Pd(OAc)$_2$-Catalyzed Carbonylation of Amines

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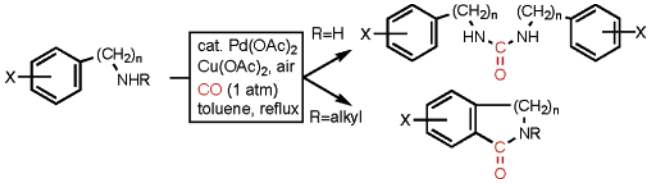

A phosphine-free catalytic system [Pd(OAc)$_2$−Cu(OAc)$_2$−air] induced a substrate-specific carbonylation of amines in boiling toluene under CO gas (1 atm). Symmetrical *N*,*N*′-dialkylureas were obtained by the carbonylation of primary amines. *N*,*N*,*N*′-Trialkylureas were selectively formed by addition of a secondary amine to the above reaction vessel. Secondary amines did not give tetraalkylureas. However, dialkylamines with a phenyl group on their alkyl chains, such as *N*-monoalkylated benzylic amine or phenethylamine derivatives, underwent a direct aromatic carbonylation to afford five- or six-membered benzolactams. In the carbonylation, the chelation effect or steric repulsion between Pd(II) and the *meta*-substituent in the *ortho*-palladation and the ring sizes of cyclopalladation products that were formed prior to carbonylation were found to generate good site selectivity and increase the reaction rate. In contrast, carbonylation of ω-arylalkylamines with a hydroxyl group gave neither ureas nor benzolactams but instead produced 1,3-oxazolidinones smoothly. Hydrochlorides of amines also underwent carbonylation to afford the corresponding amides under the conditions used. This procedure made it possible to prepare ureas of amino acid esters and *N*-alkylcarbamates in practical yields.

Introduction

Transition-metal-catalyzed carbonylation is a useful method for the formation of amide bonds.[1,2] Mono- and dicarbonylations of amines using metal catalysts (Se,[3] Tl,[4] Hg,[5] Mn,[6] Fe,[7] Co,[8] Ni,[9] Cu,[10] Ru,[11] Rh,[11b,e,f,12] Pd,[13−16] W,[17] Pt,[11b,18] Ir,[11b] or Au[19]) with CO gas have been studied, and a variety of amides, such as ureas, urethanes, oxamides, formamides, and 1,3-oxazolidinones, have been prepared.[20] The carbonylations have usually been carried out under compressed CO gas, and some have been carried out at a high temperature. For instance, metallic Se or SeCO undergoes inter- and intramolecular carbonylation of amines to give ureas, cyclic ureas, and cyclic urethanes under CO at more than 30 atm of pressure, as reported by Sonoda[3e] or Långström.[3k] Manganese-catalyzed carbonylation also produced ureas and carbamates from alkylamines[6a,b] or arylamines[6d]

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(1) For general reviews, see: (a) Colquhoun, H. M.; Thompson, D. J.; Twigg, M. V. *Carbonylation, Direct Synthesis of Carbonyl Compounds*; Plenum Press: New York, 1991. (b) Tsuji, J. *Palladium Reagents and Catalysts, Innovation in Organic Synthesis*; John Wiley & Sons: Chichester, U.K., 1995.

(2) Tkatchenko, I. In *Comprehensive Organometallic Chemistry*; Wilkinson, G., Stone, F. G. A., Abel, E. W., Eds.; Pergamon Press: Oxford, 1982; Vol. 8, pp 101−223.

(3) Se: (a) Sonoda, N.; Yasuhara, T.; Kondo, K.; Ikeda, T.; Tsutsumi, S. *J. Am. Chem. Soc.* **1971**, *93*, 6433. (b) Kondo, K.; Sonoda, N.; Tsutsumi, S. *J. Chem. Soc., Chem. Commun*. **1972**, 307. (c) Kondo, K.; Sonoda, N.; Yoshida, K.; Koishi, M.; Tsutsumi, S. *Chem. Lett*. **1972**, 401. (d) Kondo, K.; Murata, K.; Miyoshi, N.; Murai, S.; Sonoda, N. *Synthesis* **1979**, 735. (e) Yashida, T.; Kambe, N.; Murai, S.; Sonoda, N. *Tetrahedron Lett*. **1986**, *27*, 3037 *Bull. Chem. Soc. Jpn*. **1987**, *60*, 1793. (f) Fujiwara, S.; Miyoshi, N.; Ogawa, A.; Kambe, N.; Sonoda, N. *J. Phys. Org. Chem*. **1993**, *65*, 699. (g) A review, Sonoda, N. *Pure Appl. Chem*. **1993**, *65*, 699. (h) For ionic Se, see: Kim, H. S.; Kim, Y. J.; Lee, H.; Lee, S. D.; Chin, C. S. *J. Catal*. **1999**, *184*, 526. (i) Yang, Y.; Lu, S. *Tetrahedron Lett*. **1999**, *40*, 4845. (j) Kim, H. S.; Kim, Y. J.; Lee, H.; Lee, S. D.; Park, K. U.; Lee, C.; Chin, C. S. *Angew. Chem., Int. Ed.* **2002**, *41*, 4300. (k) Kihlberg, T.; Karhad, F.; Långström, B. *J. Org. Chem*. **2002**, *67*, 3687. (l) Mei, J.; Yang, Y.; Xue, Y.; Lu, S. *J. Mol. Catal. A* **2003**, *191*, 135. (m) Chen, J.; Ling, G.; Lu, S. *Tetrahedron Lett*. **2003**, *59*, 8251. (n) Ling, G.; Chen. J.; Lu, S. *J. Mol. Catal. A* **2003**, *202*, 23. (o) Ling, G.; Chen. J.; Lu, S. *J. Chem. Res., Synop*. **2003**, 442. (p) Chen, J.; Ling, G.; Lu, S. *Eur. J. Org. Chem*. **2003**, 3446. (q) Fujiwara, S.; Shikano, Y.; Shin-ike, N.; Kambe, N.; Sonoda, N. *Org. Lett*. **2002**, *67*, 6275.

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under high pressure at 131, 90, or 66 atm. Carbonylations by Pd catalyses have been extensively studied since Tsuji reported in 1966 the first Pd-catalyzed carbonylation of amines,[13a] in which $PdCl_2$ was used under CO at 100 kg/cm^2 and at 180 °C to give a mixture of *N*,*N*′-didecylurea and *N*,*N*′-didecyloxamide from decylamine in benzene. Methods for oxidative carbonylation by using $PdCl_2$ with oxidant O_2 and/or CuX or CuX_2 have been developed for preparation of ureas,[13g,m,o] carbamates,[13h,n] and oxamides or related double carbonyl compounds.[13k,l,n,p] A method for preparing cyclic mono- and dicarbonyl compounds and their chemical transformations were reported in detail by Murahashi.[13u]

Methods for oxidative carbonylation of alkylamines or aniline using a combination of Pd/C and NaI in the presence of O_2, which provided ureas and/or carbamates, were reported by Fukuoka[13f] and Chaudhari.[13o,r,s] Gabriele's procedure using PdI_2 and O_2 led to good formation of ureas, carbamates, and their cyclic derivatives.[16]

It was reported by Heck in 1974 that carbonylation using aromatic nitro compounds and aromatic primary amines under 1 atm of CO produced a mixture of *N*,*N*′-diarylureas in the presence of catalytic amounts of $PdBr_2(PPh_3)_2$, Et_4NCl, and n-Bu_3N. Under a compressed pressure of CO, unsymmetrical ureas were selectively prepared by a Se-catalyzed oxidative−reductive carbonylation similarly using nitrobenzene derivatives and primary or secondary amines, in which reduction of the nitro group into an amino group prior to the carbonylation was involved, as reported by Lu.[3l−p] Gabriele's oxidative carbonylation with PdI_2 mentioned above also gave *N*,*N*,*N*′-trisubstituted ureas from primary and secondary amines under CO at 60 atm of pressure.[16d]

Two Pd−Zr catalytic systems have been employed in the oxidative carbonylation of aniline and alkylamines.[14] One [Pd/ZrO_2−SO_4^{2-}/CO (3.5 MPa)/O_2 (0.5 MPa)] reported by Deng[14b] gave *N*-phenyl-*N*′-alkylureas.

