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Ag/CNT-catalyzed hydroamination of activated alkynes with aromatic amines

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As a nanoparticle support material, carbon nanotubes (CNTs) provide a certain potential activation of catalysis in heterogeneous catalytic organic reactions. Herein, an efficient Ag/CNT-catalyzed synthesis of enamines via hydroamination of activated alkynes with aromatic amines has been described. This catalyst still retains catalytic activity after being recycled and reused three times. In addition, it represents a green and environmentally friendly process for preparation of enamines.
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Supporting information may be found in the online version of this article.

Keywords: carbon nanotube; hydroanination; activated alkynes; aromatic amine; heterogeneous

Introduction

Carbon nanotubes (CNTs) exhibit extraordinary mechanical properties and provide a certain potential activation of catalysis in organic transformation. Since the scientist Sumio Iijima[1] discovered carbon nanotubes in 1991, there have been thousands of papers on CNTs published. Applications of CNTs have been developed in oxidative dehydrogenations,[2] selective oxidations,[3] electrochemistry and fuel cells etc.[4–6] As nanoparticle support materials, CNTs have attracted much interest in organic chemistry because of their unique electrical and structural properties in organic synthesis. Thus the development of a green and simple method to form various functionalized organic compounds is a novel field for carbon nanotubes with metal nanoparticles.[7]

The hydroamination of alkenes and alkynes is of fundamental interest in organic chemistry. It represents the most atom-economic process for the synthesis of amine derivatives that are prevalent in natural products and significant pharmaceutical compounds.[8–11] The formation of C–N bonds by hydroamination of alkynes is regarded as one of the most challenging goals in synthetic organic chemistry.[12–15] Transition metal-catalyzed inter- and intramolecular hydroamination reactions[16–20] have been proven to be the most powerful and useful tools.[21–23] More elegant processes have recently been developed using transition metal catalysts. Successful examples have been mentioned Ru, Rh, Pd, Au and Ag-catalyzed in this field. Stimulated by these results, there has been a growing effort to develop an efficient and selective hydroamination process using alkynes to form enamines.

As reagents possessing nitrogen and double bonds, enamines have a high reaction activity and can rapidly construct complex and novel heterocycles[24] under mild condition. In this paper, we have reported an efficient and high regioselective Ag/CNT-catalyzed hydroamination process of activated alkynes with anilines to synthesize enamines.

Results and Discussion

Initially, Ag/CNTs were readily prepared according to previous reports using a simple synthesis method (Fig. 1).[25,26] We chose methyl but-2-ynoate (**1a**) and aniline (**2a**) as model substrates to search for suitable reaction conditions, such as solvents, temperature and time of reaction, and the results are indicated in Table 1. Our initial efforts have focused on the optimization of solvents in the presence of Ag/CNTs at 40°C for 6 h (Table 1, entries 1–9). Screening of a series of solvents, including DMF, DMSO, DMA (N,N-dimethyl acetamide), MeCN, CH_2Cl_2, THF, EtOH, toluene and 1,4-dioxane, showed that MeCN was required for the transformation of **1a** with **2a** to form (*Z*)-methyl 3-(phenylamino) but-2-enoate (**3aa**). Other solvents also allowed the formation of the desired product **3aa** in 8–25% yield. The effects of temperature were surveyed in the following tests. Table 1 clearly indicates an important influence of the reaction temperature for this hydroamination in the presence of Ag/CNTs in MeCN. To our delight, the yield of corresponding product **3aa** increased to 69% when the reaction was carried out at 60°C (Table 1, entry 10). Further investigation demonstrated that 80°C was the most efficient temperature for hydroamination by Ag/CNT-catalyzed reaction. Subsequently, efforts attempted to improve the yield by prolonging the reaction time, and the results showed that the optimum reaction time was determined to be 10 h (Table 1, entry 15).

