# N-Heterocyclic Carbene – Palladium Complexes as Efficient Catalysts for the Oxidative Carbonylation of Amines to Ureas

by **Shuzhan Zheng**[a])[b]), **Xingao Peng**[a])[b]), **Jianming Liu**[a])[b]), **Wei Sun**[a]), and **Chungu Xia***[a])

[a]) State Key Laboratory for Oxo Synthesis and Selective Oxidation, Lanzhou Institute of Chemical Physics, Chinese Academy of Sciences, Lanzhou, 730000, P. R. China
(fax: +86 9318277088; e-mail: cgxia@lzb.ac.cn)
[b]) Graduate School of the Chinese Academy of Sciences, Beijing, 100039, P. R. China

---

A highly efficient oxidative carbonylation reaction of amines to ureas was developed making use of carbene – palladium complexes in the absence of any promoter. Both aliphatic amines and aromatic amines were transformed in good to excellent yields to the expected ureas.

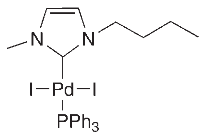
---

**Introduction.** – Since the discovery of a stable, crystalline N-heterocyclic carbene (NHC) by *Arduengo* and co-workers [1], the use of NHCs as ligands in organometallic chemistry and homogeneous catalysis has become increasingly popular in the last few years [2]. A series of highly active catalytic systems with NHC ligands for divers transformations have been developed, such as ruthenium-mediated olefin metathesis [3], iridium-catalyzed hydrogenation [4], nickel-catalyzed aerobic alcohol oxidations [5], and palladium-mediated cross-coupling reactions [6]. Recently, NHC complexes have also been used in carbonylation reactions: *Crudden* and co-workers, *Weberskirch* and co-workers, *Fernandez* and *Peris* and co-workers, and *Nuyken* and *Buchmeiser* and co-workers reported carbene – rhodium-complex-catalyzed hydroformylations of olefins [7], and *Nacci* and co-workers used a [Pd(benzothiazolylidene)] complex as catalyst for the carbonylation of aryl halides [8]. These studies showed that NHC – palladium complexes also could be efficient catalysts in carbonylation reactions.

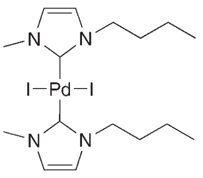
Ureas are important chemicals widely used as agrochemicals, dyes, antioxidants, resin precursors, synthetic intermediates (also for the production of carbamates and isocyanates), and HIV inhibitors [9]. The conventional methods for the preparation of ureas utilize highly toxic phosgene as the carbonyl source, which may cause serious environmental pollution and equipment corrosion [10]. In recent years, many non-phosgene routes, including those involving reductive [11] and oxidative carbonylation [12] have been extensively studied. The latter reaction is particularly attractive from the standpoint of atom economy and environmental concern; it employs an amine, carbon monoxide, and oxygen as starting materials and produces only $H_2O$ as by-product (*Eqn. 1*). The corresponding catalytic turnover frequencies (TOF), however, are still not high enough for industrial applications, and the development of more efficient catalysts is necessary. The NHC complexes are stable toward high temperature, air, and moisture and tolerant towards oxidation conditions [13]. These properties make NHC complexes ideal candidates for oxidative carbonylation reactions. However, there are few reports on oxidative carbonylations in the presence of NHC–palladium-complex catalysts. Nevertheless, it is worthy to note that *Sugiyama* and co-workers have reported on the [Pd(NHC)]-catalyzed oxidative carbonylation of phenol to diphenyl carbonate [14]. Here, we report the successful synthesis of ureas from amines by oxidative carbonylation in the presence of [Pd(NHC)] complexes.

