

나이트릴을 아마이드로 선택적 가수분해하는데 효과적인 촉매로서의 자연 고령토에 흡착된 황산

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Natural Kaolin Supported Sulfuric Acid as an Efficient Catalyst for Selective Hydrolysis of Nitriles to Amides

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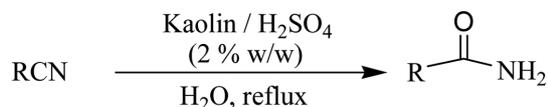
The Preparation of amides is an important transformation from both academic and industrial points of view. Amides not only constitute versatile building blocks in synthetic organic chemistry,¹ but also exhibit a wide range of industrial applications^{2,3} and pharmacological interest.⁴ Most of the known synthetic transformations leading to amides are based on the reaction of an activated carboxylic acid with an amine or ammonia.¹ Alternative preparative pathways involve the rearrangement of an oxime,⁵ and the recently reported Ritter-type reaction of an alcohol with an amine.⁶ Also, a less frequently reported amide synthesis is the coupling of a nitrile and an amine.^{7,8} Nitriles are intrinsically more reactive than carboxylic acids and direct conversion of nitriles to primary amides are more interesting in organic synthesis. However, a base-catalyzed reaction leads to a carboxylate salt, because the second step of the hydrolysis is faster than the first one, and the reaction thus proceeds to the final hydration product rather than stopping at the amide stage.¹ Although it can be possible to obtain amides in strong acidic solutions, it is then necessary to have careful control of the temperature and of the ratio of reagents in order to avoid the formation of polymers which is promoted by the exothermic character of the hydrolysis.⁹ Moreover, the final neutralization leads to an extensive salt formation with inconvenient product contamination and pollution effects.^{9,10} Introduction of a new catalyst such as tris-dim-

ethylphosphinito platinum hydride¹¹ for the selective hydrolysis of acrylonitrile with high reaction rate and turnover numbers is industrially very important. Several syntheses of primary amides from nitriles have been reported using NaBO₃/MW,¹² ZnCl₂/MW,¹³ Co(III) complex,¹⁴ ruthenium complex/sealed tube,¹⁵ ZnX₂/ketoxime combination,¹⁶ TMSCl,¹⁷ KOTMS,¹⁸ and nitrile hydratase.¹⁹ However, most of the reported methods have not been proven in general and practical in scope because of harsh condition or expensive catalyst. In this paper we introduced natural kaolin supported sulfuric acid as an efficient catalyst for the selective hydrolysis of nitriles to primary amides in aqueous conditions (*Scheme 1*).

RESULTS AND DISCUSSION

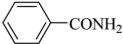
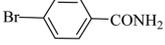
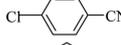
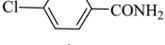
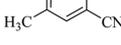
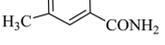
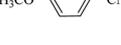
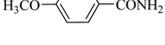
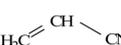
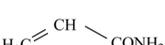
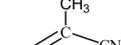
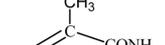
Natural kaolin is very cheap and shows good potential as support material. Currently, strong interests in such natural supports are due to ecofriendly demands in many modern industrial applications.²⁰

In a typical procedure, nitrile (4 mmol) were dissolved in water (10 mL) in the presence of kaolin and refluxed for



Scheme 1.

Table 1. Preparation of primary amides from nitriles in the presence of kaolin/sulfuric acid (2% w/w) under reflux conditions

Entry	Nitrile	Yield % ^a	Product ^b	m.p./°C	
				Found	Reported ^{ref}
1		74		125-126	126-127 ¹³
2		65		190	189-190 ²¹
3		80		171-172	170-172 ¹²
4		66		93-94	92-93 ¹³
5		69		164-165	163-165 ¹²
6		58		80-81	81.3 ²¹
7		57		114-115	114.8 ²¹
8		61		100-101	100-101 ²¹
9		55		119-120	121 ²¹
10		78		84-85	84-85 ²²
11		74		109-110	110.5 ²¹

^aIsolated yields. ^bThe products were characterized by IR and ¹H NMR spectroscopy and also their melting points are compared with authentic samples.

24 h. The best result was obtained by acidified kaolin with sulfuric acid (2% w/w). After completion of the reaction (monitored by TLC), the crude product was extracted with ethyl acetate in 55-80% yields. The results are shown in Table 1. In general, aliphatic and aromatic nitriles were successfully converted into amides. Two industrially important amides, acrylic amide and methacrylic amid were obtained in 78% and 74% yields, respectively, from corresponding nitriles.

Careful neutralization of all reaction mixtures were carried out to pH = 7 for exact monitoring of reaction for possible formation of carboxylic acid. In all reactions we only obtained amide without any contamination with carboxylic acid which was monitored with TLC, IR and NMR spectra. Only in the case of (Table 1, entry 4) about 5% carboxylic acid was formed. Then the product was purified for obtaining the pure corresponding amide for further characterization. Acidic work up destroyed the product complexes with metal cations of kaolin and increased the isolated yields but the catalyst was deformed and did not regenerate.

