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Article

Nano-sized NiLa_2O_4 spinel– NaBH_4 -mediated reduction of imines to secondary amines

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ABSTRACT

Nano-sized NiLa_2O_4 spinel was produced by thermal decomposition of Ni–La compounds via a sol-gel method. The well-crystallized spinel structure was formed after calcination at 750 °C. The physicochemical properties of the spinel were investigated using differential thermal analysis, X-ray diffraction, transmission electron microscopy, scanning electron microscopy, and particle size distribution analysis. The results show that the nanoparticles have regular shapes with well-defined crystal faces and consist of uniform quasi-spherical crystallites of average size 40 nm. The refined unit cell parameters are $a = 3.861205 \text{ \AA}$ and $c = 12.6793 \text{ \AA}$. This new nano-sized NiLa_2O_4 spinel is an efficient heterogeneous catalyst for the selective conversion of imines to the corresponding secondary amines in the presence of NaBH_4 as a reducing agent, in good to excellent yields. All the reactions were completely chemoselective at room temperature and had relatively short reaction times. Secondary amines with different aryl groups, including those bearing electron-withdrawing or electron-donating groups, were obtained under the optimum reaction conditions. The catalyst was readily recovered and was recycled four times with no significant loss of catalytic activity.

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1. Introduction

Imine reduction to the corresponding amine is a widely used and important functional group transformation reaction in synthetic organic chemistry. Many amines are used in the pharmaceutical and agricultural industries [1–7]. Two approaches are commonly used to convert imines to amines. One is catalytic hydrogenation, which requires high pressure. The other is hydride reduction, which uses metal hydrides such as LiAlH_4 or NaBH_4 [8]. LiAlH_4 is normally used in a dry organic solvent in a protective inert atmosphere [9,10]; in contrast, NaBH_4 is an inexpensive, safe, and environmentally friendly reducing agent. Various Lewis acids such as LiCl [11], TiCl_4 [12], TiCl_3 [13], Ni_2B [14], I_2 [15], ZrCl_4 [16], and CoCl_2 [17] have been used to reduce C=N bonds in the presence of NaBH_4 , but

they are not always effective.

Spinel oxides play important roles in various catalytic applications, e.g., gaseous pollutant decomposition [18] and the water-gas-shift reaction [19]. In normal spinels, AB_2O_4 , A is generally a divalent cation occupying tetrahedral sites, and B is a trivalent cation occupying octahedral sites. In inverse spinels, half of the B cations occupy tetrahedral sites, and the formula is $\text{B}(\text{AB})\text{O}_4$.

Spinel oxides are prepared using various methods, including hydrothermal synthesis [20], modified oxidation processes [21], forced hydrolysis [22], and ball-milling [23], solid-state [24], and microemulsion methods [25]. Sol-gel methods are preferred because they are effective and convenient techniques and use less energy and materials [26].

In this study, as part of our research on organic transfor-

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Scheme 1. Imines to the corresponding secondary amines by NaBH_4 and NiLa_2O_4 .

mations using simple reagents, catalysts, and reaction media [27], we investigated the direct reduction of imines to the corresponding secondary amines by NaBH_4 in the presence of a catalytic amount of nano-sized NiLa_2O_4 spinel (Scheme 1).

2. Experimental

2.1. Preparation of NiLa_2O_4 powders

Citric acid (18 mmol, 3.50 g) was gradually added to a solution of LaCl_3 (4 mmol, 1.48 g) and $\text{Ni}(\text{NO}_3)_2 \cdot 4\text{H}_2\text{O}$ (2 mmol, 0.58 g) in deionized water (10 mL), with constant magnetic stirring. The gel was heated at 80 °C for 3 h and dried at 120 °C for 24 h. It was then ground to a powder in an agate mortar and fired at 750 °C in air for 4 h.

2.2. Characterization

Decomposition of the dried polymeric gel precursor was investigated using differential thermal analysis (DTA; NETZSCH, Germany) at a heating rate of 10 °C/min in the range 25–1000 °C. Crystal structures were examined by X-ray diffraction (XRD; Xpert 200, Philips, $\text{Cu K}\alpha$ radiation) at a scanning rate of 0.02°/s in the 2θ range 0° to 70°. The morphologies and dimensions of the nanoparticles were examined using transmission electron microscopy (TEM; LEO 912AB, accelerating voltage 120 kV). The morphologies of the calcined powders were examined using scanning electron microscopy (SEM; LEO 1450VP, accelerating voltage 120 kV).

