

Supported monomeric vanadium catalyst for dehydration of amides to form nitriles†

Shoichiro Sueoka,^a Takato Mitsudome,^a Tomoo Mizugaki,^a
Koichiro Jitsukawa^a and Kiyotomi Kaneda^{*ab}

Received 7th July 2010, Accepted 3rd September 2010

DOI: 10.1039/c0cc02412k

Monomeric vanadium oxide species is created on the surface of hydrotalcite (V/HT), which acts as a reusable solid catalyst for the highly efficient dehydration of amides into the corresponding nitriles.

Nitriles are of great importance as synthetic intermediates for the preparation of pharmaceuticals, agricultural chemicals and dyes. Among the variety of known synthetic routes to nitriles, dehydration of primary amides is one of the most straightforward methods.¹ Although many reports on the useful dehydration of amides have been published, most of these methods need excess amounts of stoichiometric reagents, such as P₂O₅,^{2a} SOCl₂^{2b} and POCl₃,^{2c} which results in the production of vast amounts of environmentally damaging wastes. From the standpoint of Green Sustainable Chemistry, the development of an efficient process for the catalytic dehydration of primary amides to nitriles has been desired because, theoretically, water is the only byproduct. Several catalytic dehydration systems have appeared to date; however, excess amounts of additives are still often required to promote the reaction.³ Only two examples of the successful catalytic dehydration of amides under additive-free conditions have been reported.⁴ In these cases, monomeric metal oxo compounds of dibutyltin oxide and perrhenic acid were found to be effective catalysts.

Hydrotalcites (HTs, Mg₆Al₂(OH)₁₆CO₃) are layered anionic clays consisting of positively charged two-dimensional brucite layers and anionic species, such as hydroxide and carbonate, located in the interlayer. HTs have attracted considerable interest as catalysts because of their multifunctionality, including their cation and anion exchange ability, surface tunable basicity and metal adsorption capacity.⁵ The metal adsorption ability of HT can provide strong protocols to create monomeric metal oxide species on the HT surface which show high catalytic activities for various organic reactions.⁶ Herein, we report that a monomeric vanadium oxide species is created on the surface of HT (V/HT), which can act as a solid catalyst for the highly efficient dehydration of versatile amides into the corresponding nitriles. The advantages of the V/HT catalyst

system over the previously reported catalysts are the elimination of the need for additives and precious or toxic metals and avoidance of any tedious separation of the catalyst from the reaction mixture. Moreover, the V/HT catalyst can be reused with retention of activity.

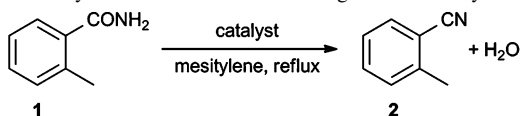
V/HT was synthesized as follows. HT (1.0 g) was added to 100 mL of an aqueous VCl₃ solution (4 mM) and then the mixture was stirred at room temperature for 3 h. The obtained slurry was filtered, washed with deionized water and dried overnight at room temperature *in vacuo* to yield V/HT (V: 1.9 wt%) as a pale gray powder. The XRD peak positions of V/HT were similar to those of the parent HT, indicating that the vanadium species is located on the surface of HT. V/HT was also characterized by X-ray absorption fine structure (XAFS) and UV-vis diffuse reflectance spectroscopy. The V K-edge X-ray absorption near-edge structure (XANES) spectrum of V/HT showed that the edge energy value of V/HT was consistent with that of Na₃VO₄ (Fig. S1, ESI†).⁷ The absorption edge was assigned to V^V species. The Fourier transform (FT) of the *k*³-weighted V K-edge EXAFS showed a peak attributed to V–O bonds and no peaks for V–V bonds on the surface of HT. The main peak of the inverse FT was well fitted to a single V–O shell (1.68 Å) with a coordination number of 4.1 (Fig. S2 and Table S1, ESI†). These results revealed that the vanadium species on the HT surface is located as a monomeric vanadium species with tetrahedral coordination similar to that in Na₃VO₄.⁸ The proposed structure of the vanadium species was also confirmed by UV-vis diffuse reflectance spectra of V/HT; the charge-transfer band at 300 nm was assigned to a monomeric VO₄ tetrahedral species (Fig. S3, ESI†).⁹

Various HT-supported metals were synthesized, and their ability to catalyze the dehydration of *o*-toluamide (**1**) was examined; the results are summarized in Table 1. Among the HT-supported metals tested, V/HT showed excellent catalytic activity to afford *o*-tolunitrile (**2**) as the sole product with 91% yield (entry 1). Other HTs such as Sn/HT, Re/HT, Mn/HT, Mo/HT, W/HT and the parent HT, however, provided low yields of **2** (entries 3–8). Next, the dehydration of **1** using supported vanadium compounds was carried out. Interestingly, good yields of **2** were obtained using V/MgO and V/SiO₂, in which the vanadium species are in monomeric states (entries 9 and 10). On the other hand, the polymeric vanadium species in V/Al₂O₃ and V/TiO₂ (Fig. S3, ESI†) were not effective (entries 11 and 12). Non-supported vanadium compounds, such as Na₃VO₄ and V₂O₅, also did not work as catalysts (entries 14 and 15). These phenomena show that V/HT had the best catalytic efficiency and a monomeric

