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Platinum nanowires catalyzed direct amidation of aldehydes and amines

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Different from the conventional synthesis methods and substrates, we designed a brand new method for synthesizing amides with platinum nanowires as catalysts and *tert*-butylhydroperoxide (TBHP) as the oxidant. Influence of factors, such as the catalyst, solvents, and the reaction temperature, were studied to determine the optimal reaction conditions. In addition, we explored the substrate generality and observed excellent yields.

aldehyde, amine, amide, amidation, Pt nanowires

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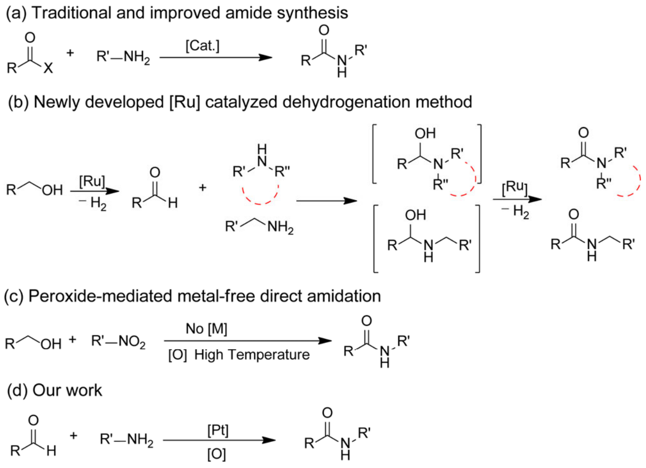
1 Introduction

The amide bond is a key feature of all natural peptides in biological systems and one of the most common functional groups in organic synthesis [1]. Amide compounds have a wide range of applications in industrial chemicals and research. They can be used as intermediates in organic synthesis, raw materials for detergents, plastics, lubricants, biologically active compounds and pharmaceuticals [2]. Much effort has been focused towards exploring the synthesis of amides. Traditionally, the preparation of amides involves the reaction of amines with activated carboxylic acid derivatives, such as acyl halides [3], mixed anhydrides [4], acyl imidazoles and acid azides (Scheme 1(a)). To simplify the procedure, the direct catalyzed amidation of amines and acids has been extended. Upon the nonmetallic catalysts, boric acid [5] and the derivatives [6] were used to promote the reaction of a carboxylic acid and amine to generate the amide bond as early as 1996. Xu *et al.* [7] synthesized amides using *N*-substituted formamide and *tert*-butyl alcohol in the presence of iodine with amide yields of up to 80%. Many metallic materials have also been used as catalysts for the synthesis of amides [8]. Chan *et al.* [9] firstly discovered



Scheme 1 Different substrates for amidation.

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*Corresponding author (email: hongwei@suda.edu.cn) that phenylacetylene and ammonium can produce oxidation reactions with the use of metal complexes of manganese as catalysts and hydrogen peroxide as an oxidant, with amide yields of up to 80%. One great step for amide synthesis is that Gunanathan *et al.* [10] achieved pretty high yields using equal amounts of alcohol and amine catalyzed by ruthenium complexes with two dehydrogenation steps (Scheme 1(b)). Other metals, Au [11], Cu [12], and Fe [13], all played an important role in the field of amide synthesis.

Although the above improved methods overcame aspects of drawbacks, such as cost, pollution, toxicity and atom efficiency, the amidation step restricts the starting materials as benzylamines and secondary cyclic amines, which obsessed lower or even no yields when it referred to phenylamines. Despite the relatively high temperature and narrow substrate extension, Shang *et al.* [14] and Deng *et al.* [15] (Scheme 1(c)) developed two different nonmetallic processes with phenylamines occasionally. Likewise, we also hope to find an efficient approach for different amide preparation. Herein, we report a new amide synthesis method directly from various aldehydes and amines in a one-pot reaction with platinum nanowires (Pt NWs, Figure S1, Supporting Information online, no Fe exists according to the ICP analysis) as catalysts. In this method, pyridine and aluminium chloride were used as co-catalysts and the oxidant, *tert*-butylhydroperoxide (TBHP), was the only source of oxygen (Scheme 1(d)). The method not only extended the scope for substrates of amines and aldehydes but also resulted in yields up to 90%.

2 Experimental

2.1 General experimental section

All reagents were used as received from commercial sources, unless otherwise specified or prepared as described in the literature. All reagents were weighed and handled in air. Flash column chromatography was performed over silica-gel powder 200–300 mesh (75–48 μm).

