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Cobalt/Rhodium Heterobimetallic Nanoparticle-Catalyzed Oxidative Carbonylation of Amines in the Presence of Carbon Monoxide and Molecular Oxygen to Ureas

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Abstract: An environmentally friendly oxidative carbonylation of aliphatic and aromatic primary amines to ureas has been successfully achieved in the presence of a catalytic amount of cobalt/rhodium heterobimetallic nanoparticles without any promoters. The catalyst system could be reused with only a slight loss of catalytic activity.

Keywords: aerobic oxidation; amines; bimetallic catalysts; carbonylation; nanoparticles; ureas

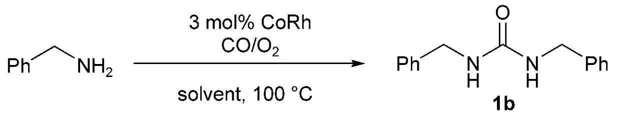
Recently, the development of new synthetic strategies that take green chemistry into consideration has become a very important topic.[1] Catalysis can be considered as one of the central themes in the green chemistry. Among the catalytic reactions, a transition metal-catalyzed oxidative transformations of amines is one of the most important functional transformations in organic synthesis, because they produce useful nitrogen compounds that are versatile building blocks and intermediates for the synthesis of biologically active nitrogen compounds.[2,3] In the context of the green chemistry, an aerobic oxidation is recognized to be very important. Thus, many methods for transition metal-catalyzed aerobic oxidative transformation of amines to the corresponding imines,[4] carbamates,[5] nitrones,[6] and ureas[7] have been explored. Particularly, most Pd-based catalysts showed high activity, but the reactions are mostly promoted by an iodine-containing promoter,[8] which is very corrosive in the reaction system.

The emergence of transition metal nanoparticles has led to an explosive growth in catalysis.[9] Transition metal naoparticles are potentially attractive catalysts due to their small size and high surface-to-volume ratio, but their small size also results in a higher surface area that makes their surface atoms very active. To sustain their high activity, it is important to stabilize catalytic metallic nanoparticles. Recently, the use of heterobimetallic nanoparticles as catalysts has attracted much attention because their catalytic performance is generally superior to that of a single nanometal by itself and there is potential to create new types of catalysts for reactions which may not be achieved by monometallic catalysts.[10] We recently reported that cobalt/rhodium nanoparticles[11] [Co_2Rh_2, derived from $Co_2Rh_2(CO)_{12}$] immobilized on charcoal (Co_2Rh_2/C) were quite useful catalysts in carbonylation reactions, including the Pauson–Khand reaction,[12] silylcarbocyclization,[13] cyclohydrocarbonylation,[14] and aminocarbonylation.[15] In the exploration of the use of Co_2Rh_2/C as a catalyst, we recently studied a Co_2Rh_2/C-catalyzed oxidative carbonylation of amines in the presence of carbon monoxide. Here, we report on our recent intriguing findings in the Co_2Rh_2/C-catalyzed oxidative carbonylation of amines to ureas.

Our catalytic system is quite effective for the oxidative carbonylation of amines to ureas in the presence of carbon monoxide and can be reused several times with only a slight loss of catalytic activity. This is the first example of the use of a nanoparticle catalyst in the oxidative carbonylation of amino compounds to ureas.

The initial investigation of oxidative carbonylation was carried out using benzylamine (**1a**) as a probe substrate to optimize the reaction conditions, and the results are summarized in Table 1. As Table 1 shows, the catalytic reaction went to completion in the absence of any promoters and the yields obtained ranged from 45% to 74%. Thus, the reaction was not highly sensitive to the pressures of CO and O_2, the ratio of CO:O_2, the reaction time, and the solvent.

Table 1. Optimization of Co_2Rh_2 catalyzed oxidative carbonylation of benzylamine.[a]



1b

Entry	Solvent	CO/O_2 [atm]	Time [h]	Yield [%][b]
1	Toluene	3/0.5	15	45
2	Toluene	4/1	12	67
3	Methanol	4/1	12	51
4	Toluene	4/1	3	64
5	Toluene	4/0.5	3	71
6	THF	4/0.5	15	68
7	Toluene	4/0.1	3	74
8	toluene	5/0	12	0[c]

[a] *Reaction conditions:* benzylamine (1.0 mmol), Co_2Rh_2 catalyst (3 mol%, 50 mg), CO, and O_2 in 2 mL solvent at 100 °C.

