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Copper-Catalyzed C–N Bond Formation *via* Oxidative Cross-Coupling of Amines with α-Aminocarbonyl Compounds

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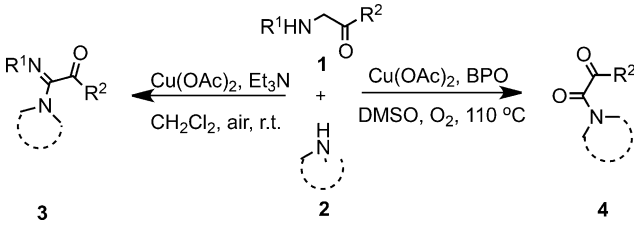
Abstract: A novel and selective method for the simple copper-catalyzed α-amination of α-aminocarbonyl compounds to afford 2-amino-2-iminocarbonyl and 2-amino-2-oxocarbonyl compounds is reported. This transformation is achieved by C(sp^3)–H and N–H bond oxidative cross-coupling and selective C–N bond oxidative cleavage. This reaction system has a broad reaction scope, providing a facile pathway for the α-functionalization of α-amino ketones.

Keywords: α-amination; α-aminocarbonyl compounds; C(sp^3)–H functionalization; copper; oxidative cross-coupling

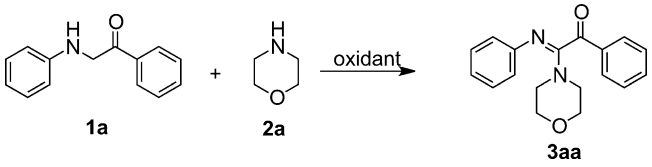
α-Aminocarbonyl compounds are important structural motifs existing widely in a large number of biologically active natural products, biomolecules and therapeutic agents.[1] The functionalization of α-C–H bonds to the carbonyl group in α-aminocarbonyl compounds has attracted considerable attention in organic and bioorganic synthesis.[2–4] In the past decade, significant progress has been achieved in developing various functionalizations of C–H bonds adjacent to a carbonyl group by employing different nucleophiles.[5–12] These reactions were mostly catalyzed by iron or copper salts in combination with stoichiometric amounts of chemical oxidants such as DTBP, DDQ, TBHP or TEMPO oxoammonium salt.[5–12] For example, Li and co-workers reported a copper-catalyzed C–H oxidative/cross-coupling of α-aminocarbonyl compounds with indoles to furnish 2-(1*H*-indol-3-yl)-2-iminocarbonyl and 2-(1*H*-indol-3-yl)-2-oxocarbonyl compounds selectively in 2012.[6] Subsequently, the same group demonstrated the copper-catalyzed α-alkylation of α-aminocarbonyl compounds with ethers *via* dual C(sp^3)–H bond oxidative cross-coupling.[8] In 2013, Yang's group described a novel protocol of copper-catalyzed oxidative phosphonation by using α-aminocarbonyls and diphenylphosphine.[10] To the best of our knowledge, the formation of C–C bonds has been reported largely, however, the cleavage of α-C(sp^3)–H bonds to the carbonyl group in α-aminocarbonyl compounds leading to C–N bond formation has rarely been studied. Herein, we present a facile route to selectively synthesize 2-amino-2-iminocarbonyl compounds **3** and 2-amino-2-oxocarbonyl compounds **4** by copper-catalyzed C–H oxidation/cross-coupling of α-aminocarbonyl compounds **1** with amines **2** to give new C–N bonds. Interestingly, the selectivity for either **3** or **4** can be tuned by a slight modification of the reaction conditions (Scheme 1).

Our initial study began with 1-phenyl-2-(phenylamino)ethanone **1a** and morpholine **2a** in the presence of 0.5 equiv. $Cu(OAc)_2$ in CH_2Cl_2 at room temperature under air (entry 1; Table 1). To our delight, the desired product 2-morpholino-1-phenyl-2-(phenylimino)ethanone **3aa** was obtained in 72% yield. Encouraged by this result, we continued optimizing the other reaction parameters. After a series of trials, we found that other oxidants such as $CuCl_2$, NIS, I_2, and AgOAc did not provide any better results (entries 1–6; Table 1). Screening revealed that the amount of



Scheme 1. Copper-catalyzed C–H oxidation.

