Heterogeneous Catalysis

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A Tungsten–Tin Mixed Hydroxide as an Efficient Heterogeneous Catalyst for Dehydration of Aldoximes to Nitriles[**]

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Nitriles are versatile synthetic intermediates for pharmaceuticals, agricultural chemicals, and dyes.[1] A nucleophilic substitution of alkyl halides with a stoichiometric amount of inorganic cyanide is a general method for the synthesis of alkyl nitriles, which is frequently accompanied by the elimination of hydrogen halides, especially with bulky alkyl halides.[1] Aromatic nitriles (benzonitriles) can be synthesized by the Sandmeyer reaction and ammoxidation.[1] Although α,β-unsaturated nitriles can be synthesized by the Wittig reaction of the corresponding aldehydes with cyanoalkyl phosphate, the method often produces a mixture of *E*- and *Z*-isomeric nitriles.[1c] Therefore, many of these conventional methods for nitrile synthesis require hazardous reagents, for example, inorganic cyanide, and can be nonselective.

The dehydration of aldoximes, which are easily prepared from the corresponding aldehydes, is a candidate for clean nitrile synthesis, and various procedures have been reported.[2–15] However, selective dehydration to the corresponding nitriles is very difficult, and many reported procedures require the use of reactive reagents in stoichiometric amounts, such as the Burgess reagent,[2] *N*-chlorosuccinimide/PPh_3,[3] and thionyl chloride.[4] Such reagents present a severe drawback for scaled-up and industrial applications. Therefore, efficient catalytic procedures for the dehydration of aldoximes are still in great demand. Oxorhenium(VII) complexes,[5] $Ga(OTf)_3$,[6] $InCl_3$,[7] $TiCl_3(OTf)$,[8] and $Cu(OAc)_2$[9] have been reported to catalyze the dehydration homogeneously, for example. Although heterogeneous dehydration systems are environmentally and technologically the most desirable procedures, widely usable truly heterogeneous catalysts are unprecedented (see Table 1 and the Supporting Information).[11–15]

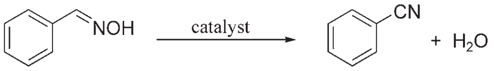
Herein, we report that a tungsten–tin mixed hydroxide (W–Sn hydroxide, Sn/W molar ratio of 1.9), prepared by the simple coprecipitation method (see the Experimental Section), can act as a reusable heterogeneous catalyst for the dehydration of various aldoximes to the corresponding nitriles [Eq. (1)]. Furthermore, the W–Sn hydroxide catalyst

$$\text{R}-\text{CH}{=}\text{NOH} \xrightarrow{\text{W–Sn hydroxide}} \text{R}-\text{CN} + \text{H}_2\text{O} \tag{1}$$

can be applied to the direct one-pot synthesis of nitriles from hydroxylamine and the corresponding aldehydes [Eq. (2)].

$$\text{R}'-\text{CHO} + \text{NH}_2\text{OH} \xrightarrow{\text{W–Sn hydroxide}} \text{R}'-\text{CN} + 2\,\text{H}_2\text{O} \tag{2}$$

Table 1: Dehydration of benzaldoxime by various catalysts.[a]



Entry	Catalyst	Conv. [%]	Select. [%]
1	W–Sn hydroxide	79	96
2	$Na_2WO_4{\cdot}2\,H_2O$[b]	4	97
3	$SnCl_4{\cdot}5\,H_2O$[c]	96	20[d]
4	$Na_2WO_4{\cdot}2\,H_2O + SnCl_4{\cdot}5\,H_2O$[e]	95	15[d]
5	H_2WO_4	18	51
6	WO_3	4	>99
7	$Sn(OH)_4$	n.d.	–
8	$WO_3 + Sn(OH)_4$[f]	8	80
9	H-mordenite	trace	–
10	H–Y	trace	–
11	SO_4^{2-}/ZrO_2[g]	11	54
12	WO_3/ZrO_2[g]	37	90
13	WO_3/SnO_2[g]	15	60
14	montmorillonite[h]	12	27
15	KF/Al_2O_3[i]	41	94
16	[{$RuCl_2$(*p*-cymene)}$_2$]/C[j]	29	60
17	MgO	8	59
18	none	n.d.	–

