrated the formation of Pd nanoclusters. From transmission electron microscopy (TEM) analysis, highly dispersed Pd nanoclusters with a mean diameter of about 70 Å (standard deviation 14 Å) were observed on the Pd_{nano}/HT surface.

Synthesis of α,β-unsaturated nitriles from nitriles and primary alcohols under O_2 atmosphere: We have previously reported hydrotalcite-supported ruthenium-catalyzed oxidation of alcohols to carbonyl compounds using molecular oxygen as a sole oxidant.[7a–c,18] Furthermore, it is well known that the surface base sites of the HT promote the aldol reaction of nitriles with aldehydes.[5,6e–f] These results encouraged us to develop a one-pot synthesis of α,β-unsaturated nitriles from alcohols and nitriles, using the Ru/HT catalyst, by consecutive Ru-catalyzed aerobic oxidation/base-catalyzed aldol condensation (Table 3). The oxidation reaction of benzyl alcohol proceeded under molecular oxygen at atmospheric pressure to afford benzaldehyde in quantitative yield. Subsequent addition of phenylacetonitrile **1a** gave (*Z*)-2-phenylcinnamonitrile in 98% yield (Table 3, entry 1). Several heteroaromatic alcohols also reacted smoothly (Table 3, entries 4 and 5). This consecutive method was applicable to active nitriles such as ethyl cyanoacetate **1b** (Table 3, entry 6) and malononitrile (Table 3, entry 7).

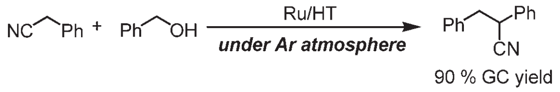
Table 3. One-pot synthesis of α,β-unsaturated nitriles using the Ru/HT under O_2 atmosphere.[a]



Entry	Nitrile	Alcohol	Product	Isolated yield [%][b]
				
1	**1a**	R = H	R = H	98
2	**1a**	R = Cl	R = Cl	98
3	**1a**	R = OMe	R = OMe	95
4[c]	**1a**			93
5[d]	**1a**			93
6[e]	 **1b**	R = H		82
7[e]		R = H		80

[a] Reaction conditions; i) alcohol (1 mmol), toluene (3 mL), Ru/HT (0.3 g; Ru: 0.015 mmol), 80 °C, 2 h, O_2 (1 atm). ii) Nitrile (1.1 mmol), 120 °C, 2 h, Ar. [b] Based on alcohol used. [c] i) 6 h. [d] i) 3 h. [e] ii) 80 °C, 1 h.

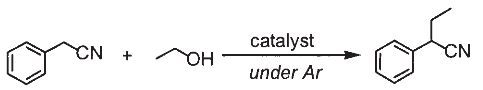
α-Alkylation of nitriles with primary alcohols using the Ru/HT catalyst: Interestingly, the reaction of **1a** with benzyl alcohol using the Ru/HT afforded an α-benzylated nitrile, 2,3-diphenylpropionitrile, as a sole product under *Ar atmosphere* [Eq. (1)]. This result led us to explore the Ru-catalyzed α-alkylation of nitriles using alcohols as alkylating reagents.[19]



(1)

A model α-alkylation of **1a** with a large excess of ethanol (**2a**) was studied in the presence of various supported Ru catalysts (Table 4). Only the Ru/HT showed high catalytic activity, giving α-ethylated phenylacetonitrile in 98% yield (Table 4, entry 1). Other solid base-supported Ru catalysts, such as Ru/Al_2O_3, Ru/MgO, $Ru/Al(OH)_3$, and $Ru/Mg(OH)_2$, were less active under the present reaction conditions (Table 4, entries 2–5). The α-alkylation did not occur at all in the presence of only parent HT or $RuCl_3 \cdot nH_2O$ (Table 4, entries 7, 8).

Table 4. α-Ethylation of **1a** using various catalysts.[a]



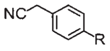
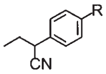
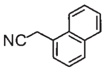
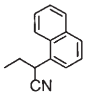
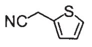
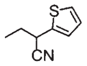
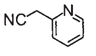
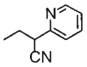
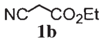
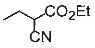
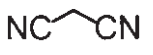
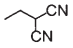
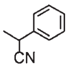
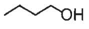
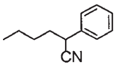
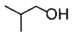
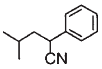
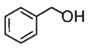
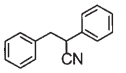
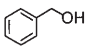
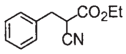
1a **2a** **3a**

Entry	Catalyst	Yield of **3a** [%][b]
1	Ru/HT	98
2	Ru/Al_2O_3	14
3	Ru/MgO	2
4	$Ru/Al(OH)_3$	5
5	$Ru/Mg(OH)_2$	2
6	Pd_{nano}/HT	trace
7[c]	HT	N.R.
8[d]	$RuCl_3 \cdot nH_2O$	N.R.

[a] Reaction conditions; **1a** (1 mmol), **2a** (2 mL), catalyst (0.15 g, 0.075 mmol of metal), 20 h, 180 °C, Ar. [b] Determined by GC. Based on **1a** used. [c] 0.15 g of HT was used. [d] 0.0075 mmol of Ru was used.

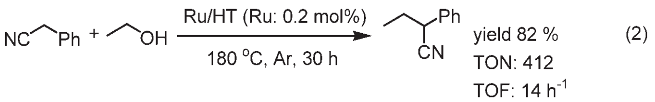
Synthetic scope: On the basis of the highest catalytic activity of the Ru/HT, we examined α-alkylations involving a variety of nitriles with aliphatic and aromatic alcohols using this catalyst, as shown in Table 5. In many reactions of aryl acetonitriles with ethanol (Table 5, entries 1–7), the corresponding ethylated products were formed in excellent yields, except for the case of 2-pyridinylacetonitrile (Table 5, entry 7). Electronic variation in the *p*-substituted phenylacetonitrile did not strongly affect the yields of the products (Table 5, entries 1–4). A sterically hindered 1-naphthylacetonitrile (Table 5, entry 5) and a nitrile containing a thiophene ring (Table 5, entry 6) were also readily reacted. To extend the scope of the alcohols employed in the Ru/HT-catalyzed α-alkylation of nitriles, methanol, *n*-butanol, isobutanol, and benzyl alcohol were investigated as potential primary alcohols. All of these substrates underwent the desired alkylation to afford important organic agents (Table 5, entries 10–13): for example, 2-phenylhexanenitrile, a precursor of the systemic fungicide Systhane,[1c] was obtained in 86% isolated yield from *n*-butanol (Table 5, entry 11). It is noteworthy that this catalyst system was applicable to a 20 mmol-scale