^a Department of Materials Engineering Science, Graduate School of Engineering Science, Osaka University, 1-3 Machikaneyama, Toyonaka, Osaka 560-8531, Japan. E-mail: kaneda@cheng.es.osaka-u.ac.jp; Fax: +81 6-6850-6260; Tel: +81 6-6850-6260

^b Research Center for Solar Energy Chemistry, Osaka University, 1-3 Machikaneyama, Toyonaka, Osaka 560-8531, Japan

† Electronic supplementary information (ESI) available: Experimental details, XAFS and UV-vis spectra of V/HT. See DOI: 10.1039/c0cc02412k

Table 1 Dehydration of *o*-toluamide using various catalysts^a


Entry	Catalyst	Yield ^b (%)
1	V/HT	91
2 ^c	V/HT	84
3	Sn/HT	36
4	Re/HT	18
5	Mn/HT	18
6	Mo/HT	16
7	W/HT	15
8	HT	16
9	V/MgO	73
10	V/SiO ₂	55
11	V/Al ₂ O ₃	33
12	V/TiO ₂	22
13	VCl ₃	27
14	Na ₃ VO ₄	8
15	V ₂ O ₅	4

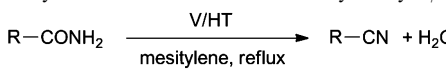
^a Reaction conditions: catalyst (metal: 0.04 mmol), *o*-toluamide (1 mmol), mesitylene (3 mL), reflux, 10 h. ^b Determined by GC analysis using internal standard technique. ^c Reuse.

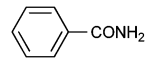
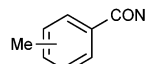
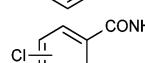
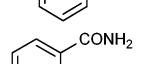
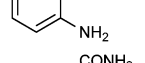
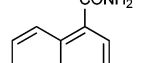
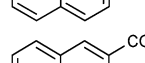
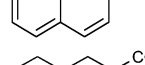
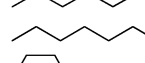
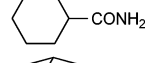
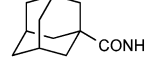
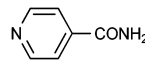
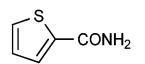
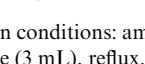
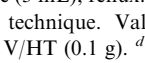
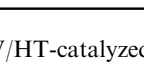
vanadium species created on the support played a crucial role in achieving high catalytic activity for the dehydration of **1**.

To determine whether or not the dehydration proceeds heterogeneously, V/HT was removed from the reaction mixture by filtration at 50% conversion of **1** followed by further stirring of the filtrate under reflux conditions. No additional product was formed. Furthermore, no vanadium ions in the filtrate were detected by inductively coupled plasma analysis (detection limit: 0.005 ppm), clearly supporting that the above dehydration occurred at the vanadium species on the surface of V/HT.

The scope of the dehydration reaction with the V/HT catalyst was investigated using various amides, as depicted in Table 2. V/HT exhibited a wide applicability towards a broad array of amides, affording the corresponding nitriles in high yields. For example, substituted benzamides were highly converted (entries 1–8). The sterically congested *ortho* and *meta*-substituted benzamides were more reactive than *para*-substituted substrates; longer reaction times were required to achieve high conversion of *para*-substituted benzamides (entries 2 and 3 vs. 4 or entries 5 and 6 vs. 7). The steric effect was also observed when naphthylamides were examined; 1-naphthylamide reacted faster than 2-naphthylamide (entry 9 vs. 10). Alicyclic and nonactivated aliphatic amides were also successfully dehydrated to the corresponding nitriles (entries 11–14). Notably, heteroaromatic amides including nitrogen and sulfur atoms were well tolerated under the reaction conditions and high yields of the desired nitriles were obtained (entries 15 and 16).

A further advantage of this solid catalytic system is its reusability. The V/HT catalyst could be separated by simple filtration upon completion of the reaction and reused twice without appreciable loss of its high catalytic activity (Table 1, entry 2). Furthermore, this solid catalyst system was applicable to scale-up conditions and **1** (20 mmol; 2.7 g) was successfully converted to **2** (88% isolated yield; 2.1 g).