With the optimal reaction conditions in hand, i.e. Ag/CNTs as catalyst, MeCN as solvent at 80°C for 10 h, we next explored the scope of hydroamination using a variety of anilines and activated alkynes. The results are summarized in Table 2. All of the substrates provided similarly good yields for the formation of enamines. The corresponding products were obtained in

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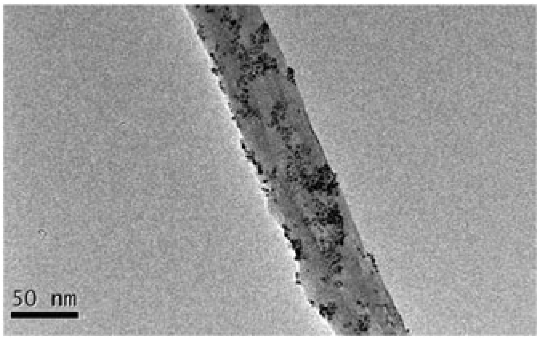
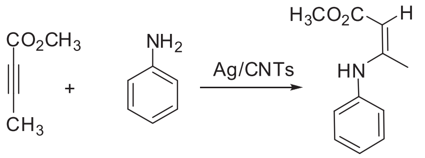


Figure 1. Transmission electron microscope images of Ag/CNTs.

Table 1. Optimization of reaction conditions[a]



1a **2a** **3aa**

Entry	Solvent	*T* (°C)	*t* (h)	Yield (%)[b]
1	DMF	40	6	19
2	DMSO	40	6	15
3[b]	DMA	40	6	17
4	MeCN	40	6	30
5	CH_2Cl_2	40	6	11
6[c]	THF	40	6	16
7	Ethanol	40	6	8
8	Toluene	40	6	21
9	1,4-Dioxine	40	6	25
10	MeCN	60	6	69
11	MeCN	80	6	74
12	MeCN	100	6	74
13	MeCN	r.t.	6	—
14	MeCN	80	8	81
15	MeCN	80	10	85
16	MeCN	80	20	85

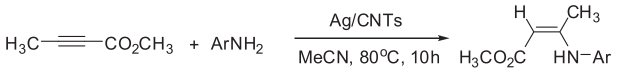
[a] Reaction conditions: **1a** (0.5 mmol); **2a** (0.6 mmol); Ag/CNTs (5 mol %); 2 mL of solvent at r.t. to 100°C for 6–24 h.

[b] Isolated yield.

moderate to good yield under the optimized conditions by using the various substituted anilines (R = *p*-CH_3, *o*-CH_3, *m*-CH_3, *p*-OCH_3, *p*-Cl, *o*-Cl, *m*-Cl, *p*-F, *p*-Br, *p*-$COCH_3$, *p*-CN, 1-naphthyl, 3,4-Cl_2).

To explore the scope of the reaction, a variety of different activated alkynes were tested to form the corresponding products in good yield under optimal conditions as shown in Table 3, such as pent-3-yn-2-one (**1b**) and ethyl 3-phenylpropiolate (**1c**). Firstly, **1b** was employed (entries 1–9) and it was indicated clearly that this transformation was applicable for hydroamination of electron-rich and electron-withdrawing groups of anilines. Meanwhile, functional groups in the *para* and *meta* position to the anilines were well tolerated in the reactions. Notably, the sterically hindered anilines also worked smoothly, affording the corresponding hydroamination products in good yield. We next

Table 2. Synthesis of enamines from methyl but-2-ynoate with anilines[a]



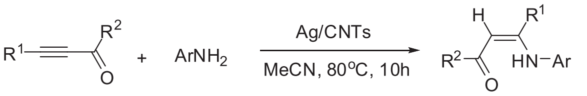
1 **2** **3**

Entry	Ar	Product[27,28]	yield (%)[b]
1	Ph–	**3aa**	81
2	4-CH_3–Ph–	**3ab**	83
3	2-CH_3–Ph–	**3ac**	82
4	3-CH_3–Ph–	**3ad**	84
5	4-CH_3O–Ph–	**3ae**	87
6	4-Cl–Ph–	**3af**	80
7	2-Cl–Ph–	**3ag**	79
8	3-Cl–Ph–	**3ah**	81
9	4-F–Ph–	**3ai**	81
10	4-Br–Ph–	**3aj**	81
11	4-CH_3CO–Ph–	**3ak**	74
12	4-CN–Ph–	**3al**	70
13	1-Naphthyl	**3am**	85
14	3,4-Cl_2–Ph–	**3an**	83

[a] Reaction conditions: **1** (0.5 mmol); **2** (0.6 mmol); Ag/CNTs (5 mol%); MeCN 2 ml at 80°C for 10 h.

