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# Methanol Promoted Palladium-catalyzed Amine Formylation with CO<sub>2</sub> and H<sub>2</sub> by the Formation of HCOOCH<sub>3</sub>

Yanyan Wang,<sup>[a,b]</sup> Bingfeng Chen,<sup>[a]</sup> Shulin Liu,<sup>[a,b]</sup> Xiaojun Shen, <sup>[a,b]</sup> Shaopeng Li, <sup>[a,b]</sup> Youdi Yang, <sup>[a,b]</sup> Huizhen Liu,<sup>\*[a,b]</sup> and Buxing Han<sup>\*[a,b]</sup>

Dedication ((optional))

**Abstract:** The N-formylation reaction of amines is one of the most effective measures to make the best use of  $CO_2$ , since the formamides have widespread applications in industry. Herein, we performed the N-formylation reaction over Mg-Al layered double hydroxide (Mg-Al LDH) supported Pd catalyst (Pd/LDH) for the first time and studied the relation between the solvent and the mechanism. In this reaction, the methanol can greatly improve the yield of the desired product by forming the HCOOCH<sub>3</sub>. The catalytic system is effective for various amines including cyclic and alkyl secondary amines. Under the optimized reaction condition, we gained 88.5%-97.4% yields of the formamides for various substrates.

Nowadays, carbon dioxide chemistry has attracted extensive interest in both academic and industrial community<sup>[1]</sup> since the greenhouse effect becomes more and more serious, where CO<sub>2</sub> contributes a lot. Catalytic chemical reduction of CO<sub>2</sub> to valuable compounds is one of the most effective measures to make waste profitable.<sup>[2]</sup> On the one hand, CO<sub>2</sub> can be converted to high value-added chemical fuels through hydrogenation,<sup>[3]</sup> such as alcohols, hydrocarbons and so on; on the other hand, via the carbonylation or methylation reaction, we can gain a series of carbonyl containing chemicals including formamides, methylamines, esters, ureas, etc.<sup>[4]</sup> Among these products, the formamide has widespread applications in industry. It can not only serve as solvent but also raw material for the synthesis of many significant chemicals.

Among various synthetic routes to formamides, the Nformylation of amines using  $CO_2$  and  $H_2$  seems to be an ideal route because the only byproduct is water. Various catalysts have been reported for the N-formylation of amines with  $CO_2$ and  $H_2$  in different solvents.<sup>[5]</sup> Ding et al. reported the homogeneous ruthenium catalyzed N-formylation reaction with THF as the solvent.<sup>[6]</sup> Shi et al. found that the heterogeneous catalyst palladium was also active for this kind of reactions with octane as the solvent.<sup>[7]</sup> Mitsudome and his co-authors reported the selective N-formylation of functionalized amines in dimethylacetamide with carbon dioxide and hydrogen.<sup>[8]</sup> Liu et al. checked the effect of solvent and found that the best solvent was methanol for the N-formylation reaction over pyridinefunctionalized organic porous polymers supported Ru catalyst.<sup>[9]</sup> According to the results reported in the literature, we found that the different solvent was used over different catalytic system.

The reaction path is also important for the N-formylation reaction. In our previous work, we proposed the mechanism of the Cu-catalyzed formylation reaction in THF, where the salt (alkyl ammonium alkyl carbamate) served as the intermediate.<sup>[10]</sup> Except for this reaction pathway, the route to N-formylation reaction with CO<sub>2</sub> and H<sub>2</sub> through formic acid was also reported, where HCOOH is formed from the hydrogenation of CO<sub>2</sub>.<sup>[8]</sup> In spite of the good performance with different catalysts in various solvents, the reports about the effect of the solvent on the performance of the reaction and the relation between the solvent and the mechanism is little up to now.

Layered double hydroxides (LDHs) are a class of synthetic anionic clay. Generally, the layered double hydroxide is represented by the formula  $[M^{2+}{}_{1-x}M^{3+}{}_x(OH)_2]^{x+}(A^{n-})_{x/n}{}^mH_2O,$  where  $A^{n-}$  represents the intercalated anion between the positive divalent and trivalent cationic layers. Because of the high adsorption capacity and composition diversity, LDHs can serve as effective supports in the immobilization of catalytically active species on the surface.^{[11]} It has been reported that LDH supported heterogeneous catalysts exhibit good performance in various reaction systems.^{[12]}

In this work, we performed the N-formylation reaction over Mg-AI layered double hydroxide (Mg-AI LDH) supported Pd catalyst (Pd/LDH) for the first time and found that the reaction intermediates were different in different solvents. The methanol can greatly improve the yield of the desired product by forming the HCOOCH<sub>3</sub>. As far as we know, this is the first work to report the solvent effect and connect the solvent with the reaction mechanism for the N-formylation reaction of various amines.