The products were characterized by IR and ¹H NMR spectroscopy and also their melting points are compared

with authentic samples. The disappearance of one strong and sharp absorption band (CN stretching band), and the appearance of two NH₂ stretching bands in 3370 and 3320 cm⁻¹ and carboxamide stretching in 1650 cm⁻¹ in the IR spectra, were evidence for the formation of primary amides. In ¹H NMR spectrum of acrylic amide, three doublet of doublets were observed for three vinylic protons at δ 5.57, 6.07 and 6.17 with expectedly vicinal and geminal splitting. NH₂ group shows two singlets at δ 7.1 and 7.5 due to amidic resonance.

The mechanism of this selective transformation is not clear. We assume that kaolin / sulfuric acid (2% w/w) acts as a Lewis or Bronsted acid making the nitrile more susceptible to nucleophilic addition. Perhaps, an efficient coordination of amide-intermediate with kaolin stopped the hydrolysis in amide stage until work up.

In conclusion, we have developed a novel and highly efficient method for the synthesis of primary amides from nitriles in the presence of the acidified kaolin (2% w/w) under reflux conditions in water. The significant advantages of this methodology are good yields without carboxylic acid contamination, a simple work-up procedure, and easy preparation and handling of the catalyst. Also,

the catalyst and solvent are both environmentally safe that means green chemistry.

EXPERIMENTAL

All materials and solvents were purchased from Merck and Fluka. Melting points were determined in open capillary tubes in an Electrothermal IA 9700 melting point apparatus. ^1H NMR spectra were recorded on a Bruker -100 MHz and 500 MHz instruments using tetramethylsilane (TMS) as an internal standard. IR spectra were recorded on a Shimadzu-IR 470 spectrophotometer. All of the products are known products and all of the isolated products gave satisfactory IR and NMR spectra.

Preparation of the Acidified Kaolin with Sulfuric Acid (2% w/w)

Kaolin (7.5 g) was treated with concentrated sulfuric acid (0.15 g, 0.08 mL) and stirred for 1 h. The prepared acidified kaolin (2% w/w), was stored for further applications.

Preparation of Primary Amides From Nitriles: Typical Procedure: The acidified kaolin (2% w/w) (150 mg) was added to a solution of nitrile (4 mmol) in water (10 mL) and refluxed for 24 h. After completion of the reaction (as indicated by TLC), the reaction mixture was cooled to room temperature and neutralized with sodium hydroxide solution (4 N) to pH=7 carefully. The reaction mixture was filtered and extracted with ethyl acetate (2×20 mL). The organic layer dried over sodium sulfate and evaporated. The crystalline amide was obtained after recrystallization from H_2O -EtOH. The products were obtained in 55-80% yields. All the products are known compounds and the spectral data and melting points were identical to those reported in the literature.

Acrylamide: Yield 78%; mp 84-85 °C; IR (KBr) 3370, 3320, 1650 cm^{-1} ; ^1H NMR (DMSO- d_6 , 500 MHz) δ 7.5 (b, 1H, NH), 7.1 (b, 1H, NH), 6.18 (dd, 1H, $J_1 = 16\text{Hz}$, $J_2 = 10\text{Hz}$), 6.07 (dd, 1H, $J_1 = 16\text{Hz}$, $J_2 = 2.2\text{Hz}$), 5.58 (dd, 1H, $J_1 = 10\text{Hz}$, $J_2 = 2.2\text{Hz}$).

4-Methoxybenzamide: Yield 69%; mp 164-165 °C; IR (KBr) 3330, 3320, 1640 cm^{-1} ; ^1H NMR (DMSO- d_6 , 500 MHz) δ 7.84 (d, 2H, $J = 7\text{Hz}$), 7.17 (b, 2H, NH_2), 6.95 (d, 2H, $J = 7\text{Hz}$), 3.78 (s, 3H).

4-Bromobenzamide: Yield 65%; mp 190 °C; IR (KBr) 3350, 3200, 1660 cm^{-1} ; ^1H NMR (Acetone- d_6 , 100 MHz) δ 7.75 (AB q, 4H), 6.8 (b, 2H, NH_2).

3-Methylbenzamide: Yield 66%; mp 93-94 °C; IR (KBr) 3350, 3200, 1660 cm^{-1} ; ^1H NMR (Acetone- d_6 , 100 MHz)

δ 7.8 (m, 2H), 7.4 (m, 4H), 2.3 (s, 3H).

n-Hexamide: Yield 61%; mp 100-101 °C; IR (KBr) 3350, 3200, 1660 cm^{-1} ; ^1H NMR (Acetone- d_6 , 100 MHz) δ 6.5 (b, 2H, NH_2), 2.55 (t, 2H, $J = 8\text{Hz}$), 2.1 (m, 2H), 1.1-1.7 (m, 4H), 0.9 (t, 3H, $J = 8\text{Hz}$).

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