Table 1. Screening for optimal reaction conditions.[a]



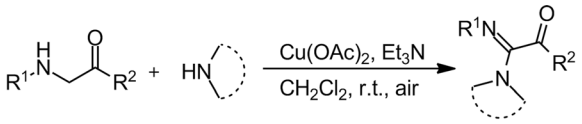
Entry	Oxidant (equiv.)	Additive (equiv.)	Solvent	Yield [%][b]
1	$Cu(OAc)_2$ (0.5)	–	CH_2Cl_2	72
2	$CuCl_2$ (0.5)	–	CH_2Cl_2	10
3	NIS (0.5)	–	CH_2Cl_2	trace
4	I_2 (0.5)	–	CH_2Cl_2	trace
5	AgOAc (0.5)	–	CH_2Cl_2	5
6[c]	TBHP (2)	–	CH_2Cl_2	trace
7	$Cu(OAc)_2$ (0.2)	–	CH_2Cl_2	65
8	$Cu(OAc)_2$ (1.0)	–	CH_2Cl_2	70
9	$Cu(OAc)_2$ (0.5)	HOAc (1.0)	CH_2Cl_2	50
10	$Cu(OAc)_2$ (0.5)	Et_3N (1.0)	CH_2Cl_2	85
11	$Cu(OAc)_2$ (0.5)	DABCO (1.0)	CH_2Cl_2	72
12	$Cu(OAc)_2$ (0.5)	DMAP (1.0)	CH_2Cl_2	60
13	$Cu(OAc)_2$ (0.5)	DIPEA (1.0)	CH_2Cl_2	72
14	$Cu(OAc)_2$ (0.5)	Et_3N (0.5)	CH_2Cl_2	83
15	**$Cu(OAc)_2$ (0.5)**	**Et_3N (1.5)**	**CH_2Cl_2**	**93**
16	$Cu(OAc)_2$ (0.5)	Et_3N (2.0)	CH_2Cl_2	92
17[d]	$Cu(OAc)_2$ (0.5)	Et_3N (1.5)	DMSO	69
18	$Cu(OAc)_2$ (0.5)	Et_3N (1.5)	MeCN	50
19	$Cu(OAc)_2$ (0.5)	Et_3N (1.5)	Dioxane	10
20[e]	$Cu(OAc)_2$ (0.5)	Et_3N (1.5)	CH_2Cl_2	70
21[f]	$Cu(OAc)_2$ (0.5)	Et_3N (1.5)	CH_2Cl_2	85
22[g]	$Cu(OAc)_2$ (0.5)	Et_3N (1.5)	CH_2Cl_2	67

[a] *Reaction conditions:* **1a** (0.2 mmol), **2a** (0.6 mmol), oxidant, additive and solvent (2 mL) under an air atmosphere at room temperature for 5 h.
[b] Yield of isolated product.
[c] TBHP (5–6 M in decane).
[d] Product **4aa** was isolated in 32% yield.
[e] Under an N_2 atmosphere.
[f] Under an O_2 (1 atm) atmosphere.
[g] $T = 50\,°C$. NIS = *N*-iodosuccinimide, TBHP = *tert*-butyl hydroperoxide, HOAc = acetic acid, Et_3N = triethylamine, DABCO = 1,4-diazabicyclo[2.2.2]octane, DMAP = dimethylaminopyridine, DIPEA = *N*,*N*-diisopropylethylamine, DMSO = dimethyl sulfoxide.

$Cu(OAc)_2$ affected the reaction, the yields were relatively lower at either 0.2 equiv. $Cu(OAc)_2$ or 1.0 equiv. $Cu(OAc)_2$ (entries 1, 7, and 8; Table 1). Subsequently, a series of additives, including HOAc, Et_3N, DABCO, DMAP, DIPEA, were examined; the desired product **3aa** was observed in 93% yield when 1.5 equiv. Et_3N were added (entries 9–16; Table 1). Among the solvents examined, CH_2Cl_2 was the most effective (entries 15, 17–19; Table 1). Surprisingly, another product, 1-morpholino-2-phenylethane-1,2-dione **4aa**, was isolated in 32% yield when DMSO was used as solvent (entry 17; Table 1). It was interesting to discover that the reaction could be carried out under an N_2 atmosphere to furnish **3aa** in 70% yield (entry 20; Table 1). Moreover, when we conducted the reaction under an O_2 atmosphere, the yield of **3aa** did not increase (entry 21; Table 1). Furthermore, increasing the temperature also could not improve the yield of **3aa** (entry 22; Table 1). After exploring different parameters, the highest yield of **3aa** was achieved when the reaction was carried out with $Cu(OAc)_2$ (0.5 equiv.) and Et_3N (1.5 equiv.) in CH_2Cl_2 under air at room temperature (entry 15; Table 1).