$$2\ RNH_2 + CO + 1/2\ O_2 \rightarrow (RNH)_2CO + H_2O \qquad (1)$$

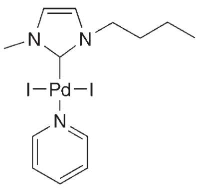
**Results and Discussion.** – The initial investigation of oxidative carbonylation with $CO/O_2$ was carried out with aniline as substrate and $[PdI_2(NHC)(PPh_3)]$ complex **1** [15] as catalyst to optimize the reaction conditions (*Table 1*). Interestingly, **1** was found to be effective even at a loading as low as 0.02 mol-%. HPLC and GC/MS Analysis of the reaction mixture revealed a 93% conversion of aniline and a high selectivity (99%). It should be noted that in most of the oxidative carbonylation reactions an excess of promoter is required [11]. In contrast, carbene–metal catalyst **1** gave good results in the absence of any promoter and within much shorter times. The catalytic system was sensitive to the reaction temperature; optimal results were obtained at 150° (*Table 1*, *Entry 2*), decreasing or increasing the temperature both resulted in a dramatic loss of catalytic activity. Additionally, the solvent played a key role. High catalytic activities were obtained in the polar solvent DMF. In less polar solvents, such as 1,4-dioxane or THF, poor conversions were achieved (*Table 1*, *Entries 6* and *7*). When using 1,2-dimethoxyethane ($MeOCH_2CH_2OMe$) as solvent, the conversion was good but the selectivity unsatisfactory (*Table 1*, *Entry 5*).



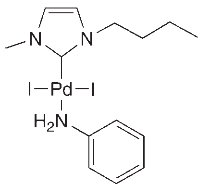
**1**



**2**



**3**



**4**

It is known that the performance of homogeneous catalysts is highly dependent on the ancillary ligand coordinated to the metal center [16], non-NHC ligands have a remarkable influence on the properties of [Pd(NHC)] complexes [15]. Thus, complexes **2**–**4** were synthesized and investigated in the oxidative carbonylation reactions, complex **2** [17] having two NHC ligands, complex **3** an NHC and a pyridine ligand, and complex **4** an NHC and an aniline ligand, as compared to the NHC and $PPh_3$ ligand of **1**. The activity of **2** (70% conversion) was lower than that of **1** (93% conversion), **3** (86% conversion), and **4** (99% conversion) under the same conditions (*Table 1*). This may be due to the fact that NHC is a tightly bound ligand hard to dissociate during catalysis to generate the active species [18]. On the other hand, $PPh_3$ and aniline were more labile ligands as compared to NHC, *i.e.*, their dissociation were more easy; thus **1** and **4** showed higher activities. Remarkably, although the activities were different, all the [Pd(NHC)] complexes **1**–**4** showed high selectivities. Especially, **4** exhibited excellent activity and selectivity. Complex **4** is a new type of Pd-complex

Table 1. *Synthesis of* N,N′-*Diphenylurea by Oxidative Carbonylation of Aniline in the Presence of Catalysts* **1**–**4**[a])

| *Entry* | Catalyst | *T* [°] | Solvent | Conversion[b]) [%] | Selectivity[b]) [%] | TOF [$h^{-1}$][c]) |
|---|---|---|---|---|---|---|
| *1* | **1** | 140 | DMF | 86 | 98 | 4200 |
| *2* | **1** | 150 | DMF | 93 | 99 | 4600 |
| *3* | **1** | 160 | DMF | 91 | 99 | 4500 |
| *4* | **1** | 170 | DMF | 86 | 99 | 4200 |
| *5* | **1** | 150 | $MeOCH_2CH_2OMe$ | 92 | 76 | 3400 |
| *6* | **1** | 150 | dioxane | 9 | 99 | 440 |
| *7* | **1** | 150 | THF | 75 | 99 | 3700 |
| *8* | **2** | 150 | DMF | 70 | 99 | 3400 |
| *9* | **3** | 150 | DMF | 86 | 99 | 4200 |
| *10* | **4** | 150 | DMF | 99 | 99 | 4900 |

[a]) Reaction conditions: catalyst (0.0044 mmol), aniline (22 mmol), solvent (6 ml); $P(CO, O_2) = 3.2, 0.8$ MPa; time 1 h. [b]) Determined by HPLC. [c]) Mol of amine converted per mol of catalyst per hour.

containing both an NHC and an aniline as ligands. The structure of **4** was confirmed by a single-crystal X-ray diffraction analysis (*Fig.*). The ORTEP diagram reveals an unusual coordination mode in the carbene–palladium complex **4**, in which an aniline and an NHC are both bound to one Pd-atom, which is a rare case. According to the above results, more labile non-NHC ligands have a remarkable influence on the catalytic activity of [Pd(NHC)] complexes in this reaction.