2.3. General procedure for imine reduction to amines

NaBH_4 (0.37 mmol, 0.014 g) was added at room temperature to a stirred mixture of the appropriate imine (0.5 mmol) and nano-sized spinel NiLa_2O_4 (0.3 mol%, 6.0 mg) in CH_2Cl_2 (1 mL). Methanol (1 mL) was added slowly under constant magnetic stirring. On completion of the reaction, which was monitored using thin-layer chromatography (TLC; *n*-hexane:ethyl acetate = 8:2), the catalyst was removed by centrifugation and the solvent was evaporated under reduced pressure. Addition of water (10 mL) gave an oily liquid; the mixture was extracted with CH_2Cl_2 (2×10 mL). The combined organic layers were dried over anhydrous Na_2SO_4 and the solvent was evaporated under reduced pressure to afford the product. The sample purity was confirmed using TLC and ^1H nuclear magnetic resonance (NMR) spectroscopy.

3. Results and discussion

3.1. Thermal analysis

Figure 1 shows the DTA curve of the NiLa_2O_4 gel precursor

Fig. 1. DTA curve of NiLa_2O_4 gel precursor obtained using the sol-gel method.

obtained using the sol-gel method. The DTA curve has a large endothermic peak at around 100 °C, which is related to the evaporation of water. The combustion of organic compounds such as citric acid causes the exothermic peak at around 200 °C. The small exothermic peak at 350 °C is attributed to the decomposition of nitrate, which decomposes completely at around 420 °C, giving a large exothermic peak [28]. The exothermic peak at 750 °C corresponds to crystallization of the NiLa_2O_4 phase. No obvious change is observed above 800 °C. It is therefore concluded that the optimum calcination temperature is 750 °C.

3.2. XRD analysis

Figure 2 shows the XRD pattern of spinel-type NiLa_2O_4 , which was formed when the gel was calcined at 750 °C for 4 h. No secondary phase is observed. The good agreement between the experimental and calculated data confirms that the sample consists of a single phase. Rietveld refinement showed that the material had a tetragonal unit cell with the I_4/mmm space group. The refined unit cell parameters were $a = 3.861205$ Å and $c = 12.6793$ Å. The unit cell volume was 189.035 Å³, which is in close agreement with the results reported in the literature [29].

3.3. Powder morphology

Figure 3 shows a TEM image of the NiLa_2O_4 nanoparticles prepared at 750 °C. It shows that nanoparticles were homogeneous and consisted of uniform quasi-spherical crystallites of

Fig. 2. XRD pattern of NiLa_2O_4 nanopowder sintered at 750 °C.

Fig. 3. TEM image of nano-sized NiLa_2O_4 spinel calcined at 750 °C.

average size 40 nm. This is in agreement with the results obtained using XRD [30].

The nanoparticle size affects many properties of nanomaterials and is a major indicator of quality and performance. Figure 4 shows the nano- NiLa_2O_4 spinel particle size distribution; this was determined from the TEM image based on more than 100 particles.

The SEM image in Fig. 5 of the NiLa_2O_4 nanoparticles prepared using the sol-gel method shows the typical morphology of the obtained powder. It shows that the nanoparticles had regular shapes with well-defined crystal faces [31].

3.4. Catalysis of reduction of imines to amines by NiLa_2O_4 spinel nanoparticles

The imines were synthesized by treatment of the corresponding carbonyl compounds with the appropriate amines, using a previously reported method [32,33]. *N*-(4-chlorobenzylidene)aniline was used as a model compound for optimization of the catalytic conditions for reductive hydrogenation.

Various solvents were screened for the reduction of *N*-(4-chlorobenzylidene)aniline with NaBH_4 using NiLa_2O_4 spinel nanoparticles as a catalyst (Table 1). The results show that CH_2Cl_2 was the best solvent in terms of activity. The polarity of CH_2Cl_2 is appropriate for dissolving the reactant, and appropriate interactions between the hydrogenated surface of the nanocatalyst and the substrate are triggered. Furthermore, CH_2Cl_2 is a solvent with a low moisture content, toxicity, and

Fig. 4. Particle size distribution for calcined nano-sized NiLa_2O_4 spinel catalyst.