Table 2 Dehydration of various amides catalyzed by V/HT^a


Entry	Substrate	Time/h	Yield ^b (%)
1		24	93 (93)
2		24	93 (93)
3 ^c		24	89 (89)
4		80	96 (86)
5		24	>99 (88)
6 ^c		24	89 (89)
7		24	50
8 ^c		24	80 (79)
9 ^c		10	92 (89)
10 ^c		24	99 (94)
11 ^d		72	93 (93)
12 ^d		24	93 (92)
13 ^d		24	87
14 ^d		24	93 (93)
15		48	83 (83)
16		72	86 (86)

^a Reaction conditions: amides (1 mmol), V/HT (0.05 g, V: 0.02 mmol), mesitylene (3 mL), reflux. ^b Determined by GC analysis using internal standard technique. Values in parentheses are isolated yields of nitriles. ^c V/HT (0.1 g). ^d Amides (0.5 mmol), V/HT (0.2 g).

The V/HT-catalyzed dehydration of amides may proceed via a pathway similar to that proposed by Ishihara and Yamamoto *et al.*^{4d} Reaction of the substrate and monomeric VO₄ species leads to a six-membered cyclic transition state. Subsequently, water and nitrile are eliminated (Scheme S1, ESI†). The high reactivity of *o*-substituted aromatic amides can be explained by a preference for the formation of the *syn* isomer in the six-membered cyclic transition state due to steric hindrance of the substituents.

In conclusion, we created a monomeric vanadium species on hydrotalcite that was found to be an effective heterogeneous catalyst for the dehydration of amides to nitriles. The V/HT catalyst system has several advantages: (I) high catalytic activity; (II) wide applicability to various amides including aromatic, aliphatic and heterocyclic substrates; (III) simple workup procedure; and (IV) reusability. The new catalyst could act as a pivotal tool in the development of economically and environmentally friendly dehydration reactions.

This work was supported by a Grant-in-Aid for Scientific Research and Scientific Research on Priority Areas (No. 18065016, "Chemistry of Concerto Catalysis") from the Ministry of Education, Culture, Sports, Science, and Technology

of Japan. We thank Dr. Uruga, Dr. Tanida, Dr. Honma, Dr. Taniguchi and Dr. Hirayama (SPRING-8) for XAFS measurements and express special thanks to the Global Center of Excellence Program “Global Education and Research Center for Bio-Environmental Chemistry” of the Osaka University.

Notes and references

- (a) D. T. Mowry, *Chem. Rev.*, 1948, **42**, 189; (b) R. E. Kent and S. M. McElvain, *Organic Syntheses*, Wiley, New York, 1955, Collect. Vol. III, p. 493; (c) S. Patai, in *The Chemistry of Functional Groups: Amides*, ed. J. Zabicky, Wiley, New York, 1970, pp. 814–816; (d) R. C. Larock, *Comprehensive Organic Transformations*, VCH Publishers, New York, 2nd edn, 1999, pp. 1983–1985.
- (a) D. B. Reisner and E. C. Horning, *Organic Syntheses*, Wiley, New York, 1963, Collect. Vol. IV, p. 144; (b) B. Rickborn and F. R. Jensen, *J. Org. Chem.*, 1962, **27**, 4608; (c) W. B. Reid Jr. and H. J. Hunter, *J. Am. Chem. Soc.*, 1948, **70**, 3515.
- (a) Y. Watanabe, F. Okuda and Y. Tsuji, *J. Mol. Catal.*, 1990, **58**, 87; (b) M.-P. Heck, A. Wagner and C. Mioskowski, *J. Org. Chem.*, 1996, **61**, 6486; (c) A. V. Narsaiah and K. Nagaiah, *Adv. Synth. Catal.*, 2004, **346**, 1271; (d) R. T. Ruck and R. G. Bergman, *Angew. Chem., Int. Ed.*, 2004, **43**, 5375; (e) S. I. Maffioli, E. Marzorati and A. Marazzi, *Org. Lett.*, 2005, **7**, 5237; (f) S. Zhou, K. Junge, D. Addis, S. Das and M. Beller, *Org. Lett.*, 2009, **11**, 2461.
- (a) D. S. Bose and B. Jayalakshmi, *J. Org. Chem.*, 1999, **64**, 1713; (b) D. S. Bose and B. Jayalakshmi, *Synthesis*, 1999, 1724; (c) K. Ishihara, Y. Furuya and H. Yamamoto, *Angew. Chem., Int. Ed.*, 2002, **41**, 2983; (d) Y. Furuya, K. Ishihara and H. Yamamoto, *Bull. Chem. Soc. Jpn.*, 2007, **80**, 400.
- A. Vaccari, *Catal. Today*, 1991, **11**, 173.
- K. Kaneda, K. Ebitani, T. Mizugaki and K. Mori, *Bull. Chem. Soc. Jpn.*, 2006, **79**, 981.
- Y. Izumi, K. Konishi, D. M. Obaid, T. Miyajima and H. Yoshitake, *Anal. Chem.*, 2007, **79**, 6933.
- F. Amamo, T. Yamaguchi and T. Tanaka, *Catal. Today*, 2007, **120**, 126.
- M. Schramil-Marth, A. Wokaun, M. Pohl and H.-L. Krauss, *J. Chem. Soc., Faraday Trans.*, 1991, **87**, 2635.