

Nano-TiCl₄.SiO₂ Promoted One-Pot Synthesis of Amides or Nitriles from Aldehydes

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Abstract

This research proposes an efficient and easy procedure for the preparation of amides or nitriles from aldehydes. Such materials were prepared via one-pot three component condensation reaction of various aldehydes in the presence of nano-TiCl₄.SiO₂ as a catalyst under thermal conditions. All reactions proceeded in high yields and in a moderately short reaction time. Meanwhile, oximes were obtained from aldehydes in the presence of nano-TiCl₄.SiO₂.

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Introduction

Amides retain critical importance both in research and industrial chemistry owing to their frequent use in detergents, lubricants, biologically-active compounds and pharmaceuticals (1). Most traditional methods for the preparation of amides are condensation of activated carboxylic acids with amines or Beckmann rearrangement (2) of oximes. In hard condition, the dehydration of oximes or amides produce nitriles which are highly important in the synthesis of 1,2-diarylimidazoles (3), thiazoles (4) and tetrazoles (5). Nitriles are widely transformed into amides, amines, esters and carboxylic acids. Hence they have been used in the synthesis of fine chemicals including agricultural chemicals, dyes and medicines. One of the most general methods for the synthesis of

nitriles is the nucleophilic substitution reaction of alkyl halides with metal cyanides. The method is however inconvenient due to high toxicity of metal cyanides and troublesome handling. Consequently, other methods such as dehydration of primary amides or aldioximes have attracted attention.

Previously, Cu(OAc)₂ (6), H₂SO₄ (7) and NaOCl/Bu₄NHSO₄ (8) were applied for one-pot conversion of aldehydes to amides procedure KF/Al₂O₃ (9). In addition, aqueous sodium dichloroiodate (10) has been reported as good catalyst for one-pot production of nitriles from aldehydes.

We have previously described the design and synthesis of some organic reactions in the presence of solid acid catalysts as a green, cheap and efficient method (11-16).

Experiments

Chemistry

The chemicals were purchased from Merck and used without any additional purification. The products were characterized by FT-IR (ATR), ¹H-NMR, and a comparison of their physical properties with those reported in the literature. FT-IR (ATR) spectra were acquired on a Bruker, Equinox 55 spectrometer. A Bruker (DRX-400 Avance) nmr was used to record the ¹H NMR spectra. In spectrophotometry (UV/Vis biotek model UVIKONXL), melting points were determined with a Thermo Scientific Electrothermal digital apparatus (Thermo Fisher Scientific Inc.).

General procedure for the synthesis of amides from aldehydes

A mixture of aldehyde (1 mmol), sodium acetate (1 mmol), hydroxyl amine hydrochloride (1 mmol) and nano-TiCl₄.SiO₂ (0.1) was heated at 120 °C. The progress of the reaction was monitored by TLC. Upon completion of the reaction, the mixture was extracted with ethylacetate and the solvents were removed. The product was purified by recrystallization from chloroform n-hexane (2:1). All products were known and characterized by physical and spectroscopic data.

General procedure for the synthesis of oximes from aldehydes

A mixture of aldehyde (1 mmol), sodium acetate (1 mmol), hydroxyl amine hydro chloride (1 mmol) and nano-TiCl₄.SiO₂ (0.1 g) was heated at 100 °C. The progress of the reaction was monitored by TLC. Upon completion of the reaction, ethyl acetate was added and filtrated to remove catalyst. After removing of ethylacetate, the product achieved pure solid state which was washed with water.

General procedure for the synthesis of nitriles from aldehydes

A mixture of aldehyde (1 mmol), sodium acetate (1 mmol), hydroxyl amine hydrochloride (1 mmol) and nano-TiCl₄.SiO₂ (0.1 g) in DMF¹ reflux was used. The progress of the reaction was monitored by TLC. Upon completion of the reaction, the mixture was filtrated for the separation of catalyst. DMF was removed in reduced pressure to give the crude nitrile. All products were known and identified through comparing their physical and spectroscopic data with those of authentic samples.

Results and discussion

In order to examine the one-pot synthesis of amides or nitriles from aldehydes we have reacted 4-nitrobenzaldehyde with hydroxylamine hydrochloride and sodium acetate in the presence of nano-TiCl₄.SiO₂ under various conditions (Table 1). Depending on to reaction conditions, we obtained various products such as amide, oxime or nitrile. Reaction under solvent-free conditions at 100 °C gave rise to the expected oxime in a good yield (Table 1, Entry 13).