Fig. 5. SEM image of nano-sized NiLa_2O_4 prepared by a sol-gel method.

boiling point, and is used in many organic transformations.

The catalytic role of the nano-sized NiLa_2O_4 spinel was clarified by performing the model reaction in the absence of a nanocatalyst and in the presence of the micro- NiLa_2O_4 spinel catalyst (Table 2, entries 1 and 2). Neither reaction was complete after 60 min. The reduction of *N*-(4-chlorobenzylidene)aniline was then performed using different molar ratios of the nanocatalyst to identify the optimum reaction conditions. The results show that the minimum amount of nanocatalyst needed to significantly affect the reduction process was 0.3 mol%, with 0.75 equiv. of NaBH_4 (Table 2, entry 9). The results also show that the use of 0.15 mol% of nanocatalyst gave a low conversion because of the lack of appropriate surface active sites at low nanocatalyst concentrations (Table 2, entry 10).

Table 1

Solvent optimization for chemoselective reduction of *N*-(4-chlorobenzylidene)aniline to *N*-(4-chlorobenzyl)aniline.

Solvent	Time (min)	Conversion ^a (%)
DMF	30	90
THF	30	88
CH_2Cl_2	5	97
CHCl_3	5	96
<i>n</i> -Hexane	5	85

Reaction conditions: *N*-(4-chlorobenzylidene)aniline 1 mmol, nano-sized NiLa_2O_4 spinel 1 mg, solvent 2 mL, NaBH_4 4 eq., room temperature.

^a Based on ^1H NMR spectroscopic integrations.

Table 2

Data for reduction of *N*-(4-chlorobenzylidene)aniline to *N*-(4-chlorobenzyl)aniline.

Entry	Nano-sized NiLa_2O_4 (mol%)	NaBH_4 (eq.)	Time (min)	<i>t</i> (°C)	Conversion ^a (%)
1	None	4	60	25	40
2	Micro- NiLa_2O_4 (1 mol %)	4	60	25	63
3	1	4	10	25	95
4	1	2	10	25	96
5	1	1	10	25	98
6	1	0.75	10	25	97
7	1	0.50	10	25	50
8	0.6	0.75	10	25	97
9	0.3	0.75	10	25	95
10	0.15	0.75	60	25	50
11	0.3	0.75	35	0	73
12	0.3	0.75	6	40	96

^a According to TLC monitoring and ^1H NMR spectroscopic integration.

Table 3Substrates tested in reduction of imines to amines with NaBH₄ in the presence of nano-sized NiLa₂O₄.

Entry	Imine	Time (min)	Sec-amine	Yield ^a (%)	TOF ^b (h ⁻¹)	Entry	Imine	Time (min)	Sec-amine	Yield ^a (%)	TOF ^b (h ⁻¹)
1		10		98	1963	10		15		92	1228
2		15		90	1202	11		2		92	9212
3		15		97	1295	12		2		88	8812
4		20		97	971	13		5		85	3405
5		5		90	3605	14		15		95	1268
6		2		95	9513	15		5		97	3885
7		2		98	9813	16		15		91	1215
8		5		92	3685	17		15		86	1155
9		10		86	1722						

Reaction conditions: Substrate 0.5 mmol, NiLa₂O₄ spinel nanoparticles 6 mg, CH₂Cl₂ 1 mL, MeOH 1 mL, NaBH₄ 0.75 eq., room temperature.^a Determined by ¹H NMR spectroscopy.^b Turnover frequency defined as mmoles of products obtained per mmoles of catalyst per hour.

Table 3 shows the general applicability of the current method in the synthesis of a wide variety of secondary amines. The reactions were performed by mixing the synthesized imines with NaBH₄ in methanol in an ambient atmosphere until TLC showed the complete disappearance of the imine and formation of the corresponding secondary amine. In all cases, excellent yields of secondary amines with different aryl groups, including those bearing electron-withdrawing or electron-donating groups, were obtained in short reaction times under the optimum reaction conditions.