Table 5. The Ru/HT-catalyzed α-alkylation of nitriles with primary alcohols.[a]

Entry	Nitrile	Alcohol	Product	Isolated yield [%][b]
				
1	R = H **1a**	EtOH **2a**	R = H	94
2	R = Me	**2a**	R = Me	99
3[c]	R = OMe	**2a**	R = OMe	92
4	R = Cl	**2a**	R = Cl	77
5		**2a**		89
6[c]		**2a**		86[d]
7		**2a**		37
8	 **1b**	**2a**		trace
9		**2a**		trace
10	**1a**	MeOH		65[d]
11	**1a**			86
12[c]	**1a**			85[d]
13[d]	**1a**			77
14[e,f]	**1b**			trace[g]

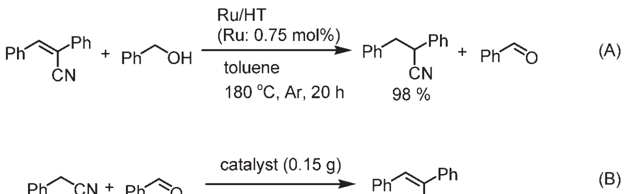
[a] Reaction conditions; nitrile (1 mmol), alcohol (2 mL), Ru/HT (0.15 g, Ru: 0.0075 mmol), 180 °C, 20 h, Ar. [b] Based on nitrile used. [c] Ru/HT (0.3 g, Ru: 0.015 mmol) was used. [d] Determined by GC using internal standard. [e] 2 mL of toluene and 1.5 mmol of alcohol were used. [f] At 100 °C. [g] Benzyl cyanoacetate was formed in a 37 % yield.

reaction of phenylacetonitrile with ethanol to afford 2-phenylbutyronitrile in 82 % yield with a TOF of 14 h^{-1} and a TON of 412 [Eq. (2)]. The above values are considerably higher than those previously reported for reactions using homogeneous Ru catalysts combined with a stoichiometric amount of Na_2CO_3 (TOF 0.77 h^{-1}; TON 18).[3]

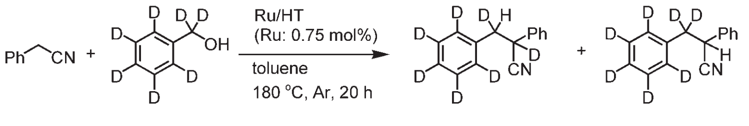


Unfortunately, the Ru/HT-catalyzed alkylation of nitriles with low pK_a values (11∼13), such as malononitrile (Table 5, entry 9) and **1b** (Table 5, entries 8 and 14), did not occur. In a separate experiment, the reaction of phenylacetonitrile with ethanol gave no product in the presence of malononitrile, which suggests that the strong coordination of highly acidic nitriles to the Ru species depressed the desired α-alkylation. In the case of ethyl cyanoacetate with benzyl alcohol, an undesirable base-catalyzed transesterification product, benzyl cyanoacetate, was formed as a major product (Table 5, entry 14). These results show that alcohols are not favorable as alkylating reagents for the reaction of cyanoesters.

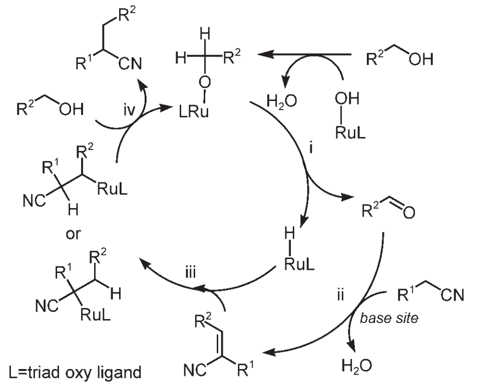
Mechanistic investigations: The reaction of (*Z*)-2-phenylcinnamonitrile with benzyl alcohol using the Ru/HT under an Ar atmosphere afforded a 98 % yield of 2,3-diphenylpropionitrile along with benzaldehyde (Scheme 2A). On the other hand, aldol condensation of phenylacetonitrile with benzaldehyde was promoted by the parent HT catalyst as well as the Ru/HT, producing (*Z*)-2-phenylcinnamonitrile (Scheme 2B). Additionally, in the α-alkylation of phenylacetonitrile with benzyl-[D_7]-alcohol ($C_6D_5CD_2OH$), 2-[D]-2-phenyl-3-[D]-3-[D_5]-phenylpropionitrile and 2-phenyl-3,3-[D_2]-3-[D_5]-phenylpropionitrile were obtained (Scheme 3). From these results, a plausible reaction pathway through three consecutive reactions was deduced and is illustrated as Scheme 4: i) oxidative dehydro-



Scheme 2.



Scheme 3.



Scheme 4.

genation of alcohols to aldehydes along with the formation of Ru–H species; ii) aldol condensation of nitriles with aldehydes, giving α,β-unsaturated nitriles, at the base sites on the HT surface; iii) hydrogenation of α,β-unsaturated nitriles by the Ru–H species;[20,21] and iv) formation of α-alkylated nitriles.[22] The IR spectrum of the benzyl alcohol-treated Ru/HT catalyst showed a signal at 2120 cm^{-1}, which is assigned to ν(Ru–H) (Figure 6).[23] In the one-pot synthesis of an α,β-unsaturated nitrile under molecular oxygen (Table 3), this Ru–H species spontaneously reacts with O_2 to give the α,β-unsaturated nitrile exclusively without the corresponding saturated nitrile.

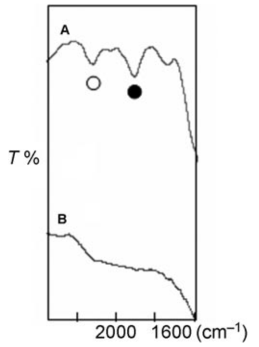
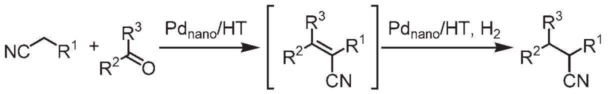


Figure 6. IR spectra of the samples A) after treatment of the Ru/HT with benzyl alcohol, B) fresh Ru/HT; ○:Ru-H species, ●: benzyl alcohol.

