Heterogeneous & Homogeneous & Bio- & Nano-

CHEMCATCHEM

CATALYSIS

Accepted Article

Title: Amide Bond Formation Catalyzed by Recyclable Copper Nanoparticles Supported on Zeolite Y under Mild Conditions

Authors: Yanina Moglie, Eduardo Buxaderas, Agustina Mancini, Francisco Alonso, and Gabriel Radivoy

To be cited as: *ChemCatChem* 10.1002/cctc.201801858

Link to VoR: http://dx.doi.org/10.1002/cctc.201801858

A Journal of

ChemPubSoc Europe

WILEY-VCH

www.chemcatchem.org

10.1002/cctc.201801858

WILEY-VCH

Amide Bond Formation Catalyzed by Recyclable Copper Nanoparticles Supported on Zeolite Y under Mild Conditions

Yanina Moglie,*[a] Eduardo Buxaderas,[a] Agustina Mancini,[a] Francisco Alonso,[b] and Gabriel Radivoy*[a]

A series of catalysts based on supported copper nanoparticles have been prepared and tested in the amide bond formation from tertiary amines and acid anhydrides, in the presence of *tert*-butyl hydroperoxide as an oxidant. Copper nanoparticles on zeolite Y (CuNPs/ZY) was found to be the most efficient catalyst for the synthesis of amides, working in acetonitrile as solvent, under ligand- and base-free conditions in air. The products were obtained in good to excellent yields and in short reaction times. The CuNPs/ZY system also exhibited higher catalytic activity than some commercially available copper and iron sources and it was reused in ten reaction cycles without any further pre-treatment. This methodology has been successfully scaled-up to a gram scale with no detriment to the yield.

Introduction

Amide bond forming reactions[1] are among the most important tools in synthetic organic chemistry since they allow access to relevant fine chemicals such as peptides, proteins and synthetic polymers.[2] Amides are also present in a large number of other biologically important compounds, pharmaceuticals and synthetic materials,[3] and they are used as ligands for stabilizing various metal centers.[4]

Traditionally, the amide synthesis involve the reaction between carboxylic acids, or their activated species, and amines, usually primary or secondary ones.[5] On the other hand, tertiary amines, which are commonly present in various natural products, are highly stable and easily available compounds, making their transformation into amides an interesting alternative.[6] Since tertiary amines are less nucleophilic, amidation of these substrates usually requires harsh conditions and/or metal catalysis. The catalytic oxidative amidation of tertiary amines with different acylating agents, mainly aldehydes and carboxylic acids, has been accomplished by using different copper or iron sources as metal catalysts. In 2013, Li and co-workers reported a new and efficient method for the $FeCl_2$-catalyzed oxidative amidation of tertiary amines with aldehydes, using *tert*-butyl hydroperoxide (TBHP) as oxidant.[6a] Right after, they improved their own method by using anhydrides as acylating agents, avoiding some of the disadvantages of the use of aldehydes, however, the use of pyridine as base was necessary to increase the reaction yield.[6b] More recently, Guan and co-workers[6c] extended the use of anhydrides as acylating agents in the amidation of tertiary amines, catalyzed by $Cu(OAc)_2$ in the presence of molecular oxygen, leading to the corresponding amides in good yields but in much longer reaction times.

The use of heterogeneous catalysis in organic transformations is favored in terms of the ease of handling, simple workup, recyclability and reusability.[7] The possibility of catalyst recovery is not only beneficial from an economic point of view, but also decreases the risk of contamination of the reaction products with transition metals. To the best of our knowledge, there is only one example in the literature concerning the direct oxidative amidation of tertiary amines by means of heterogeneous catalysis. In that paper, Phan and co-workers, reported on the use of copper-based metal-organic framework (MOF) composites for the direct oxidative amidation of *N*,*N*-dimethylanilines using anhydrides as acylating agents, in the presence of pyridine and TBHP as an oxidant.[8] The metal-organic framework $[Cu_2(EDB)_2(BPY)]$ demonstrated to be an efficient heterogeneous catalyst, and robust enough to be recycled and reused, but its synthesis is time-demanding and the scope of the method was tested with only four substrates (Figure 1a).

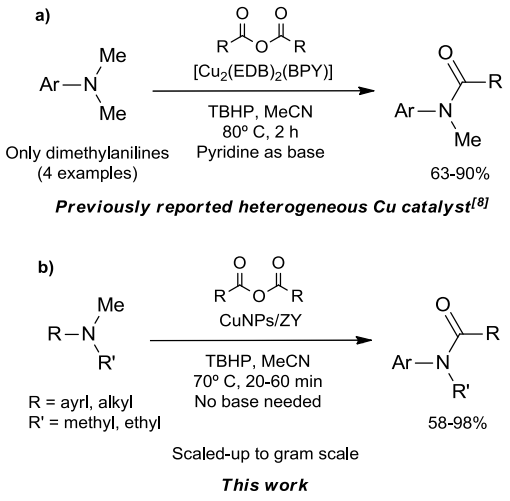


Figure 1. Heterogeneous copper catalysts for the direct amidation of tertiary amines.

[a] Dr. Y. Moglie, Dr. E. Buxaderas, A. Mancini, Prof. G. Radivoy
Departmento de Química
INQUISUR, Universidad Nacional del Sur (UNS)-CONICET
Avenida Alem 1253, Bahía Blanca, 8000, Argentina
E-mails: gradivoy@criba.edu.ar, ymoglie@uns.edu.ar
[b] Prof. Dr. Francisco Alonso
Instituto de Síntesis Orgánica (ISO) and Departamento de Química Orgánica, Facultad de Ciencias
Universidad de Alicante
Apdo. 99, 03080 Alicante, Spain

Supporting information for this article is given via a link at the end of the document.((Please delete this text if not appropriate))

Following our research on catalysis by metal nanoparticles (supported or unsupported) and its application in useful synthetic transformations,[9] we now focused our attention on the direct oxidative amidation of tertiary amines by acid anhydrides, using inexpensive and easy to prepare catalysts based on supported copper nanoparticles. We want to present herein, our results on the direct amidation of a wide range of tertiary amines with a variety of anhydrides, catalyzed by a highly efficient and recyclable CuNPs/ZY heterogeneous catalyst with low copper loading, using TBHP as oxidant and in the absence of any added base (Figure 1b).

Results and Discussion

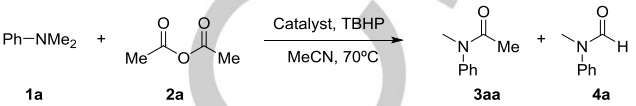
The catalysts were readily prepared by addition of the support to a suspension of freshly prepared copper nanoparticles (CuNPs). The CuNPs were generated by fast reduction of anhydrous copper(II) chloride, using lithium sand and a catalytic amount of DTBB (4,4'-di-*tert*-butylbiphenyl, 10 mol %) as reducing system, in THF at room temperature. The catalysts were ready for use as prepared, after filtration and drying, without any pre-treatment. Different inorganic materials such as activated carbon, Celite, zeolite Y and ZnO were tested as supports for the CuNPs.