With the optimal reaction conditions in hand, different sets of experiments were carried out to investigate the scope and limitations of this reaction (Table 2). This method was found to be applicable to a wide range of α-aminocarbonyl compounds **1** (leading to **3ba–3xa**). Initially, steric and electronic variations in the N-aryl moiety of α-amino ketones **1** were tested under the optimized conditions with morpholine **2a** (**3ba–3ka**). It was observed that both electron-rich and electron-deficient N-aryl moieties of α-amino ketones **1** could be smoothly transformed into the corresponding products. The reactivity of the electron-withdrawing N-aryl groups was superior to that of the electron-donating N-aryl groups, and some halogen substituents (F, Cl, or Br) were perfectly tolerated under the optimal conditions (**3ba–3ga**). However, substrate with an N-*n*-Bu group, an aliphatic group, did not lead to the desired product **3ha**. Furthermore, substituents at different positions of the N-aryl group did not affect the efficiency of the reaction. For example, substrates bearing a methyl group at the *para*-, *ortho*- or *meta*- position had high reactivity to couple with morpholine **2a** in excellent yields (**3ba**, **3ia** and **3ja**). We next set out to exploit the substitution effect on the aryl group of the 1-arylethanone moiety: a number of substituents, such as Me, OMe, Ph, F, Cl, Br or CF_3, were consistent with the optimal conditions, thus affording the corresponding products **3la–3ra** in good yields, and the electron-donating groups were superior to the electron-withdrawing groups (**3la–3ra**). Good yields were still achieved when using 2-naphthyl-substituted substrate **1u** and dichloro-substituted substrate **1v**. The reaction was also readily expanded to an aliphatic substrate, 1-(phenylamino)propan-2-one, leading to the desired product **3oa** in 85% yield. However, ethyl 2-(phenylamino)acetate failed to produce the desired product under the optimal conditions (**3xa**). Subsequently, the scope of the amines **2** was examined under the standard conditions (**3ab–3ai**). All secondary amines tested above gave rise to the desired products with moderate yields (**3ab–3af**). Disappointingly, primary amines including *p*-toluidine, cyclohexanamine and butan-1-amine failed to produce desired products (**3ag–3ai**). We speculate that maybe the reaction of primary amines with the carbonyl group of α-amino ketones is faster than the cross-coupling reaction to give the desired prod-

Table 2. $Cu(OAc)_2$-catalyzed synthesis of 2-amino-2-imino-carbonyls **3** under air[a] and X-ray structure of **3af**.[13]



1 2 3

3ba: R^1 = 4-MeC_6H_4, 84%[b] (7 h)
3ca: R^1 = 4-$OMeC_6H_4$, 83% (7 h)
3da: R^1 = 4-FC_6H_4, 92% (12 h)
3ea: R^1 = 4-ClC_6H_4, 91% (8 h)
3fa: R^1 = 4-BrC_6H_4, 93% (6 h)
3ga: R^1 = 4-$CF_3C_6H_4$, 86% (8 h)
3ha: R^1 = *n*-C_4H_9, N.D.[c] (12h)
3ia: R^1 = 2-MeC_6H_4, 89% (8 h)
3ja: R^1 = 3-MeC_6H_4, 91% (8 h)

3ka, 90%, (8 h)

3ua, 90%, (8 h)

3la: R^2 = 4-MeC_6H_4, 83% (8 h)
3ma: R^2 = 4-$OMeC_6H_4$, 90% (8 h)
3na: R^2 = 4-PhC_6H_4, 88% (8 h)
3oa: R^2 = 4-FC_6H_4, 86% (8 h)
3pa: R^2 = 4-ClC_6H_4, 74% (8 h)
3qa: R^2 = 4-BrC_6H_4, 69% (8 h)
3ra: R^2 = 4-$CF_3C_6H_4$, 83% (8 h)
3sa: R^2 = 2-$OMeC_6H_4$,70% (8 h)
3ta: R^2 = 3-$OMeC_6H_4$, 78% (8 h)

3va, 95%, (8 h)

3wa, 85%, (10 h)

3xa, N.D., (10h)

3ab, 69%, (8 h)

3ac, 55%, (8 h)

3ad, 70%, (8h)

3ae, 73%, (8 h)

3af, 55%, (8 h)

X-ray structure of **3af**

3ag, N.D., (8 h)

3ah, N.D., (8 h)

3ai, N.D., (8 h)