The above-described combination of oxidative dehydrogenation, aldol condensation, and hydrogenation in a single reactor has the following advantages over multistep procedures. First, the hydrogen-transfer reaction using the Ru/HT under Ar gave no over-oxidation products, while oxidation of primary alcohols using molecular oxygen or hydrogen peroxide often produces carboxylic acids as by-products.[24] Next, the cross-aldol reaction of relatively unreactive aryl acetonitriles with aldehydes that have α-protons of carbonyl groups often affords undesirable by-products: in a separate experiment, an aldol reaction of phenylacetonitrile with *n*-butyraldehyde formed the corresponding self-condensed product of the aldehyde, whereas no by-product was obtained in the α-alkylation of phenylacetonitrile with *n*-butanol (Table 5, entry 11). Since the concentrations of aldehydes were kept low, formation of the self-aldol products was effectively depressed. Finally, the present one-pot process achieved the hydrogen transfer-reaction without any waste, because the aldehydes were consumed as alkylating reagents. The advantages of sequential reactions in a single reactor include operational simplicity as well as the achievement of novel synthetic routes.[8]

α-Alkylation of nitriles with carbonyl compounds using the Pd_{nano}/HT catalyst: As described above, the Ru/HT catalyst could efficiently promote α-alkylation of aryl acetonitriles with primary alcohols, but reaction of nitriles with low pK_a values, such as malononitrile, cyanoesters, and 2-pyridinylacetonitrile barely occurred owing to strong coordination to the Ru species. Because of the synthetic utility of α-alkylated products from such active nitriles, we aimed to develop new synthetic routes to these α-alkylated nitriles using the Pd_{nano}/HT. The planned reaction sequence was an aldol reaction of nitriles with carbonyl compounds at base sites on the HT surface, followed by hydrogenation of the α,β-unsaturated nitriles with Pd species [Eq. (3)].[25,26]

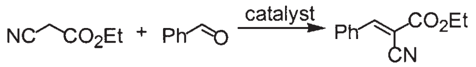


(3)

In the initial study, the aldol reaction of ethyl cyanoacetate **1b** with benzaldehyde **4** was examined using various solid catalysts (Table 6). The highest yield of an α,β-unsaturated nitrile, (*E*)-ethyl-2-cyano-3-phenylacrylate **5**, was obtained using the HT (Table 6, entry 1). The use of aluminum oxide resulted in a moderate yield (Table 6, entry 3) and other solid catalysts were inactive (Table 6, entries 4–7). The Pd_{nano}/HT was also found to be an efficient catalyst for the aldol reaction (Table 6, entry 2).

Next, the catalytic activity of the Pd_{nano}/HT for hydrogenation of **5** was compared with those of various supported palladium catalysts, as shown in Table 7. The Pd_{nano}/HT was an effective catalyst, affording an excellent yield of **3b**

Table 6. Aldol reaction of **1b** with **4** using various solid base catalysts.[a]



1b **4** **5**

Entry	Catalyst	Yield of **5** [%][b]
1	HT	99
2	Pd_{nano}/HT	99
3	Al_2O_3[c]	52
4	MgO	3
5	SiO_2[d]	N.R.
6	$Al(OH)_3$	2
7	$Mg(OH)_2$	2

[a] Reaction conditions; **1b** (1.0 mmol), **4** (1.0 mmol), catalyst (0.025 g), toluene (3 mL), 80°C, 1 h, Ar. [b] Determined by GC. [c] JRC-ALO-4. [d] JRC-SiO-5.

Table 7. Hydrogenation of α,β-unsaturated nitrile **5** with various catalysts.[a]

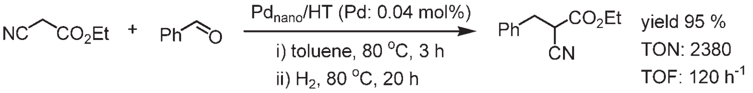
5 **3b**

Entry	Catalyst	Yield of **3b** [%][b]
1	Pd_{nano}/HT	98
2[c]	Pd^{II}/HT	76
3	Pd/Al_2O_3 (0.5 wt %)[d]	99
4	Pd/carbon (0.5 wt %)[d]	94
5	Pd/carbon (5.0 wt %)[e]	49
6	Pd/MgO	41
7	Pd/SiO (0.5 wt %)[d]	24
8	Ru/HT	trace
9	HT	trace

[a] Reaction conditions; **5** (1 mmol), catalyst (1 mol%), H_2 (1 atm), toluene (3 mL), 60 °C, 1 h, H_2 (1 atm). [b] Determined by GC. [c] 80 °C. [d] Purchased from N.E. Chemcat. [e] Purchased from Wako Pure Chemicals.

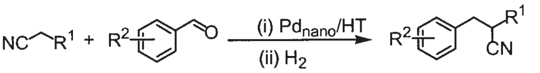
(Table 7, entry 1), while the Pd^{II}/HT afforded a moderate yield of the product (Table 7, entry 2). Several commercially available supported Pd catalysts, such as Pd/Al_2O_3 and Pd/carbon (0.5 wt %), were also effective in promoting the hydrogenation reaction (Table 7, entries 3 and 4). Pd/MgO and Pd/SiO_2 showed low activities (Table 7, entries 6 and 7), and the Ru/HT, in particular, was not effective at all (Table 7, entry 8).

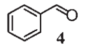
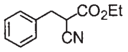
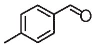
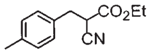
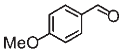
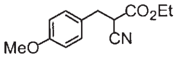
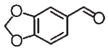
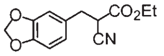
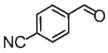
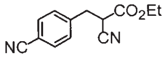
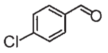
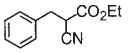
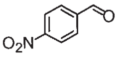
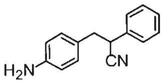
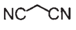
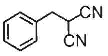
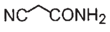
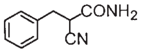
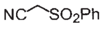
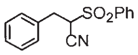
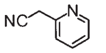
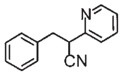
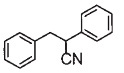
Synthetic scope: The generality of the Pd_{nano}/HT-catalyzed α-alkylation of various nitriles with benzaldehydes is illustrated in Table 8. Both electron-rich and electron-deficient benzaldehydes serve as good substrates, affording the corresponding α-benzylated ethyl cyanoacetates (Table 8, entries 1–5). Chloro and nitro groups were reduced under present reaction conditions (Table 8, entries 6 and 7); for example, the reaction of phenylacetonitrile with 4-nitrobenzaldehyde gave 3-(4-aminophenyl)-2-phenylpropionitrile in high yield (Table 8, entry 7). A variety of nitriles could be used as donors, leaving intact ester, cyano, amide, and sulfoxide groups, and a pyridine ring (Table 8, entries 1 and 7–11). Notably, some unreactive nitriles in the Ru/HT catalyst system were successfully transformed to highly useful intermediates for pharmaceutical synthesis. For example, 3-phenyl-2-(2-pyridyl)propionitrile, a precursor of antiarrhythmic agents, was obtained from 2-pyridinylacetonitrile with **4** in quantitative yield (Table 8, entry 11), while the traditional method using benzyl chloride instead of **4** in the presence of $NaNH_2$ resulted in a 52 % yield.[27] This catalyst system was applicable to 15 mmol-scale synthesis; the reaction of ethyl cyanoacetate with benzaldehyde proceeded smoothly, and the crude product was purified by simple distillation to afford a 95 % isolated yield of the product with a TON of 2380 [Eq. (4)]. As described above, the HT is a solid strong base catalyst that can promote aldol reactions of various nitriles with a wide range of pK_a values (pK_a = 11–22);[28] however, simple alkane nitriles with high pK_a values (~31)[28] did not react.