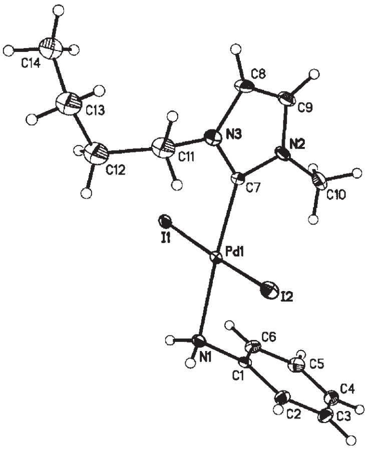


Figure. *ORTEP Diagram of* **4**. Arbitrary atom numbering. Selected distances [Å] and angles [°]: Pd(1)–I(1) 2.6052(6), Pd(1)–I(2) 2.6169(6), Pd(1)–C(7) 1.958(5), and Pd(1)–N(1) 2.147(3); Pd(1)–N(1)–C(1) 110.2(2), N(1)–Pd(1)–C(7) 174.6(2), I(1)–Pd(1)–I(2) 175.051(18), C(7)–Pd(1)–I(1) 88.18(16), and C(7)–Pd(1)–I(2) 88.56(16).

After the systematic optimization of the reaction conditions, we successfully applied the highly efficient oxidative carbonylation with $CO/O_2$ in the presence of only a [Pd(NHC)] catalyst without any promoter to other primary amines (*Table 2*). And to the best of our knowledge, this is the first time that an NHC is used in the oxidative carbonylation of amines to prepare symmetrically *N*,*N'*-disubstituted ureas. Good to excellent yields of isolated ureas were obtained. As expected, the presence of an electron-releasing or an electron-withdrawing substituent at the *para*-position of aniline strongly affected the reactivity of the substrate, electron-attracting substituents slightly retarding the reaction (87% and 60% conversion for *p*-Cl- and *p*-Ac-substituted aniline (*Entries 2* and *5*), resp.). Sterically more crowded substrates such as 2,6-dimethylaniline also gave good yields (*Entry 4*, 72%). Aliphatic amines were less reactive than aromatic ones when the reactions were performed at 150° and in DMF as solvent (*Entry 6*). This was due to the formation of formamide and oxamide as by-products. Satisfactory results were obtained for the aliphatic amines by using $MeOCH_2CH_2OMe$ as solvent at a lower temperature, *i.e.*, at 100° (*Entries 7* and *8*). Benzylamine gave also good yields (*Entry 9*).

Table 2. *Synthesis of Ureas by Oxidative Carbonylation of Primary Amines in the Presence of Catalyst* **4**[a])

| *Entry* | Substrate $RNH_2$ | Product $(RNH)_2CO$ | Yield[b]) |
|---|---|---|---|
| *1* | $4\text{-Me}-C_6H_4-NH_2$ | $(4\text{-Me}-C_6H_4-NH)_2CO$ | 99 |
| *2* | $4\text{-Cl}-C_6H_4-NH_2$ | $(4\text{-Cl}-C_6H_4-NH)_2CO$ | 87 |
| *3* | $2,4\text{-Me}_2C_6H_3-NH_2$ | $(2,4\text{-Me}_2C_6H_3-NH)_2CO$ | 85 |
| *4* | $2,6\text{-Me}_2C_6H_3-NH_2$ | $(2,6\text{-Me}_2C_6H_3-NH)_2CO$ | 72 |
| *5* | $4\text{-Ac}-C_6H_4-NH_2$ | $(4\text{-Ac}-C_6H_4-NH)_2CO$ | 60 |
| *6* | $BuNH_2$ | $(BuNH)_2CO$ | 46 |
| *7*[c]) | $BuNH_2$ | $(BuNH)_2CO$ | 75 |
| *8*[c]) | $^tBuNH_2$ | $(^tBuNH)_2CO$ | 70 |
| *9*[c]) | $PhCH_2NH_2$ | $(PhCH_2NH)_2CO$ | 75 |

