ORGANIC LETTERS

2007
Vol. 9, No. 13
2465−2468

Cobalt–Rhodium Heterobimetallic Nanoparticle-Catalyzed Synthesis of α,*β*-Unsaturated Amides from Internal Alkynes, Amines, and Carbon Monoxide

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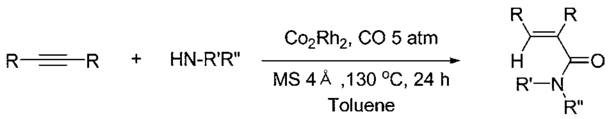
Received March 20, 2007

ABSTRACT



The first example of cobalt–rhodium heterobimetallic nanoparticle-catalyzed synthesis of alkenyl amides from alkynes, amines, and carbon monoxide is described.

α,*β*-Unsaturated amides are an important class of compounds because of their biological and insecticidal activities,[1] their presence in the structure of natural products,[2] and their role as a reaction partner in many useful reactions.[3] However, the preparation of α,*β*-unsaturated amides has scarcely been reported.[4] Only a handful of stoichiometric reactions and a few catalytic reactions have been disclosed. The most desirable method for preparing α,*β*-unsaturated amides would be a direct carbonylation of alkynes in the presence of amines, i.e., aminocarbonylation. Many palladium-catalyzed aminocarbonylation reactions have been reported.[5] However, they use aryl bromides and iodides to generate primary aromatic amides.[6] Very recently, Alper et al. reported[7] the $Pd(OAc)_2$/dppp-catalyzed aminocarbonylation of alkynes with amines in ionic liquid [bmim][Tf_2N] under mild conditions. However, their catalytic system is effective in the presence of relatively high CO pressure (200 psi) and is

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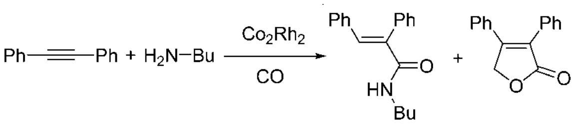
10.1021/ol0706760 CCC: $37.00

ineffective for the aminocarbonylation of internal alkynes. El Ali et al. reported[4a,b] a catalytic synthesis of amides by carbonylation of alkyl alkynes with aniline derivatives by $Pd(OAc)_2$/dppb under syngas. They also used a high pressure of CO and used hydrogen gas to generate palladium-hydride species. Recently, Ryu et al. reported[8] the radical-catalyzed aminocarbonylation of alkynes. Thus, development of a direct and clean catalytic synthesis of *trans*-α,β-unsaturated amides from readily available starting materials is needed. So far, very limited work[4a,b] has been done toward carbonylative coupling of primary and secondary amines with internal alkynes. Furthermore, heterogeneous catalysts for the aminocarbonylation are still scarce.[9] Thus, the study of aminocarbonylation of internal alkynes via new heterogeneous catalysts under relatively low CO pressure is still of interest.

Recently, the chemistry of transition-metal nanoparticles has been rapidly developed[10] and their use has widened to include many catalytic reactions, such as oxidation,[11] hydrogenation,[12] coupling reactions,[9b,13] the PKR,[14] and some photocatalytic reactions.[15] We found that cobalt/rhodium nanoparticles (Co_2Rh_2) derived from $Co_2Rh_2(CO)_{12}$ were quite useful catalysts in PKR-type reactions and related carbocyclizations.[16] In the context of our studies on the use of transition metal nanoparticles in organic reactions, we recently found that Co_2Rh_2 was quite effective for the aminocarbonylation reaction of disubstituted alkynes in the presence of amines and carbon monoxide. The catalytic reaction could be carried out under relatively low CO pressure (5 atm) and the catalytic system did not require any additives or promoters such as phosphines or ionic liquids. This is the first use of transition metal nanoparticles as catalysts in the aminocarbonylation of alkynes.

