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Silica-Sulfuric Acid: Novel, Simple, Efficient and Reusable Catalyst for Hydration of Nitrile to Amide

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Silica-sulfuric acid efficiently catalyzes conversion of aliphatic, substituted aromatic and hetero aromatic nitriles to their corresponding amides in good to excellent yields under reflux condition. Products obtained were purified by column chromatography method and characterized by ^{1}H NMR, ^{13}C NMR and mass spectral analysis.

Keywords: Silica-sulfuric acid, Nitriles, Amides, Hydration.

INTRODUCTION

The hydration of nitriles into the corresponding amides is very important in organic chemistry as well as in the chemical industry. There are a number of different methods for this conversion. Nitrile hydration is a classic transformation but one which is still difficult to achieve, even with the range of available reagents. Traditionally, various acids or bases were used as catalysts [1-9]. Transition metal catalyzed methods have been developed using Co [10,11], Mo [12], Ru [13-16], Rh [17,18], Pd [19,20], Ir [21] and Pt [22-24]. Homogeneous metal catalysis is frequently used in an industrial setting. Intimate catalyst substrate interaction, mild reaction conditions and an understanding of the catalytic process are recognized as main advantages. The catalytic hydration of nitriles (RCN) to carboxamides ($RCONH_2$) represents a fundamentally important pathway to these products in both laboratory and industrial contexts [25-34]. Since the discovery of alumina-supported ruthenium hydroxide catalysts [$Ru(OH)_x/Al_2O_3$] by Yamaguchi *et al*. [15] solid-supported ruthenium has become an important class of catalyst for nitrile hydration, demonstrating high selectivity for carboxamide formation as well as other practical advantages [35-50]. Although $RuCl_3{\cdot}nH_2O$ itself catalyzes nitrile hydration, the choice of solid support is critically important for achieving sufficient reactivity as well as for retaining Ru species on support [15,37]. Examples of supports successfully used for Ru species include inorganic Al_2O_3 [15], nanoferrite [35] and magnetic silica [36] as well as organic chitosan [51], amberlite [37] and Nafion [38]. However, these systems typically require the use of microwave irradiation [35-37,51] or high reaction temperatures (175 °C) [38]. Moreover, the tolerance of base-sensitive functional groups such as carboxylic esters has not been documented in these reports [15,35-38,51]. Such chemo-selectivity is important in modern organic synthesis [52,53], but is generally considered elusive in nitrile hydration promoted by metal-loaded heterogeneous catalysts, a single exception (Au/TiO_2) [44] notwithstanding. A number of catalysts have been developed for the synthesis of amide from nitrile such as hydrogen peroxide/DMSO [9,54], hydrogen peroxide/PTC [55], Na/FAP [56] and synthetic fluorapatites (FAP) [57]. Amide can also be prepared by metal complex such as palladium [18], rhodium [58], sodium perborate [59], ruthenium complex [60], chloromethylsilane [6] and $ZnCl_2$ under microwave condition [61]. On the other hand, heterogeneous process enhances the selectivity in this reaction. Heterogeneous catalysts such as a KF/Al_2O_3 [62], resins [63], KF/natural phosphate [64] are used for conversion of nitrile to amide.

According to the reported literature, the conversion of nitriles to amides requires an expensive catalyst and long duration time. Moreover, some of the metal catalysts are not easily available and some of the metal catalysts are to be used with high precautions during the reaction conditions. Keeping these reasons in mind, we developed a simple method for conversion of nitrile to amides without affecting any substitutions with in the molecule. However, the reported methods suffer from drawbacks such as being expensive, explosive, unavailable, low yield and polluting to environment to some extent. Furthermore, some of these methods yield acid as a side product. Therefore, a need still exists for versatile, simple and environmentally friendly process for conversion of nitrile

to amide. In this research we report silica-sulfuric acid as a simple, efficient and reusable catalyst for the transformation of amides from nitriles.

EXPERIMENTAL

^{1}H NMR and ^{13}C NMR spectrum were recorded on 400 MHz Bruker spectrometer using $CDCl_3$ solvent. Molecular weight of the synthesized compounds were checked using LC-MS Agilent 1100 series with MSD Ion trap using 0.1 % aqueous trifluoroacetic acid in acetonitrile system on C18-BDS column for a 10 min duration and GC-MS. Commercially available chemicals were procured from Sigma-Aldrich and Alfa-Aesar and used without further purification.

General procedure for the preparation of amide from nitrile: In a round bottom flask, aliphatic/substituted aromatic/hetero aromatic nitrile (1 mmol), silica-sulfuric acid (1 mmol) and toluene (10 mL) were taken under nitrogen atmosphere and refluxed for 1-3 h. Completion of the reaction was monitored on thin layer chromatography, LC-MS and GC-MS. After reaction completion, the product obtained was filtered and washed with ethyl acetate. Crude product was purified by column chromatography using 60-120 mesh silica gel with *n*-hexane-ethyl acetate solvent and recrystallized with appropriate solvents. All the purified compounds were characterized by ^{1}H NMR, ^{13}C NMR, LC-MS/GC-MS and elemental analysis.