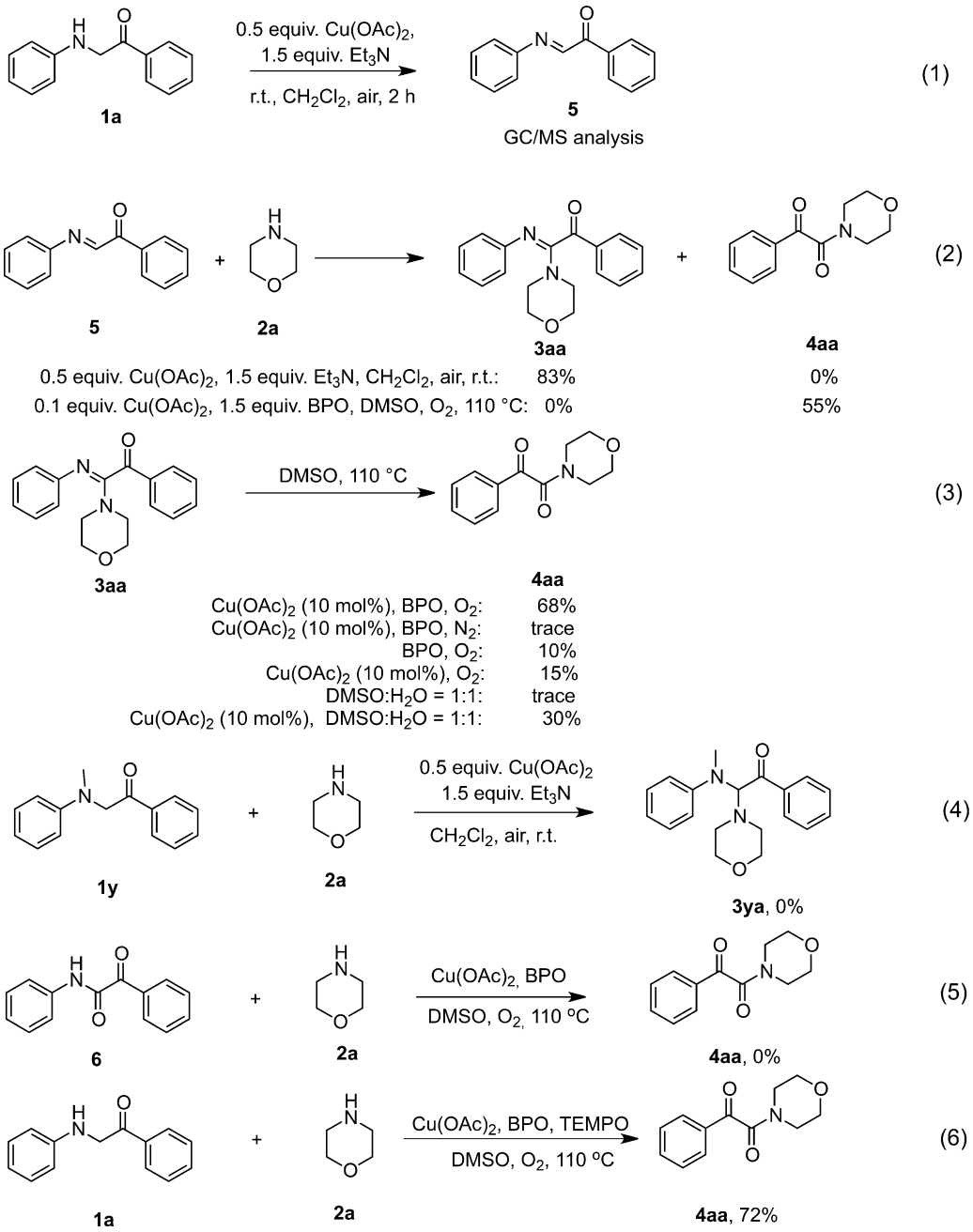
[a] *Reaction conditions:* **1** (0.2 mmol), **2** (0.6 mmol), $Cu(OAc)_2$ (0.5 equiv.), Et_3N (1.5 equiv.) and CH_2Cl_2 (2 mL) at room temperature under air.
[b] Isolated yields.
[c] N.D. = not detected.

uct. Moreover, the structure of **3af** was confirmed by X-ray crystallography (Table 2).[13]

The reaction of 1-phenyl-2-(phenylamino)ethanone **1a** with morpholine **2a** giving 1-morpholino-2-phenylethane-1,2-dione **4aa** was investigated next. We systematically explored a number of experimental variables such as reaction temperature, solvents, metal salts, additives, and other parameters (see the Supporting Information, Table S1). The experiments demonstrated that for optimal results, the reaction should be performed by the catalysis of $Cu(OAc)_2$ (10 mol%) with benzoyl peroxide (BPO; 1.5 equiv.) at 110 °C under the atmosphere of oxygen. Under the optimized conditions, **1a** reacted with **2a** smoothly to give the desired product **4aa** in 74% yield (Supporting Information, Table S1, entry 18). A series of α-aminocarbonyl compounds were examined in this reaction system. As expected, most of the α-aminocarbonyl substrates reacted smoothly under the procedure to provide the desired products in moderate to good yields. For example, the substrates bearing Me, OMe, naphthyl, Br, Cl groups all survived and gave the target molecules in moderate yields (**4la**, **4ma**, **4pa**, **4qa**, **4ua**). However, the introduction of a fluorine group on the aryl group of the 1-aryl-ethanone moiety **1o** as well as aliphatic substrates such as 2-(bu-

tylamino)-1-phenylethanone **1h** and 1-(phenylamino)-propan-2-one **1w** surprisingly had no reactivity (**4ha**, **4oa**, **4wa** and **4xa**). Unfortunately, this protocol was not general to a wide range of amines that we tested. The secondary amines including *N*-methylaniline, 1-ethylpiperazine and diethylamine and the primary amines such as *p*-toluidine, cyclohexanamine and butan-1-amine were not suitable substrates; they all gave no desired products (**4ad**–**4ai**).

