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Tetrahedron Letters
Tetrahedron Letters 48 (2007) 5883–5886

A novel and efficient (NHC)Cu^{I} (NHC = N-heterocyclic carbene) catalyst for the oxidative carbonylation of amino compounds

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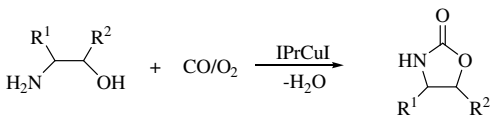
Received 16 May 2007; revised 7 June 2007; accepted 11 June 2007
Available online 14 June 2007

Abstract—Oxidative carbonylation of amino compounds to prepare corresponding 2-oxazolidinones, ureas, and carbamates selectively in the presence of (NHC)Cu^{I} without any additives was firstly achieved in good yields and selectivities.

2-Oxazolidinone, urea, and carbamate have often successfully been employed as intermediates for fine chemicals, pharmaceuticals, cosmetics, and pesticides.[1] Classical synthesis of these three N-containing carbonyl compounds are mainly conducted by phosgenation of the corresponding amino compounds with toxic phosgene or its derivatives,[2] which may result in serious environmental pollution and equipment corrosion. With the increasing environmental concerns, there is a great demand for finding some efficient and environmentally benign methods in place of such toxic and dangerous reagents. Recently, production of 2-oxazolidinone, urea, and carbamate by oxidative carbonylation of corresponding amino compounds as effective alternative have been considerably studied. Many transition metals including Rh,[3] Ru,[4] and especially Pd[5] have been reported to catalyze this process. However, the reported literatures are mostly focus on the costly noble metal catalysts, and additives such as KI and I_2 need to be used. Therefore, it is necessary to develop a non-noble metal catalytic system to mediate this reaction with an efficient performance.

Starting with the isolation of the first stable N-heterocyclic carbene (NHC) by Arduengo et al. in 1991,[6] NHCs have emerged as efficient ligands in metal-mediated reactions due to their strong σ-donor properties compared to tertiary phosphine, thereby enhancing the stability of NHC complexes toward heat and moisture. This characteristic property is very important for a catalyst to keep efficient activity in the carbonylation because they always proceed under rigorous conditions. Many catalytic applications for NHC complexes have been involved recently,[7] including several Pd or Rh NHC complexes mediated carbonylations.[8] However, very few non-expensive metal NHC complex systems were reported for all the carbonylation. So in this hand it is also necessary to develop a cheap metal NHC complex system to catalyze oxidative carbonylation reaction.

Actually, we have developed some good processes for the syntheses of 2-oxazolidinone, urea, and carbamate with good yields and selectivities.[9] As a part of our ongoing interest in the construction of N-containing carbonyl compounds with oxidative carbonylation method, we herein report a (NHC)Cu^{I} catalytic system without any additives for the oxidative carbonylation of amino compounds to synthesize 2-oxazolidinone, urea, and carbamate selectively under different reaction conditions (Eqs. 1–3). To the best of our knowledge, this is the first catalyst example for the oxidative carbonylation of amino compounds to selectively prepare three different N-containing carbonyl compounds.



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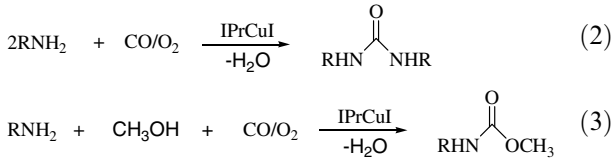
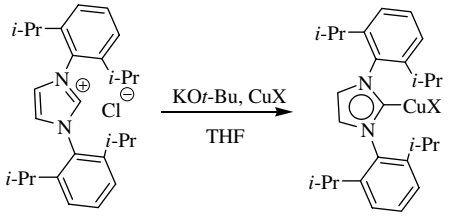
doi:10.1016/j.tetlet.2007.06.049



