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ARTICLE TYPE

An efficient copper catalyzed formylation of amines utilizing CO_2 and hydrogen

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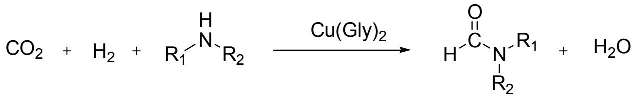
Received (in XXX, XXX) Xth XXXXXXXXX 20XX, Accepted Xth XXXXXXXXX 20XX

DOI: 10.1039/b000000x

Trans-*bis*-(glycinato)copper(II) complex was found to be highly active, economical and efficient heterogeneous catalyst for the formylation of amines utilizing CO_2 and hydrogen under solvent less conditions.

Chemical fixation of carbon dioxide (CO_2) to high value chemicals has gained considerable interest in recent years due to the gowning environmental concerns and its abundant availability at low cost. Replacement of toxic and hazardous C1 building blocks such as phosgene, carbon monoxide with non-toxic CO_2 represents a green and sustainable approach for the synthesis of carbonyl group derived industrially important chemicals such as urea, alkyl carbonates, formamides, carbamates and isocynates.[1] The formylation of amines using CO_2 and hydrogen is of great importance due to versatile applications of formamides such as solvent, in the manufacture of polyurethane leatherette, polyacronitrile fiber and pharmaceutical industry.[2] In this context a number of transition metal based catalysts such as iridium oxide cluster dispersed in titania, silica hybrid aerogels containing bidentate ruthenium complexes, $Pd(CO_3)[P(C_6H_5)_3]_2$, $RuCl_2[P(CH_3)_3]_4$ etc. have been reported.[3] However, in most of the cases the use of expensive metal catalysts, rapid deactivation of the catalyst and severe reaction conditions make the developed processes less attractive for large scale synthesis. Recently, Feng Shi et al. have demonstrated the use of Pd/Al_2O_3-NRs as efficient heterogeneous catalyst for amine formylation.[4] However, the use of expensive Pd metal, two step process of catalyst synthesis and longer reaction time still leaves a scope for the further development of an efficient and cost effective methodology for this transformation.

In the present we disclose for the first time an efficient, easily accessible and inexpensive *bis*-(glycinato)copper(II) i.e. $Cu(gly)_2$ complex as a recyclable catalyst for the formylation of various secondary amines including aliphatic and aromatic using CO_2 and H_2 under solvent less conditions (Scheme 1).



Scheme 1 $Cu(gly)_2$ catalysed formylation of amines

The $Cu(gly)_2$ complex was easily obtained from the reaction of copper chloride and glycine in ethanol under refluxing condition in almost quantitative yields. The synthesized catalyst was characterized by XRD, XPS, FT-IR, and TGA. Detailed synthetic procedure and characterization of the catalyst is given in supporting information file. The chemical nature and functionalities presented in $Cu(gly)_2$ complex were revealed by FT-IR (Fig S1). Two intense peaks at 1604 and 1389 cm^{-1} in the spectrum of $Cu(gly)_2$ are attributed to COO^- asymmetric and symmetric stretches, respectively. Furthermore, strong bands at 3334 and 1423 cm^{-1} are due to N-H stretch and bending vibrations of amino functional groups of glycine revealed the formation of $Cu(gly)_2$ complex.[5] Importantly, O-H stretching vibration do not appear in complex in the range (3450 – 3750) cm^{-1} suggesting the absence of the lattice and coordinated water. XPS analysis of $Cu(gly)_2$ complex was carried out to elucidate the chemical interaction between the $CuCl_2$ and glycine (Fig. 1). The survey scan XPS spectra explicitly demonstrated the presence of C, N, O, and Cu elements. The high-resolution Cu 2p spectrum exhibited split bands of Cu 2p peak at 936.1 and 956.8 eV due to Cu $2p_{3/2}$ and Cu $2p_{1/2}$, respectively is consistent with Cu(II) oxidation state.[6] XRD pattern of the $Cu(gly)_2$ complex (Fig. 1c), exhibits strong peaks and are found to be identical to the pure $Cu(gly)_2$ (JCPDS card No. 17-1814).[7] TG analysis results of $Cu(gly)_2$ complex is depicted in (Fig 1d). The TG curve recorded under N_2 atmosphere at 10°C/min heating rate shows a single step weight loss at temperatures ranging from 50 °C to 600 °C. It is observed that there is no weight loss until 250 °C, which further confirms the absence of lattice water molecules. TGA results are in good agreement with the results of FT-IR. The values of elemental analyses (found: C, 22.41 %; H, 3.52 %, N, 13.33 %; cal: C, 22.70%, H, 3.81%, N, 13.23 %) suggested the proposed formula of complex is $Cu(gly)_2$. These results suggested the successful formation of the substantive $Cu(gly)_2$ complex.