^{1}H and ^{13}C NMR spectra were respectively recorded at 400 and 100 MHz. Chemical shifts (δ) were expressed in parts per million.

2.2 General procedure for preparation of Pt nanowires catalyst

Pt NWs were achieved by acidic etching of FePt NWs, which was synthesized according to the procedure described by Sun *et al.* [16] and Gu *et al.* [17]. Pt(acac)$_2$ (200 mg) and oleylamine (20 mL) were mixed at room temperature under nitrogen atmosphere and heated to 120 °C under stirring, which was then maintained at 120 °C for 20 min. Fe(CO)$_5$ (150 μL) was injected into the hot solution and the temperature was raised to 160 °C gradually. The reaction was kept at this temperature for half an hour without stirring. The black solution was then cooled to room temperature and centrifuged in excess ethanol. The precipitate was redispersed in methanol and washed by ethanol for three times.

FePt NWs (100 mg, in 20 mL methanol) were firstly treated by oxygen bubbling at 100 °C, and HCl/methanol (1:1, 10 mL) solution was added into the above suspension. The solution was heated and stirred at 60 °C for 1 h, and the resultant precipitates were obtained following 10 minutes of centrifugation (3000 r/min). The dark solid was washed with methanol for at least two times and stored in methanol.

2.3 General procedure for the Pt nanowires catalyzed amides formation of aldehydes with amines

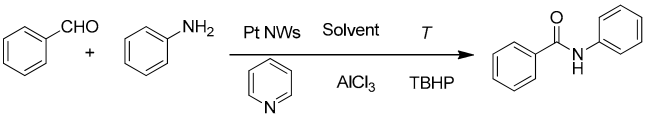
To a 25 mL screw-capped vial, Pt nanowires dispersed in methanol (500 μL, 0.01 mol/L) were added. The solvent was removed under reduced pressure. Then, a spinvane Teflon stirbar, aldehyde (1.1 mmol), amine (1.0 mmol), pyridine (1.0 mmol) and AlCl$_3$ (0.25 mmol) were added in toluene (2.0 mL) stepwise. The mixture was sealed with a Teflon-lined cap and stirred at 100 °C for 18 h (monitored by GC). The mixture was purified by flash silica gel column chromatography to give amide. The characterizations of amides are listed in the Supporting Information online.

3 Results and discussion

Initially, we selected the model reaction between aniline and benzaldehyde with TBHP as the oxidant under the co-catalysts pyridine and aluminium chloride to examine platinum-based catalysts. Pt NWs showed excellent catalytic efficiency, but platinum nanoparticles (Pt NPs) and platinum nanorods (Pt NRs) possessed lower catalytic activity in the synthesis of amides (Table S1, Supporting Information online). Pyridine and aluminium chloride, as co-catalysts, played an important role in the amidation reaction (Table S2). Without the pyridine or aluminium chloride, less than 20% of the target product was obtained.

After the catalyst and co-catalysts were determined, we tested five commonly used solvents to optimize the reaction conditions (Table 1, entries 1–5). In toluene, the phenylbenzamide had the greatest yield at 92%. Using the strongly polar solvents CH$_3$OH and CHCl$_3$, no target product was detected and most of the substrate was converted to *N*-benzylidene-benzeneamine. In 1,4-dioxane and dimethyl sulfoxide (DMSO), only 17% and 26% yields, respectively, were obtained for the target product. The reaction temperature was also investigated with toluene as solvent and Pt NWs as catalysts with the presence of pyridine and aluminium chloride. The results showed good yields at 100 °C, along with a sharp decrease as the temperature dropped (entries 5–7). Other oxidants, such as O$_2$ and H$_2$O$_2$, were also evaluated. But no target product was detected. Consequently,

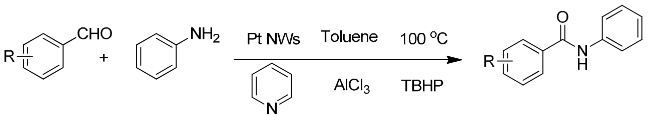
Table 1 *N*-phenylbenzamide formation in a series of reaction conditions [a)]