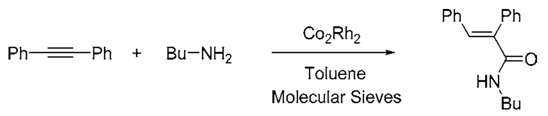


(1)

1a **2a** **3a** **4a**

Aminocarbonylation was studied using diphenyl acetylene **1a** as a model substrate and Co_2Rh_2 as a catalyst. Treatment of **1a** (1 mmol, 174 mg) with butyl amine **1b** (1 mmol, 73 mg) in the presence of a catalytic amount of Co_2Rh_2 (5 mol %, 90 mg) in 4 mL of toluene, under 5 atm of CO at 100 °C for 18 h, gave an amide **3a** and a cyclohydrocarbonylated product **4a** in 45% and 7% yields (based on **1a** used), respectively (eq 1). The catalytic cyclohydrocarbonylation of acetylenes in the presence of Co_2Rh_2 has already been reported by us.[16d] Initially, a furanone, a double carbonylation product, was always present in the product mixture. However, addition of molecular sieves to the reaction mixture practically eliminated this problem. Encouraged by this result, we screened various reaction conditions, including the CO pressure, the reaction temperature, the reaction time, and a catalyst for the aminocarbonylation of **1a** and **2a**. The result is summarized in Table 1. A trimerization product, an aromatic compound, was sometimes obtained as a side product. Thus, the yields in Table 1 were based on the butylamine used.

Table 1. Optimization of the Co_2Rh_2-Catalyzed Aminocarbonylation of **1a** with **2a**[a]



entry	catalyst	CO (atm)	*T* (°C)	time (h)	yield[b] (%)
1	Co_2Rh_2 (5 mol %)	10	100	18	53
2	Co_2Rh_2 (5 mol %)	20	130	18	42
3	Co_2Rh_2 (5 mol %)	3	130	18	60
4	Co_2Rh_2 (5 mol %)	5	130	18	69
5	Co_2Rh_2 (5 mol %)	5	130	24	79
6	Rh_4 (5 mol %)[c]	5	130	24	12
7	Co_2 (10 mol %)[c]	5	130	24	N.R.[d]
8	Co_2 (5 mol %) + Rh_4 (2.5 mol %)[c]	5	130	24	trace

[a] 1.5 mmol of alkyne and 1.0 mmol of amine were used in 4 mL of toluene. [b] Based on amine employed. [c] Rhodium and cobalt nanoparticles drived from $Rh_4(CO)_{12}$ and $Co_2(CO)_8$, respectively. [d] Reactant recovered.

As Table 1 shows, the effect of the CO pressure and the reaction temperature was noticeable (entries 1−4). Interestingly, there was an optimum CO pressure. An increase of the reaction time from 18 to 24 h (entry 4 vs 5) also resulted in a noticeable increase in the yield. For reference purposes, other relevant transition metal nanoparticles such as Rh and Co nanoparticles, and a mixture of the two were used as catalysts (entries 6−8). When the Rh nanoparticles were used as catalysts (entry 6), the expected product was obtained in 12% yield. However, neither Co nor the Co/Rh mixture was effective for the aminocarbonylation. Thus, it seemed that

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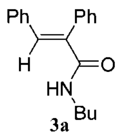
some synergistic effects arose between cobalt and rhodium nanoparticles in the Co_2Rh_2 nanoparticles. We do not have a plausible explanation for the exact nature of the synergistic effects. A similar sygnergistic phenomenon was observed other heterobimetallic nanoparticle systems.[17] Thus, the optimized reaction conditions were established as follows: 5 mol % of Co_2Rh_2, alkyne (1.5 mmol), amine (1.0 mmol), 5 atm of CO, 4 mL of toluene, 130 °C, and 24 h.

The recyclability of the Co_2Rh_2 heterobimetallic nanoparticle catalyst system for the aminocarbonylation of alkynes was investigated in toluene. Reuse of the catalyst was performed without any significant loss of its catalytic activity after six runs.