N,*N*-Dimethylaniline (**1a**) and acetic anhydride (**2a**) were used as model substrates in order to test the activity of different catalysts in the direct oxidative amidation reaction (Table 1). The reactions were performed under mild conditions, at 70 ºC, using acetonitrile as solvent and *tert*-butyl hydroperoxide (TBHP, 70% in water) as oxidant. As shown in Table 1, along with the desired *N*-methyl-*N*-phenylacetamide (**3aa**), the formation of minor amounts of formyl amide (**4a**) was observed as the only by-product in all cases. It is noteworthy that working under the present reaction conditions the use of a base as additive was not necessary.

As can be seen from the results in Table 1, a substantial difference was observed in terms of conversion and selectivity, depending on the catalyst support. Thus, CuNPs supported on activated carbon (C) or Celite (Table 1, entries 1 and 2) gave modest conversions and high selectivities towards the acetamide **3aa**, after 1 h of reaction time. When ZnO was tested as support, a detrimental effect in the Cu-catalyzed amide bond formation was observed, leading to 57% of acetamide **3aa** after 10 h of reaction (Table 1, entry 3). The use of zeolite Y (ZY) as support for the CuNPs, proved to be the best choice for the desired transformation, giving quantitative conversion and excellent selectivity towards **3aa** in only 20 min of reaction time (Table 1, entry 4).

We then studied the effect of different oxidizing agents in the course of the amidation reaction. When TBHP was replaced by O_2 (1 atm, balloon), quantitative conversion of **1a** was achieved but longer reaction time (120 min) and lower selectivity towards **3aa** was observed (Table 1, entry 5). Also H_2O_2 was tested as oxidant, however almost no conversion of the starting materials was observed after 24 h of reaction (Table 1, entry 6). With the optimized conditions in hand, some control experiments were carried out. When the reaction was conducted under N_2 atmosphere, high conversion and selectivity values were maintained but the reaction was thrice slower (Table 1, entry 7). Finally, very low conversions and selectivities were observed in the absence of the catalyst or in the presence of the support alone (Table 1, entries 8 and 9).

Table 1. Screening of catalysts and optimization of reaction conditions[a]



1a **2a** **3aa** **4a**

Entry	Catalyst	Time (min)	X (%)[b]	S (%)[c]
1	CuNPs/C	60	82	94
2	CuNPs/Celite	60	72	94
3	CuNPs/ZnO	240	52	97
4	**CuNPs/ZY**	**20**	**100**	**99**
5	CuNPs/ZY[d]	120	100	82
6	CuNPs/ZY[e]	24h	5	---
7	CuNPs/ZY[f]	60	100	99
8	---	120	46	57
9	ZY	120	19	60

[a] Conditions: **1a** (0.5 mmol), **2a** (0.6 mmol), catalyst (20 mg, 1.0 mol% Cu), TBHP (1.6 equiv.), MeCN (2 mL), 70 ºC under air. [b] Conversion determined by GC-MS using dodecane as internal standard. [c] Selectivity expressed as (moles of **3aa** / moles converted of **1a**) x 100, determined by GC-MS. [d] Reaction carried out using O_2 as oxidant. [e] Reaction carried out using H_2O_2 (1.6 equiv.) as oxidant. [f] Reaction carried out under N_2 atmosphere.

The full characterization of the CuNPs/ZY catalyst was reported by some of us elsewhere[10] (see also Supporting Information). Analysis by transmission electron microscopy (TEM) revealed the presence of well dispersed spherical nanoparticles, with diameters of *ca*. 1.7 ± 0.7 nm. Energy-dispersive X-Ray (EDX) analysis on various regions confirmed the presence of copper with energy bands of 8.04, 8.90 keV (K lines) and 0.92 keV (L line). X-ray diffraction (XRD) was consistent with the presence of zeolite Y in the catalyst, but no diffraction peaks owing to copper species were detected. XPS analysis showed four Cu $2p_{3/2}$ peaks at 932.6, 934.6, 941.5 and 944.1 eV. These peaks could be assigned to Cu_2O (932.6 eV) and CuO (934.6 eV), with the peaks at 941.5 and 944.1 eV being the satellite shake-up features characteristic of Cu^{2+} species. A copper loading of 1.15 wt% was determined by atomic absorption spectroscopy (AAS).

Catalyst recyclability was then tested. After one cycle, the CuNPs/ZY catalyst was separated by centrifugation, washed with the reaction solvent and reused in further experiments under the optimized conditions, without any previous treatment. It was found that CuNPs/ZY could be recovered and reused several times in the direct amidation of **1a** with **2a** without any

significant decrease in the catalytic activity. As shown in Figure 2, a slightly lower selectivity towards the formation of the acetamide **3aa** was observed, while the conversion value remained almost constant along ten consecutive cycles.

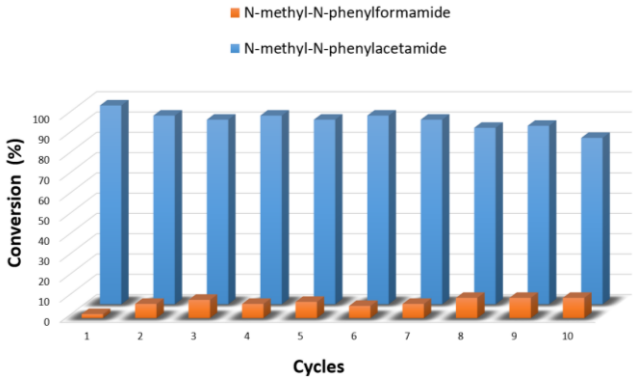


Figure 2. Recycling of the CuNPs/ZY catalyst in the synthesis of **3aa**.

Furthermore, the procedure was successfully scaled up to a 10 mmol scale, giving 98% conversion into the desired acetamide **3aa**, using a copper loading of 2.3 mol%. The kinetic profile for the amidation reaction of **1a** at 10 mmol scale is showed in the Figure 3.

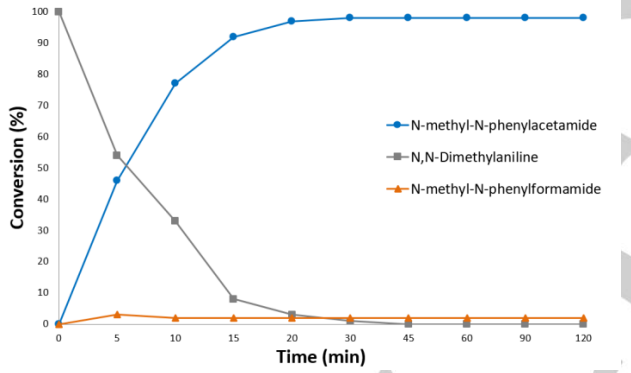
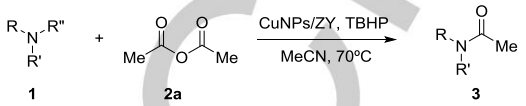


Figure 3. Kinetic profile for a 10 mmol scale synthesis of **3aa**.