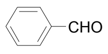
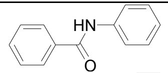
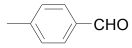
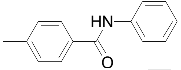
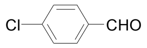
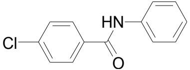
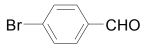
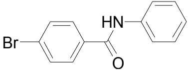
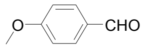
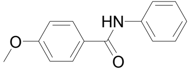
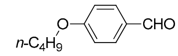
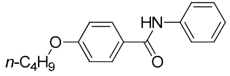
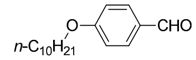
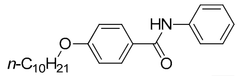
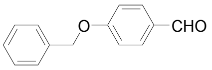
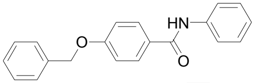
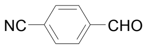
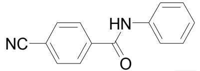
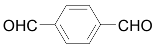
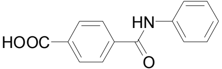
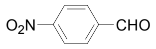
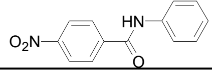


Entry	Solvent	T (°C)	Yield (%) [b)]
1	CH_3OH	50	N.D. [c)]
2	$CHCl_3$	40	N.D.
3	1,4-Dioxane	100	17
4	DMSO	100	26
5	Toluene	100	92
6	Toluene	80	13
7	Toluene	60	10
8 [d)]	Toluene	100	N.D.

a) All reactions were carried out with Pt NWs (0.5% mmol), aniline (1 mmol), benzaldehyde (1.1 mmol), $AlCl_3$ (0.25 mmol), pyridine (1 mmol), TBHP (3.6 mmol) and solvent (2 mL) for 18 h; b) GC yield; c) not detected; d) O_2 or H_2O_2 as the oxidant.

Table 2 Scope of benzaldehydes to synthesize amides [a)]



Entry	Benzaldehyde	Produce	Yield (%) [b)]
1			92
2			68
3			42
4			73 [c)]
5			58
6			59
7			94
8			50
9			57 [c)]
10			83 [c)]
11			52

a) Reaction conditions: Pt NWs (0.5% mmol), aniline (1 mmol), benzaldehydes (1.1 mmol), $AlCl_3$ (0.25 mmol), pyridine (1 mmol), TBHP (3.6 mmol) and toluene (2 mL), 100 °C for 18 h; b) GC yield; c) isolated yield.

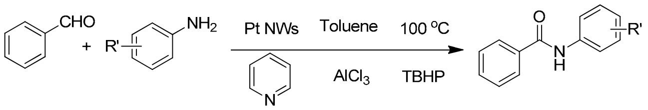
we selected Pt NWs as the catalyst, pyridine and aluminium chloride as the co-catalysts, TBHP as the oxidant, toluene as the solvent, and a reaction temperature of 100 °C for the optimized reaction condition.

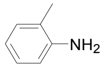
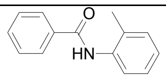
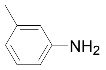
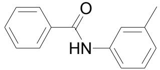
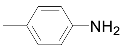
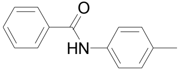
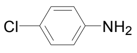
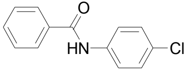
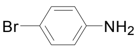
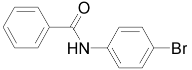
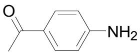
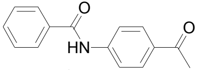
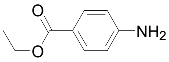
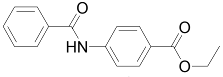
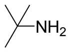
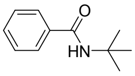
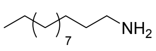
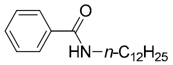
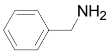
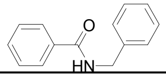
With the optimized reaction conditions, the scope for substrates was studied. A range of benzaldehydes were examined and a series of amides were successfully prepared under the optimized reaction conditions (Table 2). The reactions with aromatic benzaldehydes bearing electron-donating groups and electron-withdrawing substituents proceeded smoothly to give the desired products in good to excellent yields (50%–94%). The longer-chain alkane of the aromatic benzaldehyde gave higher yields at 94% (Table 2, entry 7), where 4-(decyloxy) benzaldehyde produced 4-(decyloxy)-*N*-phenylbenzamide. For halogen-containing substrates of aromatic benzaldehydes, the activity of the bromine substituent was higher than the chlorine-substituted, giving 73% and 42% yields, respectively (entries 3, 4). Because of the serious dehalogenation of 4-iodobenzaldehyde, it is too difficult to get the corresponding amide. Electron-withdrawing substituents formed the corresponding amide compounds in reasonable yields (entries 9–11). Notably, an excellent yield of 83% was obtained when terephthalaldehyde was used (entry 10); one of the aldehyde groups was reacted with aniline and the other was oxidized to a carboxyl group. However, other aliphatic aldehydes including pivalaldehyde, 2-phenylpropanal and heptanal were not effective substrates for this kind of reaction.