Carbonylations of primary or secondary alkylamines and primary or secondary α,ω-diamines were carried out using $W(CO)_6$ as a catalyst and I_2 as an oxidant at 60−100 atm of CO to afford symmetrical dialkyl- or tetraalkylureas and cyclic ureas. The method was applied to the synthesis of seven-membered cyclic ureas related to HIV protease inhibitors.[17h] Gold also produced diarylureas and *N*-arylcarbamates by oxidative carbonylation using a polymer-immobilized Au catalyst prepared from $HAuCl_4{\cdot}4H_2O$.[19]

Methods for carbonylation of amines in an atmosphere of pressure to ureas have been limited to oxidative carbonylation with Se,[3a,f] $CuCl_2$,[10] $PdCl_2$,[13h,m] $Pd(OAc)_2$ on clay,[13q] and a homogeneous catalyst, $[Ru(CO)_3I_3]NBu_4$,[11f] to oxidative−reductive carbonylation with $PdBr_2(PPh_3)_2$ using nitrobenzene and anilines,[13b] and to electrochemical carbonylation with $PdCl_2(PPh_3)_2$−$Cu(OAc)_2$[15a] or $Pd(OAc)_2(PPh_3)_2$−NaOAc.[15c]

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(4) Tl: Sonoda, N.; Yasuhara, T.; Kondo, K.; Ikeda, T.; Tsutsumi, S. *Bull. Chem. Soc. Jpn*. **1981**, *54*, 1460.

(5) Hg: Tsuji, J.; Iwamoto, N. Japan Patent 6904096; *Chem. Abstr.* **1969**, *71*, 12792. Nefedov, B. R.; Sergeeva, N. S.; Eidus, Ya. T. *Izv. Akad. Nauk. SSSR, Khim*. **1973**, 807; *Chem. Abstr*. **1973**, *79*, 31813.

(6) Mn: (a) Calderazzo, F. *Inorg. Chem*. **1965**, *4*, 293. (b) Dombek, D.; Angelici, R. J. *J. Organomet. Chem*. **1977**, *134*, 203. (c) Srivastava, S. C.; Shrimal, A. K.; Srivastava, A. *J. Organomet. Chem*. **1991**, *414*, 65. (d) Li, K.-T.; Peng, Y.-J. *J. Catal*. **1993**, *143*, 631.

(7) Fe: (a) Dombeck, B. K.; Eidus, Ya. T. *Izv. Akad. Nauk. SSSR, Khim*. **1976**, 1782; *Chem. Abstr*. **1977**, *86*, 16056. German Patent 1170396; *Chem. Abstr*. **1964**, *61*, 2979. (b) Sampson, H. J., Jr. U.S. Patent 2589289; *Chem. Abstr*. **1952**, *46*, 11234. (c) Dombek, B. D.; Angelici, R. J. *J. Catal*. **1977**, *48*, 433.

(8) Co: (a) Sternberg, H. W.; Wender, I.; Friedel, R. A.; Orchin, M. *J. Am. Chem. Soc*. **1953**, *75*, 3148. (b) Rosenthal, A. *Can. J. Chem*. **1962**, *40*, 1718. (c) Benedini, F.; Nali, M.; Rindone, B.; Tollari, S.; Cenini, S.; Monica, G. La; Porta, F. *J. Mol. Catal*. **1986**, *3*, 155. (d) Bassoli, A.; Rindone, B.; Tollari, S.; Chioccara, F. *J. Mol. Catal*. **1990**, *60*, 41.

(9) Ni: (a) Aliev, Ya. Yu.; Romanova, I. B.; Freidlin, L. Kh. *Uzb. Khim. Zh*. **1961**, *5*, 54; *Chem. Abstr*. **1962**, *57*, 8413. (b) Aliev, Ya. Yu.; Romanova, I. B. *Neftekhim., Akad. Nauk Turkm., SSR* **1963**, 204; *Chem. Abstr*. **1964**, *61*, 6913. (c) Martin, W. E.; Farona, M. F. *J. Organomet. Chem*. **1981**, *206*, 393. (d) Hoberg, H.; Fañanás, F. J.; Riegel, H. J. *J. Organomet. Chem*. **1983**, *254*, 267. (e) Giannoccaro, P.; Nobile, C. F.; Mastrorilli, P.; Ravasio, N. *J. Organomet. Chem*. **1991**, *419*, 251.

(10) Cu: Brackman, W. *Discuss. Faraday Soc*. **1968**, 122.

(11) Ru: (a) Byerley, J. J.; Rempel, G. L.; Takebe, N. *J. Chem. Soc., Chem. Commun*. **1971**, 1482. Lassau, C.; Cheuvin, Y.; Lefevro, G. Ger. Offen. 1902560; *Chem. Abstr*. **1970**, 72, 21358. Yamahara, T.; Takamatsu, S.; Hirose, K. Japan Kokai 72 34341; *Chem. Abstr*. **1973**, *78*, 43087. (b) With Rh, Pt and Ir: Fukuoka, S.; Chono, M.; Kohno, M. *J. Org. Chem*. **1984**, *49*, 1458. (c) Taqui Khan, M. M.; Halligudi, S. B.; Abdi, S. H. R.; Shukla, S. *J. Mol. Catal*. **1988**, *48*, 25. (d) Taqui Khan, M. M.; Halligudi, S. B.; Shukla, S.; Abdi, S. H. R. *J. Mol. Catal*. **1989**, *51*, 129. (e) With Rh, Mulla, S. A. R.; Gupte, S. P.; Chaudhari, R. V. *J. Mol. Catal*. **1991**, *67*, L7. (f) With Rh, Mulla, S. A. R.; Rode, C. V.; Kelkar, A. A.; Gupte, S. P. *J. Mol. Catal. A* **1997**, *122*, 103. (g) Kondo, T.; Kotachi, S.; Tsuji, Y.; Watanabe, Y.; Mitsudo, T. *Organometallics* **1997**, *16*, 2562.

(12) Rh: Durand, D.; Lassau, C. *Tetrahedron* **1969**, *28*, 2329.

(13) Pd: (a) Tsuji, J.; Iwamoto, N. *Chem. Commun*. **1966**, 380. (b) Schoenberg, A.; Heck, R. F. *J. Org. Chem*. **1974**, *39*, 3327. Dieck, H. A.; Laine, R. M.; Heck, R. F. *J. Org. Chem*. **1975**, *40*, 2819. (c) Ozawa, F.; Soyama, H.; Yamamoto, T.; Yamamoto, A. *Tetrahedron Lett*. **1982**, *23*, 3383. (d) Ozawa, F.; Sugimoto, T.; Yuasa, Y.; Santra, M.; Yamamoto, T.; Yamamoto, A. *Organometallics* **1984**, *3*, 683. (e) Ozawa, F.; Sugimoto, T.; Yamamoto, T.; Yamamoto, A. *Organometallics* **1984**, *3*, 692. (f) Fukuoka, S.; Chono, M.; Kohno, M. *J. Chem. Soc., Chem. Commun*. **1984**, 399. (g) Sheludyakov, Y. L.; Golodov, V. A. *Bull. Chem. Soc. Jpn*. **1984**, *57*, 251. (h) Alper, H.; Hartstock, F. W. *J. Chem. Soc., Chem. Commun*. **1985**, 1142. (i) Ozawa, F.; Soyama, H.; Yanagihara, H.; Aoyama, I.; Takino, H.; Izawa, K.; Yamamoto, T.; Yamamoto, A. *J. Am. Chem. Soc*. **1985**, *107*, 3235. (j) Ozawa, F.; Yanagihara, H.; Yamamoto, A. *J. Org. Chem*. **1986**, *51*, 415. (k) Tam, W. *J. Org. Chem*. **1986**, *51*, 2977. (l) Murahashi, S.; Mitsue, Y.; Ike, K. *J. Chem. Soc., Chem. Commun*. **1987**, 125. (m) Giannoccaro, P. *J. Organomet. Chem*. **1987**, *336*, 271. (n) Alper, H.; Vasapollo, G.; Hartstock, F. W.; Mlekuz, M. *Organometallics* **1987**, *6*, 2391. (o) Gupte, S. P.; Chaudhari, R. V. *J. Catal*. **1988**, *114*, 246. (p) Pri-Bar, I.; Alper, H. *Can. J. Chem*. **1990**, *68*, 1544. (q) Choudary, B. M.; Rao, K. K.; Pirozhkov, S. D.; Lapidus, A. L. *Synth. Commun*. **1991**, *21*, 1923. (r) Kelkar, A. A.; Kolhe, D. S.; Kanagasabapathy, S. R.; Chaudhari, V. *Ind. Eng. Chem. Res*. **1992**, *31*, 172. (s) Cf. Gupte, S. P.; Chaudhari, R. V. *Ind. Eng. Chem. Res*. **1992**, *31*, 2069. (t) Dahlen, G. M.; Sen, A. *Macromolecules* **1993**, *26*, 1784. (u) Imada, Y.; Mitsui, Y.; Ike, K.; Washizuka, K.; Murahashi, S. *Bull. Chem. Soc. Jpn*. **1996**, *69*, 2079.