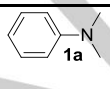
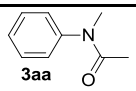
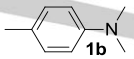
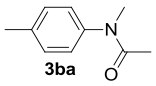
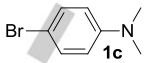
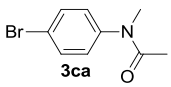
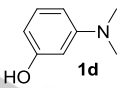
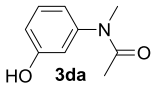
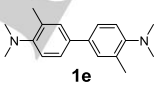
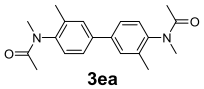
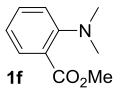
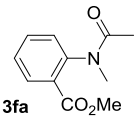
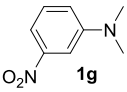
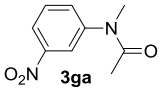
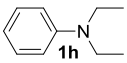
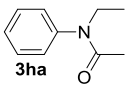
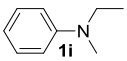
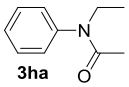
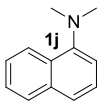
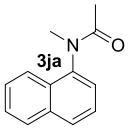
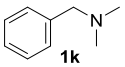
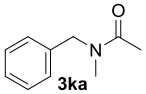
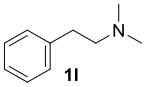
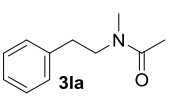
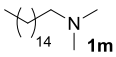
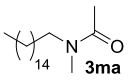
Chemical structure of neat zeolite Y, fresh CuNPs/ZY and spent catalyst were characterized by FTIR spectroscopy (see Supporting Information). For neat zeolite Y, a broad band located around 3500 cm^{-1} was observed due to stretching vibration of O-H groups on the zeolite surface. A band located at approximately 1630 cm^{-1} could be assigned to bending vibration of O-H groups. The main characteristic band for zeolite Y was observed at 1200-1000 cm^{-1}, which could be ascribed to stretching vibrations of Si-O and Al-O groups. The presence of copper led to small changes in the chemical structure of the support as the main bands were located at the same wavenumbers. The appearance of new bands located at 1500-1400 cm^{-1} could be assigned to the interaction between Cu and Si-O or Al-O bonds. Also, a new band observed at 876 cm-1 could be assigned to the Cu-O-H stretching. The FTIR spectra of spent catalyst showed small differences with the spectra corresponding to the fresh catalyst, only a deacrease in the bands intensity was observed.

The optimized conditions for the direct amidation of *N*,*N*-dimethylaniline using acetic anhydride as acylating agent were then applied to a range of tertiary amines (Table 2).

Table 2. Scope of the amidation of tertiary amines with acetic anhydride[a]



1 2a 3

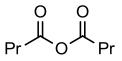
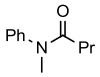
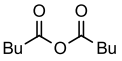
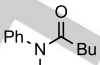
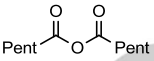
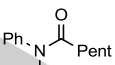
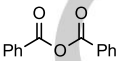
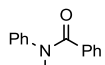
Entry	Starting amine	Time (min)	Product	Yield (%)[b]
1	 1a	20	 3aa	98
2	 1b	30	 3ba	81
3	 1c	30	 3ca	92
4	 1d	60	 3da	90
5	 1e	120	 3ea	96
6	 1f	24h	 3fa	20
7	 1g	24h	 3ga	17
8	 1h	45	 3ha	78
9	 1i	45	 3ha	70
10	 1j	60	 3ja	73
11	 1k	60	 3ka	88
12	 1l	30	 3la	88
13	 1m	120	 3ma	58

14	 **1n**	60	 **3na**	89

[a] Tertiary amine (**1**, 0.5 mmol), acetic anhydride (**2a**, 0.6 mmol), CuNPs/ZY catalyst (20 mg, 1.0 mol% Cu), TBHP (1.6 equiv) in MeCN (2 mL) at 70° C under air. [b] Determined by GC-MS using dodecane as internal standard.

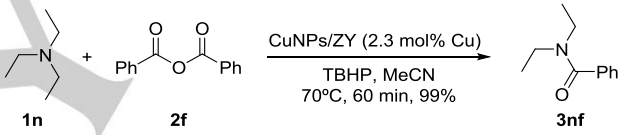
As shown in Table 2, both *N*,*N*-dimethyl-*p*-toluidine (**1b**) and 4-bromo-*N*,*N*-dimethylaniline (**1c**) gave the corresponding acetamides **3ba** and **3ca** in good yields after 30 min of reaction time (Table 2, entries 2 and 3, respectively). Notably, the catalytic system was equally effective when applied to the acidic phenolic derivative **1d** and the sterically hindered benzidine **1e** (entries 4 and 5). On the contrary, anilines **1f** and **1g**, which are substituted with electron-withdrawing groups, gave poor yields, probably due to the lower electron density of the aniline which would suppress the oxidative amidation reaction[6c] (entries 6 and 7). Not only *N*-methyl groups but also *N*-ethyl ones reacted under the reaction conditions. Thus, *N*,*N*-diethylaniline (**1h**), gave the corresponding amide **3ha** in 78% yield (Table 2, entry 8). Furthermore, in the case of unsymmetrical tertiary anilines such as *N*-ethyl-*N*-methylaniline, the catalyst showed to be highly selective towards the cleavage of the methyl group, as acetamide **3ha** was formed as the major amidation product (Table 2, entry 9). Also naphthylamines could be converted in the corresponding tertiary amides, although in longer reaction times. As an example, *N*,*N*-dimethylnaphthalen-1-amine (**1j**) was transformed into acetamide **3ja** in 73% yield, after 60 min of reaction (Table 2, entry 10). The non-aromatic tertiary amines **1k** and **1l** also gave the corresponding acetamides in good yields (Table 2, entries 11 and 12, respectively). Unexpectedly, *N*,*N*-dimethylhexadecan-1-amine was sluggish to react under the optimized conditions giving the corresponding acetamide **3ma** in low yield (Table 1, entry 13). In contrast, triethylamine (**1j**) was converted into the corresponding acetamide **3na** in 89% yield (Table 2, entry 14).

