

Tetrahedron 58 (2002) 10323-10328

TETRAHEDRON

A direct synthesis of nitriles and amides from aldehydes using dry or wet alumina in solvent free conditions

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Received 7 August 2002; revised 7 October 2002; accepted 31 October 2002

Abstract—An efficient and simple procedure for the direct conversion of aldehydes into the corresponding nitriles with NH₂OH·HCl/dry Al₂O₃/MeSO₂Cl or amides with NH₂OH·HCl/wet Al₂O₃/MeSO₂Cl are studied. © 2002 Elsevier Science Ltd. All rights reserved.

1. Introduction

Synthetic chemists continue to explore new methods to carry out chemical transformations. One of these new methods is to run reactions on the surface of solids. As the surfaces have properties that are not duplicated in the solution or gas phase, entirely new chemistry may occur. Even in the absence of new chemistry, a surface reaction may be more desirable than a solution counterpart, because the reaction is more convenient to run, or a high yield of product is attained. For these reasons, synthetic surface organic chemistry is a rapidly growing field of study.

Experiments using these solid phase catalysts generally have the following features; (i) it is often easy to isolate the products and to separate the catalyst; (ii) comparing the reaction conditions with those of related homogeneous reactions, they are so mild that a high yield of specific products and suppression of by-product formation are expected; (iii) selectivity and activity of the catalysts are often comparable to those of enzymes.¹ Several classes of solids have commonly been used for surface organic chemistry including aluminas, silica gels, and clays.² Acidic alumina, the material used commonly for column chromatography, is certainly one of the most interesting of these solids because it has surface properties that suggest that a very rich organic chemistry may occur there.

This report describes the efficient application of dry or wet alumina in synthesis of nitriles and amides directly from aldehydes.

The conversion of aldehydes into nitriles is a useful transformation³ and a topic of current interest to organic

chemists. As a result, a number of reagents have been emerged for this purpose, such as triethylamine sulfurdioxide,⁴ sulphuryl chloride fluoride,⁵ montmorillonite KSF,⁶ formamide,⁷ etc.⁸ However, some of these methods suffer from disadvantages such as, preparation of triethylamine sulfurdioxide and sulphuryl chloride fluoride is inconvenient (-70° C), dehydration with KSF, zeolite,^{8b,c} and envirocat EPZG^{8d} requires high temperature or long reaction times.

Therefore, we reasoned that use of an immobilized system, via the application of solid phase reagents, could lead to a more efficient and cleaner route to these important materials.

Here, we decided to apply an inexpensive and environmentally friendly catalyst, dry-alumina, for the preparation of nitriles from aldehydes in one-pot without solvents. The reaction of aldehydes with hydroxylamine hydrochloride (NH₂OH·HCl) and methanesulfonyl chloride (MeSO₂Cl) in dry-alumina to prepare nitriles were found to be clean and fast with high yields. Therefore, the preparation of different alkyl, aryl and heterocyclic nitriles (**2a**-**s**) was performed in dry-alumina, at 100°C in an oil bath (Fig. 1, method A and Table 1). This heterogeneous system offers an easy work-up that includes only a mixing with a suitable solvent, simple filtration to remove the solid material, extraction with water and evaporation of the solvent.



Figure 1.

Keywords: graphite; dry-alumina; wet-alumina; aldehyde.

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Table 1. Conversion of aldehydes into nitriles using dry-alumina

Entry	Reactant 1	Product 2 ^a	t (min)	Yield (%) ^b	IR (KBr) (lit.) ^c	Mp or bp °C/Torr (lit)
a b	CH ₃ CH ₂ CH ₂ CHO CH ₃ CHO	CH ₃ CH ₂ CH ₂ CN CH ₃ CN	45 45	95 92	2248 CN (2222) 2231 CN (2222)	110/760 (118/760) ¹² 80/760 (81/760) ¹²
с	С _s сно		30	85	2224 CN (2222)	190/760 (192/760) ¹⁰
d	CHO	CN N	35	90	2229 CN (2230)	47 (50) ¹²
e	СНО	CN CN	35	90	2213 CN (2220)	34 (35) ⁷
f	СНО	C CN	25	90	2218 CN (2240)	187/760 (190/760) ^{9a}
g	СНО	CN CN	30	97	2235 CN (2222)	160 (162) ¹²
h	CHO	CN	30	95	2243 CN	210
i	СНО	CN CN	35	90	2218 CN (2222)	260/760 (263.8/760) ¹²
j	СІСНО		20	98	2226 CN	140 (145) ¹⁰
k	CHO NH ₂	NH ₂ ^{CN}	20	97	2231 CN (2222)	48 (53) ¹²
1	CHO OH	OH CN	15	94	2237 CN (2222)	80 (83) ¹²
m	CHO NO ₂	CN NO ₂	20	97	2235 CN (2222)	117 (117) ¹²
n	CHO Me	CN Me	25	90	2225 CN (2222)	210/760 (213/760) ¹²
0	Me	Me	20	95	2227 CN (2240)	216/760 (218/760) ^{9a}
р	O ₂ N CHO	O ₂ N CN	25	95	2232CN (2240)	148 (147) ^{9a}
q	CHO NO ₂	CN NO ₂	40	86	2233 CN	109 (109) ¹²
r	СНО	CN OH	35	90	2223 CN	96 (97) ⁷
S	CHO	CN	40	90	2214CN (2222)	42 (42) ⁷
^a Products ^b Yields r ^c Ref. 12.	s were characterized by thei refer to pure isolated produc	r melting points, IR, and N ts.	MR spectra.			