(14) Pd on Zr: (a) Giannoccaro, P.; Nobile, C. F.; Moro, G.; Ginestra, A. La; Ferragina, C.; Massucci, M. A.; Patrono, P. *J. Mol. Catal*. **1989**, *53*, 349. (b) Shi, F.; Deng, Y.; SiMa, T.; Yang, H. *Tetrahedron Lett*. **2001**, *42*, 2161.

(15) Pd in electrolytic oxidation: (a) Yang, H.; Deng, Y.; Shi, F. *J. Mol. Catal. A* **2001**, *176*, 73. (b) Chiarotto, I.; Feroci, M. *Tetrahedron Lett*. **2001**, *42*, 3451. (c) Chiarotto, I.; Feroci, M. *J. Org. Chem*. **2003**, *68*, 7137.

(16) PdI_2: (a) Gabriele, B.; Salerno, G.; Brindisi, D.; Costa, M.; Chiusoli, G. P. *Org. Lett*. **2000**, *2*, 625. (b) Gabriele, B.; Mancuso, R.; Salerno, G.; Costa, M. *J. Org. Chem*. **2003**, *68*, 601. (c) Gabriele, B.; Mancuso, R.; Salerno, G.; Costa, M. *Chem. Commun*. **2003**, 406. (d) Gabriele, B.; Salerno, G.; Mancuso, R.; Costa, M. *J. Org. Chem*. **2004**, *69*, 4741.

(17) W: (a) Patterson, J. A.; Atwell, H. V. U.S. Patent 2993931; *Chem. Abstr*. **1962**, *56*, 1392. (b) German Patent 1158494; *Chem. Abstr*. **1964**, *61*, 11900. (c) German Patent 1163311; *Chem. Abstr*. **1964**, *60*, 15744. (d) McCusker, J. E.; Grasso, C. A.; Main, A. D.; McElwee-White, L. *Org. Lett*. **1999**, *1*, 961 (e) McCusker, J. E.; Qian, F.; McElwee-White, L. *J. Mol. Catal. A* **2000**, *159*, 11. (f) McCusker, J. E.; Main, A. D.; Johnson, K. S.; Grasso, C. A.; McElwee-White, L. *J. Org. Chem*. **2000**, *65*, 5216. (g) Qian, F.; McCusker, J. E.; Zhang, Y.; Main, A. D.; Chlebowski, M.; Kokka, M.; McElwee-White, L. *J. Org. Chem*. **2002**, *67*, 4086. (h) Hylton, K.-G.; Main, A. D.; McElwee-White, L. *J. Org. Chem*. **2003**, *68*, 1615.

(18) Pt: (a) Kucheryavyi. I.; Gorlovskii, D. M.; Al'tshuler, L. N.; Zinov'ev, G. N.; Karlik, A. B.; Klopina, N. A. USR 371210; *Chem. Abstr*. **1973**, *79*, 18161.

(19) Au: Shi, F.; Y. Deng, Y. *J. Catal*. **2002**, *211*, 548.

(20) For classical methods for preparation of ureic derivatives using phosgene and other carbonylation reagents and their biological activities, see Gabriele's well-reviewed paper, ref 16d and references therein.

In this paper, we report the oxidative carbonylation of amines with CO in a $Pd(OAc)_2-Cu(OAc)_2-O_2$ catalytic system in an atmosphere of pressure of CO gas. The method provides ureas, carbamates, 1,3-oxazolidinones, and benzolactams.

Results and Discussion

Carbonylation of Primary Amines. First, we describe the selective formation of *N*,*N*′-dialkylureas and *N*,*N*,*N*′-trialkylureas from primary amines by this phosphine-free catalytic system. A stirred mixture of a primary amine, $Pd(OAc)_2$ (5 mol %), and $Cu(OAc)_2$ (50 mol %) in 0.1 M toluene solution was heated at reflux under 1 atm of CO containing air (0.25 molar equiv of O_2) delivered from a toy balloon.[21]

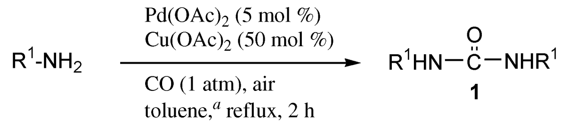
Most of the *n*-alkylamines were converted to the corresponding ureas almost quantitatively within 2 h. As shown in Table 1, alkoxy-substituted benzylic amines or phenethylamines, including amines **g** and **h** with a bromine atom at their *ortho*-position (entries 7 and 8), gave ureas **1c**−**h** in good yields, although it has been reported that the interaction of such phenylalkylamines with $Pd(OAc)_2$ affords cyclopalladation products.[22]

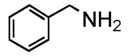
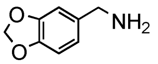
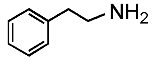
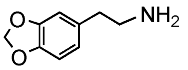
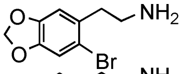
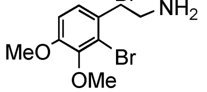
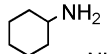
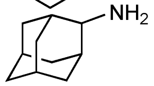
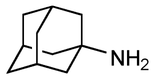
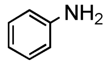
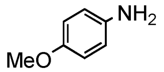
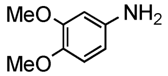
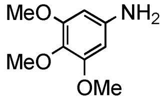
Primary alkylamines with a *sec*-alkyl group underwent carbonylation smoothly (**i** and **j**). Carbonylation of primary amines with a *tert*-alkyl group, such as *t*-BuNH$_2$ (**k**) and 1-aminoadamantane (**l**), resulted in a low yield of the corresponding urea (34% for **1k** and 43% for **1l**).

Carbonylation of primary amines in the presence of a secondary amine (1.2 equiv) and air (0.5 molar equiv of O_2) produced an unsymmetrical urea, such as **2cs**, **2ct**, **2cu**, or **2cv** (66−86%), predominantly over symmetrical urea **1c** (Table 2).[23] Marked selectivity was also observed in carbonylation of bulky primary amines, **j** and **k**, in the presence of a secondary amine. The use of 2.0 equiv of the respective secondary amine suppressed the formation of symmetrical ureas and increased the yields of unsymmetrical ureas (**2cs**, **2ct**, **2cu**, **2cv**, and **2lt**) to 84−93%. No tetraalkylurea,[17e] which consists of two molecules of secondary amines, was produced.

Carbonylation of arylamines **m**−**p** did not proceed well under the conditions used, as shown in Table 1, because of the predominant formation of the corresponding azobenzenes.[24] The addition of a secondary amine to the system resulted in the exclusive formation of unsymmetrical ureas (**2mt** and **2pt**). Similarly, unsymmetrical ureas **2qt** and **2rt** were obtained in good yields from arylamines **q** and **r** with an electron-deficient substituent, which did not give any symmetrical urea even in the absence of a secondary amine.

TABLE 1. Preparation of Symmetrical *N*,*N*′-Disubstituted Ureas



entry	substrate	(type)	product	yield
1	BuNH$_2$	(**a**)	**1a**:	80%
2	HexylNH$_2$	(**b**)	**1b**:	87%
3		(**c**)	**1c**:	94%
4		(**d**)	**1d**:	82%
5		(**e**)	**1e**:	90%
6		(**f**)	**1f**:	82%
7		(**g**)	**1g**:	79%
8		(**h**)	**1h**:	70%
9		(**i**)	**1i**:	76%
10		(**j**)	**1j**:	74%
11	t-BuNH$_2$	(**k**)	**1k**:	34%
12		(**l**)	**1l**:	43%
13		(**m**)	**1m**:	14%
14		(**n**)	**1n**:	18%
15		(**o**)	**1o**:	20%
16		(**p**)	**1p**:	25%

[a] Solutions of 0.1 M amine−toluene were used.