Then, a series of anhydrides other than **2a** were tested as acylating agents in the amidation of *N*,*N*-dimethylaniline (**1a**). As can be seen in Table 3, working under the optimized conditions all of the alkyl anhydrides tested (**2b**-**2e**) and also benzoic anhydride (**2f**) smoothly reacted with **1a** to give the corresponding amides **3ab**-**3af** in excellent yields, even though in longer reaction times than that of the amidation reaction using acetic anhydride as acylating agent.

2	 **2c**	45	 **3ac**	83
3	 **2d**	45	 **3ad**	88
4	 **2e**	45	 **3ae**	89
5	 **2f**	60	 **3af**	83

[a] *N*,*N*-dimethylaniline (**1a**, 0.5 mmol), anhydride (**2**, 0.6 mmol), CuNPs/ZY catalyst (20 mg, 1.0 mol% Cu), TBHP (1.6 equiv) in MeCN (2 mL) at 70° C under air. [b] Determined by GC-MS using dodecane as internal standard.

In view of these results, we decided to test our methodology in the synthesis of *N*,*N*-diethylbenzamide, a well-known commercial tertiary amide used in many mosquito repellent formulations. As shown in Scheme 1, the CuNPs/ZY-catalyzed direct amidation of triethylamine with benzoic anhydride, quantitatively giving the desired benzamide **3nf** in 60 min of reaction time.

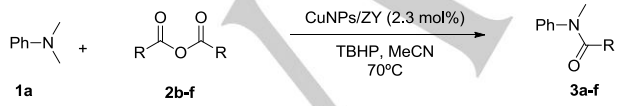


1n **2f** **3nf**

Scheme 1. Synthesis of *N*,*N*-diethylbenzamide (**3nf**) from triethylamine and benzoic anhydride.

For the sake of comparison, we decided to carry out the direct amidation of *N*,*N*-dimethylaniline (**1a**) with acetic anhydride (**2a**) in the presence of a variety of commercial copper sources as catalysts. As shown in Table 4, the CuNPs/ZY catalyst proved to be more active than any of the commercial copper sources tested, at lower metal loading and with the possibility of being recovered and reused. On the other hand, it can be inferred that the presence of copper(II) species is relevant to achieve both high conversions and selectivities to the desired amide product **3aa** (compare entries 1-3 with entries 4-7 in Table 4).

Table 3. Direct amidation of **1a** with different anhydrides[a]



1a **2b-f** **3a-f**

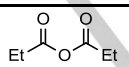
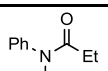
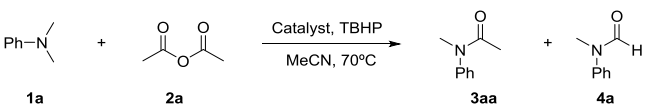
Entry	Anhydride 2	Time (min)	Product	Yield (%)[b]
1	 **2b**	30	 **3ab**	92

Table 4. Comparison of CuNPs/ZY with commercial copper sources as catalysts[a]



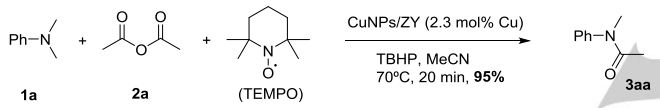
1a **2a** **3aa** **4a**

Entry	Catalyst	Conversion (%)[b]	Selectivity (%)[c]
1	Cu	30/80	70/73
2	Cu_2O	60/99	50/76
3	CuI	49/80	55/83

4	CuO	70/99	89/93
5	$Cu(OAc)_2$	60/99	74/81
6	$CuCl_2{\cdot}2H_2O$	75/82	80/90
7	CuNPs/ZY[d]	100	99/99

[a] Conditions: **1a** (0.5 mmol), **2a** (0.6 mmol), catalyst (5 mol% Cu), TBHP (1.6 equiv) in MeCN (2 mL) at 70 ºC under air. [b] Conversion at 20 min and 2 h of reaction, respectively, based on **1a**. **D**etermined by GC-MS using dodecane as internal standard. [c] Selectivity expressed as (moles of **3aa** / moles converted of **1a**) x 100, determined by GC-MS. [d] Reaction performed using 20 mg of catalyst (1.0 mol% Cu).

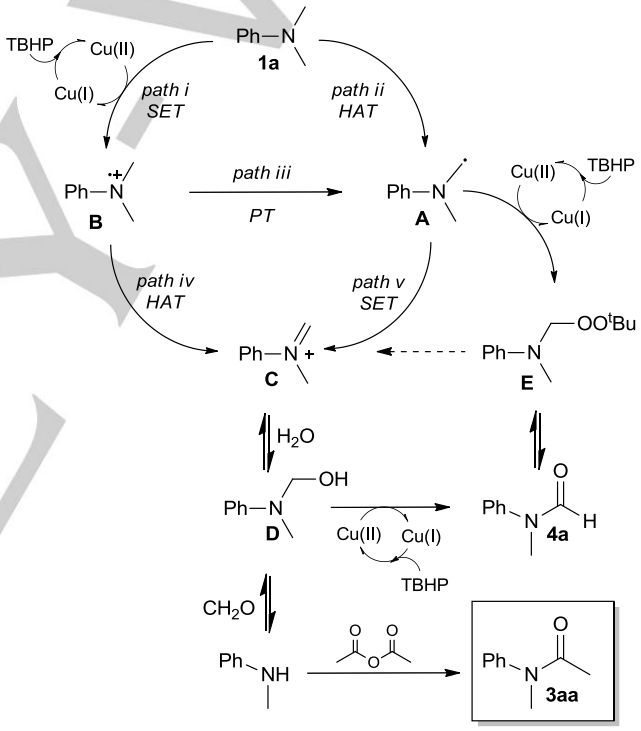
In order to get some information about the plausible mechanistic pathway, and based on previous reports by other authors,[6],[8] we next studied the effect of the addition of TEMPO to the reaction mixture as radical scavenger. Thus, the reaction of **1a** and **2a** under the optimized conditions was not affected by the presence of TEMPO, giving **3aa** with the same rate and yield as in the absence of this additive (Scheme 2). It is worthy of note, that this experimental evidence is in contrast with the results by Phan and co-workers,[8] as they reported that no further reaction progress was detected for the same transformation catalyzed by the Cu-MOF $[Cu_2(EDB)_2(BPY)]$, after addition of TEMPO.



Scheme 2. Direct amidation of **1a** with **3a** in the presence of TEMPO.

In general, it is commonly accepted that tertiary amine oxidation occurs via generation of an α-amino radical intermediate. As exemplified in Scheme 3 for the amidation of **1a**, this intermediate (**A**) could be generated through two different routes, one of them would involve a single electron transfer (SET) catalyzed by Cu(II) to give an aminium radical cation (**B**) followed by a proton transfer (PT) step (Scheme 3, *path i* followed by *path iii*). Another way in which the intermediate **A** could be formed implies a direct hydrogen atom transfer (HAT) from the tertiary amine (Scheme 3, *path ii*).