[a] Reaction conditions: benzaldoxime (1 mmol), catalyst (0.1 g), *o*-xylene (3 mL), 153 °C, 0.5 h. Conversion and selectivity were determined by GC analysis with biphenyl as an internal standard. Main by-products were benzamide and benzaldehyde. n.d. = nitrile not detected. [b] $Na_2WO_4{\cdot}2\,H_2O$ (0.17 mmol). [c] $SnCl_4{\cdot}5\,H_2O$ (0.33 mmol). [d] Unidentified by-products (ca. 50% selectivity) were formed. [e] $Na_2WO_4{\cdot}2\,H_2O$ (0.17 mmol) + $SnCl_4{\cdot}5\,H_2O$ (0.33 mmol). [f] WO_3 (0.045 g) + $Sn(OH)_4$ (0.049 g). [g] Prepared according to reference [20]. [h] Montmorillonite KSF. Purchased from Alfa Aesar. [i] Purchased from Aldrich (40 wt% KF on Al_2O_3; 0.69 mmol; 69 mol%). [j] Prepared according to reference [11]; 0.1 g (Ru: 2.2 mol%). A similar result was obtained when the reaction was performed with [{$RuCl_2$(*p*-cymene)}$_2$]/C in the presence of M.S. (4 Å, 200 mass% with respect to substrate).

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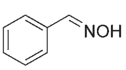
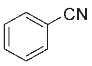
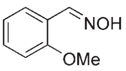
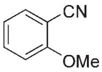
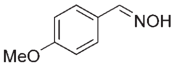
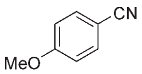
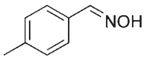
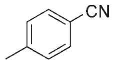
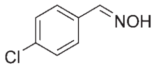
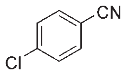
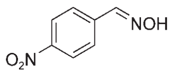
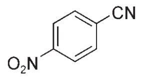
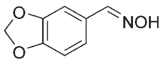
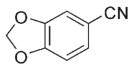
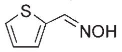
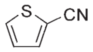
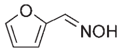
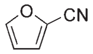
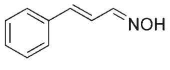
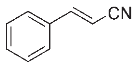
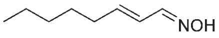
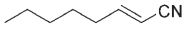
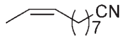
Supporting information for this article is available on the WWW under http://www.angewandte.org or from the author.

First, the dehydration of benzaldoxime as a model substrate was carried out with various catalysts, including previously reported solid catalysts (Table 1). The W–Sn hydroxide showed the highest catalytic activity for the dehydration of benzaldoxime among various catalysts tested (Table 1, entry 1).[16] To verify whether the observed catalysis is truly heterogeneous or not, the W–Sn hydroxide was separated from the reaction mixture by filtration at the reaction temperature, and the reaction was again carried out with the filtrate under the same conditions. The dehydration was completely stopped by the removal of the W–Sn hydroxide. Furthermore, it was confirmed by inductively coupled plasma–atomic emission spectrometry (ICP–AES) analysis that tungsten and tin species were hardly detected in the filtrate ($W < 0.0032\,\%$, $Sn < 0.0025\,\%$). These results show that the nature of the observed catalysis is truly heterogeneous.[17] The dehydration hardly proceeded in the absence of catalysts (Table 1, entry 18) or in the presence of $Na_2WO_4{\cdot}2H_2O$ (Table 1, entry 2). In the presence of $SnCl_4{\cdot}5H_2O$, the selectivity for benzonitrile was very low, and many unidentified by-products were formed (Table 1, entry 3). WO_3, H_2WO_4, $Sn(OH)_4$, and a physical mixture of WO_3 and $Sn(OH)_4$ were not effective for the dehydration (Table 1, entries 5–8). According to our experiments, previously reported solid catalysts such as montmorillonite,[12] KF/Al_2O_3,[15] and $[\{RuCl_2(p\text{-cymene})\}_2]/C$[11] were not effective for dehydration under the present conditions (Table 1, entries 14–16). In the case of montmorillonite, benzaldehyde was obtained as a main product (73 % selectivity).