(4)

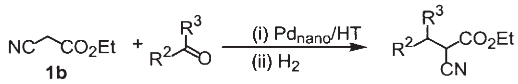
Table 8. α-Alkylation of various nitriles with benzaldehydes using the Pd_{nano}/HT.[a]

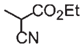
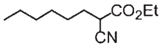
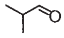
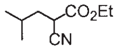
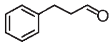
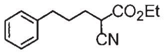
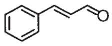
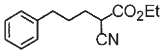
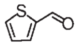
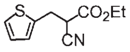
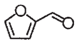
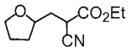
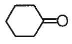
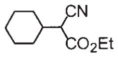
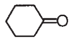
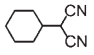
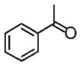
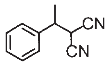


Entry	Nitrile	Aldehyde	Time of (ii) [h]	Product	Isolated yield [%]
1	**1b**	 **4**	1		94
2	**1b**		3		95
3	**1b**		2		90
4	**1b**		3		99
5	**1b**		9		83
6[b]	**1b**		4		87[c]
7[d]	**1a**		23		84[c]
8		**4**	5		82[c]
9[b,e]		**4**	4		64
10		**4**	2		98
11		**4**	2.5		99
12[d]	**1a**	**4**	4		83

[a] Reaction conditions; (i) nitrile (1 mmol), carbonyl compounds (1 mmol), Pd_{nano}/HT (0.1 g; Pd: 0.01 mml), toluene (3 mL), 2 h, 80 °C, Ar. (ii) 60 °C, H_2 (1 atm). [b] DMF (3 mL) was used as solvent. [c] Determined by GC using an internal standard. [d] At 120 °C for aldol reaction. [e] 18 h for aldol reaction.

Table 9. α-Alkylation of **1b** with various carbonyl compounds using the Pd_{nano}/HT.[a]



Entry	Carbonyl compound	Time of (ii) [h]	Product	Isolated yield [%]
1[b,c]	CH_2O	1		91[d]
2		1		81
3		1		92
4		1		99[d]
5		2		98[d]
6		24		19[d,e]
7		3		88
8[f]		1		66
9[g]		6.5		92
10[g]		–		trace[h]

[a] Reaction conditions; i) nitrile (1 mmol), carbonyl compounds (1 mmol), Pd_{nano}/HT (0.1 g; Pd: 0.01 mml), toluene (3 mL), 2 h, 80 °C, Ar. ii) 60 °C, H_2 (1 atm). [b] DMF (3 mL) was used as solvent. [c] 37 % aqueous HCHO was used, 3 h for aldol reaction. [d] Determined by GC using an internal standard. [e] 80 % of the unsaturated nitrile was obtained. [f] At 100 °C for aldol reaction. [g] Malononitrile (1 mmol) was used instead of ethyl cyanoacetate. [h] Aldol reaction scarcely occurred.

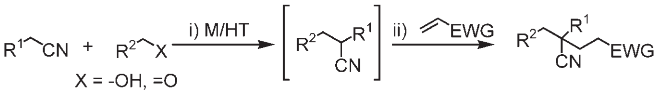
The α-alkylation of **1b** with **4** was examined using various solvents. Toluene and dimethylformamide (DMF) were found to be effective solvents for both the aldol reaction and hydrogenation, affording the corresponding alkylated product. Although a high yield of the α,β-unsaturated nitrile was obtained using ethanol as a solvent, the reaction rate for hydrogenation was slightly low. A nonpolar solvent, *n*-heptane, was found to be ineffective for the aldol reaction.

In addition to the benzaldehyde derivatives, α-alkylations of **1b** with linear and branched aliphatic aldehydes occurred smoothly (Table 9, entries 1–4). Formaldehyde is an important electrophilic reagent in the C1 chemistry. α-Alkylation effectively proceeded even in the presence of water: a 91 % yield of 2-cyanopropionic acid ethyl ester was obtained from ethyl cyanoacetate with a commercial aqueous 37 % solution of formaldehyde, a convenient formaldehyde source (Table 9, entry 1).[29] The aldol reaction with 2-thiophenaldehyde took place readily, but hydrogenation of the unsaturated nitrile occurred to only slight extent under the present reaction conditions owing to strong coordination of the sulfur atom to the Pd species (Table 9, entry 6). To extend the scope of carbonyl substrates, the use of ketones was also examined: ethyl cyanoacetate and malononitrile reacted with cyclohexanone, affording good to excellent yields of the corresponding products (Table 9, entries 8 and 9), but the aldol reaction with acetophenone barely occurred (Table 9, entry 10).

After the reaction of **1b** with **4**, the used Pd_{nano}/HT catalyst was easily recovered from the reaction mixture by simple filtration, and ICP analysis of the filtrate confirmed that the Pd content was below the detection limit (0.03 ppm). The recovered Pd_{nano}/HT catalyst was found to be recyclable with retention of its high catalytic activity and selectivity; the first, second, and third runs afforded 95, 93, and 93 % yield of the product, respectively.

The IR spectra of both the HT and Pd_{nano}/HT, upon treatment with **5**, revealed a shift of the ν(CN) band toward 2147 cm^{-1} in comparison with the free cyano group at 2224 cm^{-1}. This suggests that the large positive electric potential of the HT surface induces a high concentration of nitrile compounds close to the surface,[30] enhancing hydrogenation and aldol reaction rates. It seems that the HT would be an ideal catalyst support for efficient reactions of various polarized organic compounds.