Based on previous literature reports on this subject,[11],[6b] *path ii* in Scheme 3 would be suppressed by the presence of a radical scavenger. On this basis, and since the presence of TEMPO did not inhibit the reaction under our conditions (Scheme 2), we consider that a single electron transfer followed by a proton transfer (*path i* and then *path iii*) is more likely to occur in the formation of intermediate **A**. A further SET process from radical **A** (*path v*) would led to iminium cation **C** which is the key intermediate in the way to the desired amide product.[6],[8],[12] Alternatively, as depicted in Scheme 3, the formation of **C** through elimination from peroxide intermediate **E**, or even through a direct hydrogen atom transfer (HAT) from **B**, could not be disregarded. Nevertheless, it should be noted that this last HAT process (*path iv*) could be inhibited by the presence of a radical scavenger. Finally, hydrolysis of **C**, *via N*-hydroxymethylamine **D**, would render the corresponding secondary amine, which would react with the anhydride to give the desired amide **3aa**. In order to confirm our assumption, we carried out the same reaction but in the absence of the acylating agent. Under these conditions, the secondary amine (*N*-methyl aniline) was observed as the major reaction product (63%) together with minor amounts of formamide **4a** (7%) and the unreacted starting amine **1a** (30%). This result is concordant with the fact that the electron-poor *N,N*-dimethylanilines **1f** and **1g** were reluctant to react, because of the lower nucleophilic character of the intermediate secondary amine. Even though the specific copper species involved in the reaction pathway remain unclear at this stage, we speculate that a Cu(II)/Cu(I) redox couple is required.[10a] With regard to the role of TBHP, by reaction with Cu(I) catalyst, it would generate Cu(II) peroxide species which would act as an oxidant in the initial SET process (Scheme 3, *path i*).[13] Besides, TBHP would regenerate the Cu(II) species needed to restart the catalytic cycle, and it could also be acting as oxidant in the formation of peroxide intermediate **E** and/or formamide by-product **4a**.



Scheme 3. Plausible mechanistic pathway.

Conclusions

In summary, we have developed a highly efficient method for the direct amidation of tertiary amines with anhydrides, catalyzed by CuNPs supported on zeolite Y. The heterogeneous CuNPs/ZY catalyst is easy to prepare and can be recovered and reused several times without any pre-treatment. The reported methodology has proven to be wide in scope, being applicable to the amidation of a range of aryl- and alkyl amines with a variety of anhydrides under mild conditions. In addition, the procedure could be succesfully scaled up to a gram scale with

no detriment to the yield of the desired amide. Further studies are now under way to explore other useful synthetic applications of this catalytic system.

Experimental Section

General

All moisture sensitive reactions were carried out under a nitrogen atmosphere. Anhydrous tetrahydrofuran was freshly distilled from sodium/benzophenone ketyl. All starting materials were of the best available grade (Aldrich, Merck) and were used without further purification. Starting *N*,*N*-dimethylanilines **1d**, **1e**, **1f** and **1g** were prepared from the corresponding anilines using dimethyl sulfate as methylating agent (See Supporting Information). Commercially available copper(II) chloride dihydrate was dehydrated upon heating in oven (150 ºC, 45 min) prior to use for the preparation of CuNPs. Column chromatography was performed with Merck silica gel 60 (0.040–0.063 μm, 240–400 mesh) and hexane/EtOAc as eluent. Reactions were monitored by thin-layer chromatography on silica gel plates (60F-254) visualized under UV light and/or using 0.2% ninhydrin in ethanol. Nuclear magnetic resonance (NMR) spectra were recorded on a Bruker ARX-300 spectrometer using $CDCl_3$ as the solvent and tetramethylsilane (TMS) as internal reference. Mass spectra (EI) were obtained at 70 eV on a Hewlett Packard HP-5890 GC/MS instrument equipped with a HP-5972 selective mass detector. High resolution mass spectra were recorded on Thermo Fisher LTQ Orbitrap XL, (for EI) and a Finnigen MAT 95 (for ESI). Infrared (FT-IR) spectra were obtained on a Nicolet-Nexus spectrophotometer.

Preparation of the CuNPs/ZY catalyst

Anhydrous copper(II) chloride (135 mg, 1 mmol) was added to a suspension of lithium (14 mg, 2 mmol) and 4,4'-di-*tert*-butylbiphenyl (DTBB, 27 mg, 0.1 mmol) in THF (2 mL) at room temperature under a nitrogen atmosphere. The reaction mixture, which was initially dark blue, rapidly changed to black, indicating that the suspension of copper nanoparticles was formed. This suspension was diluted with THF (18 mL) followed by the addition of the sodium Y zeolite (1.28 g). The resulting mixture was stirred for 1 h at room temperature, filtered, and the solid successively washed with THF (5 mL) and diethyl ether (10 mL), and then dried under vacuum.

General procedure for the synthesis of amides catalyzed by CuNPs/ZY

The amine (0.5 mmol), the anhydride (0.60 mmol) and *t*-BuOOH (1 Equiv.) were added to a reactor tube containing CuNPs/ZY (20 mg, 1.0 mol% Cu) in MeCN (2 mL) under air. The reaction mixture was warmed to 70 ºC and monitored by TLC and/or GLC until total conversion of the starting material. The solvent was removed in vacuo and the product was purified by flash column chromatography (hexane-EtOAc) to give the corresponding tertiary amide. Compounds **3aa**,[14] **3ba**,[15] **3ca**,[16] **3ha**,[17] **3ja**,[18] **3ka**,[19] **3la**,[20] **3na**,[21] **3ab**,[22] **3ac**,[23] **3ad**,[24] **3ae**,[24] **3af**[25], **3nf**[26], **3fa**[27], **3ga**[28] were characterized by comparison of their physical and spectroscopic data with those described in the literature.

Full data for the new compounds **3da**, **3ea** and **3ma** are provided below.

N-Methyl-*N*-phenylacetamide (**3aa**): White solid. 68.6 mg, 92% yield. 1H NMR (300 MHz, $CDCl_3$) δ 7.40– 7.19 (m, 3H), 7.16 – 7.07 (m, 2H), 3.20 (s, 3H), 1.80 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.8, 144.7, 129.8, 127.8, 127.2, 37.3, 22.5.

N-Methyl-N-(p-tolyl)acetamide (**3ba**): Pale yellow solid. 63.2 mg, 78% yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.14 (d, J = 8.0 Hz, 2H), 6.99 (d, *J* = 8.2 Hz, 2H), 3.17 (s, 3H), 2.30 (s, 3H), 1.79 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.8, 142.0, 137.6, 130.3, 126.8, 37.2, 22.3, 21.0.