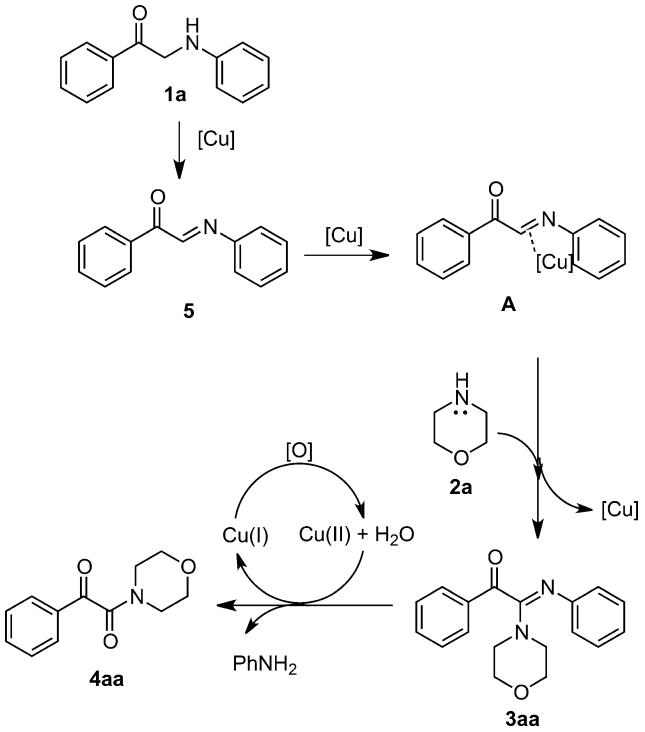
To elucidate the mechanism, some control experiments were conducted (Scheme 2). According to the results of the transformations, we proposed that the imine **5** may in fact be a crucial intermediate in the reaction. Therefore, we conducted the first control experiment involving oxidation of **1a** in the absence of amines under standard conditions. The GC-MS trace analysis showed that **1a** was converted almost completely into **5** within 2 h [Scheme 2, Eq. (1)]. As shown in Eq. (2), the reactions between **2a** and **5** were investigated. Under the optimized conditions, the product **3aa** and **4aa** both could be furnished in 83% and 55% yields [Scheme 2, Eq. (2)]. The results demonstrated that the reaction includes the direct formation of an imine intermediate from α-aminocarbonyl compounds **1**. Additionally, **3aa** could be converted into **4aa** in 68% yield using the $Cu(OAc)_2$/



Scheme 2. Different control experiments.

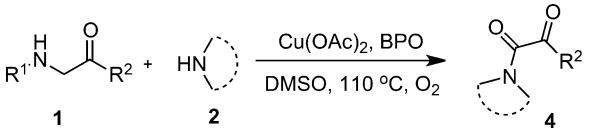
BPO/O_2 system [Scheme 2, Eq. (3)]. However, the conversion decreased sharply in the absence of O_2, BPO or $Cu(OAc)_2$. The results indicated that $Cu(OAc)_2$, BPO, and O_2 are important factors in the conversion of **3aa** into **4aa**. To our surprise, **4aa** could be obtained in 28% yield in the presence of $Cu(OAc)_2$ (10 mol%) in DMSO/H_2O (1:1); disappointedly **4aa** was detected only in trace yield in the absence of $Cu(OAc)_2$ in DMSO/H_2O (1:1) [Scheme 2, Eq. (3)]. On the basis of the above results in Eq. (3), the Cu(II) species is the real catalyst for hydrolyzing imine **3**.[6] Notably, 1-phenyl-2-(phenylamino)propan-1-one **1y** and 2-oxo-*N*,2-diphenylacetamide **6** both were not suitable substrates for the reaction [Scheme 2, Eq. (4) and Eq. (5)]. Moreover, the reaction could proceed smoothly by adding 1.0 equivalent of the radical-trapping reagent 2,2,6,6 tetramethylpiperidine *N*-oxyl (TEMPO), giving the desired product **4aa** in 72% yield [Scheme 2, Eq. (6)]. The result implied that the present reaction does not include a radical process.

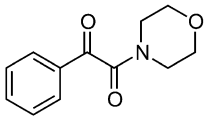
Based on the above results and literature reports,[5c,6,9,10] the proposed mechanism is outlined in Scheme 3. Initially, **1a** is oxidized by $Cu(OAc)_2$ to



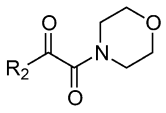
Scheme 3. Possible mechanism.