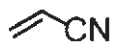
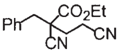
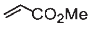
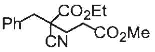
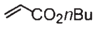
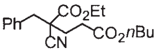
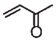
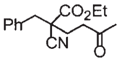
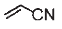
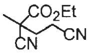
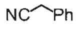
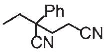
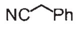
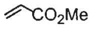
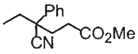
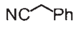
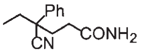
One-pot synthesis of α,α-dialkylated nitriles: As the Ru/HT and Pd_{nano}/HT possess catalytically active metal and base sites, the applicability of hydrotalcite-supported metals (M/HTs) as multifunctional catalysts is highlighted by their ability to catalyze consecutive transformations of α-alkylated nitriles in a single reactor. Here, we attempted a one-pot synthesis of glutaronitrile derivatives by Michael reaction of α-alkylated nitriles with electron-deficient olefins on the base sites of the HT [Eq. (5); ii)] after the M/HT-catalyzed α-alkylation [Eq. (5); i)].



(5)

Table 10 shows the results of consecutive α-alkylation/Michael reaction for various substrates using Pd_{nano}/HT and Ru/HT. For example, after the α-alkylation of **1b** with **4** using the Pd_{nano}/HT catalyst, acrylonitrile was added to the same flask and further reaction under an Ar atmosphere afforded 2-benzyl-2-carboethyoxyglutaronitrile in 94 % overall yield (Table 10, entry 1). The Pd_{nano}/HT catalyst also promoted successive reaction using methyl acrylate, *n*-butyl

Table 10. One-pot α,α-dialkylation of nitriles using the M/HTs.[a]

Entry	Nitrile	Aldehyde or Alcohol	Olefin	Method	Product	Isolated yield [%][b]
1	**1b**	**4**		**A**		94
2	**1b**	**4**		**A**		98
3[c]	**1b**	**4**		**A**		79
4[d]	**1b**	**4**		**A**		79
5[e]	**1b**	HCHO		**A**		63
6[f]		EtOH		**B**		93[g]
7		EtOH		**B**		80
8		EtOH		**B**		84[g]

[a] Reaction conditions; Method A: i) nitrile (1 mmol), carbonyl compounds (1 mmol), Pd_{nano}/HT (0.1 g; Pd: 0.01 mml), toluene (3 mL), 2 h, 80 °C, Ar. After the completion of aldol reaction, the reaction mixture was further treated at 60 °C for 1 h under H_2 (1 atm). ii) Olefin (1.5 mmol), 5 h, 70 °C, Ar. Method B: i) nitrile (1 mmol), alcohol (2 mL), Ru/HT (0.15 g: 0.0075 mmol), 180 °C, 20 h, Ar. ii) Olefin (3 mmol), DMSO (2 mL), 150 °C, 1 h, Ar. [b] Overall yield based on nitrile. [c] At 110 °C, 12 h for Michael reaction. [d] A solution of methyl vinyl ketone (1.5 mmol) in toluene (2 mL) was slowly added over 6 h and further reacted for 4 h. [e] DMF (3 mL) was used as solvent. [f] DMF (3 mL) was used as solvent for Michael reaction. [g] Determined by GC by an internal standard.

acrylate, and methyl vinyl ketone (Table 10, entries 2–4). The Ru/HT-catalyzed α-ethylation of phenylacetonitrile proceeded smoothly, followed by Michael reaction with acrylonitrile to give 2-ethyl-2-phenylglutaronitrile in 93 % overall yield (Table 10, entry 6), while the traditional method using iodoethane and Triton B afforded only a 39 % yield of the above product.[1b] Methyl acrylate and acrylamide were also found to be good acceptors (Table 10, entries 7 and 8). It can be said that α,α-dialkylation of nitriles using the M/HT catalysts is a powerful protocol for one-pot synthesis of highly substituted glutaronitrile derivatives. Unfortunately, α,β-disubstituted olefins, such as crotononitrile and 2-cyclohexen-1-one, were less active under these reaction conditions.

Conclusion

Hydrotalcite-supported ruthenium and palladium compounds have been developed and explored as highly active multifunctional catalysts for novel environmentally friendly α-alkylation of various nitriles with alcohols and carbonyl compounds. These catalysts are reusable and applicable to one-pot α,α-dialkylation for synthesis of glutaronitrile derivatives. One-pot syntheses using heterogeneous catalysts based on the HT, which posses both active metal species and strong base sites will contribute strongly to development of "green" chemical processes.

Experimental Section

General: ^{1}H and ^{13}C NMR spectra were obtained on JEOL GSX-270 or JNM-AL400 spectrometers at 270 or 400 MHz in $CDCl_3$ with TMS as an internal standard. Infrared spectra were obtained with a JASCO FTIR-410. Analytical GLC and GLC-mass were performed using a Shimadzu GC-8 A PF with flame ionization detector equipped with KOCL 3000T, Silicon SE-30, and OV-17 columns, and a Shimadzu GCMS QP5000 equipped with ULBON HR-1 columns. A JEOL JMS-700 mass spectrometer was used for HRMS analyses. Powder X-ray diffraction patterns were recorded using Philips X'Pert-MPD with $Cu_{K\alpha}$ radiation. XPS were measured on Shimadzu ESCA-KM using $Mg_{K\alpha}$ radiation. Inductively coupled plasma measurement was performed using a Nippon Jarrell-Ash ICAP-575 Mark II. Ru and Pd K-edge X-ray absorption spectra were recorded at the beam line 01B1 station attached to the Si(311) monochromator at SPring-8 for JASRI, Harima, Japan (2004 A0489-NXa-np and 2005 A0296-NXa-np). Fluorescence yield was collected at room temperature. Data analyses were performed with the FACOM M-780 computer system of the Data Processing Center of Kyoto University and the "REX2000 ver. 2.3" program (RIGAKU). The detailed procedures for data analysis are described elsewhere.[31] The inverse FTs and curve-fitting results of the Ru/HT and Pd/HTs are shown as Figures 7 and 8, respectively.

A hydrotalcite (HT), $Mg_6Al_2(OH)_{16}CO_3$, was obtained from TOMITA Pharmaceutical Co. Ltd., Japan. MgO, $Mg(OH)_2$, and $Al(OH)_3$ were purchased from Wako Pure Chemicals. γ-Al_2O_3 (JRC-ALO-4) was also used. $RuCl_3{\cdot}nH_2O$, $PdCl_2$, and supported Pd catalysts (Pd/carbon, Pd/Al_2O_3, Pd/SiO_2, Pd/TiO_2) were obtained from N. E. Chemcat and Wako Pure Chemical. Nitriles, alcohols, carbonyl compounds, and solvents were purchased from Wako, Tokyo Kasei, and Aldrich, and purified by the stand-