The Mg-Al LDH was prepared by the co-precipitation method which was similar to that reported previously.<sup>[13]</sup> The supported Pd catalyst was prepared by impregnation method with NaBH<sub>4</sub> as the reducing agent (the details are shown in the supporting information).

Figure 1a shows the transmission electron microscopy (TEM) image of the prepared Pd/LDH, in which the nanoparticles with an average diameter of about 2.8 nm (Figure 1b) are immobilized uniformly on the support. The crystalline structure of the catalyst was characterized by the X-ray diffraction (XRD) and the result is shown in Figure 1c. It is noteworthy that no obvious diffraction peaks of metallic Pd were observed, which is due to very small size and well dispersion of the Pd particles. The crystal planes of (003), (006), (012), (015), (018), (110) and (113) were obviously observed, which is corresponding to a typical layered double hydroxide material.<sup>[14]</sup> The XPS measurement was used to study the surface electronic

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state of the palladium catalyst. The peak at 335.54 eV is assigned to the Pd<sup>0</sup>  $3d_{5/2}$  and the peak at 337.08 eV is assigned to the Pd<sup>2+</sup>  $3d_{5/2}$ . The other spin-orbit component,  $3d_{3/2}$ , appears at 340.62 eV and 342.41 eV for Pd<sup>0</sup> and Pd<sup>2+</sup>, respectively.<sup>[15]</sup> It is demonstrated that 86.5% of the palladium species have been reduced to Pd<sup>0</sup> in spite of a small quantity of Pd<sup>2+</sup> after reduction. The ICP-AES suggests that the palladium content is 2.9%.



**Figure 1.** (a) TEM image of the Pd/LDH. (b) the corresponding size analysis of the Pd nanoparticles. (c) XRD patterns of the Pd/LDH. (d) XPS spectra of the Pd/LDH.

Initially, we optimized the reaction conditions in methanol using the N-formylation of morpholine as the model reaction and the results are shown in Table S1. The optimized reaction temperature is 140 °C and the optimized catalyst dosage was 1 mol% of the substrate. 3.0 MPa  $CO_2$  and 3.0 MPa  $H_2$  was the optimized pressure, and 16 h was enough to realize the high yield of the product.

The effect of different solvents were checked under the optimized reaction conditions for the N-formylation reaction of morpholine and the carbon balance values were calculated from morpholine, N-formylmorpholine (Table 1). In hexane, the conversion of morpholine reached up to 94.6% while the yield of the N-formylmorpholine was 3.6% with only 9.0% carbon balance value (Table 1, Entry 1). In THF, the conversion of the morpholine was 47.2% with a 34.8% yield of the Nformylmorpholine and the carbon balance value was 87.6% (Table 1, Entry 2). The carbon balance values far from 100% in THF and hexane mean that there are other products besides Nformylmorpholine in these solvents. That is to say, the yield of the by-products in hexane is more than that in THF. The carbon balance values in the other solvents are near 100% (Table 1, Entries 3-5), which illustrates that N-formylmorpholine is the only product in these solvents. Under optimal reaction conditions, methanol exhibits the best performance for the N-formylation reaction of morpholine with 92.7% conversion and 91.4% yield (Table 1, Entry 5).

It has been reported that the amine can quickly react with CO<sub>2</sub> to form the corresponding alkyl ammonium alkyl carbamate.<sup>[16]</sup> The existence of alkyl ammonium alkyl carbamate was also proved by the white solid product from reacting 1 mmol morpholine with 3 MPa CO<sub>2</sub> at room temperature for 10 min in our experiment. The solubility of alkyl ammonium alkyl carbamate was checked in different solvents. The test methods

for solubility were shown in supporting information. The results showed that 2.6% and 53.4% of alkyl ammonium alkyl carbamate produced from 1 mmol morpholine and 3 MPa  $CO_2$  can be dissolved in 2 mL hexane and in 2 mL THF, respectively. We didn't observe the solid products in 2 mL methanol, ethanol and the mixed solvent of THF and methanol (1:1 in volume). It is obvious that the solubility of the alkyl ammonium alkyl carbamate in various solvents is related to the carbon balance value. The poorer the solubility of the alkyl ammonium alkyl carbamate in the solvent, the lower the carbon balance value. The carbon balance value in hexane and THF is far less than 100% because the insoluble salts can't be detected by gas phase chromatography.