Table 3. $Cu(OAc)_2$-catalyzed synthesis of 2-amino-2-oxocarbonyls **4** with the aid of BPO under O_2.[a]

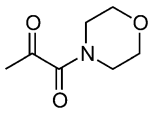




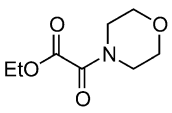
4aa: R^1 = C_6H_5, 74%, [b] (15 h)
4ba: R^1 = 4-MeC_6H_4, 70%, (15 h)
4ca: R^1 = 4-$OMeC_6H_4$, 76% , (15 h)
4da: R^1 = 4-FC_6H_4, 72%, (15 h)
4ea: R^1 = 4-ClC_6H_4, 73%, (15 h)
4fa: R^1 = 4-BrC_6H_4, 60%, (15 h)
4ga: R^1 = 4-$CF_3C_6H_4$, 59%, (15 h)
4ha: R^1 = *n*-C_4H_9, N.D.,[c] (15 h)
4ia: R_1 = 2-MeC_6H_4, 60%, (15 h)
4ja: R^1 = 3-MeC_6H_4, 63%, (15 h)
4ka: R^1 = 1-naphthyl, 67%, (15 h)



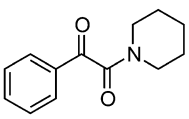
4la: R^2 = 4-MeC_6H_4, 70%, (15 h)
4ma: R^2 = 4-$OMeC_6H_4$, 65% , (15 h)
4na: R^2 = 4-PhC_6H_4, 71% , (15 h)
4oa: R^2 = 4-FC_6H_4, trace , (15 h)
4pa: R^2 = 4-ClC_6H_4, 35% , (15 h)
4qa: R^2 = 4-BrC_6H_4, 40% , (15 h)
4ra: R^2 = 4-$CF_3C_6H_4$, 50% , (15 h)
4sa: R^2 = 2-$OMeC_6H_4$, 61% , (15 h)
4ta: R^2 = 3-$OMeC_6H_4$, 63% , (15 h)
4ua: R^2 = 2-naphthyl, 67% , (15 h)
4va: R^2 = 3,4-$DiClC_6H_4$, 30% ,(15 h)



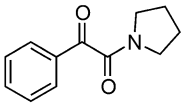
4wa, N.D., (15 h)



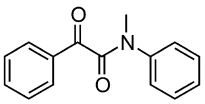
4xa, N.D., (15 h)



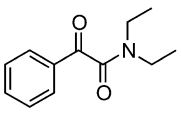
4ab, 70%, (12 h)



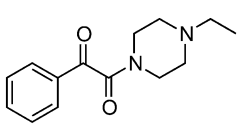
4ac, 50%, (14 h)



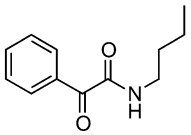
4ad, N.D., (20 h)



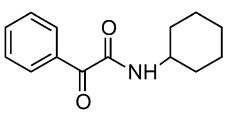
4ae, N.D., (15 h)



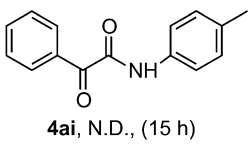
4af, N.D., (20 h)



4ag, N.D., (15 h)



4ah, N.D., (15 h)



4ai, N.D., (15 h)

[a] *Reaction conditions:* **1** (0.2 mmol), **2** (0.6 mmol), $Cu(OAc)_2$ (10 mol%), BPO (1.5 equiv.) and DMSO (2 mL) at 110 °C under oxygen.
[b] Isolated yields.
[c] N.D. = not detected.

generate the imine intermediate **5**,[6,9,10] but only after the copper salt has coordinated with **5** to form the activated copper complex **A**.[5c,10] Consequently, the morpholine **2a** undergoes nucleophilic attack to **A** to produce product **3aa**.[6,10] Product **3aa** is hydrolyzed by H_2O to produce **4aa** with the aid of $Cu(OAc)_2$, BPO, and O_2.[6]

In summary, we have presented a general and efficient method for C–N oxidative cross-coupling through direct C(sp^3)–H bond functionalization of α-aminocarbonyl compounds with amines using inexpensive copper salts as catalysis. This transformation could selectively furnish 2-amino-2-iminocarbonyl and 2-amino-2-oxocarbonyl compounds by slightly modifying the reaction conditions. A variety of substituted α-aminocarbonyl compounds could be tolerated by this procedure which proceeds smoothly in moderate to good yields. Thus, it represents a facile pathway for the functionalization of α-amino ketones.