The mechanism of heterogeneous hydrogenation is unclear, partly because the reactive sites on the metal surface cannot be as precisely described as can small molecule reagents in solution. However, it is probable that hydrogen is adsorbed onto the surface of the catalyst, forming metal–hydrogen bonds; this type of intermediate has been implicated in the hydrogenation

of unsaturated double bonds, particularly on the nanoscale [34–36]. A suggested mechanism for the reduction of imines to their corresponding secondary amines over the nano-sized NiLa₂O₄ spinel catalyst in the presence of NaBH₄ is shown schematically in Scheme 2.

The nano-sized NiLa₂O₄ spinel catalyst is insoluble in organic solvents, therefore it can easily be recovered. The catalyst reusability was examined under the optimum reaction conditions, using *N*-(4-chlorobenzylidene)aniline reduction as a model reaction. In each cycle, the catalyst was recovered, washed with ethyl acetate, and dried before use in the next reaction. It is important to note that the catalyst was reused four times without significant loss of activity and selectivity, as shown in Fig. 6.

The SEM and TEM images of the nano-sized NiLa₂O₄ spinel after the fourth cycle are shown in Fig. 7. The surface rough-

Scheme 2. Proposed mechanism for the reduction of imines to secondary amines.

Fig. 6. Recycling of NiLa_2O_4 spinel nanopowder in selective reductive hydrogenation of imines to corresponding secondary amines.

Fig. 7. SEM (a) and TEM (b) images of nano-sized NiLa_2O_4 spinel after fourth cycle.

ness of the used catalyst increased, which could be attributed to carbon deposition on the catalyst surface, but its activity did not decrease significantly.

A literature survey was performed to compare this method with some previously reported methods, including NaBH_4 reductive hydrogenation of imines. As shown in Table 4, the nano-sized NiLa_2O_4 spinel is an efficient catalyst for this selective reduction.

Table 4

Comparison of some other catalysts with nano-sized NiLa_2O_4 spinel.

Catalyst	Amount of catalyst (eq.)	Temperature ($^{\circ}\text{C}$)	Time (min)	Amount of NaBH_4 (eq.)	Yield (%)	Ref.
H_3BO_3	1	r.t.	40	1	80	[37]
Al_2O_3	1.4	r.t.	5–15	3	80–98	[38]
Rany Ni	27–55 mol%	40–60	10–30	3.2	75–93	[39]
Nano-sized NiLa_2O_4	0.75 mol%	r.t.	2–20	0.75	90–98	This work

4. Conclusions

We developed a novel, highly efficient, and easy protocol for the synthesis of secondary amines from the corresponding imines in the presence of NaBH_4 . The procedure has several advantages over other methods, including improved yields, cleaner reactions, a simple experimental procedure, and the use of easily prepared and inexpensive starting materials. This approach is therefore a useful and attractive strategy in synthetic organic chemistry.

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Graphical Abstract

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The well-crystallized nano-sized NiLa_2O_4 spinel structure is formed and applies as an efficient heterogeneous catalyst for selective conversion of imines to the corresponding secondary amines in the presence of NaBH_4 as reducing agent.

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纳米尺度 NiLa_2O_4 尖晶石催化 NaBH_4 还原亚胺制仲胺

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摘要: 由溶胶-凝胶法制得的Ni-La化合物经热分解制备了纳米尺度 NiLa_2O_4 尖晶石, 在750 °C焙烧后形成了结晶良好的尖晶石结构. 采用差热分析、X射线衍射、透射电镜、扫描电镜和粒度分布分析等手段表征了该尖晶石的物理化学性质. 结果表明, 该纳米颗粒有规则的外形和确定的晶面, 由平均粒径为40 nm的规整半球晶粒组成. 精修的晶胞参数 $a = 3.861205 \text{ \AA}$ 和 $c = 12.6793 \text{ \AA}$. 在 NaBH_4 选择还原亚胺制相应仲胺的反应中, 该新型纳米 NiLa_2O_4 尖晶石可用作高效多相催化剂, 得到了较高的产物产率. 所有反应可在室温和相对较短的时间内完成. 在优化的反应条件下, 均可得到带有不同芳基的, 包括带有吸电子和供电子基团的仲胺. 该催化剂回收简便, 重复使用4次, 其催化活性未见明显下降.

关键词: 亚胺; 还原; 仲胺; 硼氢化钠; 纳米尺度尖晶石; 镧酸镍

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