Table 2. Conversion of aldehydes into amides using wet alumina

Entry	Reactant 1	Product 3 ^a	Mp (°C, lit)	<i>t</i> (h)	Yield (%) ^b
a b	CH ₃ CH ₂ CH ₂ CHO CH ₃ CHO	$CH_3CH_2CH_2CONH_2$ CH_3CONH_2	113 (114.8) ¹² 79 (81) ¹²	2 2	90 90
c	CHO N	CONH_2	125 (125) ¹²	3	87
d	СНО	CONH ₂	200 (204) ¹²	1.5	96
e	CHO CI	CI CONH ₂	135 (135.5) ¹²	1	95
f	CHO OH	OH CONH ₂	170 (170.5) ¹²	1	94
g	СНО	CONH ₂	183	2	90
h	CHO NO ₂	NO ₂	140 (141) ¹¹	1	94
i	CHO Me	CONH ₂ Me	92 (95) ¹¹	1	90
j	носно	HO CONH ₂	160 (162) ¹²	1.5	95
k	Me	Mé CONH ₂	163 (163) ¹¹	1.5	94
1	O2N CHO	O ₂ N CONH ₂	200 (201) ¹²	1.5	87
m	CHO OH	CONH ₂ OH	140 (142) ¹²	1	90
n	CHO NO ₂	CONH ₂ NO ₂	176 (176.6) ¹²	3	85
0	CHO	CONH ₂ Cl	142 (142.4) ¹²	3	86
p	CHO NH ₂	NH ₂	79 (80) ¹²	2	90
q	H ₂ N CHO	H ₂ N CONH ₂	183 (183) ¹²	1.5	97
r	CHO NH ₂	CONH ₂ NH ₂	110 (110) ¹²	2.5	88
s	СНО	CONH ₂	130 (127) ¹¹	1.5	90

 $^{\rm a}$ Products were characterized by their melting points, IR, and NMR spectra. $^{\rm b}$ Yields refer to pure isolated products.

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Figure 2.

Table 3. Conversion of aldoximes into nitriles or amides using dry or wet alumina

Entry	Reactant	Reaction condition	Products	t/min	Yield (%) ^a
a	CH ₃ CH ₂ CH ₂ CH=NOH	Dry-Al2O3/MeSO2Cl	CH ₃ CH ₂ CH ₂ CN	5	95
b	⟨_ _S ↓ _{CH=NOH}	Dry-Al ₂ O ₃ /MeSO ₂ Cl		8	85
с	CH=NOH	Dry-Al ₂ O ₃ /MeSO ₂ Cl	CN CCN	15	90
d	Me0 CH=NOH	Dry-Al ₂ O ₃ /MeSO ₂ Cl	MeO	10	94
e	CH=NOH NO ₂	Dry-Al ₂ O ₃ /MeSO ₂ Cl	CN NO ₂	4	97
f	CH=NOH Me	Dry-Al ₂ O ₃ /MeSO ₂ Cl	CN Me	5	90
g	CH=NOH OH	Dry-Al ₂ O ₃ /MeSO ₂ Cl	CN OH	5	94
h	CH=NOH	Wet-Al ₂ O ₃ /MeSO ₂ Cl	CONH ₂	15	90
i	CH ₃ (CH ₂) ₃ CH=NOH	Wet-Al ₂ O ₃ /MeSO ₂ Cl	CH ₃ (CH ₂) ₃ CONH ₂	20	92
j	HO CH=NOH	Wet-Al ₂ O ₃ /MeSO ₂ Cl	HO CONH ₂	15	90
k	CI CH=NOH	Wet-Al ₂ O ₃ /MeSO ₂ Cl	CI CONH ₂	20	97
1	CH=NOH OMe	Wet-Al ₂ O ₃ /MeSO ₂ Cl	CONH ₂ OMe	18	94

^a Yields refer to pure isolated products.

We found that, under the same reaction conditions, when the alumina was wet, amides were obtained in high yields. Now, we report a high yield preparation of amides from aldehydes with wet-alumina under solvent-free conditions (Fig 1, method B, Table 2).

The results indicate that this methodology gives good yields of aryl, alkyl and heterocyclic amides from aldehydes when reacted with a mixture of $NH_2OH \cdot HCl/wet$ alumina/MeSO₂Cl at 100°C without use of any solvents (Table 2). The work-up of the reaction mixture was clean

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and a quick process, and the yields of the products were high.