Experimental Section

Typical Experimental Procedure for the Cu-Catalyzed Synthesis of 2-Amino-2-iminocarbonyl Compounds (3)

An oven-dried tube with a magnetic stir bar was charged with the α-aminocarbonyl compound **1** (0.2 mmol), amine **2** (0.6 mmol), $Cu(OAc)_2$ (0.5 equiv.), Et_3N (1.5 equiv.) and CH_2Cl_2 (2 mL). Then the reaction mixture was stirred at room temperature under air for the indicated time (Table 2) until complete consumption of the starting material as monitored by TLC. After the reaction was finished, the mixture was concentrated in vacuum, and the residues were purified by silica gel column chromatography (hexane/ethyl acetate = 5:1) to afford the desired product **3**.

Typical Experimental Procedure for the Cu-Catalyzed Synthesis of 2-Amino-2-oxocarbonyl Compounds (4)

0.2 mmol of α-aminocarbonyl compound **1**, 0.6 mmol of amine **2**, 10 mol% of $Cu(OAc)_2$, 1.5 equiv. of BPO and 2 mL of DMSO were added to a test tube equipped with a magnetic stir bar. The reaction tube was evacuated and backfilled with O_2 (3 times, balloon). Then the reaction mixture was stirred at 110 °C under O_2 balloon for the indicated time (Table 3) until complete consumption of the starting material as monitored by TLC. After the reaction was finished, the reaction mixture was washed with brine. The organic extracts were dried over Na_2SO_4, concentrated in vacuum, and the resulting residue was purified by silica gel column chromatography (hexane/ethyl acetate = 4:1) to afford the desired product **4**.

References

[1] a) S. Hunt, *Chemistry and Biochemistry of the Amino Acids*, (Ed.: G. C. Barrett), Chapman and Hall, London, **1985**, p 55; b) R. M. Williams, *Synthesis of optically active α-amino acids*, in: *Organic Chemistry Series*, Pergamon, New York, **1989**; c) Y. Ohfune, *Acc. Chem. Res.* **1992**, *25*, 360; d) S. H. Gellman, *Acc. Chem. Res.* **1998**, *31*, 173; e) F. D. Klingler, *Acc. Chem. Res.* **2007**, *40*, 1367; f) J. M. Concellon, H. Rodriguez-Solla, *Curr. Org. Chem.* **2008**, *12*, 524.

[2] a) D. Obrecht, M. Altorfer, C. Lehmann, P. Schçnholzer, K. Müller, *J. Org. Chem.* **1996**, *61*, 4080; b) D. Obrecht, U. Bohdal, C. Broger, D. Bur, C. Lehmann, R. Ruffieux, P. Schçnholzer, C. Spiegler, K. Müller, *Helv. Chim. Acta* **1995**, *78*, 563; c) D. D. Schoepp, D. E. Jane, J. A. Monn, *Neuropharmacology* **1999**, *38*, 1431; d) A. Takahashi, H. Naganawa, D. Ikeda, Y. Okami, *Tetrahedron* **1991**, *47*, 3621; e) D. Schirlin, F. Gerhart, J. M. Hornsperger, M. Hamon, J. Wagner, M. J. Jung, *J. Med. Chem.* **1988**, *31*, 30; f) J. J. Walsh, D. E. Metzler, D. Powell, R. A. Jacobson, *J. Am. Chem. Soc.* **1980**, *102*, 7136; g) V. Lupi, M. Penso, F. Foschi, F. Gassa, V. Mihali, A. Tagliabue, *Chem. Commun.* **2009**, 5012; h) M. A. Beenen, D. J. Weix, J. A. Ellman, *J. Am. Chem. Soc.* **2006**, *128*, 6304; i) L. Zhao, C.-J. Li, *Angew. Chem.* **2008**, *120*, 7183; *Angew. Chem. Int. Ed.* **2008**, *47*, 7075; j) B.-X. Tang, R.-J. Song, C.-Y. Wu, Z.-Q. Wang, Y. Liu, X.-C. Huang, Y.-X. Xie, J.-H. Li, *Chem. Sci.* **2011**, *2*, 2131.

[3] a) O. Gaertzen, S. L. Buchwald, *J. Org. Chem.* **2002**, *67*, 465; b) X. Liu, J. F. Hartwig, *Org. Lett.* **2003**, *5*, 1915; c) S. Lee, N. A. Beare, J. F. Hartwig, *J. Am. Chem. Soc.* **2001**, *123*, 8410; d) M. S. Sigman, E. N. Jacobsen, *J. Am. Chem. Soc.* **1998**, *120*, 5315; e) M. S. Sigman, E. N. Jacobsen, *J. Am. Chem. Soc.* **1998**, *120*, 4901; f) K. L. Reddy, K. B. Sharpless, *J. Am. Chem. Soc.* **1998**, *120*, 1207; g) M. Chaari, A. Jenhi, J.-P. Lavergne, P. Viallefont, *Tetrahedron* **1991**, *47*, 4619; h) M. J. O'Donnell, W. D. Bennett, W. N. Jacobsen, Y. Ma, J. C. Huffman, *Tetrahedron Lett.* **1989**, *30*, 3909; i) B. M. Trost, X. Aeiza, *J. Am. Chem. Soc.* **1999**, *121*, 10727; j) M. Hocek, *Heterocycles* **2004**, *63*, 1673; k) S. P. Marsden, E. L. Watson, S. A. Raw, *Org. Lett.* **2008**, *10*, 2905.