A main reaction pathway to ureas is shown in Scheme 1. A primary amine reacts with $Pd(OAc)_2$ to give a palladium amide, **i**, on which the insertion of a CO molecule takes place to afford a carbamoyl intermediate, **ii** (an isocyanate equivalent).[6b] A nucleophilic attack by an amino group to the carbonyl carbon produces urea **1** or **2** and Pd(0), and the predominant formation of **2** may be accounted for by the higher nucleophilicity of the secondary amine. Regeneration of $Pd(OAc)_2$ by oxidation of Pd(0) with $Cu(OAc)_2$ starts this catalytic cycle in a manner similar to that of the Wacker process.[25]

Carbonylation of Secondary Amines. Secondary amines did not give ureas under the conditions used, but *N*-benzyl- or *N*-phenethylpropylamines afforded five- or six-membered benzolactams (Scheme 2), as described in a preliminary paper.[26]

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(21) A little more air (oxygen) is slowly supplied through the surface of the balloon during the reaction (Knudsen flow; for a review, see: Steckelmacher, W. *Rep. Prog. Phys.* **1986**, *49*, 1083).

(22) (a) Fuchita, Y. Tsuchiya, H. *Polyhedron* **1993**, *12*, 2079; *Inorg. Chim. Acta* **1993**, *209*, 229. (b) Vicente, J.; Saura-Llamas, I.; Palin, M. J.; Jones, P. G.; Ramírez de Arellano, M. C. *Organometallics* **1997**, *16*, 826.

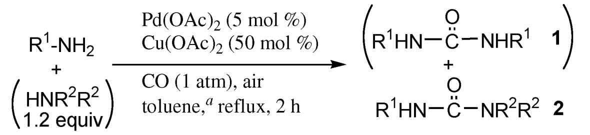
(23) Orito, K.; Horibata, A.; Nakamura, T.; Ushito, H.; Nagasaki, H.; Tokuda, M. Presented at the 31th Congress of Heterocyclic Chemistry, Kitakyushu, Japan, October 2000; Abstract, p 147.

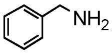
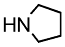
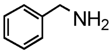
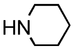
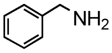
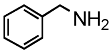
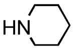
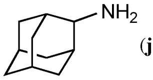
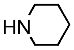
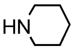
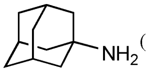
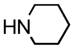
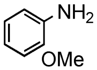
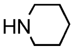
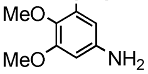
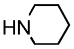
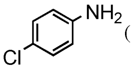
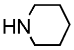
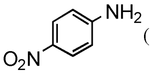
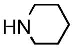
(24) The corresponding azobenzenes were formed without $Pd(OAc)_2$.

(25) Hosokawa, T.; Murahashi, S. *Acc. Chem. Res.* **1990**, *23*, 49.

(26) Orito, K.; Horibata, A.; Nakamura, T.; Ushito, H.; Nagasaki, H.; Yuguchi, M.; Yamashita, M.; Tokuda, M. *J. Am. Chem. Soc.* **2004**, *126*, 14342.

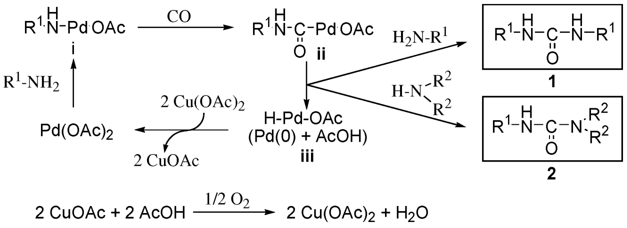
TABLE 2. Preparation of *N*,*N*,*N*′-Trisubstituted Ureas



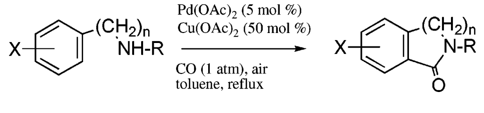
entry	substrate (type)	additive (type)	product	yield (**1**:**2**)^b
1	 (**c**)	 1(**s**)	**2cs**:	82% (4:96) 93% (0:100)^c
2	 (**c**)	 (**t**)	**2ct**:	86% (2:98) 87% (0:100)^c
3	 (**c**)	$HNPr_2$ (**u**)	**2cu**:	77% (4:96) 87% (0:100)^c
4	 (**c**)	$HNBu_2$ (**v**)	**2cv**:	66% (21:79) 84% (0:100)^c
5	$HexylNH_2$ (**b**)	 (**t**)	**2bt**:	80% (7:93)
6	 (**j**)	 (**t**)	**2jt**:	81% (0:100)
7	t-$BuNH_2$ (**k**)	 (**t**)	**2kt**:	43% (0:100)
8	 (**l**)	 (**t**)	**2lt**:	69% (5:95) 87% (0:100)^c
9	 (**m**)	 (**t**)	**2mt**:	79% (0:100)
10	 (**p**)	 (**t**)	**2pt**:	70% (0:100)
11	 (**q**)	 (**t**)	**2qt**:	92% (0:100)
12	 (**r**)	 (**t**)	**2rt**:	64% (0:100) 96% (0:100)^c

^{a} Solutions of 0.1 M amine−toluene were used. ^{b} Ratios of **1** and **2** in crude products determined by ^1H NMR analysis. ^{c} A 2.0 equiv sample of the appropriate secondary amine was used.

SCHEME 1. Carbonylation of Primary Amines



SCHEME 2. Carbonylation of Secondary Amines



Preparation of benzolactams by direct carbonylation of azobenzenes and benzalimines has been reported by Murahashi's and Rosenthal's groups and also by Tsuji and his colleagues using carbonyl complexes of Co, Mo, or Cr.[27] Carbonylation of some cyclopalladation products of *N*,*N*-dialkylbenzylamines and benzalimines was also reported to afford benzolactams.[28,29] Some methods for direct aromatic carbonylation using a Pd, Ir, Ru, or Rh catalyst have also been reported.[30−33] The indirect aromatic carbonylation via a halogen−metal exchange developed by Mori and Ban[34] has become one of the standard Pd(0)-

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[27] Preparation of benzolactams by direct carbonylation of azobenzenes and benzalimines using carbonyl complexes of Co, Mo, or Cr as catalysts has been reported. For $Co_2(CO)_8$, see: (a) Murahash, S.; Horiie, S. *J. Am. Chem. Soc*. **1955**, *77*, 6403. (b) Murahashi, S.; Horiie, S. *J. Am. Chem. Soc*. **1956**, *78*, 4816. (c) Rosenthal, A.; Astbury, R. F.; Hubscher, A. *J. Am. Chem. Soc*. **1958**, *23*, 1037. (d) Rosenthal, A. *Can. J. Chem*. **1960**, *38*, 2025. (e) Rosenthal, A.; Hubscher, H. *J. Org. Chem*. **1969**, *25*, 1562. (f) Rosenthal, A.; Weir, M. R. S. *Can. J. Chem*. **1962**, *40*, 610; *J. Org. Chem*. **1963**, *28*, 3025. (g) Rosenthal, A.; Millward, S. *Can. J. Chem*. **1963**, *41*, 2504; **1964**, *42*, 956. (h) Rosenthal, A.; Gervay, J. *Can. J. Chem*. **1964**, *42*, 1490. (i) Rosenthal, A.; Yalpani, M. *Can. J. Chem*. **1965**, *43*, 711, 3449. (j) Murahashi, S.; Horiie, T.; Jo, T. *Bull. Chem. Soc. Jpn*. **1960**, *33*, 81. (k) Horiie, S.; Murahashi, S. *Bull. Chem. Soc. Jpn*. **1960**, *33*, 88. (l) Horiie, S.; Murahashi, S. *Bull. Chem. Soc. Jpn*. **1960**, *33*, 247. (m) Kajimoto, T.; Tsuji, J. *J. Org. Chem*. **1983**, *48*, 1685. For $Co_2(CO)_8$, $Mo(CO)_6$, $[CpMo(CO)_3]_2$, $Cr(CO)_6$, see: (n) Mori, Y.; Tsuji, J. *Tetrahedron* **1971**, *27*, 3811.

[28] For recent reviews on carbonylation of cyclopalladation products, see: (a) Ryabov, A. D. *Synthesis* **1985**, 233. (b) Reference 1b, pp 87−94.