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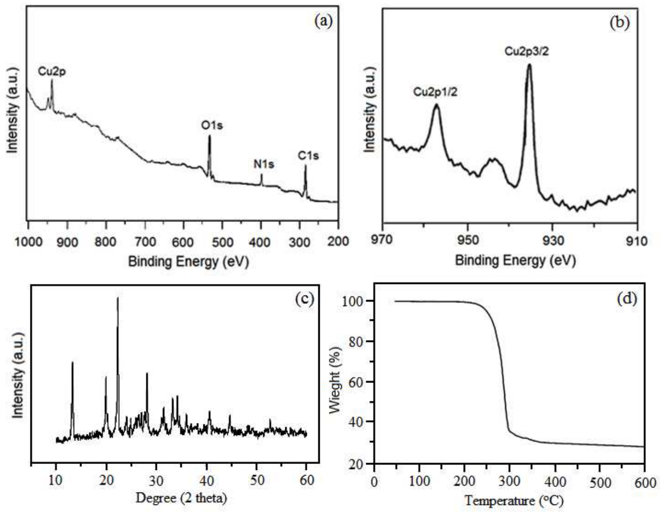

Fig 1: a) Broad scan XPS spectra of Cu(gly)$_2$; b) High resolution XPS spectra of Cu2p; c) XRD of Cu(gly)$_2$; d) TGA of Cu(gly)$_2$

The catalytic activity of the synthesized heterogeneous catalyst i.e. Cu(gly)$_2$ was tested for the formylation of various primary and secondary amines including aliphatic and aromatic to the corresponding formamides by using CO_2 and hydrogen. At first, diethyl amine was chosen as a model substrate to optimize the reaction conditions. The experiments were carried out in a stainless steel 15 ml autoclave under stirring at 85 °C and 50 bar pressure for 4h. The maximum formylation of diethyl amine under the optimized reaction condition was found to be 95 % as shown in Table 1, entry 4.

In the absence of any catalyst, no reaction was taken place under identical experimental conditions (Table 1, entry 1). In order to compare the catalytic activity of the developed heterogeneous catalyst with its homogeneous analogue, we also carried out the formylation of diethyl amine from hydrogen and CO_2 using homogeneous copper $CuCl_2$ and mix of $CuCl_2$/glycine as catalyst under described experimental conditions. The results are summarized in Table 1 (entry 2-3).

Table 1 Catalytic activity of Cu(gly)$_2$ over its analogue

Entry	Catalyst (mol %)	Yield (%)	Selectivity (%)
1.	-	-	-
2.	$CuCl_2$	21	75
3.	$CuCl_2$/Glycine	39	71
4.	*Trans*-Cu-(Gly)$_2$	95	98
5.	*Cis*-Cu(Gly)$_2$.H_2O	71	95
6.	*Trans*-Cu(Gly)$_2$.H_2O	70	92

^{a} Reaction conditions: diethyl amine (5 ml); catalyst (0.1g); molar ratio of CO_2/H_2 (1.25); Total pressure of reaction (50 bar); reaction time 4h.

In the present study, we observed that *trans*-Cu(gly)$_2$ complex exhibited higher catalytic activity as compared to its hydrated *cis*- and *trans*-analogues (Table 1, entry 4-6). The lower catalytic activity of the hydrated complexes might be due to the presence of water molecules on the axial position[8] which hindered the copper to interact with hydrogen from one side. While in case of *trans*-Cu(gly)$_2$ both the axial positions are free to interact with hydrogen and therefore gave higher rate of the reaction. Besides these experiments, we also investigated the effect of temperature, molar ratio of CO_2 and H_2, and reaction time on the formylation of diethyl amine under described reaction conditions. At ambient temperature (25 °C), the reaction rate was found to be slow and depended on the CO_2 pressure applied (Fig. 2a). Among the various conditions 85 °C temperature and 50 bar CO_2 pressure was found to be optimum for maximum conversion of diethylamine to corresponding formamide. Further increase in temperature (120 °C) was found to be unsuitable and exhibited significant decrease in the formylation of diethyl amine. This may be due to the formation of undesired N-methylated by-products. In addition, the reaction was found to be increased with increasing the molar ratio of CO_2 and H_2 up to 1.25 (Fig. 2b). Further increase in CO_2/H_2 molar ratio did not affect the reaction to any significant extent (Fig 2b). Next, we studied the effect of the reaction time on the yield of the formylated product (Fig 2c). The yield of the desired product was found to be increased with time up to 4h, however further increase in reaction time did not influence the reaction to any considerable level.