Rising of temperature to 150 °C, 4-nitrobenzamide was produced (Table 1, Entry 11). In addition, using reflux condition in DMF achieved 4-nitrobenzoxime (Table 1, Entry 14). The catalyst could be reused up to 3 times without losing its activity in amide formation at 150 °C as shown in Figure. 1 and Table 1, Entries 15 and 16. Then, the optimized protocol was applied to other substrates in order to study the scope of the amide formation (Table 2, Scheme 1). The reaction gave an excellent result about electron-withdrawing group bearing substrates with any influence of position of substituent in yields (Table 2, Entries 4-6).

¹. *N,N*-Dimethylformide (DMF)

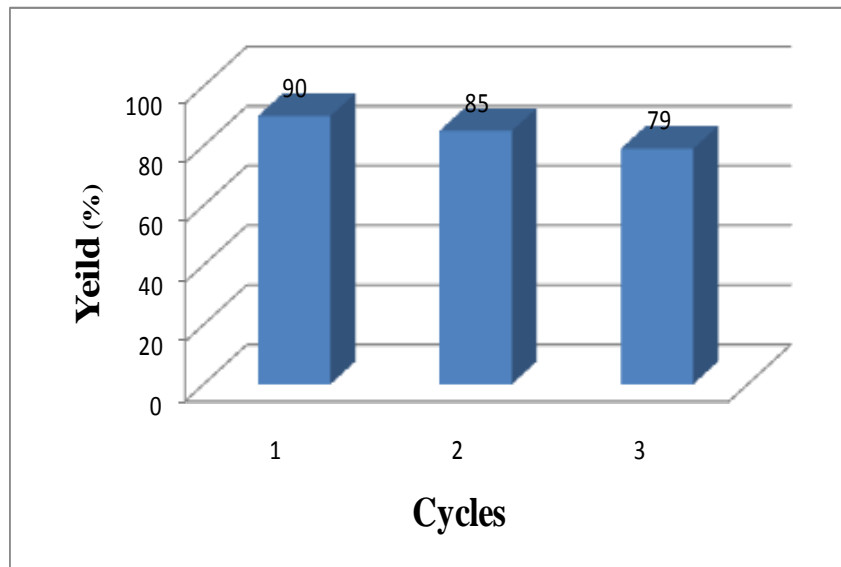
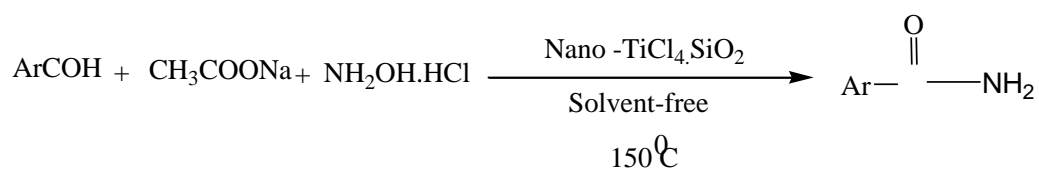


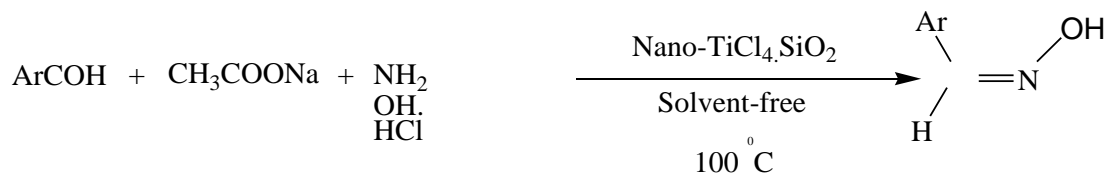
Figure 1. The catalyst could be reused up to 3 times without losing its activity in amide formation at 150°C.