The acid strength of the W–Sn hydroxide (as prepared) was estimated by the Hammett indicator method.[18] The W–Sn hydroxide reacted with benzeneazodiphenylamine ($pK_a = +1.5$) and did not react with dicinnamalacetone ($pK_a = -3.0$), showing that the H_0 value of the W–Sn hydroxide lies between $+1.5$ and -3.0. This result suggests that the W–Sn hydroxide is much less acidic than the zeolites.[18,19] However, the reaction hardly proceeded in the presence of zeolites (Table 1, entries 9 and 10). SO_4^{2-}/ZrO_2, WO_3/ZrO_2, and WO_3/SnO_2, which have been reported to be solid superacids,[20] were much less active for this reaction than the W–Sn hydroxide (Table 1, entries 11–13). In addition, strong solid bases such as KF/Al_2O_3 and MgO were less active (Table 1, entries 15 and 17). These results show that the present dehydration is not a simple acid- or base-catalyzed reaction. It is likely that the dehydration proceeds efficiently in the presence of catalysts with a suitable acidity. Detailed studies are in progress.

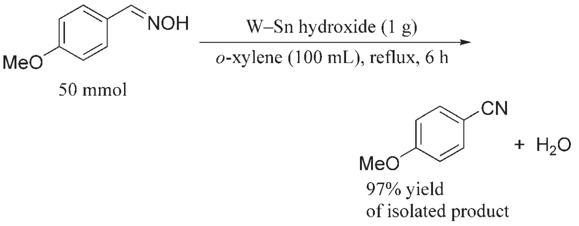
The scope of the present W–Sn hydroxide-catalyzed system with regard to various kinds of structurally diverse aldoximes was examined. The W–Sn hydroxide showed high catalytic activities for the dehydration of activated, non-activated, and heteroatom-containing aldoximes, as summarized in Table 2. In the dehydration of benzaldoximes, the substrates were smoothly converted to the corresponding benzonitriles in excellent yields (Table 2, entries 1–9). Not only aromatic aldoximes but also aliphatic ones could be dehydrated to the corresponding aliphatic nitriles (Table 2, entries 11–13). The present system was also effective for acid-sensitive piperonaldoxime (Table 2, entry 10). The dehydration of 2-thiophenealdoxime and 2-furaldoxime gave the corresponding nitriles in 80 and 73 % selectivity, respectively, because of the formation of amides as by-products (Table 2,

Table 2: Dehydration of various aldoximes by W–Sn hydroxide.[a]

Entry	Substrate	Product	t [h]	Conv. [%]	Select. [%]
1			1	94 (82)	91
2[b]			1	90	94
3[b]			1	87	94
4[b]			1	87	95
5			1	> 99 (91)	98
6			1	> 99 (82)	96
7			1	95 (85)	94
8			1.5	96 (87)	91
9			3	94 (72)	86
10			1	97 (86)	94
11	$n\text{-}C_7H_{15}CH{=}NOH$	$n\text{-}C_7H_{15}CN$	1	98 (89)	97
12	$n\text{-}C_9H_{19}CH{=}NOH$	$n\text{-}C_9H_{19}CN$	1	> 99 (90)	98
13	$n\text{-}C_{11}H_{23}CH{=}NOH$	$n\text{-}C_{11}H_{23}CN$	1	96 (95)	95
14			1.5	> 99 (65)	80
15			4.5	88[c]	73
16			3	97 (94)	96
17			5.5	89 (73)	91
18			1.5	> 99 (95)	98