With optimal conditions in hand, we next investigated the aminocarbonylation of various alkynes in the presence of a variety of amines (Table 3). Disubstituted alkynes with dialkyl, alkyl aryl, and diaryl termini were good substrates. When dialkyl-substituted symmetric alkynes (entry 1 and 2) were used, the expected products were isolated in 85% and 64% yields, respectively. Treatment of unsymmetric alkynes led to isolation of two isomeric amides in a ratio of 1.2:1−1.5:1 depending upon the substituents (entries 3−6). The overall yields varied greatly depending upon the substituents. In cases of alkyl,aryl-disubstituted alkynes (entries 3 and 4), the yields were relatively high (75% and 81% yields, respectively). However, a relatively lower yield (48%, respectively) was obtained for diaryl-substituted alkyne with an electron-donating group (entry 5). In the case of entry 5, increasing the reaction time to 36 h increased the yield up to 56%.

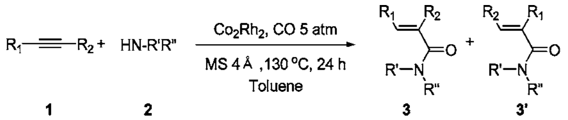
Table 2. Reuse of Co_2Rh_2 Catalyst for Aminocarbonylation Reaction of **1a** with **2a**[a]

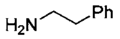
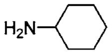
entry	catalyst	alkyne	amine	product	yield (%)
1	Co_2Rh_2 5 mol %	Ph—≡—Ph **1a**	H_2N−Bu **2a**	 **3a**	79
2	recovered from #1				75
3	recovered from #2				76
4	recovered from #3				72
5	recovered from #4				74
6	recovered from #5				75

[a] 1.5 mmol of **1a**, 1.0 mmol of **2a**, and 5 mol % of Co_2Rh_2 catalyst were used at 130 °C for 24 h in 4 mL of toluene.

When the aminocarbonylation of dipropylacetylene was compared to those of diphenylacetylene, relatively high yields were observed for the aminocarbonylation of dipropylacetylene. Reasonably high yields (50−77%) were obtained for all primary amines used (entries 6−14). However, a relatively low yield (24%) was observed for the secondary amine (entry 15).

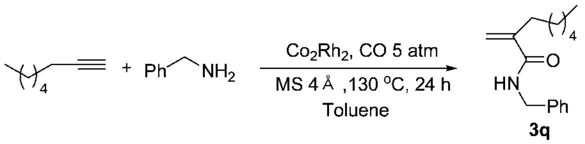
Table 3. Co_2Rh_2-Catalyzed Aminocarbonylation of Alkynes and Amines[a]



entry	alkyne	amine	product	yield (%)[b]
1	Pr—≡—Pr **(1b)**	H_2N−Bu **(2a)**	**3b**	85
2	Et—≡—Et **(1c)**	**2a**	**3c**	64
3	Ph—≡—Et **(1d)**	**2a**	**3d + 3d'**	75(1.1:1)[c]
4	Ph—≡—Bu **(1e)**	**2a**	**3e + 3e'**	81(1.5:1)[c]
5	$H_3COC_6H_4$—≡—Ph **(1f)**	**2a**	**3f + 3f'**	48(1:1.2)[c] 56[d]
6	**1a**	H_2N−Octyl **(2b)**	**3g**	64
7	**1b**	**2b**	**3h**	77
8	**1a**	H_2N−Dodecyl **(2c)**	**3i**	53
9	**1b**	**2c**	**3j**	60
10	**1a**	H_2N−Benzyl **(2d)**	**3k**	64
11	**1b**	**2d**	**3l**	73
12	**1a**	 **(2e)**	**3m**	54
13	**1a**	 **(2f)**	**3n**	50
14	**1b**	**2f**	**3o**	70
15	**1a**	HN−Et_2 **(2g)**	**3p**	24

[a] 1.5 mmol of alkyne, 1.0 mmol of amine, and 5 mol % of Co_2Rh_2 catalyst were used at 130 °C for 24 h in 4 mL of toluene. [b] Isolated yield. [c] Product ratio is determined by ^1H NMR spectroscopy. [d] Reaction time: 36 h.