To further explore the scope of the reaction, a number of substituted aniline derivatives were reacted with benzaldehyde (Table 3). In general, both aromatic and aliphatic amines were found to be suitable substrates and produced the corresponding amides in good to excellent yields under the standard optimized reaction conditions. The position of the substituents on the phenyl ring of anilines only slightly affected the reaction yield (Table 3, entries 1–3). Halogen groups were tolerated under the optimized conditions, and the reaction of 4-chlorobenzenamine and 4-bromobenzenamine with benzaldehyde resulted in the desired products with 69% and 55% yields, respectively. Aromatic amines bearing electron-withdrawing groups as acyl and acyloxy groups gave good yields (Table 3, entries 6, 7). Additionally, both linear and branched aliphatic amines possessed higher yields (entries 8, 9) and the benzylamine gave a 72% yield (entry 10).

Based on experimental results (Figure 1), a mechanism is proposed for the reaction between benzaldehyde and aniline (Scheme 2). In the initial stages of the reaction, the amine combined with the aldehyde and rapidly dehydrated to form the imine **A**. As the reaction proceeded, electron transfer between the resulting imine and pyridine was catalyzed by Pt NWs to generate the negatively charged active intermediate **B**. During the reaction, the oxidizing agent, TBHP, was rapidly decomposed in the presence of the Pt NWs to form the active oxygen species. Upon oxidation of the active oxygen, B generated the desired product **C**. During the reaction, only a small amount of imines directly generated

Table 3 Scope of amines to synthesize amides [a)]



Entry	Aniline	Produce	Yield (%) [b)]
1			77
2			85
3			89
4			69
5			55
6			93 [c)]
7			58 [c)]
8			95 [c)]
9			95
10			72 [c)]

a) Reaction conditions: Pt NWs (0.5% mmol), benzaldehyde (1.1 mmol), anilines (1 mmol), $AlCl_3$ (0.25 mmol), pyridine (1 mmol), TBHP (3.6 mmol) and toluene (2 mL), 100 °C for 18 h; b) GC yield; c) isolated yield.

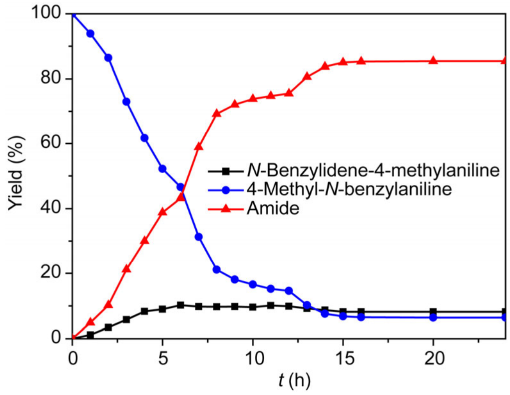
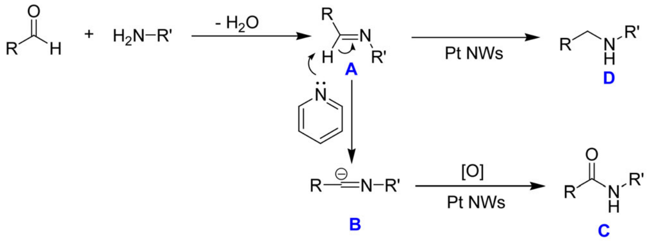


Figure 1 Time-dependent conversion plot for the model reaction between benzaldehyde and *p*-toluidine.



Scheme 2 Proposed mechanism for the reaction of benzaldehyde and aniline.

the secondary amine byproduct **D**. Because **D** was only produced in the initial stages of the reaction, the reaction yield did not change with time.

4 Conclusions

In conclusion, we have developed an efficient method for the direct amidation of benzaldehydes and anilines in a one-pot synthesis using stable and highly active Pt NWs as the catalyst, which expanded the amides synthesis substrates. The reaction exhibited good functional group tolerance. Various amides were formed in good to excellent yields (up to 94%). This new synthetic method using Pt NWs as the catalyst in a one-pot synthesis may contribute to advancing other relevant catalytic synthesis processes.

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Conflict of interest The authors declare that they have no conflict of interest.

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