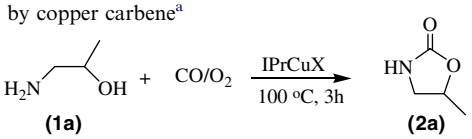
The air- and moisture-stable NHC–Cu^{I} complexes were readily prepared by deprotonation of 1,3-bis(2,6-di-isopropylphenyl)-imidazolium chloride with KO*t*-Bu in the presence of different CuX with good yields (Scheme 1).[10] And initial investigation of oxidative carbonylation was carried out using 1-amino-2-propanol (**1a**) as a probe substrate to optimize the reaction conditions, and the results are listed in Table 1. The influence of halogen anions on the NHC–Cu^{I} catalyst was first examined in the preparation of 5-methyloxazolin-2-one (**2a**). IPrCuI shows excellent reactivity (100% conv. and 99% sel.) (Table 1, entry 1), surprisingly IPrCuBr gives poor results and IPrCuCl has no reactivity at all. The results indicate that the anions on the metal center have a remarkable influence on the activity of the NHC–Cu^{I}, this phenomenon is similar to that of the Pd based system.[5e,9a] A comparison experiment was also done using CuI as the catalyst, and only 53% conversion of **1a** was observed (Table 1, entry 4). We considered that the bulky NHC ligand pushed a positive effect on Cu(I),



IPrCuCl: X=Cl; IPrCuBr: X=Br; IPrCuI: X=I

Scheme 1. Synthesis of copper N-heterocyclic carbene.

Table 1. Oxidative cyclocarbonylation of 1-amino-2-propanol catalyzed by copper carbene[a]



(1a) (2a)

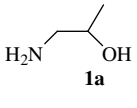
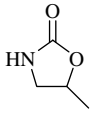
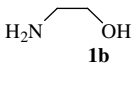
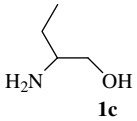
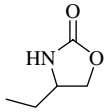
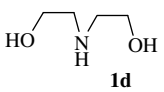
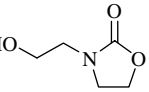
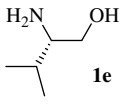
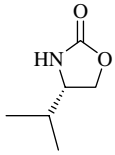
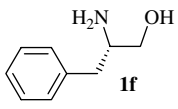
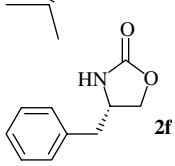
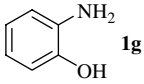
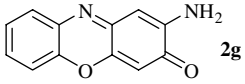
Entry	Catalyst	Solvent	Conversion (%)	Selectivity (%)
1	IPrCuI	Dioxane	100	99 (96[b])
2	IPrCuBr	Dioxane	8	87
3	IPrCuCl	Dioxane	—	—
4	CuI	Dioxane	53	96
5	IPrCuI	THF	100	99
6	IPrCuI	Toluene	100	37
7	IPrCuI	Acetonitrile	100	99
8	IPrCuI	DMF	99	6
9	IPrCuI	DME	99	5

[a] Reaction condition: 0.01 mmol of catalyst, 1 mmol of 1-amino-2-propanol, solvent (4 ml), $P_{CO} = 4.8$ MPa, $P_{O_2} = 0.2$ MPa, 100 °C for 3 h.
[b] Isolated yield.

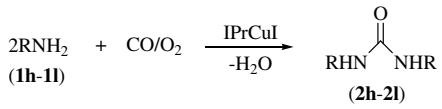
and its catalytic activity was enhanced. It is also worth to note here that there is no need to add any other iodide-containing promoters in this catalyst system to obtain good yield. On the other hand, solvents also play a key role in the activity and selectivity. The effects of different solvents on the reaction were investigated with IPrCuI as catalyst, it is seen that acetonitrile, 1,4-dioxane and THF have proved to be a suitable reaction medium (Table 1, entries 1, 5, and 7), whereas toluene afforded lower yields (Table 1, entry 6). Poor results were observed when the reaction was carried out in 1,2-dimethoxyethane (DME) and DMF (Table 1, entries 8 and 9).