N-(4-Bromophenyl)-*N*-methylacetamide (**3ca**): Light yellow solid. 101.0 mg, 89% yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.54 (d, J = 8.5 Hz, 2H), 7.07 (d, *J* = 8.5 Hz, 2H), 3.23 (s, 3H), 1.87 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.5, 143.7, 133.1, 128.9, 121.5, 37.2, 22.5.

N-(3-hydroxyphenyl)-*N*-methylacetamide (**3da**): Red oil. 70.1 mg, 85% yield. IR (neat) ν: 3276, 2929, 1696, 1499, 1372, 1213, 1180, 698 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.47 – 7.37 (m, 1H), 7.12 – 7.05 (m, 2H), 6.99 – 6.94 (m, 1H), 3.26 (s, 3H), 2.31 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.9, 158.28, 151.4, 130.5, 124.5, 121.2, 120.8, 37.3, 22.5 ppm. MS m/z 165 (M^+, 35), 123 (100), 122 (33), 94 (12); HRMS (EI) calc. for $C_9H_{11}NO_2$ 165.0790, found 165.0786.

N,N'-(3,3'-dimethyl-[1,1'-biphenyl]-4,4'-diyl)bis(*N*-methylacetamide) (**3ea**): Orange oil. 142.6 mg, 88% yield. IR (neat) ν: 2966, 2921, 1699, 1495, 1384, 833, 796 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.46 – 7.41 (m, 2H), 7.39 – 7.36 (m, 2H), 7.15 – 7.11 (m, 2H), 3.15 (s, 6H), 2.24 (s, 6H), 1.76 (s, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.9, 142.7, 140.3, 135.9, 130.2, 128.4, 126.3, 36.1, 22.1, 17.6 ppm. MS m/z 325 (M^{+1}, 10), 324 (M^+, 44), 281 (15), 227 (29), 165 (16), 56 (100); HRMS (EI) calc. for $C_{20}H_{24}N_2O_2$ 324.1838, found 324.1842.

N-Ethyl-*N*-phenylacetamide (**3ha**): White solid. 60.3 mg, 74% yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.46 – 7.34 (m, 3H), 7.20 – 7.13 (m, 2H), 3.75 (q, *J* = 7.2 Hz, 1H), 1.83 (s, 3H), 1.11 (t, *J* = 7.2 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.1, 142.9, 129.7, 128.2, 127.9, 43.9, 22.8, 13.1.

N-Methyl-*N*-(naphthalen-1-yl)acetamide (**3ja**): White solid. 67.7 mg, 68% yield. 1H NMR (300 MHz, $CDCl_3$) δ 7.98 – 7.85 (m, 2H), 7.84 – 7.78 (m, 1H), 7.60 – 7.47 (m, 3H), 7.40 – 7.33 (m, 1H), 3.37 (s, 3H), 1.77 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.4, 140.8, 134. 8, 130.1, 128.7, 127.5, 126.8, 125.9, 125.3, 122.3, 37.0, 21.9.

N-Benzyl-*N*-methylacetamide (**3ka**): Yellow-brown oil. 66.9 mg, 82% yield. The product was obtained as a mixture of two rotamers in its ^{1}H and ^{13}C NMR spectra. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.41 – 7.20 (m, 8H), 7.19 – 7.14 (m, 2H), 4.59 (s, 2H, major rotamer), 4.53 (s, 2H, major rotamer), 2.94 (s, 3H, minor rotamer), 2.92 (s, 3H, major rotamer), 2.16 (s, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.1, 170.8, 137.3, 136.5, 129.0, 128.6, 128.0, 127.6, 127.3, 126.3, 54.3, 50.6, 35.5, 33.7, 21.8, 21.4.

N-Methyl-*N*-phenethylacetamide (**3la**): White solid. 70.8 mg, 80% yield. The product was obtained as a mixture of two

rotamers in its ^{1}H and ^{13}C NMR spectra. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.32 – 7.20 (m, 8H), 7.18 – 7.13 (m, 2H), 3.62 – 3.54 (m, 2H), 3.52 – 3.46 (m, 2H), 2.94 (s, 3H), 2.86 (s, 3H), 2.90 – 2.79 (m, 4H), 2.05 (s, 3H), 1.84 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.6, 170.4, 139.3, 138.6, 128.9, 128.8, 128.7, 128.5, 126.8, 126.3, 52.6, 49.8, 36.9, 34.8, 33.8, 33.4, 22.0, 21.0.

N-Hexadecyl-*N*-methylacetamide (**3ma**): Yellow oil. 74.3 mg, 50% yield. IR (neat) ν: 2929, 2855, 1699, 1462 cm^{-1}. This product was obtained as a mixture of two rotamers in its ^{1}H and ^{13}C NMR spectra. ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.36 – 3.28 (m, 2H), 3.26 – 3.20 (m, 2H), 2.96 (s, 3H), 2.90 (s, 3H), 2.08 (s, 3H), 2.06 (s, 3H), 1.58 – 1.47 (m, 4H), 1.26 – 1.22 (m, 52H), 0.87 (t, *J* = 6.6 Hz, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.5, 170.4, 51.0, 47.7, 36.2, 33.4, 32.1, 29.8 x 3, 29.7 x 2, 29.6, 29.5, 28.5, 27.5, 27.0, 26.9, 22.8, 22.1, 21.4, 14.3 ppm. MS m/z 297 (M^+, 4), 283 (21), 282 (100), 114 (17), 100 (19), 87 (55), 86 (74), 74 (11), 55 (11); HRMS (EI) calc. for $C_{19}H_{39}NO$ 297.3032, found 297.3036.

N,N-Diethylacetamide (**3na**): Yellow oil. 49.9 mg, 85% yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.41 – 3.27 (m, 4H), 2.08 (s, 3H), 1.18 (t, *J* = 7.0 Hz, 3H), 1.12 (t, *J* = 7.0 Hz, 3H. ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.8, 42.9, 40.1, 21.6, 14.3, 13.2.

N-Methyl-*N*-phenylpropionamide (**3ab**): Yellow oil. 71.8 mg, 88% yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.44 – 7.36 (m, 2H), 7.34 – 7.27 (m, 2H), 7.20 – 7.30 (m, 1H), 3.25 (s, 3H), 2.15 – 1.98 (m, 2H), 1.03 (t, *J* = 7.5 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 174.1, 144.3, 129.8, 127.4, 122.5, 37.4, 27.6, 9.8.

N-Methyl-*N*-phenylbutyramide (**3ac**): Orange oil. 69.1 mg, 78% yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.39 – 7.31 (m, 2H), 7.30 – 7.24 (m, 1H), 7.15 – 7.07 (m, 2H), 3.19 (s, 3H), 2.03 – 1.95 (m, 2H), 1.58 – 1.46 (m, 2H), 0.74 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.5, 144.3, 129.8, 127.8, 127.4, 37.4, 36.1, 19.0, 13.9.