Table 1. N-formylation of morpholine with CO2 and H2 in various solvents

Entry	Solvent	Conversion (%)	Yield (%)	Carbon balance
1	hexane	94.6	3.6	9.0%
2	THF	47.2	34.8	87.6%
3	CH <sub>3</sub> CH <sub>2</sub> OH	56.0	55.8	99.8%
4	THF+CH <sub>3</sub> OH	55.3	54.6	99.3%
5	CH₃OH	92.7	91.4	98.7%

Reaction conditions: morpholine (1 mmol), Pd/LDH (1 mol% of the substrate), solvent (2 mL),  $P_{H2}$  (3 MPa),  $P_{CO2}$  (3 MPa), temperature (140 °C), reaction time (16 h).

Entry 4, THF: CH<sub>3</sub>OH = 1:1 in volume

Generally, CO<sub>2</sub> can be reduced to HCOOH or HCOOCH<sub>3</sub> depending upon the catalytic system used and reaction conditions operated. In this work, we also investigated HCOOH or HCOOCH<sub>3</sub> as the C1 source to find out their performances in N-formylation reaction of morpholine, and the results are given in Table 2. With the increase of HCOOH or HCOOCH<sub>3</sub>, the yield increased gradually. Interestingly, at the same concentration of C1 source, HCOOCH<sub>3</sub> gave higher yield of N-formylmorpholine. When 0.5 mmol HCOOH was used as the C1 source in methanol, the yield of N-formylmorpholine was only 1.8% (Table 2, Entry 1). However, the yield could reach up to 54.3% by using 0.5 mmol HCOOCH<sub>3</sub> as the C1 source (Table 2, Entry 4). 1.0 mmol HCOOCH<sub>3</sub> was enough to realize the high yield of morpholine (Table 2, Entry 5). However, with the same amount HCOOH, the yield was only 16.3% (Table 2, Entry 2). When we increased the amount of HCOOH to 2.5 mmol, we also gained high yield of the product (Table 2, Entry 3), which is consistent with the HCOOH-mediated formylation reaction report.<sup>[8]</sup> Besides, we compared the reaction rate using the same amount of HCOOH and HCOOCH<sub>3</sub> as C1 source in other solvents and other catalytic systems for the N-formylation reaction. In THF, there was no product detected with HCOOH as the carbon source (Table 2, Entry 7), while the yield of N-formylmorpholine can reach up to 91.7% by using HCOOCH<sub>3</sub> under the same conditions (Table 2, Entry 8). With commercial 5% Pd/C as the catalyst, the yield of the product was 84.8% by using HCOOCH<sub>3</sub> (Table 2, Entry10), while there was little product detected by using HCOOH (Table 2, Entry 9). In commercial 1% Pd/Al<sub>2</sub>O<sub>3</sub> catalytic system, the yields of the product by using HCOOH and

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HCOOCH<sub>3</sub> were 52.3% and 90.2%, respectively (Table 2, Entries 11-12). These results illustrate that the HCOOCH<sub>3</sub>mediated reaction pathway is superior to the HCOOH-mediated pathway for the N-formylation reaction. More importantly, the superiority of the HCOOCH<sub>3</sub>-mediated reaction pathway is universal but not limited to our catalytic system.

When the N-formylation reaction of morpholine with CO<sub>2</sub> and H<sub>2</sub> was performed in methanol, we detected a small amount of methyl formate. It means that the HCOOCH<sub>3</sub> is the reaction intermediate in CH<sub>3</sub>OH. When the reaction was performed in THF or in ethanol, the reaction went only through the salt or HCOOH-mediated pathway since HCOOCH<sub>3</sub> can't be produced in these reaction systems. The absence of HCOOCH<sub>3</sub> intermediate in THF and ethanol greatly slowed down the reaction rate and resulted in the lower yields than that in methanol.