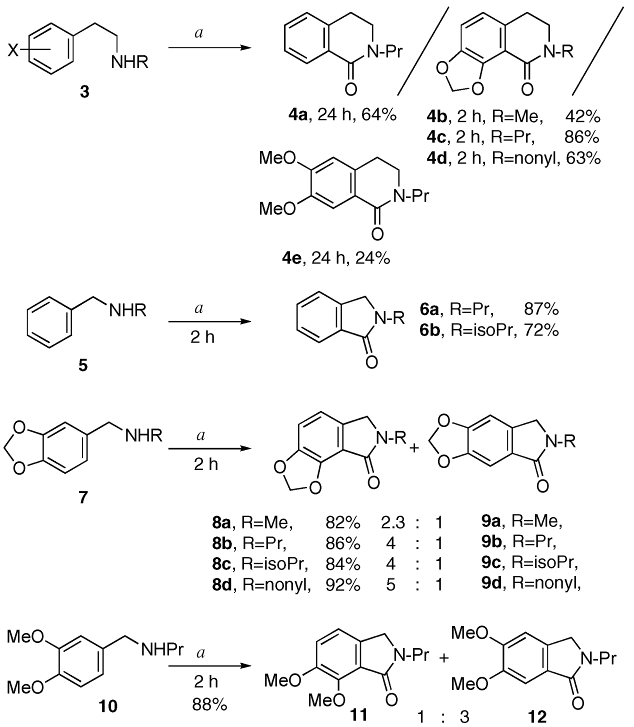
[29] For carbonylation of cyclopalladation products, leading to the formation of benzolactams, see: (a) Takahashi, H.; Tsuji, J. *J. Organomet. Chem*. **1967**, *10*, 511. (b) Thompson, J. M.; Heck, R. F. *J. Org. Chem*. **1975**, *40*, 2667. (c) Yamamoto, Y.; Yamazaki, H. *Synthesis* **1976**, 750. For esters, see: (d) Izumi, T.; Katou, T.; Kusahara, A.; Hanaya, K. *Bull. Chem. Soc. Jpn*. **1978**, *51*, 3407. (e) Kasahara, A.; Izumi, T.; Maemura, M. *Bull. Chem. Soc. Jpn*. **1977**, *50*, 1878. (f) Kamiyama, S. I.; Kamura, T. Kasahara, A.; Izumi, T.; Maemura, M. *Bull. Chem. Soc. Jpn*. **1979**, *52*, 142. (g) Kasahara, A.; Izumi, T.; Watanabe, H. *Bull. Chem. Soc. Jpn*. **1979**, *52*, 957. (h) Sokolov, V. I.; Troitskaya, L. L.; Reutov, O. A. *J. Organomet. Chem*. **1979**, *182*, 537. (i) Nielson, A. J. *J. Chem. Soc., Dalton Trans*. **1981**, 205. (j) Izumi, T.; Maemura, M.; Endoh, K.; Oikawa, T.; Zakozi, S.; Kasahara, A. *Bull. Chem. Soc. Jpn*. **1981**, *54*, 836. (k) Horino, H.; Inoue, N. *J. Org. Chem*. **1981**, *46*, 4416. (l) Troitskaya, L. L.; Khruschova, N. S.; Sokolov, V. I.; Reutov, O. A. *Zh. Org. Khim*. **1982**, *18*, 2606; *Chem. Abstr*. **1983**, *98*, 126327. (m) Sokolov, V. I. *Pure Appl. Chem*. **1984**, *55*, 1837.

[30] Other examples of direct aromatic carbonylations. For Pd(II)-catalyzed carbonylation of benzene to benzoic acid, see: (a) Fujiwara, Y.; Kawauchi, T.; Taniguchi, H. *J. Chem. Soc., Chem. Commun*. **1980**, 220. (b) Jintoku, T.; Taniguchi, H.; Fujiwara, Y. *Chem. Lett*. **1987**, 1159. (c) Jintoku, T.; Fujiwara, Y.; Kawata, I.; Kawauchi, T.; Taniguchi, H. *J. Organomet. Chem*. **1990**, *385*, 297. (d) Taniguchi, Y.; Yamaoka, Y.; Nakata, K.; Takaki, K.; Fujiwara, Y. *Chem. Lett*. **1995**, 345. (e) Lu, W.; Yamaoka, Y.; Taniguchi, Y.; Kitamura, T.; Takaki, K.; Fujiwara, Y. *J. Organomet. Chem*. **1999**, *580*, 290. For reviews, see: (f) Fujiwara, Y.; Takaki, K. Taniguchi, Y. *Synlett* **1996**, 591. (g) Jia, C.; Kitamura, T.; Fujiwara, Y. *Acc. Chem. Res*. **2001**, *34*, 633.

[31] For photochemical carbonylation with IrH(CO)(dppe), IrH(CO)-(dppe), $IrCl(CO)(PPh_3)_2$, and $RhCl(CO)(PPh_3)_2$, see: (a) Fisher, B. J.; Eisenberg, R. K. *Organometallics* **1983**, *2*, 764. (b) Kunin, A. J.; Eisenberg, R. K. *J. Am. Chem. Soc*. **1986**, *108*, 535. (c) Kunin, A. J.; Eisenberg, R. K. *Organometallics* **1988**, *7*, 2124. For $RhCl(CO)(PMe_3)_2$, see: (d) Sakakura, T.; Tanaka, M. *Chem. Lett*. **1987**, 249. (e) Sakakura, T.; Sodeyama, T.; Sasaki, K.; Wada, K.; Tanaka, M. *J. Am. Chem. Soc*. **1990**, *112*, 7221. (f) Boyd, S. E.; Field, L. D.; Partridge, M. G. *J. Am. Chem. Soc*. **1994**, *116*, 9492. (g) Rosini, G. P.; Boese, W. T.; Goldman, A. S. *J. Am. Chem. Soc*. **1994**, *116*, 9498. For $Ru(CO)_4(PPh_3)$, see: (h) Gordon, E. M.; Eisenberg, R. *J. Mol. Catal*. **1988**, *45*, 57.

[32] For other examples of direct aromatic carbonylations with $Ru_3(CO)_{12}$, see: (a) Moore, E. J.; Pretzer, W. R.; O'Connell, T. J.; Harris, J.; LaBounty, L.; Chou, L.; Grimmer, S. S. *J. Am. Chem. Soc*. **1992**, *114*, 5888. (b) Chatani, N.; Fukuyama, T.; Kakiuchi, F.; Murai, S. *J. Am. Chem. Soc*. **1966**, *118*, 493. (c) Chatani, N.; Ie, Y.; Kakiuchi, F.; Murai, S. *J. Org. Chem*. **1997**, *62*, 2604. (d) Fukuyama, T.; Chatani, N.; Kakiuchi, F.; Murai, S. *J. Org. Chem*. **1997**, *62*, 5647. (e) Chatani, N.; Ishii, Y.; Ie, Y.; Kakiuchi, F.; Murai, S. *J. Org. Chem*. **1998**, *63*, 5129. (f) Fukuyama, T.; Chatani, N.; Tatsumi, J.; Kakiuchi, F.; Murai, S. *J. Am. Chem. Soc*. **1998**, *120*, 11522. (g) Ie, Y.; Chatani, N.; Ogo, T.; Marshall, D. R.; Fukuyama, T.; Kakiuchi, F.; Murai, S. *J. Org. Chem*. **2000**, *65*, 1475. (h) Chatani, N.; Fukuyama, T.; Tatamidani, H.; Kakiuchi, F.; Murai, S. *J. Org. Chem*. **2000**, *65*, 4039. (i) Chatani, N.; Yorimitsu, S.; Asaumi, T.; Kakiuchi, F.; Murai, S. *J. Org. Chem*. **2002**, *67*, 7557. (j) Asaumi, T.; Chatani, N.; Matsuo, T.; Kakiuchi, F.; Murai, S. *J. Org. Chem*. **2003**, *68*, 7538. For $Rh_4(CO)_{12}$, see: (k) Asaumi, T.; Matsuo, T.; Fukuyama, T.; Ie, Y.; Kakiuchi, F.; Chatani, N. *J. Org. Chem*. **2004**, *69*, 4433. (l) Hong, P.; Yamazaki, H. *Chem. Lett*. **1979**, 1335. For $RhCl(PPh_3)_3$ and $[Rh(COD)Cl]_2$, see: (m) Takeuchi, R.; Yasue, H. *J. Org. Chem*. **1993**, *58*, 5386. (n) Kokubo, K.; Matsumasa, K.; Miura, M.; Nomura, M. *J. Org. Chem*. **1996**, *61*, 6941.