Acrylamide (2a): ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.5 (d, 1H), 6 (m, 2H), 7.1 (s, 1H), 8.0 (s, 1 H).^{13}C NMR (400 MHz, $CDCl_3$): δ = 126, 132, 167; GC-MS: *m/z* = 71 (M^+); Anal. calculated for C_3H_5NO; C, 50.69; H, 7.09; N, 19.71; Found: C, 50.70; H, 6.98; N, 19.72.

2-Hydroxyacetamide (2b): ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.7 (d, 2H), 5.3 (t, 2H), 7.2 (s, 2H); ^{13}C NMR (400 MHz, $CDCl_3$): δ = 34, 116, 194 GC-MS: *m/z* = 75 (M^+); Anal. calculated for $C_2H_5NO_2$; C, 32.00; H, 6.71; N, 18.66; Found: C, 31.58; H, 6.68; N, 18.63.

Benzamide (2c): ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.4 (m, 2H), 7.5 (m, 1H), 7.8 (m, 2H), 9.49 (s, 1H), 9.89 (s, 1H); ^{13}C NMR (400 MHz, $CDCl_3$): δ = 127, 128, 132, 133, 169; LC-MS: *m/z* = 121 (M^+); Anal. calculated for C_7H_7NO; C, 69.41; H, 5.82; N, 11.56; Found: C, 69.38; H, 5.83; N, 11.55.

3-Amino-4-methoxybenzamide (2d): ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.7 (s, 3H), 4.7 (s, 2H), 6.78 (d, 1H), 7.0 (d, 1H), 7.1 (s, 1H), 7.16 (s, 1H), 7.6 (s, 1H);^{13}C NMR (400 MHz, $CDCl_3$): δ = 55, 109, 113, 116, 127, 137, 149, 168; LC-MS: *m/z* = 166 (M^+); Anal. calculated for $C_8H_{10}N_2O_2$; C, 57.82; H, 6.07; N, 16.86; Found: C, 57.79; H, 6.04; N, 16.87.

2,6-Dichlorobenzamide (2e): ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.33 (d, 2H), 7.4 (t, 1H) ^{13}C NMR (400 MHz $CDCl_3$): δ = 127, 134, 135, 136, 169; LC-MS: *m/z* = 190 (M^+); Anal. calculated for $C_7H_5NOCl_2$; C, 44.25; H, 2.65; N, 7.37; Found; C, 44.21; H, 2.64; N, 7.37.

3-Aminobenzamide (2f): ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.1 (s, 2H), 6.7 (s, 1H), 6.98 (dd, 1H), 7.0 (d, 2H), 7.1 (s, 1H), 7.70 (s, 1H); ^{13}C NMR (400 MHz, $CDCl_3$): δ = 113, 115, 118, 129, 135, 149, LC-MS: *m/z* = 136 (M^+); Anal. calculated for $C_7H_8N_2O$; C, 61.75; H, 5.92; N, 20.58; Found: C, 61.76; H, 5.91; N, 20.56.

4-Aminobenzamide (2g): ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.5 (s, 2H), 6.5 (dd, 2H), 6.8 (s, 1H), 7.50 (s, 1H), 7.6 (dd, 2H): ^{13}C NMR (400 MHz, $CDCl_3$): δ = 115, 123, 128, 150, 169; LC-MS: *m/z* = 136 (M^+); Anal. calculated for $C_7H_8N_2O$; C, 61.75; H, 5.92; N, 20.58; Found: C, 61.74; H, 5.90; N, 20.59.

2-Amino-5-chlorobenzamide (2h): ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.6 (s, 2H), 7.15 (d, 2H), 7.6 (s, 1H), 7.80 (s, 1H); ^{13}C NMR (400 MHz, $CDCl_3$): δ = 114, 117, 118, 128, 132, 149, 170; LC-MS: *m/z* = 170 (M^+); Anal. calculated for $C_7H_7N_2OCl$; C, 49.28; H, 4.14; N, 16.42; Found: C, 49.29; H, 4.15; N, 16.41.

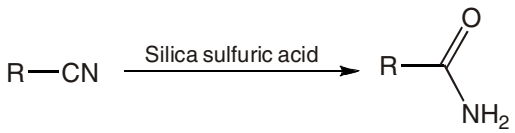
***tert*-Butyl 2-(4-carbamoylphenyl)acetate (2i):** ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.35 (s, 9H), 3.59 (s, 2H), 7.25 (d, 2H), 7.8 (d, 2H), 9.4 (s, 1H), 9.8 (s, 1H); ^{13}C NMR (400 MHz, $CDCl_3$): δ = 9, 12, 29, 73, 127, 130, 138, 173; LC-MS: *m/z* = 235 (M^+); Anal. calculated for $C_{13}H_{17}NO_3$; C, 66.36; H, 7.28; N, 5.95; Found: C, 66.33; H, 7.27; N, 5.98.