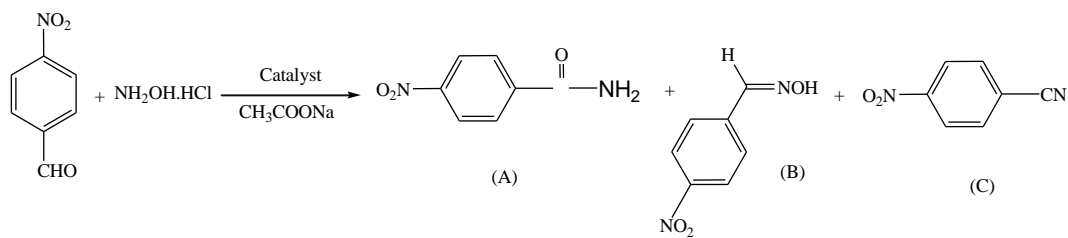


Scheme 1

Oximes have been achieved by the same protocol under lower temperature. Various aldehydes have converted to corresponding oximes in the presence

of nano-TiCl₄.SiO₂ under solvent-free conditions at 100°C (Scheme 2 and Table 3).



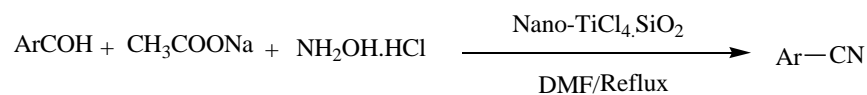


Scheme 2

Table 1. Synthesis of 4-nitrobenzamide (A), 4-nitrobenzaloxime (B) and 4-nitrobenzonitrile (C) from 4-nitrobenzaldehyde under various conditions. The molar ratio of 4-nitrobenzaldehyde: sodium acetate: hydroxyl amine hydrochloride: is 1:1:1.

Entry	Catalyst(g)	Solvent	Conditions	Time (h)	Yield (%) Amide (A) ^{Ref}	Yield (%) Oxime (B) ^{Ref}	Yield (%) Nitrile (C) ^{Ref}
1	TiCl ₄ .SiO ₂ (0.2)	Solvent-free	100 °C	3	trace	80	-
2	TiCl ₄ .SiO ₂ (0.2)	Solvent free	150 °C	5	80	trace	-
3	TiCl ₄ .SiO ₂ (0.2)	Solvent free	150 °C	5	85	trace	-
4	TiCl ₄ .SiO ₂ (0.2)	Solvent free	150 °C	5	90	trace	-
5	Nano-TiCl ₄ .SiO ₂ (0.1)	DMF	Reflux	3	45	trace	55
6	Nano-TiCl ₄ .SiO ₂ (0.1)	Toluene	Reflux	3	42	trace	45
7	Nano-TiCl ₄ .SiO ₂ (0.1)	Dioxane	Reflux	3	30	trace	32
8	Nano-TiCl ₄ .SiO ₂ (0.1)	Solvent free	MM ^b	40 min	-	-	-
9	Nano-TiCl ₄ .SiO ₂ (0.1)	EtOAc	Sonication ^c	30 min	-	-	-
10	Nano-TiCl ₄ .SiO ₂ (0.1)	Solvent free	MW ^d	20 min	60	30	-
11	Nano-TiCl ₄ .SiO ₂ (0.1)	Solvent-free	150 °C	3	90	trace	-
12	Nano-TiCl ₄ .SiO ₂ (0.05)	Solvent-free	150 °C	3	82	trace	-
13	Nano-TiCl ₄ .SiO ₂ (0.1)	Solvent-free	100 °C	1.5	trace	92	-
14	Nano-TiCl ₄ .SiO ₂ (0.1)	DMF	Reflux	7	-	-	98
15	Nano-TiCl ₄ .SiO ₂ (0.1), 2 nd run	Solvent-free	150 °C	3	85	trace	-
16	Nano-TiCl ₄ .SiO ₂ (0.1), 3 rd run	Solvent-free	150 °C	3	79	trace	-
17	2mol% Cu(OAc) ₂	H ₂ O	110 °C	2d	99 ⁶	-	-
18	H ₂ SO ₄	CH ₃ CN	Reflux	8	80 ⁷	-	-
19	NaOCl/Bu ₄ NHSO ₄	PEG-40	120 °C	-	50 ⁸	-	-
20	2mol% Cu(OAc) ₂	Dioxane	110 °C	3d	-	99 ⁶	-
21	KF/Al ₂ O ₃	DMF	100 °C	4	-	-	89 ⁹
22	Aqueous sodium dichloroiodate	Aqueous ammonia	r.t.	4	-	-	90 ¹⁰

Nitriles have been synthesis by the similar procedure under reflux condition in the presence of nano-TiCl₄.SiO₂. Various aldehydes have converted to corresponding oximes in DMF under solvent-free conditions at 100 °C (Scheme 3 and Table 4).