SCHEME 3. Preparation of Benzolactams by Pd(OAc)$_2$-Catalyzed Aromatic Carbonylation 1



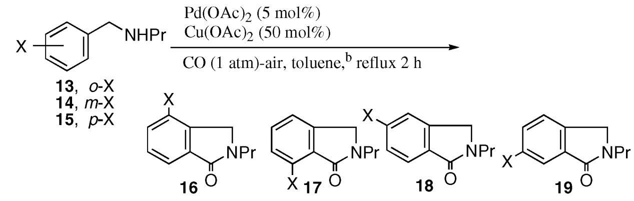
[a] Reagents and conditions: Pd(OAc)$_2$ (5 mol %), Cu(OAc)$_2$ (50 mol %), CO (1 atm) containing air (0.5 molar equiv of O$_2$), toluene, reflux.

catalyzed reactions for syntheses of a variety of heterocyclic compounds. However, a method for *catalytic transformation of ω-arylalkylamines by a direct aromatic metalation to the corresponding benzolactams* has not been established.

Carbonylation of *N*-methyl derivative **3b** of 3,4-(methylenedioxy)phenethylamine resulted in a lower yield of a six-membered benzolactam, **4b**, compared with yields obtained by using other phenethylamines with a more bulky *N*-alkyl group, such as a propyl or nonyl group, but in a good regioselectivity (Scheme 3). Carbonylation of 3,4-dimethoxyphenethylamine **3e** gave only 6,7-dimethoxybenzolactam **4e** with regioselectivity different from that of its methylenedioxy derivatives **4b**−**d**.[35,36] Carbonylation of benzylic amines **5**, **7**, and **10** proceeded faster than did carbonylation of phenethylamines. 3,4-Methylenedioxybenzylamine **7** and 3,4-dimethoxybenzylamine **10** gave two lactams, **8** and **9**, and **11** and **12**, respectively.

Carbonylation of *ortho*- or *para*-substituted benzylic amines **13** or **15** proceeds smoothly to give the corresponding 4- or 6-substituted isoindolin-1-ones **16** or **19**, although *meta*-substituted derivatives **14** gave a mixture of 5- and 7-substituted isoindolin-1-ones **17** and **18** in the respective ratios (Scheme 4), in which two potential abilities of substituents, that is, steric effect and cheletion to Pd, were reflected, as described before (Scheme 5).[26]

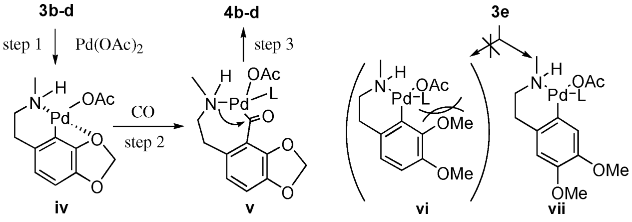
SCHEME 4. Preparation of Benzolactams by Pd(OAc)$_2$-Catalyzed Aromatic Carbonylation 2[a]



	16	17	18	19
a, X=OMe	78% (67%)	48% (36%)	49% (38%)	79% (67%)
b, X=Me	92% (76%)	25% (18%))	68% (59%)	85% (72%)
c, X=Cl	81% (73%)[c]	45% (21%)	45% (31%)	82% (71%)
d, X=Br	55% (50%)[c]	28% (22%)	58% (54%)	79% (68%)
e, X=CN		51% (27%)	45% (24%)	93% (74%)
f, X=NO$_2$	90% (69%)	0%	81% (68%)	81% (72%)
g. X=CF$_3$				75% (71%)
h. X=F				80% (74%)
i. X=COOMe				89% (72%)

[a] ^{1}H NMR yields; isolated yields are in parentheses. [b] Solutions of 0.1 M amine−toluene were used. [c] **2d** was also formed probably via a halogen−metal exchange with a Pd(0) catalyst generated in situ in 5% and 30% yields from **5e** and **5d**, respectively.

SCHEME 5. Carbonylation of *N*-Alkylphenethylamines



m-Nitrobenzylamine (**14f**) gave a single benzolactam, 5-nitroisoindolin-1-one **18f**, exclusively. 3,5-Dinitrobenzylamine thus gave no benzolactam at all. Additional results for carbonylation of benzylic amines with an electron-deficient sustitution at their *para*-position were shown in conversion of **15g**−**i** to **19g**−**i**. Carbonylation of 1-benzylaminobenzocycles **20** did not produce a carbonylative product (**21**) at the *peri*-position but produced isoindolin-1-ones **22** slowly. Carbonylation of 2-benzylpyrrolidine (**23a**) produced benz[*b*]indolizidin-5-one (**24a**) in good yield. Its homologues **24b,c** were similarly prepared but not in good yields (Scheme 6).

Carbonylation of *N*-benzylphenethylamine (**25a**) and its homologues with one (**25b,c**)[26] or two (**25d**−**f**) methylenedioxy groups was examined (Scheme 7). Five-membered ring closure proceeds 11 or 10 times faster than does six-membered ring closure (entries 1 and 4). The presence of a 3,4-methylenedioxy group enhanced the reaction rate by 10-fold in six-membered ring closure (entry 2), and its efficient chelation to Pd(II) was induced with its small steric repulsion[36] to produce a single six-membered benzolactam with a 7,8-methylenedioxy group (entries 2, 4, and 5) and a 6,7-methylenedioxyisoindoline together with its regioisomer with a 5,6-methylenedioxy group in a 4:1 ratio in five-membered ring closure (entries 3, 4, and 6).

Carbonylation of substrates with an electron-withdrawing substituent proceeds well to afford the corresponding benzolac-

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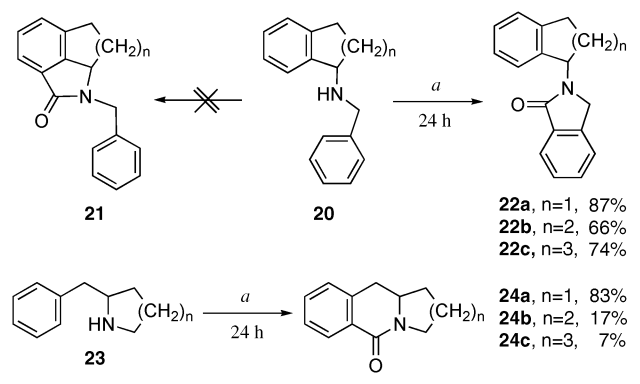
(33) For other examples of direct aromatic carbonylations via *O*-aryl palladium species, see: (a) Koyasu, Y.; Matsuzaka, H.; Hiroe, Y.; Uchida, Y.; Hidai, M. *J. Chem. Soc., Chem. Commun.* **1987**, 575. (b) Matsuzaka, H.; Hiroe, Y.; Iwasaki, M.; Ishii, Y.; Koyasu, Y.; Hidai, M. *Chem. Lett.* **1988**, 377. (c) Matsuzaka, H.; Hiroe, Y.; Iwasaki, M.; Ishii, Y.; Koyasu, Y.; Hidai, M. *J. Org. Chem.* **1988**, *53*, 3832. (d) Iwasaki, M.; Matsuzaka, H.; Hiroi, Y.; Ishii, Y.; Koyasu, Y.; Hidai, M. *Chem. Lett.* **1988**, 1159. (e) Chatani, N.; Fukuyama, T.; Kakiuchi, F.; Murai, S. *J. Am. Chem. Soc.* **1996**, *118*, 493. (f) Ishii, Y.; Hidai, M. *J. Organomet. Chem.* **1992**, *428*, 279.

(34) (a) Mori, M.; Chiba, K.; Ban, Y. *J. Org. Chem.* **1978**, *43*, 1684. (b) Mori, M.; Chiba, K.; Inotsume, N.; Ban, M. *Heterocycles* **1979**, *12*, 921.

(35) A similar steric effect of a vicinal dimethoxy group has been observed in cyclometalation using Pd(OAc)$_2$, Ru(H)$_2$(CO)(PPh$_3$)$_3$, or Ru$_3$(CO)$_{12}$; see: (a) Liang, C. D. *Tetrahedron Lett.* **1986**, *27*, 1971. (b) Sonoda, M.; Kakiuchi, F.; Chatani, N.; Murai, S. *Bull. Chem. Soc. Jpn.* **1997**, *70*, 3117 and references therein. (c) Reference 32g.

(36) Orito, K.; Hatakeyama, T.; Takeo, M.; Uchiito, S.; Tokuda, M.; Suginome, H. *Tetrahedron* **1998**, *54*, 8403.