[b] Isolated yield.

[c] *N*-Benzylformamide was obtained in 34% yield.

However, each affected the yield of the reaction to a certain extent. As the pressure of oxygen decreased, the yield gradually increased. Interestingly, without any oxygen, *N*-benzylformamide instead of urea was obtained in 34% yield. The best yield (74%) was obtained when the reaction was carried out in toluene under CO and O_2 (4 atm/0.1 atm) for 3 h.

To check the recyclability, Co_2Rh_2/C was separated and reused 4 times (Table 2, entries 1, 2, 5, and 6). Unfortunately, the activity of the catalytic system gradually decreased from 74% to 58%, 35%, and 31%, respectively. An ICP-AES study shows that the percentages of cobalt and rhodium bled from Co_2Rh_2/C after the first catalytic run was *ca.* 0.24% of the original cobalt and 0.2% of the original rhodium, respectively. Thus, the leaching was negligible. When the recovered catalyst after the first run was treated with 1 atm of CO for 20 min, the yield of the reaction slightly increased to 65%. However, when the same catalyst was treated with hydrogen, the yield of the reaction was 54%.

Table 2. Reuse of Co_2Rh_2 catalyst for oxidative carbonylation reaction of benzylamine.[a]

Entry	Catalyst	Yield [%][b]
1	1st run	74
2	2nd run	58
3[c]	2nd run (after treatment with CO)	65
4[d]	2nd run (after treatment with H_2)	54
5	3rd run	35
6	4th run	31

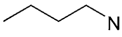
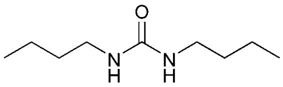
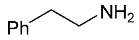
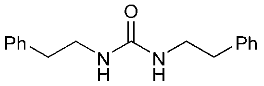
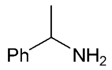
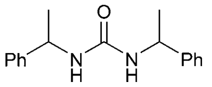
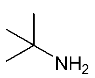
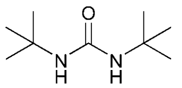
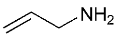
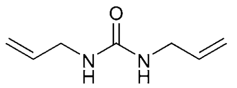
[a] *Reaction conditions:* benzylamine (1.0 mmol), CO (5 atm), O_2 (0.1 atm), and Co_2Rh_2 catalyst in 2 mL toluene at 100 °C for 3 h.

[b] Isolated yield.

[c] The recovered catalyst after the first run was treated with CO bubbling for 20 min in toluene.

[d] The recovered catalyst after the first run was treated with H_2 bubbling for 20 min in toluene.

Table 3. Co_2Rh_2-catalyzed oxidative carbonylation of various aliphatic amines.[a]

Entry	Amine	Urea		Yield [%][b]
1			**2b**	84
2			**3b**	73
3			**4b**	71
4			**5b**	59
5			**6b**	44

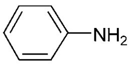
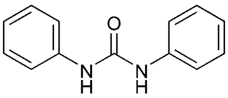
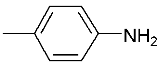
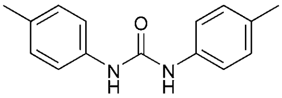
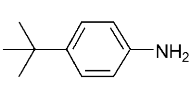
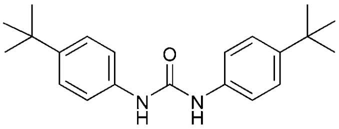
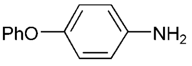
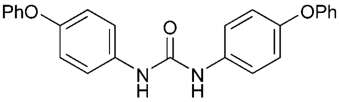
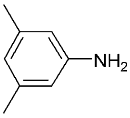
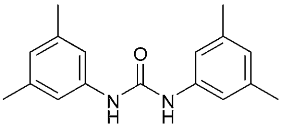
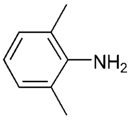
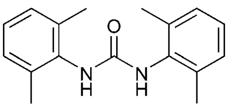
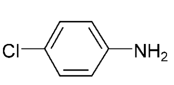
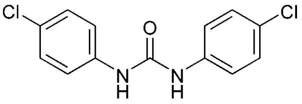
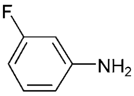
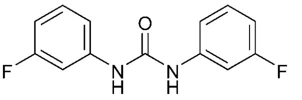
[a] *Reaction conditions:* aliphatic amine (1.0 mmol), CO (5 atm), O_2 (0.1 atm), and Co_2Rh_2 catalyst (3 mol%, 50 mg) in 2 mL toluene at 100 °C for 3 h.