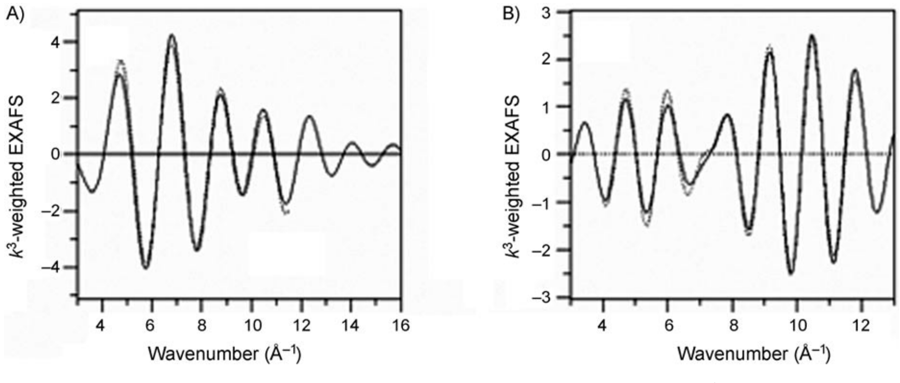


Figure 7. The inverse FTs of the Ru/HT performed in the 0.9–2.0 (A) and 1.9–3.0 Å (B) ranges. The dotted lines in (A) and (B) show the results of curve-fitting analysis using five Ru−O (A), and one Ru−O, and Ru−Mg (B) shell parameters.

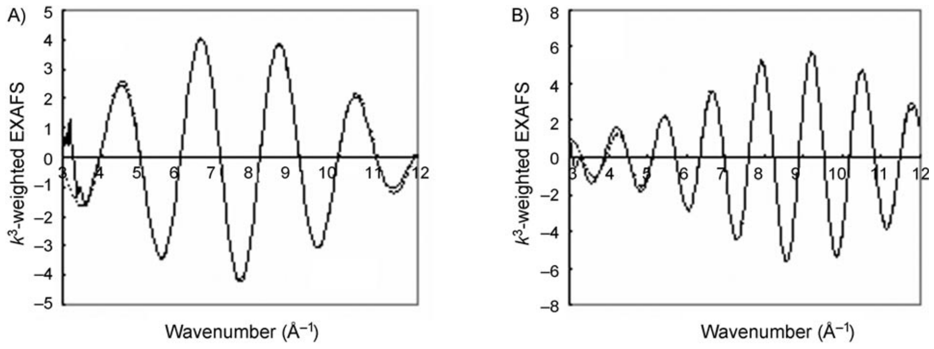


Figure 8. The inverse FTs of A) Pd^{II}/HT and B) Pd_{nano}/HT performed in the 1.2–2.0 Å (A) and 2.0–2.9 Å (B) ranges. The dotted lines show the results of curve-fitting analysis using A) four Pd−O, and B) Pd−Pd shell parameters.

ard procedures prior to experiments. The identities of products were confirmed by comparison with reported mass and NMR data. All new products were characterized by ^{1}H and ^{13}C NMR spectra, infrared spectra, mass spectra, and HRMS analysis.

Preparation of the Ru-grafted hydrotalcite: The HT, $Mg_6Al_2(OH)_{16}CO_3$ (1.0 g), was added to an aqueous solution of $RuCl_3{\cdot}n\,H_2O$ (5.0×10^{-4} M, 100 mL). The resulting heterogeneous mixture was stirred at 25 °C for 1 h under air. The solid product was separated by centrifugation, washed thoroughly with deionized water, and dried in vacuo at room temperature, affording Ru/HT as a gray powder (Ru content: 0.5 wt %). X-ray diffraction studies showed the retention of a layered structure with a basal spacing of 7.7 Å. Various ruthenium-supported solid base catalysts, such as Ru/MgO, Ru/Al_2O_3, Ru/$Mg(OH)_2$, and Ru/$Al(OH)_3$ were synthesized by the same procedure.

Preparation of the hydrotalcite-supported Pd nanoparticles: The HT, $Mg_6Al_2(OH)_{16}CO_3$, (1.0 g) was added to an aqueous solution of $PdCl_2$ (100 mL, 0.1 mmol) containing KCl (0.1 g). The heterogeneous mixture was stirred at 25 °C for 1 h under air to afford a pale yellow powder and was then successively reduced in the presence of H_2 (1 atm) at 100 °C for 8 h. The solid product was separated by centrifugation, washed thoroughly with deionized water, and dried at 110 °C for 12 h, affording the Pd_{nano}/HT as a black powder (Pd content: 1.0 wt %). Pd/MgO was prepared by the same procedure.

A typical example for the Ru/HT-catalyzed α-alkylation of nitriles with alcohols: The Ru/HT (0.15 g, Ru: 0.0075 mmol), ethanol (2 mL), and phenylacetonitrile (1.0 mmol) were placed in a pyrex pressure tube (15 mL). The resulting mixture was vigorously stirred at 180 °C under Ar. After 20 h, the catalyst was separated by filtration and the GC analysis of the filtrate showed a 98 % yield of 2-phenylbutyronitrile. The filtrate was evaporated and the crude product was purified by column chromatography using silica (hexane/ethyl acetate 9:1) to afford a pure product (0.136 g, 94 % isolated yield).

Procedure for the large-scale α-alkylation of phenylacetonitrile with ethanol: The Ru/HT (0.8 g, Ru: 0.04 mmol), ethanol (5 mL), and phenylacetonitrile (20 mmol) were placed in a pyrex pressure tube (15 mL). The reaction mixture was vigorously stirred at 180 °C under Ar for 30 h. The catalyst was then separated by filtration and the GC analysis of the filtrate showed an 82 % yield of 2-phenylbutyronitrile.

Hydrogen-transfer reaction of benzyl alcohol with 2-phenylcinnamonitrile: The Ru/HT (0.15 g, Ru: 0.0075 mmol), toluene (2 mL), benzyl alcohol (1.5 mmol), and (*Z*)-2-phenylcinnamonitrile (1.0 mmol) were placed in a pyrex pressure tube (15 mL). The reaction mixture was vigorously stirred at 180 °C under Ar. After 20 h, the catalyst was separated by filtration and the GC analysis of the filtrate showed a 98 % yield of 2,3-diphenylpropionitrile together with benzaldehyde.

Aldol condensation of phenylacetonitrile with benzaldehyde: The parent HT (0.15 g), toluene (2 mL), benzaldehyde (1.5 mmol), and phenylacetonitrile (1.0 mmol) were placed in a pyrex pressure tube (15 mL). The reaction mixture was vigorously stirred at 180 °C under Ar. After 7 h, the catalyst was separated by filtration and the GC analysis of the filtrate showed a 98 % yield of (*Z*)-2-phenylcinnamonitrile. The Ru/HT also promotes this condensation to afford (*Z*)-2-phenylcinnamonitrile in 96 % yield.