Scheme 3

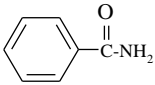
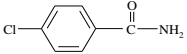
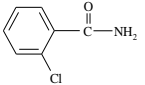
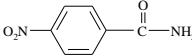
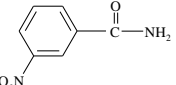
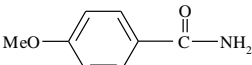
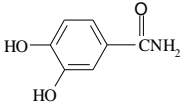
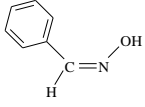
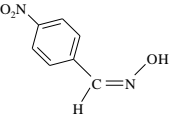
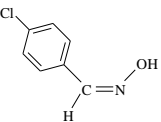
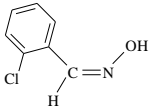
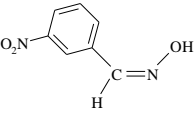
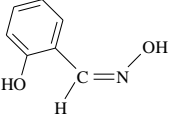
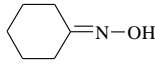
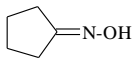
Entry	Products	Time (h)	Yield ^b
1		3	90
2		3	92
3		3	91
4		2.5	93
5		2.5	93
6		4	87
7		4	89

Table 2. One-pot preparation of amides from aldehydes in the presence of nano-TiCl₄.SiO₂a. A mixture of aldehyde (1 mmol): sodium acetate (1 mmol): hydroxyl amine hydrochloride (1 mmol) and nano-TiCl₄.SiO₂ (0.1 g) was heated at 150 °C.

Table 3. Preparation of oximes from aldehydes in the presence of nano-TiCl₄.SiO₂. The ratio of aldehyde (mmol): sodium acetate

Entry	Products	Time (h)	Yield ^a
1		1.5	90
2		1.5	92
3		2	91
4		2	89
5		1.5	93
6		3	87
7		3	72
8		3	78

(mmol): hydroxyl aminhydrochloride (mmol): nano-TiCl₄.SiO₂ (g) is 1: 1: 1: 0.1.

Representative data for the selected synthesis compounds

4-Chlorobenzamide (Table 2, entry 2):

Yield: 92%, White crystal, mp 172-74 °C. FT-IR: $\bar{\nu}$ (ATR) = 3364, 3169, 1653, 1590, 1566, 1492, 1403, 1272, 1086, 844 cm⁻¹

4-Chlorobenzaldehyde Oxime (Table 3, entry 3):

Yield: 91%, White crystal, mp 106-107 °C, FT-IR: $\bar{\nu}$ (ATR) = 3238, 2924, 1657, 1596, 1561, 1492, 1407, 1090, 971, 872, 821 cm⁻¹

4-Chlorobenzonitril (Table 4, entry 6):

Yield: 94%, White crystal, mp 88-89 °C, FT-IR: $\bar{\nu}$ (ATR) = 3092, 2226, 1656, 1592, 1484, 1398, 1089, 828 cm⁻¹

Benzamide (Table 1, entry 1):

Yield: 90%, White crystal, mp 124-126 °C. FT-IR: $\bar{\nu}$ (ATR) = 3362, 3166, 1622, 1577, 1448, 1395 cm⁻¹

Benzaldehyde Oxime (Table 3, entry 1):

Yield: 90%, White crystal, mp 31-33 °C. FT-IR: $\bar{\nu}$ (ATR) = 3032, 1682, 1591, 1409, 1286, 936, 805, 754 cm⁻¹

Benzonitril (Table 4, entry 1):

Yield: 95%, White crystal, mp 214-216 °C. FT-IR: $\bar{\nu}$ (ATR) = 3066, 2229, 1599, 1491, 1448, 1288, 1178, 1071, 1026, 972, 760, 688 cm⁻¹

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2-Chlorobenzamide (Table 2, entry 3):

Yield: 91%, White crystal, mp 141-143 °C. FT-IR: $\bar{\nu}$ (ATR) = 3372, 3182, 2927, 1661, 1592, 1532, 1473, 1436, 1401, 1053, 756, 670 cm⁻¹.