However, a terminal alkyne such as 1-octyne was not a good substrate under our reaction conditions (eq 2).



(2)

3q

24%

In order to obtain insights into the reaction mechanism, we carried out the following experiments. Treatment of diphenylacetylene with acetamide or *N*-methylformamide yielded no reaction. However, a reaction of benzylamine with carbon monoxide under our reaction conditions led to isolation of N-benzylacetamide in 76% yield (eq 3). These

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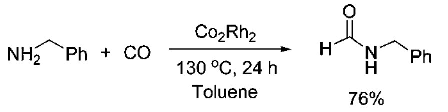
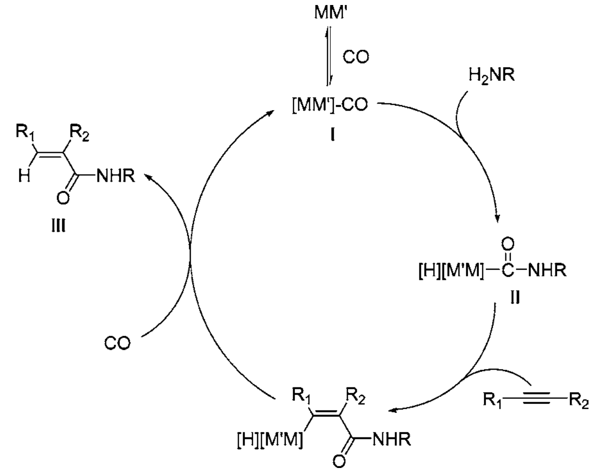
observations suggested that metal carbonyl species might react with an amine prior to an alkyne substrate on the reaction cycle.



(3)

A general mechanistic view has so far remained elusive. However, a plausible reaction mechanism is shown in Scheme 1.

Scheme 1. Proposed Reaction Mechanism



Coordination of carbon monoxide to Co_2Rh_2 generates **I** as an intermediate. Initially, it was expected that CO would compete with either the alkyne or amine for coordination to the active metal center in the catalytic cycle. However, the dependence of the yield upon the CO pressure implied an initial CO coordination. Insertion of an amine into the metal−carbon monoxide in **I** generates intermediate **II**. Insertion of alkyne followed by a reductive elimination leads to the generation of aminocarbonylated product, **III**, and intermediate **I**. While we proposed a plausible reaction mechanism, the stepwise details for this aminocarbonylation process are still open to debate and remain subject to investigate in our lab.[18]

In conclusion, we have demonstrated that the aminocarbonylation of alkynes was readily accomplished by Co_2Rh_2 heterobimetallic nanoparticles in the presence of 5 atm of CO and amines. Internal alkynes with substituents such as an alkyl and an aryl were efficiently aminocarbonylated, giving the α,β-Unsaturated amides in moderate-to-high yields. Neither a toxic phosphine/phosphite nor a corrosive acid was needed for our process. Furthermore, the Co_2Rh_2 catalyst is recyclable, and no cyclohydrocarbonylated byproduct was obtained.

Acknowledgment. This work was supported by Grant No. R01-2005-000-10548-0 from the Basic Research Program of the Korea Science & Engineering Foundation (KOSEF) and by Grant No. R11-2005-065 through the SRC/ERC Program of MOST/KOSEF We thank Dr. K. H. Park for his initial study of this project.

Supporting Information Available: Experimental procedures and spectroscopic data for all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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[18] Formation of a byproduct 4a suggested that another reaction mechanism might operate in the catalytic cycle (see below). For general discussions on the mechanism of aminocarbonylation, see: (a) Joh, T.; Doyama, K.; Onitsuka, K.; Shiohara, T.; Takahashi, S. *Organometallics* **1991**, *10*, 2493. (b) Scrivanti, A.; Beghetto, V.; Campagna, E.; Zanato, M.; Matteoli, U. *Organometallics* **1998**, *17*, 630.