[b] Isolated yield.

After optimization, oxidative carbonylations of other aliphatic primary amines were studied (Table 3). As seen in Table 3, all the reaction went to completion within 3 h under relatively mild reaction conditions and the yield was highly dependent upon the substrate. When butylamine (entry 1) was the substrate, the yield was 84%. The sterically bulky *tert*-butylamine (entry 4) gave the corresponding urea **5b** in 59% yield, and allylamine (entry 5) gave **6b** in 44% yield. Studies on the transition metal-catalyzed oxidative carbonylation of allylamine are quite rare.[16] Thus it is not easy to draw any conclusions. It seems that the presence of a double bond is not helpful for the yield of the reaction.

We also investigated the Co_2Rh_2/C-catalyzed oxidative carbonylation of aromatic primary amines (Table 4). In this case, due to their low solubility in toluene, tetrahydrofuran (THF) was used and the reaction time was lengthened to 15 h. The presence of an electron-donating or an electron-withdrawing substituent at the *para*- or *meta*-position of aniline strongly affected the yield of the reaction. High yields were obtained for anilines bearing an electron-donating group (entries 2–4). However, with an electron-withdrawing group such as *p*-Cl and *m*-F, the yields abruptly dropped to 12% and 26%. Steric crowded-

Table 4. Co_2Rh_2-catalyzed oxidative carbonylation of various aromatic amines.[a]

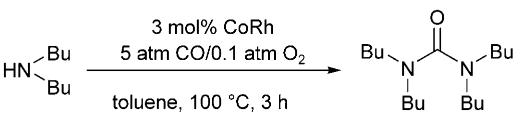
Entry	Aniline	Urea		Yield [%][b]
1			**7b**	81
2			**8b**	89
3			**9b**	80
4			**10b**	85
5			**11b**	63
6			**12b**	28
7			**13b**	12
8			**14b**	26

[a] *Reaction conditions:* aromatic amine (1.0 mmol), CO (5 atm), O_2 (0.1 atm), and Co_2Rh_2 catalyst (3 mol%, 50 mg) in 2 mL THF at 100 °C for 15 h.

[b] Isolated yield.

ness also affected the yield of the reaction. Compared to that (63%) of 3,5-dimethylaniline (entry 5), the yield of 2,6-dimethylaniline (entry 6) was quite poor (28%).

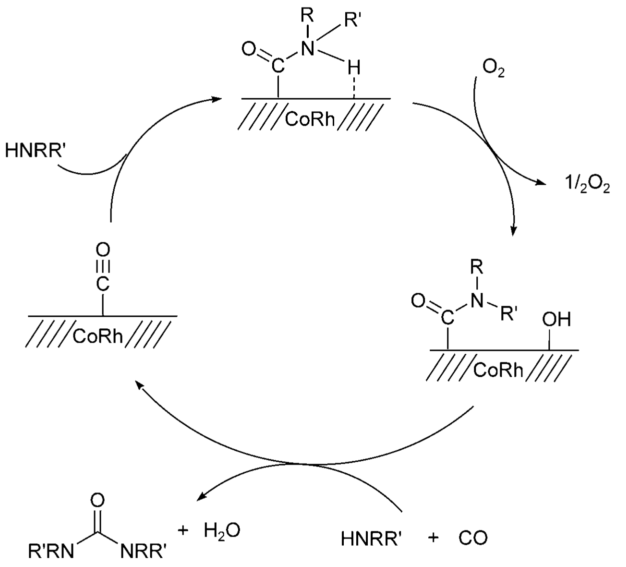
Compared to the carbonylation of aliphatic and aromatic primary amines to 1,3-disubstituted ureas, the catalytic carbonylation of secondary amines to tetrasubstituted ureas is less well explored.[8c,17] Thus we investigated the Co_2Rh_2/C-catalyzed oxidative carbonylation of dibutylamine under the same reaction conditions [Eq. (1)]. After work-up, the corresponding urea was obtained 38% yield. Interestingly, Alper et al.[8c] obtained the same compound in 2% yield using $Pd(OAc)_2$[6b] as the catalyst, a base (K_2CO_3), and a promoter (I_2). Deng et al. reported[17b] 12% in the presence of ZrO_2-SO_4^{2-}-supported palladium catalyst. It has been known[18] that the palladium-catalyzed oxidative carbonylation proceeded through an isocyanate intermediate. For the secondary amine, an isocyanate intermediate could not be formed. Thus we envisioned that our reaction mechanism might be different from that of the palladium-catalyzed reaction.