Entry	Carbon source	Amount (mmol)	Yield (%)
1	НСООН	0.5	1.8
2	НСООН	1.0	16.3
3	НСООН	2.5	92.1
4	HCOOCH₃	0.5	54.3
5	HCOOCH₃	1.0	88.6
6	HCOOCH₃	2.5	92.7
7 <sup>[a]</sup>	НСООН	1.0	0
8 <sup>[a]</sup>	HCOOCH₃	1.0	91.7
<b>9</b> <sup>[b]</sup>	НСООН	1.0	1.2
10 <sup>[b]</sup>	HCOOCH <sub>3</sub>	1.0	84.8
11 <sup>[c]</sup>	НСООН	1.0	52.3
12 <sup>[c]</sup>	HCOOCH <sub>3</sub>	1.0	90.2

Reaction conditions: morpholine (1 mmol), Pd/LDH (1 mol% of the substrate), solvent (2 mL CH<sub>3</sub>OH), temperature (140 °C), reaction time (16 h)

[a] solvent (2 mL THF), reaction time (12 h)

[b] commercial 5% Pd/C (1 mol% of the substrate), solvent (2 mL THF), reaction time (12 h)

[c] commercial 1% Pd/Al\_2O\_3 (0.33 mol% of the substrate), solvent (2 mL THF), reaction time (12 h)

The possible reason for the superiority of the HCOOCH<sub>3</sub>mediated reaction pathway to the HCOOH-mediated reaction pathway is also discussed. The possible reaction paths involved in HCOOH and HCOOCH<sub>3</sub> are shown in Scheme 1. Formamides are obtained through the nucleophilic attack of the amines to HCOOH or HCOOCH<sub>3</sub>. Amine could form corresponding quaternary ammonium salt in the presence of HCOOH, which will lower the ability for nucleophilic attack of the amine in the reaction system. However, the amines with lone electron pairs can directly attack the HCOOCH<sub>3</sub> intermediate to obtain the corresponding products in the  $HCOOCH_3$ -mediated reaction pathway.



Scheme 1. The possible reaction paths involved in HCOOH (a) and  $\mbox{HCOOCH}_3$  (b).

To test the versatility of the Pd/LDH catalytic system, we explored the formylation of various substrates with CO2 and H2 (Table 3). By using 1-methylpiperizine as the substrate, we gained the desired product with 88.5% yield (Table 3, Entry 1). Besides, the N-formylation reactions of other cyclic secondary amines, such as tetrahydropyrrole and 4-methylpiperidine, also proceeded smoothly and the yield of the desired product was 96.4% and 95.0%, respectively (Table 3, Entries 2 and 3). The catalytic system exhibited excellent performance not only for the cyclic secondary amines, but also for the secondary alkyl amines. Both the yields of the desired product were higher than 90.0% when we used N-methylpropylamine and Nmethylbutylamine as the substrates (Table 3, Entries 4 and 5). Excitingly, the reaction also went smoothly by employing the primary amine as the substrate. The yield of the butylformamide can reach up to 97.4% (Table 3, Entry 6).

#### Table 3. N-formylation of other substrates with $CO_2$ and $H_2$



In conclusion, with the Pd/LDH catalytic system, the formylation reaction of amines with  $CO_2$  and  $H_2$  in methanol exhibited unique superiority compared to that in other solvents. Methanol plays a significant role in accelerating the formylation

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reaction rates since it provides another reaction pathway where  $HCOOCH_3$  behaves as the intermediate. Under the optimized reaction condition, 88.5%-97.4% yields of the formamides were obtained for various substrates in methanol. This work provides a guideline for the choice of the solvent for the N-formylation reaction, also a direction for the research on the relation between the reaction mechanism and the solvent employed in the reaction system.

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Layout 1:

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We performed the N-formylation reaction of amines with  $CO_2$  and  $H_2$ over Mg-Al layered double hydroxide (Mg-Al LDH) supported Pd catalyst (Pd/LDH) in various solvents. Among the solvents we checked, methanol exhibits unique performance since it provides a new HCOOCH<sub>3</sub>-mediated reaction pathway, which can greatly accelerate the reaction rate. This catalytic system is also effective for various amines including cyclic and alkyl secondary amines.



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