N-Methyl-*N*-phenylpentanamide (**3ad**): Colorless liquid. 74.7 mg, 81% yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.45 – 7.37 (m, 2H), 7.36 – 7.31 (m, 1H), 7.20 – 7.14 (m, 2H), 3.26 (s, 3H), 2.07 (t, *J* = 7.5 Hz, 2H), 1.50 – 1.57 (m, 2H), 1.14 – 1.27 (m, 2H), 0.80 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.5, 144.4, 129.8, 127.8, 127.4, 37.5, 33.9, 27.8, 22.5, 13.9.

N-Methyl-*N*-phenylhexanamide (**3ae**): Light yellow liquid. 73.8 mg, 72% yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.45 – 7.37 (m, 2H), 7.36 – 7.28 (m, 1H), 7.20 – 7.12 (m, 2H), 3.25 (s, 3H), 2.05 (t, *J* = 7.6 Hz, 2H), 1.51 – 1.60 (m, 2H), 1.23 – 1.09 (m, 4H), 0.81 (t, *J* = 6.8 Hz, 3H).^{13}C NMR (75 MHz, $CDCl_3$) δ 173.6, 144.4, 129.8, 127.8, 127.4, 37.5, 34.2, 31.6, 25.4, 22.5, 14.0.

N-Methyl-*N*-phenylbenzamide (**3af**): White solid. 73.9 mg, 70% yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.32 – 7.11 (m, 8H), 7.06 – 7.00 (m, 2H), 3.49 (s, 3H).^{13}C NMR (75 MHz, $CDCl_3$) δ 170.8, 144.9, 135.9, 129.7, 129.2, 128.8, 127.8, 127. 0, 126.6, 38.5.

N,N-Diethylbenzamide (**3nf**): Light yellow liquid. 60.0 mg, 81% yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.38 (s, 5H), 3.55 (s, 2H), 3.25 (s, 2H), 1.26 (2, 3H), 1.11 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.6, 137.1, 130.1, 129.3, 128.5, 126.4, 43.4, 39.5, 14.3, 13.0.

Methyl 2-(N-methylacetamido)benzoate (**3fa**): White solid. 12.4 mg, 12% yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.10 (d, *J* = 7.9 Hz, 1H), 7.70 (t, *J* = 7.7 Hz, 1H), 7.49 (t, *J* = 7.6 Hz, 1H), 7.39 (d, *J* = 7.9 Hz, 1H), 3.92 (s, 3H), 3.32 (s, 3H), 1.92 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.3, 167.9, 141.2, 131.6, 129.1, 123.2, 122.5, 122.2, 52.4, 37.2, 22.6.

N-Methyl-*N*-(3-nitrophenyl)acetamide (**3ga**): Yellow solid. 9.7 mg, 10% yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.21 – 8.20 (m, 1H), 8.12 – 8.10 (m, 1H), 7.56 – 7.62 (m, 2H), 3.34 (s, 3H), 1.92 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.1, 148.1, 142.3, 132.1, 130.2, 118.2, 114.9, 38.2, 21.8.

Gram scale synthesis of *N*-methyl-*N*-phenylacetamide (3aa)

N,N-dimetyhaniline (10 mmol, 1267 μL), acetic anhydride (12 mmol, 1134 μL) and *tert*-butyl hydroperoxide (10 equiv.) were added to a suspension of CuNPs/ZY (400 mg, 1.0 mol% Cu) in MeCN (40 mL) under air. The reaction mixture was warmed to 70 ºC and monitored by TLC and/or GLC until total conversion of the starting material. The solvent was removed in vacuo and the product was purified by flash column chromatography to give *N*-methyl-*N*-phenylacetamide in 93% yield (1.39 g).

Acknowledgements

This work was generously supported by the Argentinian Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET, PIP-2011-268) and Agencia Nacional de Promoción Científica y Tecnológica (ANPCyT, Prest. BID, PICT-2014-2171), the Spanish Ministerio de Economía y Competitividad (MINECO; grant no. CTQ2017-88171-P) and the Generalitat Valenciana (GV; grant no. AICO/2017/007), and the Universidad Nacional del Sur (UNS, PGI 24/Q072), Argentina. The authors want to thank Prof. M. A. Volpe for TPR analyses of the catalyst and helpful discussions.

Keywords: Copper Nanoparticles • Direct Oxidative Amidation • Heterogeneous Catalysis • Tertiary Amines

[1] a) A. Ojeda-Porras, D. Gamba-Sánchez, *J. Org. Chem.* **2016**, *81*, 11548-11555; b) *The Amide Linkage: Selected Structural Aspects in Chemistry, Biochemistry, and Materials Science* (Eds.: A. Greenberg, C. M. Breneman, J. F. Liebman), Wiley-VCH, Weinheim, **2000**.

[2] a) T. Wieland, M. Bodanszky in *The World of Peptides: A Brief History of Peptide Chemistry*, Springer-Verlag, New York, **1991**; b) R. M. de Figueiredo, J.-S. Suppo, J.-M. Campagne, *Chem. Rev.* **2016**, *116*, 12029-12122; d) J. R. Dunetz, J. Magano, G. A. Weisenburger, *Org. Process Res. Dev.* **2016**, *20*, 140-177.

[3] a) W.-P. Mai, G. Song, J.-W. Yuan, L.-R. Yang, G.-C. Sun, Y.-M. Xiao, P. Maoa, L.-B. Qu *RSC Adv.* **2013**, *3*, 3869-3872; b) S. Roy, S. Roy, G. W. Gribble *Tetrahedron* **2012**, *68*, 9867-9923; c) C. Liana Allen, J. M. J. Williams *Chem. Soc. Rev.* **2011**, *40*, 3405-3415; d) E. Valeur, M. Bradley *Chem. Soc. Rev.* **2009**, *38*, 606-631.

[4] a) L. Zhao, H. Ding, B. Zhao, C. Lu, Y. Yao *Polyhedron* **2014**, *83*, 50-59; b) J. C.-H. Yim, J. A. Bexrud, R. O. Ayinla, D. C. Leitch, L. L. Schafer *J. Org. Chem.* **2014**, *79*, 2015-2028; c) H. Cheng, B. Zhao, Y. Yao, C. Lua *Green Chem.* **2015**, *17*, 1675-1682; d) N. Kumagai, M. Shibasaki *Angew. Chem. Int. Ed.* **2013**, *52*, 223-234.

[5] For amidation reactions between acids and derivatives and amines, see: a) Ref. 1a) this paper; b) H. Lundberg, F. Tinnis, N. Selander, H. Adolfsson *Chem. Soc. Rev.* **2014**, *43*, 2714-2742.

[6] a) Y. Li, F. Jia, Z. Li *Chem. Eur. J.* **2013**, *19*, 82-86; b) Y. Li, L. Ma, F. Jia, Z. Li *J. Org. Chem.* **2013**, *78*, 5638-5646; c) H.-C. Cheng, W.-J. Hou, Z.-W. Li, M.-Y. Liua, B.-T. Guan *Chem. Commun.* **2015**, *51*, 17596-17599.