[a]) Reaction conditions: Catalyst **4** (0.0044 mmol), substrate (22 mmol), DMF (6 ml); $P(CO, O_2) = 3.2, 0.8$ MPa; time 1 h, temp. 150°. [b]) Yields of isolated material. [c]) Temp. 100°, time 10 h, solvent $MeOCH_2CH_2OMe$.

**Conclusions.** – In summary, a by-product-free catalytic method for the synthesis of symmetrically *N*,*N'*-substituted ureas from amines, CO, and $O_2$ was developed. Therein, the carbene–palladium complexes were highly efficient catalysts at a low loading and in the absence of any promoter. Both aliphatic and aromatic amines gave good to excellent yields of ureas. Efforts are underway to elucidate the mechanistic details of this oxidative carbonylation reaction catalyzed by [Pd(NHC)] complexes.

We gratefully acknowledge financial support from the *National Science Foundation of China* (20533080, 20625308). We thank Dr. *Jun Zhang* for assistance in performing the X-ray crystal-structure analysis.

## Experimental Part

*General.* THF was purified by distillation from sodium/benzophenone immediately before use as solvent. Unless otherwise noted, all chemicals were purchased from commercial suppliers and used without further purification. Flash chromatography (FC): silica gel 200–300 mesh. GC Analyses: *HP 6890/5973-GC-MS* and *HP 5890-GC* apparatus. IR Spectra: $\tilde{\nu}$ in $cm^{-1}$. NMR Spectra: *Varian 400-MHz-FT-NMR* spectrometer; $\delta$ in ppm, $J$ in Hz.

*(1-Butyl-1,3-dihydro-3-methyl-2*H*-imidazol-2-ylidene)diiodopyridinepalladium* (**3**). To a soln. of bis(1-butyl-1,3-dihydro-3-methyl-2*H*-imidazol-2-ylidene)di-$\mu$-iododiiododipalladium (150 mg) [17] in THF (2 ml), pyridine (25 µl) was added and the mixture was stirred for 10 min at r.t. (red → yellow). Then, hexane (10 ml) was added and the yellow precipitate filtered, washed with hexane (3 ×), and dried *in vacuo:* **3** (166 mg, 96%). $^1$H-NMR (400 MHz, $CDCl_3$): 9.02 (*q*, *J* = 4.8, 2 H, Py); 7.71 (*t*, *J* = 7.6, 1 H, Py); 7.30 (*t*, *J* = 6.8, 2 H, Py); 6.91 (*d*, *J* = 2.0, 2 CHN); 4.37 (*t*, *J* = 7.6, $CH_2N$); 3.95 (*s*, MeN); 2.01 (*m*, 1 $CH_2$), 1.45 (*m*, 1 $CH_2$), 1.01 (*t*, *J* = 7.6, Me). $^{13}$C-NMR (100 MHz, $CDCl_3$): 153.8 ($CN_2$); 139.7 (Py); 124.4 (Py); 123.1 (Py); 121.5 (CHN); 109.8 (CHN); 51.3 ($CH_2N$); 39.2 (MeN); 31.4 ($CH_2$); 19.9 ($CH_2$); 13.7 (Me). Anal. calc. for $C_{13}H_{19}I_2N_3Pd$: C 27.04, H 3.32, N 7.27; found: C 26.96, H 3.50, N 7.44.