[4] a) P. Beak, W. J. Zajdel, D. B. Reitz, *Chem. Rev.* **1984**, *84*, 471; b) A. I. Meyers, *Aldrichimica Acta* **1985**, *18*, 59; c) K. Maruoka, T. Ooi, *Chem. Rev.* **2003**, *103*, 3013; d) T. Hashimoto, K. Maruoka, *Chem. Rev.* **2007**, *107*, 5656; e) L. Li, Y.-L. Zhao, Q. Wang, T. Lin, Q. Liu, *Org. Lett.* **2015**, *17*, 370; f) R.-L. Yan, X. Kang, X.-Q. Zhou, X.-N. Li, X.-X. Liu, L.-K. Xiang, Y.-M. Li, G.-S. Huang, *J. Org. Chem.* **2014**, *79*, 465; g) W. Xu, B. J. Nachtsheim, *Org. Lett.* **2015**, *17*, 1585.

[5] a) L. Zhao, O. Baslé, C.-J. Li, *Proc. Natl. Acad. Sci. USA* **2009**, *106*, 4106; b) G. Zhang, Y. Zhang, R. Wang, *Angew. Chem.* **2011**, *123*, 10613; *Angew. Chem. Int. Ed.* **2011**, *50*, 10429; c) J. Xie, Z.-Z. Huang, *Angew. Chem.* **2010**, *122*, 10379; *Angew. Chem. Int. Ed.* **2010**, *49*, 10181; d) X. Jia, Y. Wang, F. Peng, C. Huo, L. Yu, J. Liu, X. Wang, *J. Org. Chem.* **2013**, *78*, 9450; e) R. Rohlmann, T. Stopka, H. Richter, O. G. Mancheço, *J. Org. Chem.* **2013**, *78*, 6050; f) P. Liu, Z. Wang, J. Lin, X. Hu, *Eur. J. Org. Chem.* **2012**, 1583; g) P. Liu, Y. Li, H. Wang, Z. Wang, X. Hu, *Tetrahedron Lett.* **2012**, *53*, 6654; h) S. Zhu, M. Rueping, *Chem. Commun.* **2012**, *48*, 11960; i) C. Huo, C. Wang, M. Wu, X. Jia, H. Xie,

Y. Yuan, *Adv. Synth. Catal.* **2014**, *356*, 411; j) C. Huo, C. Wang, C. Sun, X. Jia, X. Wang, W. Chang, M. Wu, *Adv. Synth. Catal.* **2013**, *355*, 1911; k) X. Jia, F. Peng, C. Qing, C. Huo, X. Wang, *Org. Lett.* **2012**, *14*, 4030; l) H. Richter, O. G. Mancheço, *Org. Lett.* **2011**, *13*, 6066.

[6] J.-C. Wu, R.-J. Song, Z.-Q. Wang, X.-C. Huang, Y.-X. Xie, J.-H. Li, *Angew. Chem.* **2012**, *124*, 3509; *Angew. Chem. Int. Ed.* **2012**, *51*, 3453.

[7] Z.-Q. Wang, M. Hu, X.-C. Huang, L.-B. Gong, Y.-X. Xie, J.-H. Li, *J. Org. Chem.* **2012**, *77*, 8705.

[8] W.-T. Wei, R.-J. Song, J.-H. Li, *Adv. Synth. Catal.* **2014**, *356*, 1703.

[9] R.-Y. Tang, X.-K. Guo, J.-N. Xiang, J.-H. Li, *J. Org. Chem.* **2013**, *78*, 11163.

[10] B. Yang, T.-T. Yang, X.-A. Li, J.-J. Wang, S.-D. Yang, *Org. Lett.* **2013**, *15*, 5024.

[11] H.-B. Peng, J.-T. Yu, Y. Jiang, H.-T. Yang, J. Cheng, *J. Org. Chem.* **2014**, *79*, 9847.

[12] C.-D. Huo, Y. Yuan, M.-X. Wu, X.-D. Jia, X.-C. Wang, F.-J. Chen, J. Tang, *Angew. Chem.* **2014**, *126*, 13762; *Angew. Chem. Int. Ed.* **2014**, *53*, 13544.

[13] CCDC 1448052 (**3af**) contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre *via* www.ccdc.cam.ac.uk/data_request/cif.