[7] a) M. J. Climent, A. Corma, S. Iborra, M. J. Sabater, *Chem. Rev.* **2014**, *4*, 870-891; b) S. Nishimura, K. Ebitani *ChemCatChem* **2016**, *8*, 2303-2316; c) F. Alonso, M. Yus *ACS Catal.* **2012**, *2*, 1441-1451.

[8] G. H. Dang, T. D. Nguyen, D. T. Le, T. Truong, N. T. S. Phan *ChemPlusChem* **2014**, *79*, 1129-1137.

[9] Selected papers on unsupported NPs: a) V. Gutierrez, E. Mascaró, F. Alonso, Y. Moglie, G. Radivoy *RSC Adv.* **2015**, *5*, 65739-65744; b) F. Nador, M. A. Volpe, F. Alonso, A. Feldhoff, A. Kirschning, G. Radivoy *App. Catal. A: Gen.* **2013**, *455*, 39-45; c) Y. Moglie, E. Mascaró, V. Gutierrez, F. Alonso, G. Radivoy *J. Org. Chem.* **2016**, *81*, 1813-1818; d) Y. Moglie, F. Alonso, M. Yus, G. Radivoy *App. Catal. A: Gen.* **2006**, *313*, 94-100; selected papers on supported CuNPs: e) E. Buxaderas, M. Graziano-Mayer, M. A. Volpe, G. Radivoy *Synthesis* **2017**, *49*, 1387-1393.

[10] a) F. Alonso, A. Arroyo, I. Martín-García, Y. Moglie *Adv. Synth. Catal.* **2015**, *357*, 3549-3561. b) A. Y. Mitrofanov, A. V. Murashkina, I. Martín-García, F. Alonso, I. P. Beletskaya, *Catal. Sci. Technol.* **2017**, *7*, 4401–4412.

[11] a) S. Murata, M. Miura, M. Nomura *J. Chem. Soc., Chem. Commun.* **1989**, 116-118; b) S. Murata, K. Suzuki, A. Tamatani, M. Miura, M. Nomura *J. Chem. Soc., Perkin Trans. I* **1992**, 1387-1392.

[12] a) S. Guo, B. Qian, Y. Xie, C. Xia, H. Huang *Org. Lett.*, **2011**, *13*, 522–525; b) X. Chen, T. Chen, Q. Li, Y. Zhou, L.-B. Han, S.-F. Yin *Chem. Eur. J.*, **2014**, *20*, 12234–12238; c) J. Ji, Z. Liu, P. Liu, P. Sun *Org. Biomol. Chem.*, **2016**, *14*, 7018–723.

[13] a) A. E. Wendlandt, A. M. Suess, S. S. Stahl *Angew. Chem. Int. Ed.* **2011**, *50*, 11062-11087; b) M. R. Maurya, P. Saini, C. Haldar, A. K. Chandrakar, S. Chand *J. Coord. Chem.* **2012**, *65*, 2903-2918.

[14] H. Xua, C. Wolf, *Chem. Commun*. **2009**, *0*, 1715-1717.

[15] E. J. Linstad, A. L. Vāvere, B. Hu, J. J. Kempinger, S. E. Snyderc, S. G. DiMagno *Org. Biomol. Chem*., **2017**, *15*, 2246–2252.

[16] B. Huang, Y. Zhao, C. Yang, Y. Gao, W. Xia *Org. Lett.*, **2017**, *19*, 3799–3802.

[17] H.-C. Cheng, W.-J. Hou, Z.-W. Li, M.-Y. Liua, B.-T. Guan *Chem. Commun.*, **2015**, *51*, 17596-17599.

[18] Y. Li, L. Ma, F. Jia, Z. Li, *J. Org. Chem.*, **2013**, *78*, 5638-5646.

[19] D. Liu, C. Liu, H. Li, A. Lei *Angew. Chem. Int. Ed.* **2013**, *52*, 4453-4456.

[20] H. Liu, L. Zhao, Y. Yuan, Z. Xu, K. Chen, S. Qiu, H. Tan, *ACS Catal*., **2016**, *6*, 1732-1736.

[21] G. A. Meshram, V. D. Patil, *Synth. Commun.* **2009**, *39*, 4384-4395.

[22] D. Ameena, T. J. Snapeb, *Tetrahedron Lett.* **2015**, *56*, 1816-1819.

[23] P. Drouhin, T. E. Hurst, A. C. Whitwood, R. J. K. Taylor, *Org. Lett*., **2014**, 16, 4900-4903.

[24] J.-S. Li, Y.-D. Da, G.-Q. Chen, Q. Yang, Z.-W. Li, F. Yang, P. - M. Huang, *ChemistrySelect* **2017**, *2*, 1770-1773.

[25] C. Wang, L. Huang, M. Lu, B. Zhao, Y. Wang, Y. Zhang, Q. Shen, Y. Yao *RSC Adv.* **2015**, *5*, 94768-94775.

[26] H. Yang, W. Hu, S. Deng, T. Wu, H. Cen, Y. Chen, D. Zhanga, B. Wang, *New J. Chem.*, **2015**, *39*, 5912-5915.

[27] a) A. B. Miltojević, N. S. Radulović, *RSC Adv.*, **2015**, *5*, 53569-53585.

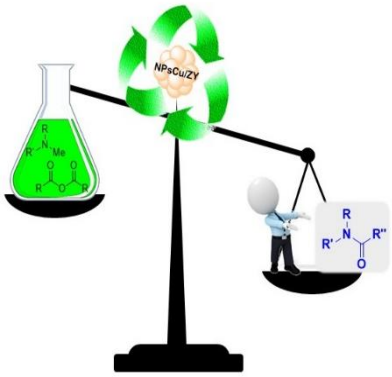
[28] R. Yamasaki, A. Tanatani, I. Azumaya, S. Saito, K. Yamaguchi, H. Kagechika, *Org. Lett.*, **2003**, 5, 1265-1267.

Entry for the Table of Contents (Please choose one layout)

Layout 1:

FULL PAPER

Better Call Copper: If you need tertiary amides, this is a case for copper! Recyclable copper nanoparticles (CuNPs) supported on Zeolite Y allow access to a variety of tertiary amides in a simple and economic way, even in gram scale.



Y. Moglie, E. Buxaderas, A. Mancini, F. Alonso, G. Radivoy**

Page No. – Page No.
Amide Bond Formation Catalyzed by Recyclable Copper Nanoparticles Supported on Zeolite Y under Mild Conditions

Layout 2:

FULL PAPER

((Insert TOC Graphic here; max. width: 11.5 cm; max. height: 2.5 cm))

Text for Table of Contents