[a] Reaction conditions: aldoxime (1 mmol), W–Sn hydroxide (0.1 g), o-xylene (3 mL), 149 °C. Conversion and selectivity were determined by GC analysis with diphenyl or naphthalene as an internal standard. Main by-products were amides and aldehydes. Values in parentheses are yields of isolated product after complete consumption of aldoximes. [b] Reuse experiments; reuse 1 (entry 2), reuse 2 (entry 3), and reuse 3 (entry 4). The initial rates for the reuse runs were almost the same as for the first run with a fresh catalyst. [c] Not isolated.

entries 14 and 15). The dehydration of olefinic aldoximes such as *trans*-cinnamaldoxime, *trans*-2-octenaldoxime, and *cis*-8-undecenaldoxime efficiently proceeded to afford the corresponding nitriles without isomerization of the double bond (Table 2, entries 16–18). The W–Sn hydroxide was reused in the dehydration of benzaldoxime, and the high catalytic activity and selectivity were maintained even after the third reuse (Table 2, entries 2–4). The present system was applicable to larger-scale production (50 mmol, heating at reflux, bath temperature 170 °C), and the corresponding nitrile could be isolated in 97 % yield after 6 h [Eq. (3)].



(3)

Interestingly, the W–Sn hydroxide could be employed in the one-pot syntheses of nitriles through the dehydrative condensation of aldehydes and hydroxylamine with subsequent dehydration (Table 3).[21] The dehydrative condensation of benzaldehyde and hydroxylamine hardly proceeded in the absence of catalyst at 80 °C. The rate in the presence of the W–Sn hydroxide was 4.0 mm min^{-1} and more than two orders of magnitude larger than that in the absence of catalyst (0.035 mm min^{-1}), showing that the W–Sn hydroxide efficiently catalyzes not only the dehydration of aldoximes but also aldoxime formation. In this one-pot synthesis, the catalysis was also heterogeneous in nature, and the catalyst could be reused without a significant loss of catalytic activity. Although this tandem one-pot synthesis of nitriles is a very useful transformation and a topic of current interest in organic synthesis, stoichiometric reagents such as triethylamine sulfur dioxide, sulphuryl chloride fluoride, methanesulfonyl chloride with dry Al_2O_3, and KF/Al_2O_3 have been utilized for the transformation.[21,22]

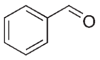
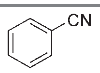
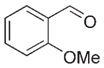
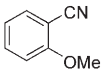
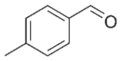
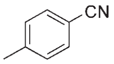
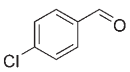
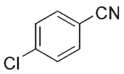
In conclusion, we have reported herein the noteworthy features of the easily prepared W–Sn hydroxide for the heterogeneously catalyzed dehydration of aldoximes and the one-pot syntheses of nitriles. This catalyst could be applied to various functional transformations.