*(Benzenamine)(1-butyl-1,3-dihydro-3-methyl-2*H*-imidazol-2-ylidene)diiodopalladium* (**4**). As described for **3**, with bis(1-butyl-1,3-dihydro-3-methyl-2*H*-imidazol-2-ylidene)di-$\mu$-iododiiododipalladium [17], THF (2 ml), and aniline (30 µl): **4** (170 mg, 98%). Crystals of **4** suitable for X-ray crystallographic analysis were obtained from a sat. soln. in THF by slow evaporation of the solvent at r.t. IR (KBr): 3272, 3221, 1599, 1581, 1491, 1469, 1068, 755, 690. $^1$H-NMR (400 MHz, $CDCl_3$): 7.44 (*d*, *J* = 8.4, 2 H, Ph); 7.29 (*t*, *J* = 7.6, 2 H, Ph); 7.11 (*t*, *J* = 7.2, 1 H, Ph); 6.91 (*d*, *J* = 2.0, 1 CHN); 6.85 (*d*, *J* = 2.0, 1 CHN); 4.45 (*s*, $NH_2$); 4.16 (*t*, *J* = 8.0, $CH_2N$); 3.79 (*s*, MeN); 1.88 (*m*, 1 $CH_2$); 1.31 (*m*, 1 $CH_2$); 0.89 (*t*, *J* = 7.2, $CH_3$). $^{13}$C-NMR (100 MHz, $CDCl_3$): 144.8 ($N_2C$); 139.7 (Ph); 128.9 (Ph); 124.8 (Ph); 123.0 (Ph); 121.7 (CHN); 121.6 (CHN); 51.3 ($CH_2N$); 39.1 (MeN); 31.4 ($CH_2$); 19.8 ($CH_2$); 13.6 (Me). Anal. calc. for $C_{14}H_{21}I_2N_3Pd$: C 28.42, H 3.57, N 7.10; found: C 29.10, H 3.69, N 6.94.

CCDC-624386 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge *via* www.ccdc.cam.ac.uk/data_request/cif.

*Catalytic Oxidative Carbonylation: General Procedure.* A 75-ml autoclave equipped with a magnetic stirring bar and automatic temp. control was charged with the mentioned amounts of an amine, catalyst, and solvent (6 ml) and then pressurized with CO (3.2 MPa) and $O_2$ (0.8 MPa) to a total pressure of 4.0 MPa. The reactor was heated at the specified temp. for 1 h. After cooling, the autoclave was degassed and the mixture analyzed by HPLC and GC/MS. Then, $H_2O$ was poured into the mixture to precipitate the crude product, which was purified by washing with acetone: pure product as white solid. The filtrate was concentrated and the residue washed with acetone to afford another crop of the product.

## REFERENCES

[1] A. J. Arduengo III, R. L. Harlow, M. Kline, *J. Am. Chem. Soc.* **1991**, *113*, 361.

[2] N. M. Scott, S. P. Nolan, *Eur. J. Inorg. Chem.* **2005**, 1815; W. A. Herrmann, *Angew. Chem., Int. Ed.* **2002**, *41*, 1290; D. Bourissou, O. Guerret, F. P. Gabbai, G. Bertrand, *Chem. Rev. (Washington, DC, U.S.)* **2000**, *100*, 39; A. J. Arduengo, *Acc. Chem. Res.* **1999**, *32*, 913.

[3] L. Jafarpour, S. P. Nolan, *Adv. Organomet. Chem.* **2001**, *46*, 181; T. M. Trnka, R. H. Grubbs, *Acc. Chem. Res.* **2001**, *34*, 18.

[4] H. M. Lee, T. Jiang, E. D. Stevens, S. P. Nolan, *Organometallics* **2001**, *20*, 1255; A. C. Hillier, H. M. Lee, E. D. Stevens, S. P. Nolan, *Organometallics* **2001**, *20*, 4246.

[5] B. R. Dible, M. S. Sigman, *J. Am. Chem. Soc.* **2003**, *125*, 872.

[6] O. Navarro, R. A. Kelly, S. P. Nolan, *J. Am. Chem. Soc.* **2003**, *125*, 16194; M. S. Viciu, R. F. Germaneau, S. P. Nolan, *Org. Lett.* **2002**, *4*, 4053; W. A. Herrmann, M. Elison, J. Fischer, C. Kocher, G. R. J. Artus, *Angew. Chem., Int. Ed.* **1995**, *34*, 2371.