The effect of dry and wet alumina was evaluated in these reactions. As shown in Fig. 2, the first step, in both reactions, involves the formation of an aldoxime followed by its reaction with MeSO₂Cl to generate compound 4, as the key intermediate. In the presence of dry-alumina (method A) compound 4 subsequently undergoes elimination thermally to produce nitrile 2 with the liberation of MeSO₃H. On the other hand, when wet-alumina was used (method B), the nitrile 2 underwent rapid hydration to produce amide 3.

According to Fig. 2, we found that our new methods also be useful for conversion of aldoximes in the presence of dryalumina to produce nitriles and in the presence of wetalumina to produce amides in high yields. Some of these results are summarized in Table 3.

In summary, this paper shows a simple and efficient general access to pure nitriles and amides. These two important materials could be synthesized in overall yields of 85-97% from their corresponding aldehydes. The catalysts, dry and wet alumina, which have been used here for the first time for such conversions are inexpensive and commercially available. The reaction was carried out in dry media and no solvents were used. The work-ups were easy and the experimental procedures are environmentally benign.

2. Experimental

2.1. Typical procedure for synthesis of nitriles in the presence of dry-alumina (Table 1)

Aldehyde (1 mmol), NH₂OH·HCl (0.3 g, 0.4 mmol), MeSO₂Cl (0.075 mL, 1 mmol) and dry Alumina (0.5 g, 4.9 mmol, Fluka type 405 acidic, dried in an oven for 5 h) were thoroughly mixed with a mechanical stirrer. The resulting fine powder was transferred to a round-bottom flask (5 mL) and heated in an oil bath at 100°C for appropriate time (Table 1). Then diethyl ether (10 mL) was added to the reaction mixture and alumina was removed by filtration. The filtrate was extracted with water (2×10 mL), dried over Na₂SO₄ and the solvent evaporated in vaccuo to give the crude product, which solids were purified by recrystallization from EtOH and liquids by distillation.

2.1.1. 1-Phenylethyl cyanide (entry h, Table 1). Hydratropaldehyde (0.13 g, 1 mmol), NH₂OH·HCl (0.3 g, 0.4 mmol), MeSO₂Cl (0.075 mL, 1 mmol) and dry Alumina (0.5 g, 4.9 mmol, Fluka type 405 acidic) were thoroughly mixed with a mechanical stirrer. The resulting fine powder was transferred to a round-bottom flask (5 mL) and heated in an oil bath at 100°C for 40 min. Then diethyl ether (10 mL) was added to the reaction mixture and alumina was removed by filtration. The filtrate was extracted with water (2×10 mL), dried over Na₂SO₄ and the solvent evaporated in vaccuo. Purification of the crude product by recrystallization from EtOH gave the title compound (95%) as a white solid. Mp 210°C; ν_{max} (KBr) 3146, 2243, 1683, 1496, 1454, 1078, 1029, 835, 765, 703 cm⁻¹; $\delta_{\rm H}$ (250 MHz, CDCl₃)

7.10–7.27 (5H, m, Ph), 4.33 (1H, m, CHMe), 1.70 (3H, d, Me); $\delta_{\rm C}$ (250 MHz, CDCl₃) 20.47, 28.79, 120.75, 126.22, 126.78, 129.33, 132.8; MS: M⁺ (131).

2.2. Typical procedure for synthesis of amides in the presence of wet-alumina (Table 2)

Aldehyde (1 mmol), NH₂OH·HCl (0.3 g, 0.4 mmol), MeSO₂Cl (0.075 mL, 1 mmol) and wet Alumina (0.5 g, 4.9 mmol, Fluka type 405 acidic, to make it wet only one drop of water was added) were thoroughly mixed with a mechanical stirrer. The resulting fine powder was transferred to a round-bottom flask (5 mL) and heated in an oil bath at 100°C for appropriate time (Table 2). Then ethyl acetate was added to the reaction mixture and alumina was removed by filtration. The filtrate was extracted with water (2×10 mL), dried over Na₂SO₄ and the solvent evaporated in vaccuo to give the crude product, which was purified by recrystallization from EtOH.

2.3. Typical procedure for synthesis of nitriles or amides from oximes in the presence of dry or wet alumina (Table 3)

A mixture of aldoxime (1 mmol), CH_3SO_2Cl (1 mmol, 0.075 mL) and dry or wet alumina (0.5 g, 4.9 mmol) was heated in an oil bath at 100°C. The progress of the reaction was monitored by TLC. After the reaction was complete, ethyl acetate was added to the reaction mixture and alumina was removed by filtration. It was then washed with water (2×10 mL) and dried over anhydrous Na_2SO_4 . After removal of the solvent, the crude product was obtained and purified by recrystallization from EtOH.

Acknowledgements

We gratefully acknowledge the support of this work by the Shiraz University Research Council.

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