Experimental Section

The W–Sn hydroxide was prepared as follows: $Na_2WO_4{\cdot}2\,H_2O$ (2.47 g, 7.5 mmol) was dissolved in deionized water (15 mL) and $SnCl_4{\cdot}5\,H_2O$ (5.26 g, 15 mmol) was immediately added in one portion. After stirring the solution for 1 h at room temperature, deionized water (60 mL) was added to the solution in one portion, and the initially colorless solution gradually turned into a white slurry. After stirring the slurry for 24 h at room temperature, the resulting white precipitate of W–Sn hydroxide was filtered off, washed with a large amount of deionized water, and dried in vacuo to afford the W–Sn hydroxide as a white powder (4.4 g). BET surface area: 149 m^2 g^{-1}. Pore volume: 0.074 cm^3 g^{-1}. The IR spectrum showed a very broad ν(OH) band in the range of 3000–3700 cm^{-1}. The X-ray photoelectron spectrum of the W–Sn hydroxide showed that the W 4f$_{7/2}$, W 4f$_{5/2}$, Sn 3d$_{5/2}$, and Sn 3d$_{3/2}$ binding energies of the W–Sn hydroxide were 36.2 eV (full width at the half maximum (FWHM) 1.3 eV), 38.4 eV (FWHM 1.3 eV), 487.7 eV (FWHM 1.5 eV), and 496.1 eV (FWHM 1.5 eV), respectively, indicating that the respective oxidation states of W and Sn species in the W–Sn hydroxide are +6 and +4.[23] The contents of W, Sn, Cl, and Na were 26.2, 31.8, 5.0, and less than 0.01 %, respectively, and the formulation of the W–Sn hydroxide was expressed by $Sn_{1.9}WClO_{6.3}{\cdot}9\,H_2O$. The Raman spectrum of the W–Sn hydroxide showed an intense band at 959 cm^{-1} corresponding to ν(W=O). No bands arising from WO_3 were observed in the Raman spectrum. The X-ray diffraction patterns of the W–Sn hydroxide (Figure S1 in the Supporting Information) showed broad signals at $d = 3.3422$, 2.6384, and 1.7619 Å. The signal positions almost agreed with those of SnO_2 (rutile). Signals associated with SnO and WO_3 phases were not detected. All these results suggest that a SnO_2-like phase was predominantly formed in the W–Sn hydroxide and that tungsten species were highly dispersed on SnO_2 and/or incorporated into the SnO_2 matrix.

A typical procedure for the dehydration was as follows: W–Sn hydroxide (0.1 g), benzaldoxime (1 mmol), and *o*-xylene (3 mL) were successively placed into a glass vial. The reaction mixture was stirred (800 rpm with a magnetic stir bar) at 149 °C under 1 atm of Ar. The conversion and product selectivity were periodically determined by GC analysis. After the reaction was finished, the spent catalyst was separated by filtration, washed with acetone, and dried in vacuo prior to being recycled. The products were isolated by column chromatography (eluent: initially *n*-pentane, after *o*-xylene was eluted *n*-pentane/diethyl ether (1:1)). All products were known and available as authentic samples. The products were confirmed by the comparison of their GC retention times, mass spectra, and ^{1}H and ^{13}C NMR spectra with those of the authentic samples.

Table 3: One-pot synthesis of nitriles by W–Sn hydroxide.[a]

Entry	Substrate	Product	*t* [h]	Conv. [%]	Select. [%]
1			7	99 (89)	92
2			6.5	> 99 (94)	99
3			9.5	99 (87)	92
4			13	99 (72)	87
5	*n*-$C_9H_{19}CHO$	*n*-$C_9H_{19}CN$	4	99 (86)	97
6	*n*-$C_{11}H_{23}CHO$	*n*-$C_{11}H_{23}CN$	5	98 (89)	93

[a] Reaction conditions: Aldehyde (1 mmol), $NH_2OH{\cdot}HCl$ (2 mmol), W–Sn hydroxide (0.1 g), *o*-xylene (3 mL), 133 °C. Conversion and selectivity were determined by GC analysis with diphenyl as an internal standard. Values in parentheses are yields of isolated product after complete consumption of aldehydes.

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[16] Three kinds of W–Sn hydroxide catalysts with different Sn/W molar ratios (0.9, 1.9, and 5.2) were prepared and used for the dehydration of benzaldoxime. The W–Sn hydroxide with the Sn/W molar ratio of 1.9 showed the highest catalytic activity, and the order of reactivity was as follows: $\text{Sn/W} = 1.9\,(79) > 5.2\,(9) > 0.9\,(7)$, where the values in the parentheses are the percent conversion of benzaldoxime under the conditions given in Table 1.

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