SCHEME 6. Preparation of Benzolactams by $Pd(OAc)_2$-Catalyzed Aromatic Carbonylation 3



[a] Reagents and conditions: $Pd(OAc)_2$ (5 mol %), $Cu(OAc)_2$ (50 mol %), CO (1 atm) containing air (0.5 molar equiv of O_2), toluene, reflux.

tams (Scheme 8). 4-Methoxy-4′-nitrodibenzylamine (**29a**) also underwent carbonylation smoothly to give a 1:1 mixture of two benzolactams, **30a** and **31a** (entry 1). In entry 2, a 2,3-methylenedioxy group did not show any enhancement of the carbonylation rate, in contrast to the above-mentioned great acceleration effect of a 3,4-methylenedioxy group. A nitro group at the *meta*-position deactivated the carbonylation, as shown in its product ratio of 2.5:1 for **30c** and **31c** or **30d** and **31d** (entries 3 and 4). An *o*-methyl group enhanced the carbonylation rate 1.5-fold (entry 5). These suggest that the present cyclopalladation involves a slightly electrophilic factor.

Carbonylation of Phenylalkylamines with a Hydroxy Group. Carbonylation of phenylalkylamines with a hydroxy group at their 2-position afforded neither benzolactams nor ureas under the same conditions but, instead, produced the corresponding 1,3-oxazolidinones **32a**−**f** within 2 h in good isolated yields (Scheme 9). Methods under compressed CO gas with $PdCl_2$,[13u] PdI_2,[16a,b] and Se[3e,k] and an electrochemical method with $Pd(OAc)_2$/NaOAc[15b] have been reported. Our results prove that 1,3-oxazolidinones can be obtained more readily under CO gas at 1 atm of pressure.

Carbonylation of HCl Salts of Primary Amines. HCl salts of amines are also useful substrates. Hydrochlorides of amino acid esters, such as glycine (**34a**), alanine (**34b**), and phenylalanine (**34c**) ethyl ester, gave their urea derivatives **35a**−**c** (Scheme 10). Alkylamine hydrochlorides **36** and **38** underwent carbonylation smoothly in boiling EtOH to give carbamic acid ethyl esters **37** and **39a,b**, although carbonylation of hydrochlorides of aniline and substituted anilines failed to give the corresponding carbamates, in contrast to our expectations.[13h]

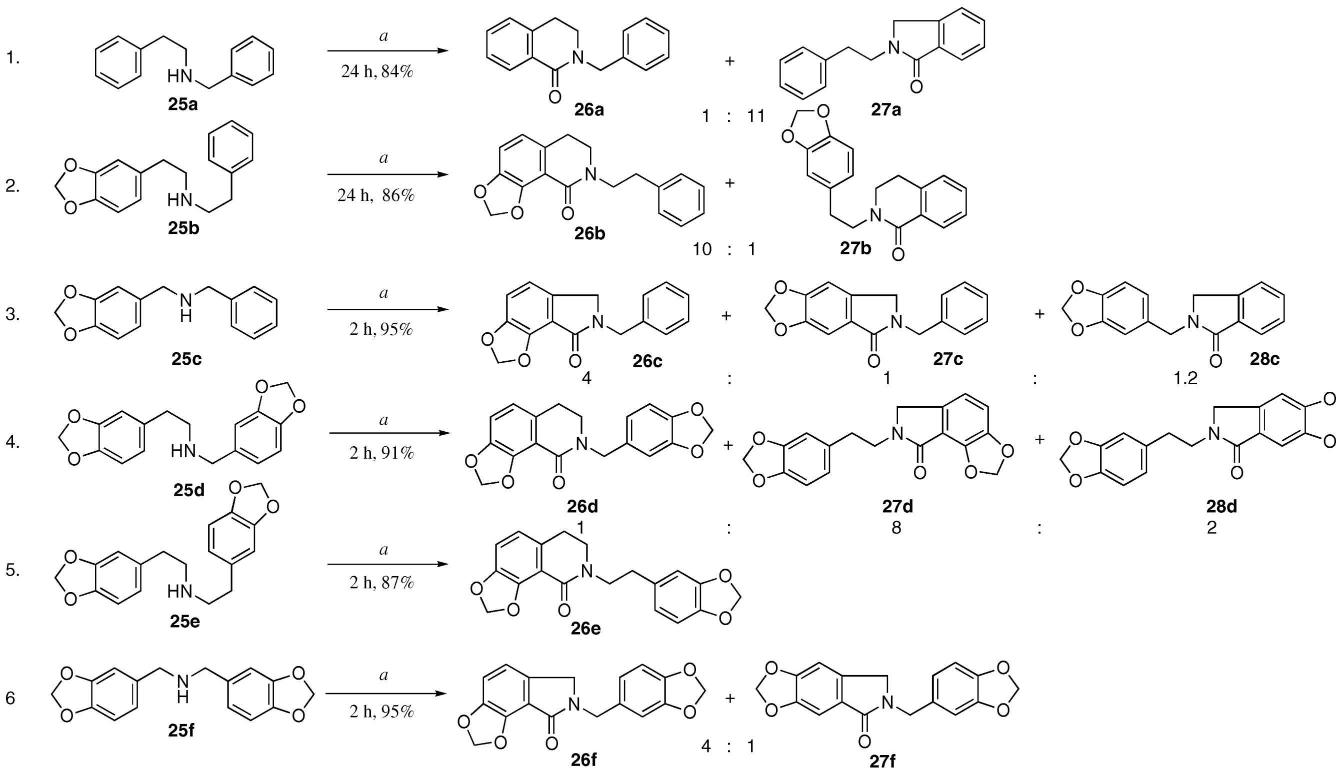
In summary, we have presented general methods based on a substrate-selective carbonylation of amines in a phosphine-free catalytic system, $Pd(OAc)_2$−$Cu(OAc)_2$, in an atmosphere of CO gas for preparation of *N*,*N*′-di- and *N*,*N*,*N*′-trisubstituted ureas, benzolactams, 1,3-oxazolidinones, and carbamic acid esters.

Experimental Section

All melting points were uncorrected. Mass spectrometric data were obtained by electron ionization at 70 eV. ^1H NMR spectra were obtained in $CDCl_3$ at 270 MHz using TMS as an internal reference. Preparative TLC was carried out on silica gel. For preparation of the reactants (amines) and characterization of all products (amides and lactams), see the Supporting Information.

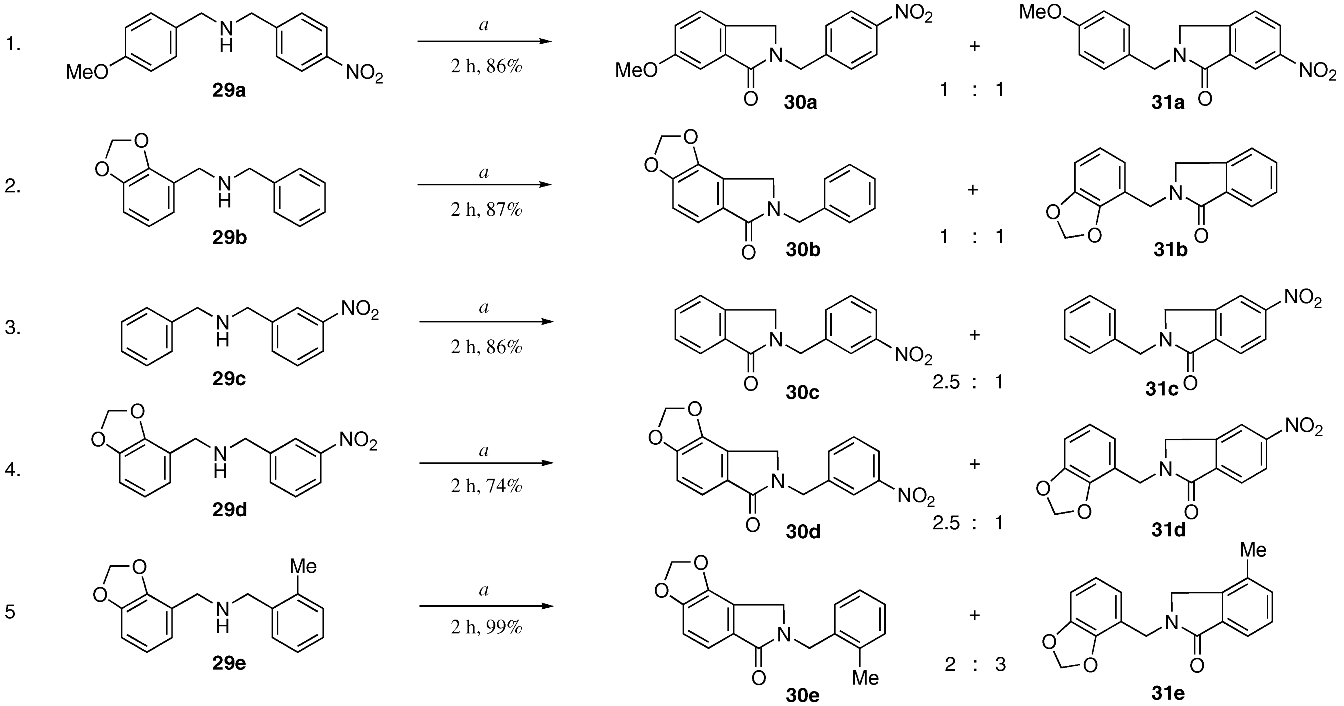
General Procedure for Preparation of Ureas 1a−p and 2cs−rt. A stirred suspension of $Pd(OAc)_2$ (2.2 mg, 0.01 mmol), $Cu(OAc)_2$ (18.1 mg, 0.1 mmol), and a primary amine (0.2 mmol) in toluene (2 mL) in an atmosphere of CO gas (ca. 1−1.5 L) containing air (6 mL, corresponding to 0.05 mmol of O_2) delivered from a