[b] Isolated yield.

Table 3. Ag/CNT-catalyzed synthesis of enamines[a]

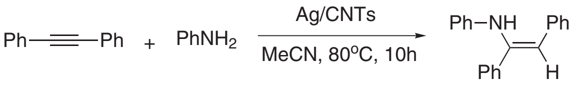


1 **2** **3**

Entry	R^1	R^2	Ar	Product[27,28]	Yield (%)[b]
1	Ph	EtO	Ph–	**3ba**	82
2	Ph	EtO	4-CH_3–Ph–	**3bb**	87
3	Ph	EtO	2-CH_3–Ph–	**3bc**	81
4	Ph	EtO	4-CH_3O–Ph–	**3be**	87
5	Ph	EtO	4-Cl–Ph–	**3bf**	80
6	Ph	EtO	4-F–Ph–	**3gi**	78
7	Ph	EtO	4-Br–Ph–	**3bj**	82
8	Ph	EtO	1-Naphthyl	**3bm**	86
9	Ph	EtO	3,4-Cl_2–Ph–	**3bn**	79
10	CH_3	CH_3	2-CH_3–Ph–	**3cc**	80

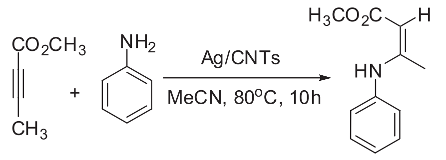
[a] Reaction conditions: **1** (0.5 mmol); **2** (0.6 mmol); Ag/CNTs (5 mol%); MeCN 2 ml at 80°C for 10 h.

[b] Isolated yield.



Scheme 1. Reaction of 1,2-diphenylethyne with aniline.

Table 4. Efficiency of catalyst reuse[a]



1a **2a** **3aa**

Entry	Run	*t* (h)	Yield (%)
1	1	10	81
2	1st reuse	10	81
3	2nd reuse	10	80
4	3rd reuse	10	79

[a] Isolated yields.

tested **1c** and the result indicated that the product **3 cc** was obtained in 80% yield (entry 10). Unfortunately, the corresponding products were not observed by GC-MS when 1,2-diphenylethyne was used as substrate, as shown in Scheme 1. These results have shown that this process is stereoselective and provides *cis* product due to formation of a hydrogen bond between N–H and oxygen in the carbonyl group. These compounds were characterized by previous reports.[27,28]

We investigated the efficiency of catalyst reuse and recycling in the following steps. As shown in Table 4, the results clearly indicated that the Ag/CNTs catalyst could be efficiently recycled and separated by filtration. The catalytic activity of heterogeneous catalyst remained unchanged after reusing three times in the reaction.

Conclusions

In summary, we have reported a convenient heterogeneous catalytic hydroamination process by Ag/CNT catalysts. It represents an efficient method for synthesis of enamines that have a high reaction activity to rapidly construct complex and novel heterocycles. This heterogeneous catalytic system is reusable and applicable, and can be used efficiently for intermolecular hydroamination. Our study has indicated the ability of Ag/CNT catalysts to promote a regioselective hydroamination of activated alkynes with aromatic amine.

Experimental

General Information

The reactions were performed at 80°C under air atmosphere. NMR spectra and ^{13}H NMR spectra were recorded with a Bruker 300 or 400 spectrometer in a $CDCl_3$ solution with tetramethylsilane as internal standard. **1a–1c** were purchased from Aldrich Chemicals. All products were isolated by short chromatography on a silica gel (200–300 mesh) column. ^{1}H and ^{13}CNMR data are provided as supporting information.

General Procedure for Synthesis of Product 3

Compound **1a** 0.5 mmol, **2a** 0.6 mmol and 5% mol Ag/CNTs were stirred at 80°C in MeCN for 10 h. When all starting material was consumed (thin-layer chromatographic analysis) the mixture was cooled to room temperature and the Ag/CNTs were deposited on the button. The catalyst was recovered by filtration and washed three times with water (2×4 ml).The aqueous solution was extracted with diethyl ether (3×10 ml) and the combined extract was dried with anhydrous $MgSO_4$. The solution was removed by evaporating to dryness under reduced pressure and the crude product was purified by column chromatography to give a sample of **3aa**.

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