α-Alkylation using deuterated benzyl alcohol: The Ru/HT (0.15 g, Ru: 0.15 mmol), toluene (2 mL), benzyl-[D_7]-alcohol (1.5 mmol), and phenylacetonitrile (1.0 mmol) were placed in a pyrex pressure tube (15 mL). The reaction mixture was vigorously stirred at 180 °C under Ar. After 20 h, the catalyst was separated by filtration, and the ^{1}H NMR analysis of the filtrate showed the formation of deuterated α-alkylated products, 2-[D]-2-phenyl-3-[D]-3-[D_5]-phenylpropionitrile and 2-phenyl-3-[D_2]-3-[D_5]-phenylpropionitrile, in a ratio of 3:4.

A typical example of the Pd_{nano}/HT-catalyzed α-alkylation of nitriles with alcohols: Ethyl cyanoacetate (1 mmol), benzaldehyde (1 mmol), the Pd_{nano}/HT (0.1 g, Pd: 0.01 mmol), and toluene (3 mL) were added into a glass reactor. After the aldol reaction (80 °C, 2 h) and the hydrogenation (60 °C, 1 h), the catalyst was filtered out and GC analysis of the filtrate showed a 98 % yield of ethyl-2-cyano-3-phenylpropanoate. The filtrate was evaporated and the crude product was purified by column chromatography using silica (hexane/ethyl acetate = 9:1) to afford a pure product (94 % isolated yield).

3-(4-Aminophenyl)-2-phenylpropionitrile: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.05 (m, 2 H), 3.62 (br, 2 H), 3.92 (dd, J = 6.8, 8.0 Hz, 1 H), 6.59 (d, J = 8.4 Hz, 2 H), 6.90 (d, J = 8.4 Hz, 2 H), 7.23–7.37 ppm (m, 5 H); ^{13}C {^{1}H} NMR (100.4 MHz, $CDCl_3$): δ = 40.2, 41.6, 115.1, 120.5, 126.1, 127.5, 128.0, 128.8, 130.1, 135.4, 145.5 ppm; IR (KBr): $\tilde{\nu}_{max}$ = 3400, 3336, 3056, 3030, 2931, 2849, 2315, 2246, 1868, 1683, 1653, 1633, 1558, 1541, 1515, 1457, 1338, 1272, 1177, 835, 791, 744, 694, 576, 509 cm^{-1}; MS (EI): m/z (%): 211 [M^+−H], 193, 176, 165, 139, 128, 116, 106 (100), 89, 77, 63, 51; HRMS calcd for $C_{15}H_{14}N_2$: 222.1157; found: 222.1175.

Procedure for the large-scale α-alkylation of ethyl cyanoacetate with benzaldehyde: Ethyl cyanoacetate (1.70 g, 15 mmol), benzaldehyde (1.59 g, 15 mmol), the Pd_{nano}/HT (0.1 wt %, 0.60 g, Pd: 0.006 mmol), and toluene (20 mL) were added into a glass reactor. After the aldol reaction (80 °C, 3 h) and the hydrogenation (80 °C, 20 h), the catalyst was filtered out and GC analysis of the filtrate showed a 97 % yield of ethyl-2-cyano-3-phenylpropanoate. The filtrate was evaporated and the crude product was purified by distillation (180 °C/5.0 mmHg) to afford pure product (2.9 g, 95 % yield, TON = 2380).

Synthesis of α,α-dialkyl phenylacetonitriles using the Pd_{nano}/HT: Ethyl cyanoacetate (1 mmol), benzaldehyde (1 mmol), the Pd_{nano}/HT (0.1 g, Pd: 0.01 mmol), and toluene (3 mL) were added into a glass reactor. After the aldol reaction (80 °C, 2 h) and the hydrogenation (60 °C, 1 h), acrylonitrile (1.5 mmol) was added to the same flask and further reacted at 70 °C under an Ar atmosphere. After 5 h, the catalyst was filtered out. The filtrate was evaporated and the crude product was purified by column chromatography using silica to afford pure 2-carboethoxy-2-benzyl glutaronitrile (94 % yield).

2-Benzyl-2-carboethoxyglutaronitrile: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.21 (t, J = 7.0 Hz, 3 H), 2.10–2.18 (m, 1 H), 2.39–2.52 (m, 2 H), 2.57–2.65 (m, 1 H), 3.17 (dd, J = 13.4, 56.4 Hz, 2 H), 4.21 (q, J = 7.2 Hz, 2 H), 7.24–7.36 ppm (m, 5 H); ^{13}C{^{1}H} NMR (100.4 MHz, $CDCl_3$): δ = 13.8, 14.0, 32.1, 43.2, 50.2, 63.4, 117.28, 117.29, 128.2, 128.7, 129.8, 132.8, 167.0 ppm; IR (KBr): $\tilde{\nu}_{max}$ = 3033, 2981, 2938, 2250, 1742, 1673, 1641, 1497, 1455, 1371, 1231, 1091, 1014, 857, 773, 743, 702 cm^{-1}; MS (EI): m/z (%): 256 [M^+], 227, 211, 200, 183, 158, 142, 131, 115, 91 (100), 78, 65, 51; HRMS calcd for $C_{15}H_{16}N_2O_2$: 256.1212; found: 256.1222.

4-Carboethoxy-4-cyano-5-phenylpentanioc acid methyl ester: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.17 (t, J = 7.0 Hz, 3 H), 2.15–2.23 (m, 1 H), 2.33–2.46 (m, 2 H), 2.57–2.65 (m, 1 H), 3.15 (dd, J = 13.6, 52.8 Hz, 2 H), 3.69 (s, 3H), 4.15 (q, $J = 7.2$ Hz, 2H), 7.25–7.34 ppm (m, 5H); ^{13}C{^{1}H} NMR (100.4 MHz, $CDCl_3$): $\delta = 13.9$, 30.1, 32.0, 43.2, 50.5, 51.9, 62.9, 118.1, 127.8, 128.5, 129.8, 133.6, 167.7, 171.7 ppm; IR (KBr): $\tilde{\nu}_{max} = 2985$, 2955, 2246, 1740, 1499, 1448, 1381, 1227, 1203, 1091, 1016, 857, 773, 745, 702 cm^{-1}; MS (EI): m/z (%): 289 [M^+], 258, 212, 202, 184, 174, 155, 142, 129, 115, 91 (100), 77; HRMS calcd for $C_{16}H_{19}NO_4$: 289.1314; found: 289.1299.