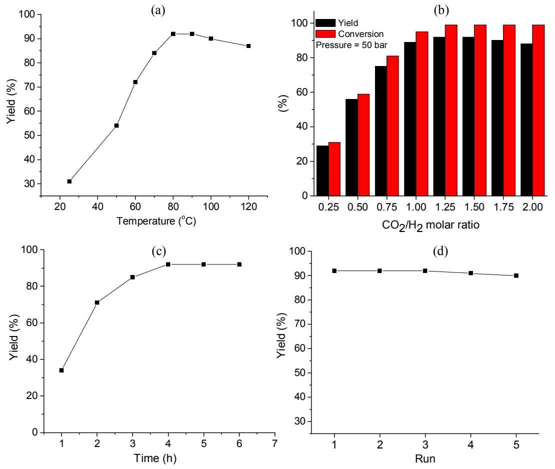

Fig. 2 a) Effect of temperature on the yield of product at 50 bar ; b) effect of molar ratio of CO_2/H_2 on the yield of product keeping reaction pressure 50 bar at 85°C; c) effect of time on the yield of product at 85°C and 50 bar CO_2 pressure; d) recyclability of the catalyst

Furthermore, we checked the recycling ability of the recovered catalyst. The results of the recycling experiments are summarized in Fig 2d. The recovered catalyst exhibited almost similar activity under identical conditions at least for five runs. Moreover, to ascertain the leaching of metal, we analyzed the reaction mixture after separating catalyst by ICP-AES analysis. No detectable leaching of copper could be observed during the course of reaction which further proved that the developed catalyst is truly heterogeneous in nature.

Furthermore, the reaction was extended to a variety of secondary amines including aliphatic and aromatic under the optimized reaction conditions. The results of these experiments are summarized in Table 2. The reaction proceeded successfully and afforded 81-95 % yield of the desired product in all cases (Table 2, entry 1,2,4-8) except in *N*-methyl aniline (Table 1, entry 3). The lower reactivity of *N*-methyl aniline might be due to the

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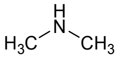
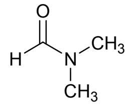
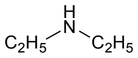
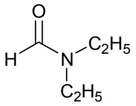
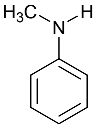
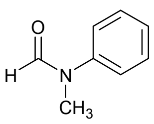
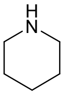
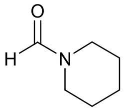
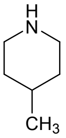
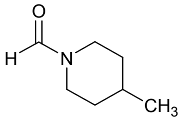
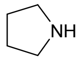
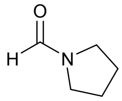
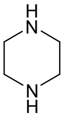
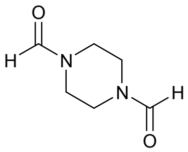
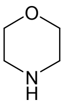
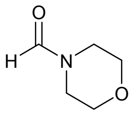
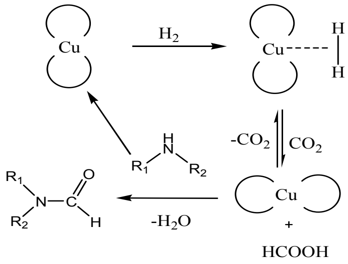
presence of aromatic ring and steric hindrance.

Table 2 Cu(Gly)$_2$ catalyzed formylation of amines

Entry	Substrate	Product	Yield (%)	Select. (%)
1.			91	96
2.			95	98
3.			41	85
4.			95	97
5.			91	97
6.			90	96
7.			81	91
8.			92	95

[a] Reaction conditions: amine (5 mL); catalyst (0.1 g); molar ratio of CO_2/H_2 =1.25; Total pressure of reaction 50 bar; 85 °C; 4 h

Although, the exact mechanism of the reaction is not clear at this stage, based on the existing literature reports,[9] a plausible mechanism for the reaction is shown in Scheme 2. In analogy to the previous reports, we presumed that Cu activates the H_2 which reacts with CO_2 to give HCOOH. Formic acid subsequently reacts with amine in the dehydration step to give corresponding formamides. It is also clear from the mechanism that high pressure of CO_2 is favourable to shift the equilibrium towards forward direction.



Scheme 2 Possible Reaction Mechanism

In summary, we have developed an easily accessible, cost effective copper (II) glycinato to be used as highly efficient, recyclable and selective catalyst for the formylation of secondary amines directly from the reaction of CO_2 and H_2 without using any solvent.

Notes and references

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† Electronic Supplementary Information (ESI) available: [Experimental, FT-IR, XRD, TGA and Proton NMR data of products]. See DOI: 10.1039/b000000x/

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