Methyl 2-(4-carbamoylphenyl)acetate (2j): ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.51 (s, 2H), 3.7 (s, 3H), 6 (2H, br), 7.24 (d, 2H). 7.83 (d, 2H); ^{13}C NMR (400 MHz, $CDCl_3$): δ = 38, 48, 51, 127, 130, 134, 142, 173; LC-MS: *m/z* = 193 (M^+); Anal. calculated for $C_{10}H_{11}NO_3$; C, 62.17; H, 5.74; N, 7.25; Found: C, 62.23; H, 5.71; N, 7.28.

2-Aminopyridine 6-carbaxalmide (2k): ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4 (2H br), 6.3 (2H), 7.1 (d, 1H), 7.7 (d, 1H), 7.9 (s, 1H); ^{13}C NMR (400 MHz, $CDCl_3$): δ = 112, 140, 149, 159, 169; LC-MS: *m/z* = 137 (M^+); Anal. calculated for $C_6H_7N_3O$; C, 52.55; H, 5.14; N, 30.64; Found: C, 52.51; H, 5.19; N, 30.62.

RESULTS AND DISCUSSION

In continuation of our effort for the development of synthetic methods in organic synthesis [65,66] and pharmacologically active heterocyclic compounds [67-69], herewith we have focused our attention on the preparation of amides from nitriles catalyzed by silica-sulfuric acid (**Scheme-I**) in good to excellent yields as shown in Table-1.

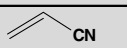
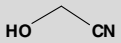
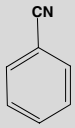
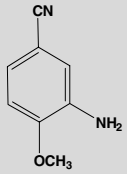
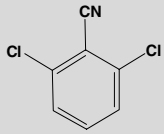
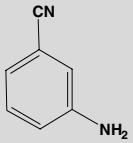
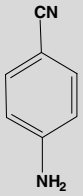
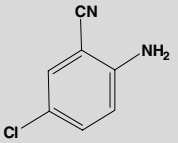
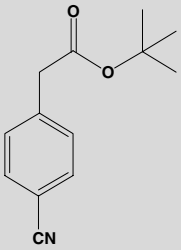
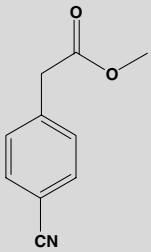
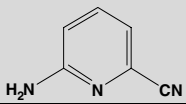


R = aliphatic, substituted aromatic and hetero aromatic

Scheme-I: Hydration of nitrile group to amide group

To demonstrate the protocol, we selected benzonitrile and substituted benzonitrile as model substrates, which smoothly converted to benzamide in excellent yield (Table-1, entry-3) and the same reaction was extended to substituted benzonitrile also (entry 4-8 and 10). Interestingly, we observed that *tert*-butyl group was unaffected under this reaction condition (entry-9). Heterocyclic nitrile such as a pyridine moiety smoothly converted to amide in excellent yield (entry-11). We also observed that an aliphatic nitrile such as acrylonitrile yields acrylamide (entry1) in excellent yield without affecting the double bond which was not possible in DMSO condition. This was an added advantage of this method and that 2-hydroxy acetonitrile also underwent this conversion in excellent yield (entry 2). Silica-sulfuric acid catalyst can also be used up to three times without losing its catalytic activity.

TABLE-1
PHYSICAL CONSTANTS OF CONVERSION OF NITRILE TO AMIDE (**1-11**)

Entry	Nitrile	Product	Reaction time (h)[a]	Yield (%)[b]
1		**2a**	2	88
2		**2b**	2.5	79
3		**2c**	3	90
4		**2d**	3	83
5		**2e**	2	88
6		**2f**	3	90
7		**2g**	3	90
8		**2h**	2.5	97
9		**2i**	3	87
10		**2j**	2	76
11		**2k**	3	90

[a]Reactions were monitored through LC-MS, GC-MS and TLC analysis
[b]Yields refers to the isolated pure products after flash chromatography All the purified compounds were characterized by ^{1}H NMR, ^{13}C NMR, LC-MS/GC-MS and spectroscopic methods.

Conclusion

Silica-sulfuric acid efficiently catalyzes conversion of aliphatic, substituted aromatic and hetero aromatic nitriles to their corresponding amides in good to excellent yields under reflux condition without affecting any other substituent in the molecule. It is also made observation on new method of synthesis. The reactions performed are ecofriendly and the used catalysts are easily available with low cost.

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