15b
38%

(1)

According to the experimental results, primary aromatic amines were less reactive than aliphatic ones in the Co_2Rh_2-catalyzed oxidative carbonylation. This means that nitrogen nucleophilicity plays an important role in the reactivity. Moreover, this was confirmed by the observation that the presence of an electron-withdrawing or electron-releasing substituent at the *para* position of the ring strongly affected substrate reactivity.



Scheme 1. Possible mechanism for the Co_2Rh_2 catalyzed oxidative carbonylation of primary/secondary amines to ureas.

Considering the results obtained above, we postulate a reaction mechanism for this newly developed oxidative carbonylation of amines, as shown in Scheme 1. Under the pressure of carbon monoxide, carbon monoxide first adsorbs on the nanoparticle surface. This makes the carbonyl susceptible to nucleophilic attack by the amine. The resulting intermediate (a CO-amine adduct) reacts with O_2 to give the amide and the hydroxy species. Attack of another amine and carbon monoxide gives the product, urea and water, and regeneration of the initial state.

In summary, a by-product-free catalytic method for the synthesis of symmetrically *N*,*N*′-substituted ureas from amine, CO, and O_2 has been developed. The catalytic system used in this study can be applied to both aliphatic and aromatic amines to give ureas.

Experimental Section

Immobilization of Co/Rh Nanoparticles on Charcoal

To a two-neck flask were added *o*-dichlorobenzene (10 mL), oleic acid (0.2 mL), and trioctylphosphine oxide (0.4 g). While the solution was heated at 180 °C, a solution of the metal carbonyl $Co_2Rh_2(CO)_{12}$ (0.8 g) in 25 mL *o*-dichlorobenzene was injected into the flask. The resulting solution was heated to 180 °C for 2 h and then concentrated to a volume of 5 mL. The concentrated solution was cooled to room temperature. To the cooled solution was added 30 mL of THF. After the solution had been well stirred for 10 min, flame-dried charcoal (1.6 g) was added to the solution. After the resulting solution had been refluxed for 12 h, the precipitates were filtered and washed with diethyl ether (20 mL), dichloromethane (20 mL), acetone (20 mL), and methanol (20 mL). Vacuum drying gave a black solid.

General Procedure for CoRh-Catalyzed Oxidative Carbonylation of Alkylamines to 1,3-Dialkylureas

Reactions were performed in a 100-mL stainless steel autoclave equipped with a stirring bar and the following were placed in the autoclave in the order, alkylamine (1.0 mmol), toluene (2 mL), and 3 mol% Co_2Rh_2 (50 mg of the immobilized Co_2Rh_2). The reactor was purged with O_2 gas, and charged with 5 atm of CO and heated at 100 °C for 3 h. After the reactor had been cooled to room temperature, the solution was filtered and concentrated, and the product was isolated by chromatography on a silica gel column eluting with hexane and ethyl acetate (v/v, 1:3).

General Procedure for CoRh-Catalyzed Oxidative Carbonylation of Arylamines to 1,3-Diarylurea

Reactions were performed in a 100-mL stainless steel autoclave equipped with a stirring bar and the following were placed in the autoclave in the order, arylamine (1.0 mmol), THF (2 mL), and 3 mol% Co_2Rh_2 (50 mg of the immobilized Co_2Rh_2). The reactor was purged with O_2 gas, and charged with 5 atm of CO and heated at 100 °C for 15 h. After the reactor had been cooled to room temperature, the solution was filtered and concentrated. Additionally, 5 mL DMF were added to the mixture and the resulting solution was stirred for 5 min. Then, excess H_2O was poured into the solution to precipitate the crude product, which was purified by washing with various solvent.

Recycling Experiment

In order to recycle the catalyst, it was separated by centrifugation from the reaction solution and washed twice with DMF/acetone and dried under vacuum. The recovered catalyst was then used *with/without* regeneration under same reaction conditions

Regeneration methods: The recovered catalyst after the first run was treated with CO or H_2 gas bubbling for 20 min in toluene.

Acknowledgements

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