[7] A. C. Chen, L. Ren, A. Decken, C. M. Crudden, *Organometallics* **2000**, *19*, 3459; M. T. Zarka, M. Bortenschlager, K. Wurst, O. Nuyken, R. Weberskirch, *Organometallics* **2004**, *23*, 4817; M. Poyatos, P. Uriz, J. A. Mata, C. Claver, E. Fernandez, E. Peris, *Organometallics* **2003**, *22*, 440; M. Bortenschlager, J. Schütz, D. von Preysing, O. Nuyken, W. A. Herrmann, R. Weberskirch, *J. Organomet. Chem.* **2005**, *690*, 6233; M. Bortenschlager, M. Mayr, O. Nuyken, M. R. Buchmeiser, *J. Mol. Catal. A* **2005**, *233*, 67.

[8] V. Calò, P. Giannoccaro, A. Nacci, A. Monopoli, *J. Organomet. Chem.* **2002**, *645*, 152.

[9] T. P. Vishnyakova, I. A. Golubeva, E. V. Glebova, *Russ. Chem. Rev. (Engl. Transl.)* **1985**, *54*, 249; K. G. Hylton, A. D. Main, L. McElwee-White, *J. Org. Chem.* **2003**, *68*, 1615.

[10] M. B. Smith, J. March, 'March's Advanced Organic Chemistry. Reactions, Mechanisms, and Structure', 5th edn., Wiley Interscience, New York – Chichester – Brisbane – Toronto – Singapore, 2001; H. J. Knölker, T. Braxmeier, G. Schlechtingen, *Angew. Chem., Int. Ed.* **1995**, *34*, 2497.

[11] A. M. Tafesh, J. Weiguny, *Chem. Rev. (Washington, DC, U.S.)* **1996**, *96*, 2035.

[12] I. Chiarotto, M. Feroci, *J. Org. Chem.* **2003**, *68*, 7137; B. Gabriele, R. Mancuso, G. Salerno, M. Costa, *J. Org. Chem.* **2003**, *68*, 601; B. Gabriele, G. Salerno, R. Mancuso, M. Costa, *J. Org. Chem.* **2004**, *69*, 4741; B. Gabriele, G. Salerno, D. Brindisi, M. Costa, G. P. Chiusoli, *Org. Lett.* **2000**, *2*, 625; B. Gabriele, R. Mancuso, G. Salerno, M. Costa, *Chem. Commun.* **2003**, *4*, 486; H. S. Kim, Y. J. Kim, H. Lee, S. D. Lee, C. S. Chin, *J. Catal.* **1999**, *184*, 526; F. Li, C. G. Xia, *J. Catal.* **2004**, *227*, 542.

[13] W. A. Herrmann, C. Kocher, *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 2163.

[14] K. Okuyama, J. Sugiyama, R. Nagahata, M. Asai, M. Ueda, K. Takeuchi, *J. Mol. Catal. A* **2003**, *203*, 21; K. Okuyama, J. Sugiyama, R. Nagahata, M. Asai, M. Ueda, K. Takeuchi, *Green Chem.* **2003**, *5*, 563.

[15] W. A. Herrmann, V. P. W. Böhm, C. W. K. Gstöttmayr, M. Grosche, C.-P. Reisinger, T. Weskamp, *J. Organomet. Chem.* **2001**, *617/618*, 616.

[16] 'Transition Metals for Organic Synthesis', Eds. M. Beller and C. Bolm, Wiley-VCH, Weinheim, 1998.

[17] W. A. Herrmann, M. Elison, J. Fisher, C. Köcher, G. R. Artus, *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 2371.

[18] T. Weskamp, F. J. Kohl, W. Hieringer, D. Gleich, W. A. Herrmann, *Angew. Chem., Int. Ed.* **1999**, *38*, 2416.

*Received January 29, 2007*