After optimization of the reaction conditions, oxidative carbonylation of other β-aminoalcohols were further tested. As seen in Table 2, IPrCuI catalyst shows excellent catalytic activity to almost all the employed β-aminoalcohols under mild conditions, providing the corresponding 2-oxazolidinones in high isolated yields. The diethanolamine (Table 2, entry 4) could also be converted to the corresponding 2-oxazolidinones through the oxidative carbonylation reaction. To our delight, optical activity of 2-oxazolidinones could be efficiently

Table 2. Synthesis of 2-oxazolidinones catalyzed by IPrCuI[a]

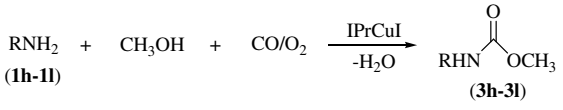
Entry	Substrate	Product	Yield[b] (%)
1	 **1a**	 **2a**	96
2	 **1b**	 **2b**	86
3	 **1c**	 **2c**	91
4	 **1d**	 **2d**	90
5	 **1e**	 **2e**	93[c]
6	 **1f**	 **2f**	86[d]
7	 **1g**	 **2g**	90

[a] Reaction condition: 0.01 mmol of IPrCuI, 1 mmol of aminoalcohol, dioxane (4 ml), $P_{CO} = 4.8$ MPa, $P_{O_2} = 0.2$ MPa, 100 °C for 3 h.
[b] Isolated yield.
[c] $[\alpha]_D^{20}$ −15 (*c* 2, ethanol).
[d] $[\alpha]_D^{20}$ −62 (*c* 1, chloroform).



R = n-C_3H_7 **2h**, 86%; R = n-C_4H_9 **2i**, 96%; R = t-C_4H_9 **2j**, 93%; R = cyclohexyl **2k**, 19%; R = C_6H_5 **2l**, <5%

Reaction condition : 0.01mmol of IPrCuI, 1mmol of amine, dioxane (4ml), P_{CO} =4.8MPa, P_{O2} =0.2MPa, 100 °C for 3h.



R = n-C_3H_7 **3h**, 98%; R = n-C_4H_9 **3i**, 98%; R = t-C_4H_9 **3j**, 93%; R = cyclohexyl **3k**, 89%; R = C_6H_5 **3l**, <10%

Reaction condition : 0.01mmol of IPrCuI, 1mmol of amine, CH_3OH (4ml), P_{CO} =4.8MPa, P_{O2} =0.2MPa, 100 °C for 3h.

Scheme 2. Selective synthesis of urea and carbamate by IPrCuI catalyzed oxidative carbonylation of primary amines under optimized conditions.

obtained from corresponding chiral β-aminoalcohols without racemization based on the polarimetric characterization (Table 2, entries 5 and 6). When 2-aminophenol (**1g**) was used as the reaction substrate, only traces of product were observed (Table 2, entry 7). We confirmed the main product 2-aminophenoxazin-3-one (**2g**) was derived from an oxidative dimerization process without CO incorporation.[5c]

Further investigation showed that this efficient copper NHC catalytic process could also be applied to the oxidative carbonylation of primary amines to prepare the corresponding ureas and carbamates with or without CH_3OH included in the catalytic cycle, the results are shown in Scheme 2. Excellent isolated yields (86–98%) of ureas and carbamates were obtained from *n*-propylamine, *n*-butylamine and *t*-butylamine, respectively. When cyclohexylamine is used as the substrate, the yield of corresponding carbamate (**3k**) is good (89%), but its activity toward preparation of urea (**2k**) was poor (19%). GC–MS analysis shows that there is imine in the reaction mixture, it indicates that there is an oxidation reaction as a side reaction.[12] The low yield of 1,3-cyclohexylurea (**2k**) may be ascribed to the oxidation of secondary amine to imine is faster than urea formation. It was regrettable that the present methodology could not be applied to aromatic amines, it was clear that the reactivity difference between the two classes of amines must be due to the differences of their basicity and nucleophilicy.[11]

In summary, we have successfully developed an efficient and simple copper N-heterocyclic carbene catalyst system without any additive for the oxidative carbonylation of β-aminoalcohols and primary amines to produce 2-oxazolidinones, disubstituted ureas and carbamates, respectively. It is the first time that a copper complex was used in the oxidative carbonylation of amino alcohols and amines. This methodology represents an economic and environmentally benign non-phosgene alternative for the preparation of these three important N-containing carbonyl compounds. The understanding of the reaction mechanism is ongoing in our laboratory.

Acknowledgements

We are grateful to the Chinese National Sciences Foundation (20533080) and The National Science Fund for Distinguished Young Scholars (20625308) for financial support.

Supplementary data

Experimental procedures and spectral data for the compounds are given in the Supplementary data. Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2007.06.049.

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