2-Chlorobenzaldehyde Oxime (Table 4, entry 4):

Yield: 89%, White crystal, mp 69-71 °C. FT-IR: $\bar{\nu}$ (ATR) = 3279, 1628, 1592, 1566, 1480, 1308, 753, 629 cm⁻¹

3-Nitrobenzamide (Table 2, entry 5):

Yield: 93%, White crystal, mp 131-133 °C. FT-IR: $\bar{\nu}$ (ATR) = 3382, 3171, 2932, 2843, 1704, 1640, 1573, 1414, 1045, 804, 647 cm⁻¹

3-Nitrobenzaldehyde Oxime (Table 3, entry 5):

Yield: 93%, White crystal, mp 121-122 °C (Lit. [207] 119-120 °C).

FT-IR: $\bar{\nu}$ (ATR) = 3295, 1619, 1537, 1467, 1351, 981, 842, 734, 670 cm⁻¹

3-Nitrobenzonitril (Table 4, entry 5):

Yield: 95%, White crystal, mp 112-114 °C. FT-IR: $\bar{\nu}$ (ATR) = 3080, 2237, 1619, 1534, 1474, 1356, 903, 816, 789, 734, 668 cm⁻¹

4-Nitrobenzamide (Table 2, entry 4):

Yield: 93%, White crystal, mp 201-203 °C. FT-IR: $\bar{\nu}$ (ATR) = 3315, 3179, 3075, 2924, 1708, 1670, 1524, 1347, 859 cm⁻¹

4-Nitrobenzaldehyde Oxime (Table 3, entry 2):

Yield: 92%, White crystal, mp 132-133 °C. FT-IR: $\bar{\nu}$ (ATR) = 3303, 1606, 1537, 1530, 1321, 1108, 969, 845 cm⁻¹

4-Nitrobenzonitril (Table 4, entry 4):

Yield: 98%, White crystal, mp 147-149 °C (Lit. [208] 144-147 °C).

FT-IR: $\bar{\nu}$ (ATR) = 3106, 2233, 1602, 1525, 1488, 1349, 859 cm⁻¹

4-Methoxybenzamide (Table 2, entry 6):

Yield: 84%, White crystal, mp 162-163 °C. FT-IR: $\bar{\nu}$ (ATR) = 3378, 3175, 1656, 1606, 1574, 1510, 1399, 1258, 1175, 1024, 831 cm⁻¹

4-Methoxybenzonitril (Table 4, entry 8):


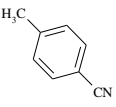
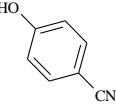
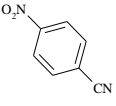
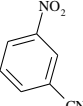
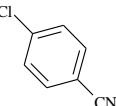
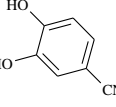
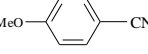
Yield: 84%, White crystal, mp 57-58 °C. FT-IR: $\bar{\nu}$ (ATR) = 3038, 2923, 2225, 1663, 1603, 1509, 1274, 1198, 818 cm⁻¹

3, 4-dihydroxybenzamide (Table 2, entry 7):

Yield: 87%, White crystal, mp 150-151 °C. FT-IR: $\bar{\nu}$ (ATR) = 3324, 3142, 2929, 1651, 1601, 1523, 1403, 1290, 1265, 1115, 951, 812 cm⁻¹

3, 4-Dihydroxybenzonitril (Table 4, entry 7):

Yield: 91%, White crystal, mp 155-156 °C. FT-IR: $\bar{\nu}$ (ATR) = 3289, 2233, 1613, 1586, 1500, 1439, 1364, 1284, 837, 702 cm⁻¹

Entry	Products	Time (h)	Yield ^b
1		7	95
2		8	92
3		8	91
4		7	98
5		7	95
6		8.5	94
7		8	89
8		7	84

Conclusion

Nano-TiCl₄.SiO₂ has shown to be highly efficient and reusable catalyst for one-pot synthesis of amides or nitriles from aldehydes under various conditions. Meanwhile, oximes were obtained from aldehydes in the presence of this catalyst with good to excellent yields.

Acknowledgment

Authors would like to acknowledge the Research Council of Yazd University for financial support in the design and synthesis of the compounds.

Table 4: One-pot synthesis of nitriles from aldehydes in the presence of nano-TiCl₄.SiO₂a ^aThe ratio of aldehyde (mmol): sodium acetate (mmol): hydroxyl amin hydro chloride (mmol): nano-TiCl₄.SiO₂ (g) is 1: 1: 1: 0.1.

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