SCHEME 7. Preparation of Benzolactams by $Pd(OAc)_2$-Catalyzed Aromatic Carbonylation 4



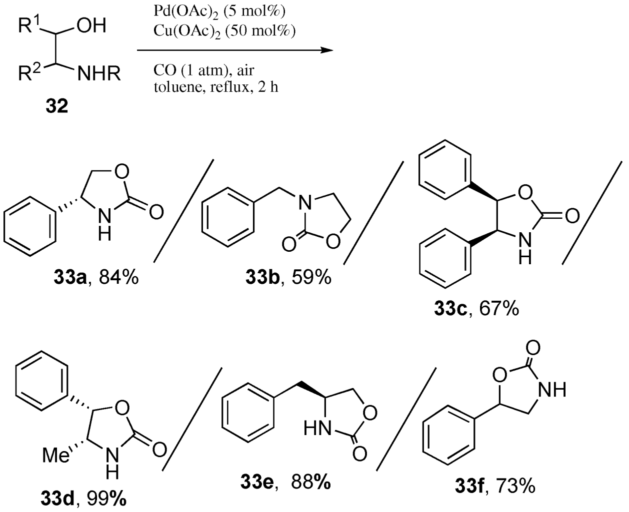
[a] Reagents and conditions: $Pd(OAc)_2$ (5 mol %), $Cu(OAc)_2$ (50 mol %), CO (1 atm) containing air (0.5 molar equiv of O_2), toluene, reflux.

SCHEME 8. Preparation of Benzolactams by Pd(OAc)$_2$-Catalyzed Aromatic Carbonylation 5



[a] Reagents and conditions: Pd(OAc)$_2$ (5 mol %), Cu(OAc)$_2$ (50 mol %), CO (1 atm) containing air (0.5 molar equiv of O$_2$), toluene, reflux.

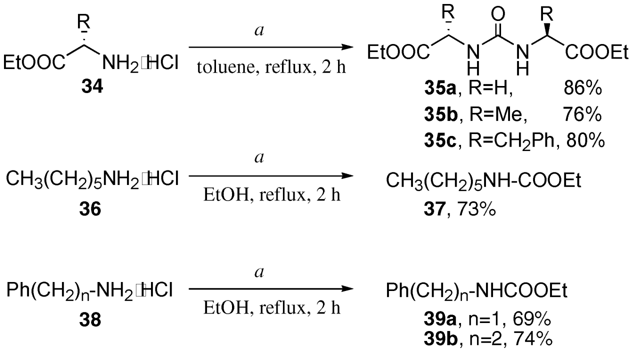
SCHEME 9. Carbonylation of 2-Amino-1-alkanols



toy balloon was gently refluxed in an oil bath at 120 °C for 2 h. Precipitates were removed by filtration through a powdered MgSO$_4$ pad, and the solvent was evaporated to afford the crude product, which was purified by crystallization from the appropriate solvents to give the corresponding symmetrical ureas **1a−p**. For preparation of unsymmetrical trisubstituted ureas **2cs−rt**, a secondary amine (0.24 or 0.4 mmol), pyrrolidine, piperidine, or dipropylamine, and air (12 mL) were added into the reaction mixture.

General Procedure for Pd(OAc)$_2$-Catalyzed Carbonylation of Benzylic Amines 5a,b, 7a−d, 10, 13a−d,f, 14a−f, 15a−i, and 20a−c, Phenethylamines 3a−d and 23a−c, Dibenzylamines 25c,f and 29a−e, *N*-Benzylphenethylamines 25a,d, and Diphenethylamines 25b,e. A stirred mixture of a freshly prepared appropriate secondary amine (0.2 mmol), Pd(OAc)$_2$ (2.24 mg, 0.01 mmol), and Cu(OAc)$_2$ (18.1 mg, 0.1 mmol) in toluene (2 mL) was refluxed in an oil bath at 120 °C in an atmosphere of CO gas (ca. 1−1.5 L)

SCHEME 10. Preparation of Ureas and Carbamates from HCl Salts of Amines



[a] Reactions were carried out in boiling toluene or EtOH (0.1 M) with Pd(OAc)$_2$ (5 mol %) and Cu(OAc)$_2$ (50 mol %) in an atmosphere of CO containing air (0.25 or 0.5 molar equiv of O$_2$) delivered from a toy balloon.

containing air (12 mL, corresponding to 0.1 mmol of O$_2$) delivered from a toy balloon for 2 h. The reaction mixture was cooled to rt and filtered through a thin pad of powdered MgSO$_4$. Toluene was removed in a rotary evaporator. The residue was crystallized from the appropriate solvents or subjected to preparative TLC on silica gel to afford the corresponding benzolactam.

General Procedure for Preparation of 2-Oxazolidinones 33a−f. A stirred mixture of an appropriate 2-amino alcohol (0.2 mmol), Pd(OAc)$_2$ (2.24 mg, 0.01 mmol), and Cu(OAc)$_2$ (36.2 mg, 0.2 mmol) in toluene (2 mL) was refluxed in an oil bath at 120 °C in an atmosphere of carbon monoxide (ca. 1−1.5 L) containing air (12 mL, corresponding to 0.1 mmol of O$_2$) delivered from a toy balloon for 2 h. The reaction mixture was cooled to rt and filtered through a thin pad of powdered MgSO$_4$. The filtrate was concentrated in a rotary evaporator. The residue was crystallized from benzene to afford colorless crystals of the corresponding 2-oxazolidinone.

General Procedure for Carbonylation of Primary Amine Hydrochlorides 34, 36, and 38 to Ureas 35a−c and Carbamates 37 and 39a,b. A stirred mixture of hydrochloride, **34a**, **34b**, or **34c** (0.2 mmol), Pd(OAc)$_2$ (2.24 mg, 0.01 mmol), and Cu(OAc)$_2$ (36.2 mg, 0.2 mmol) in toluene (2 mL) was refluxed in an oil bath at 120 °C in an atmosphere of CO gas (ca. 1−1.5 L) containing air (6 mL, corresponding to 0.05 mmol of O$_2$) delivered from a toy balloon for 2 h. The reaction mixture was cooled to rt and filtered through a thin pad of powdered MgSO$_4$. The filtrate was washed with 0.5 N HCl solution (2 mL) and water (2 mL) and dried over Na$_2$SO$_4$. The solvent was removed in a rotary evaporator. The residue was crystallized from the appropriate solvent to give urea **35a**, **35b**, or **35c**. The carbonylation of hydrochloride **36** or **38a,b** was carried out using 99.5% EtOH (2 mL) and air (12 mL) for 2 h, and EtOH was removed in a rotary evaporator. The residue was dissolved in CH$_2$Cl$_2$ (5 mL), washed with 0.5 N HCl solution (2 mL) and water (2 mL), and dried over Na$_2$SO$_4$. The solvent was removed in a rotary evaporator. The residue was subjected to preparative silica gel TLC developed with 5% MeOH−CH$_2$Cl$_2$ for **37** and **39a** or 1:1 EtOAc/hexane for **39b**.

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Supporting Information Available: Experimental procedures and characterization data for substrates and products. This material is available free of charge via the Internet at http://pubs.acs.org.

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