4-Carboethoxy-4-cyano-5-phenylpentanoic acid *n*-butyl ester: ^{1}H NMR (270 MHz, $CDCl_3$): $\delta = 0.93$ (t, $J = 7.4$ Hz, 3H), 1.17 (t, $J = 7.1$ Hz, 3H), 1.30–1.44 (m, 2H), 1.55–1.66 (m, 2H), 2.14–2.65 (m, 4H), 3.15 (dd, $J = 13.5$, 37.2 Hz, 2H), 4.12 (m, 4H), 7.25–7.34 ppm (m, 5H); ^{13}C{^{1}H} NMR (67.8 MHz, $CDCl_3$): $\delta = 13.6$, 13.9, 19.1, 30.3, 30.5, 32.0, 43.1, 50.5, 62.8, 64.7, 118.1, 127.8, 128.4, 129.7, 133.6, 167.7, 171.2 ppm; IR (KBr): $\tilde{\nu}_{max} = 3033$, 2964, 2939, 2874, 2246, 1736, 1498, 1455, 1397, 1371, 1292, 1229, 1186, 1089, 1065, 1018, 964, 945, 857, 771, 743, 701 cm^{-1}; MS (EI): m/z (%): 331 [M^+], 302, 285, 272, 258, 243, 230, 212, 202, 184, 174, 155, 142, 129, 115, 103, 91 (100), 74, 55; HRMS calcd for $C_{19}H_{25}NO_4$: 331.1784; found: 331.1810.

4-Carboethoxy-4-cyano-5-phenyl-2-hexanone: ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 1.17$ (t, $J = 7.2$ Hz, 3H), 2.08–2.76 (m, 4H), 2.16 (s, 3H), 3.14 (dd, $J = 13.4$, 54.6 Hz, 2H), 4.15 (q, $J = 7.2$ Hz, 2H), 7.23–7.34 ppm (m, 5H); ^{13}C{^{1}H} NMR (100.4 MHz, $CDCl_3$): $\delta = 13.9$, 29.9, 30.7, 39.2, 43.2, 50.5, 62.8, 118.4, 127.8, 128.4, 129.8, 133.7, 167.9, 205.3 ppm; IR (KBr): $\tilde{\nu}_{max} = 3064$, 3034, 2983, 2936, 2245, 1957, 1887, 1739, 1676, 1644, 1543, 1496, 1448, 1367, 1223, 1167, 1094, 1022, 961, 917, 859, 775, 743, 702, 618, 571, 481 cm^{-}; MS (EI): m/z (%): 273 [M^+], 255, 244, 228, 216, 203, 182, 174, 158, 142, 130, 115, 103, 91 (100), 71, 78, 65, 43; HRMS calcd for $C_{16}H_{19}NO_3$: 273.1365; found: 273.1383.

Synthesis of α,α-dialkyl phenylacetonitriles using the Ru/HT: The Ru/HT (0.15 g, Ru: 0.0075 mmol), ethanol (2 mL), and phenylacetonitrile (1.0 mmol) were placed into a pyrex pressure tube (15 mL). The reaction mixture was vigorously stirred at 180 °C under Ar for 20 h. After completion of the alkylation, excess ethanol was evaporated. Acrylonitrile (3.0 mmol) and DMF (2 mL) were then added to the same pressure tube and further reaction occurred at 150 °C. After 1 h, the catalyst was separated by filtration, and the GC analysis of the filtrate showed a 93 % yield of 2-ethyl-2-phenylglutarodinitrile based on phenylacetonitrile. For the reactions of methyl acrylate and acryl amide as Michael acceptors, the solvent used was DMSO instead of DMF.

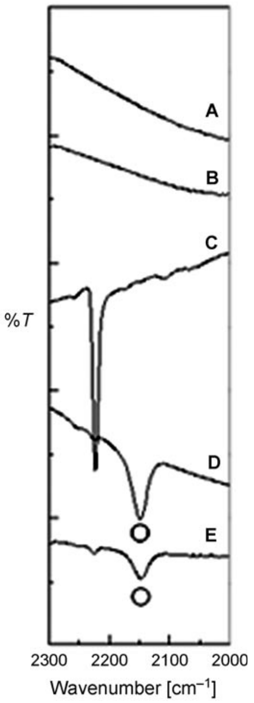


Figure 9. IR spectra of the samples A) HT, B) Pd_{nano}/HT, C) free **5**, D) after treatment of the HT with **5**, and E) after treatment of the Pd_{nano}/HT with **5**; ○: adsorbed CN group of **5** on the HT surface.

4-Cyano-4-phenylhexanoic acid methyl ester: ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 0.85$ (t, $J = 7.4$ Hz, 3H), 1.85–2.44 (m, 6H), 3.54 (s, 3H), 7.22–7.37 ppm (m, 5H); ^{13}C {^{1}H} NMR (100.4 MHz, $CDCl_3$): $\delta = 9.6$, 30.2, 34.3, 35.4, 48.4, 51.7, 121.5, 125.9, 127.9, 128.9, 137.0, 172.5 ppm; IR (KBr): $\tilde{\nu}_{max} = 2974$, 2880, 2236, 1738, 1493, 1448, 1438, 1375, 1337, 1296, 1257, 1201, 1173, 1030, 1011, 899, 882, 762, 700, 624, 517 cm^{-1}; MS (EI): m/z (%): 231 [M^+], 216, 204, 200, 189, 170, 157, 142 (100), 129, 115, 103, 91, 77; HRMS calcd for $C_{14}H_{17}NO_2$: 231.1259; found: 231.1282.

4-Cyano-4-phenylhexanoic acid amide: ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 0.91$ (t, $J = 7.4$ Hz, 3H), 1.93–2.08 (m, 3H), 2.18–2.43 (m, 3H), 5.25–5.88 (br, 2H), 7.28–7.39 ppm (m, 5H); ^{13}C {^{1}H} NMR (100.4 MHz, $CDCl_3$): $\delta = 10.4$, 32.2, 35.2, 36.2, 49.2, 122.5, 126.6, 128.6, 129.6, 137.8, 174.2 ppm; IR (KBr): $\tilde{\nu}_{max} = 3433$, 3201, 2974, 2935, 2236, 1669, 1455, 1416, 1025, 762, 700, 584, 519 cm^{-1}; MS (EI): m/z (%): 216 [M^+], 199, 187, 170, 158, 144, 129, 115, 103, 91, 77, 73, 59 (100), 44; HRMS calcd for $C_{13}H_{16}N_2O$: 216.1263; found: 216.1275.

IR measurements: After treatment of the HT, Ru/HT, and Pd_{nano}/HT with substrates in toluene, the solid catalysts were filtered, dried under an atmospheric pressure, and made into a disk with KBr. All manipulations for the measurement of Ru−H species were carried out under an Ar atmosphere. Figure 9 shows the IR spectra of both the HT and Pd_{nano}/HT upon treatment with **5**.

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