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Palladium(II)-catalyzed Oxidative Aminocarbonylation of Unsaturated Carbamates

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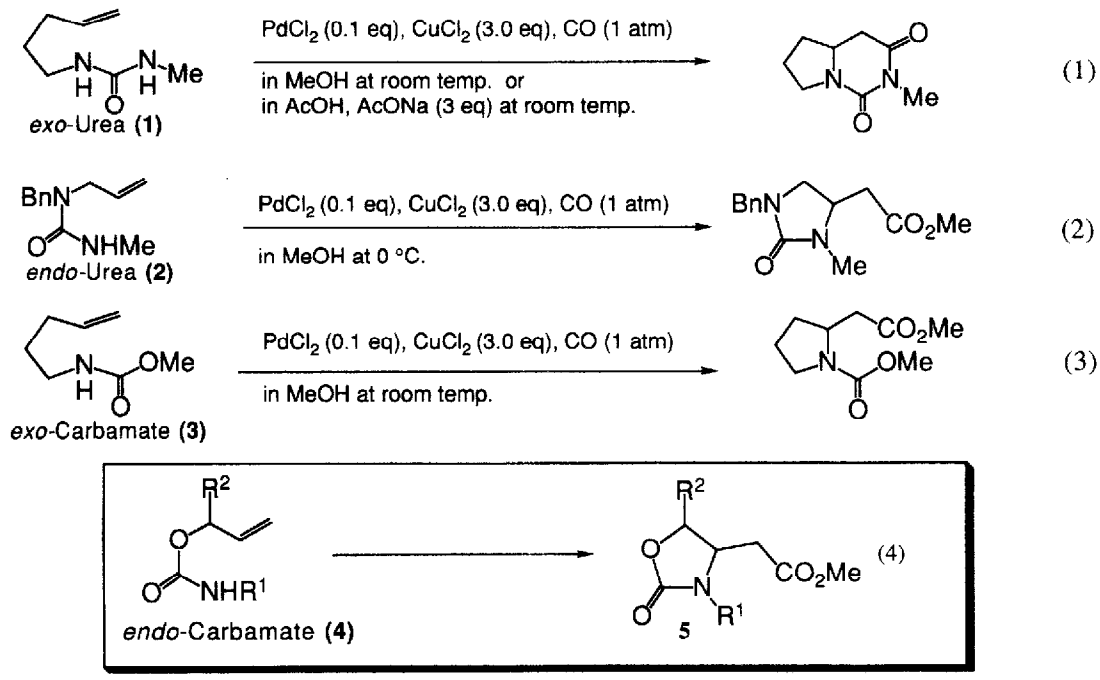
Summary: *N*-Tosyl *O*-2-propenyl carbamates **4** undergo aminocarbonylation to provide *N*-tosyl-2-oxazolidinone 4-acetic acid esters **5** by the catalysis of $PdCl_2$ under 1 atm of CO.

In recent papers,[1] we have disclosed that ureas[2] of types **1** and **2** and carbamates[3] of type **3** undergo smooth aminocarbonylations by the use of catalytic amounts of $PdCl_2$ (Scheme I). At the same time, we reported that carbamate of type **4** was completely indifferent to the aminocarbonylation[1b] (equation 4, Scheme 1). In view of the higher reactivity of *endo*-urea **2** than *exo*-urea **1** (cf. the reaction conditions shown in equations 1 and 2), the reason for the exceedingly low reactivity of *endo*-carbamate **4**, as compared with *exo*-carbamate **3**, has been a question of long standing to us.

Scheme 1. Pd(II)-catalyzed Oxidative Aminocarbonylation of Unsaturated Ureas and Carbamates



Here we report the first successful palladium(II)-catalyzed aminocarbonylation of *endo*-carbamates **4**, which proceeds in a quite different mechanism from those for **1** - **3**. The reaction of *endo*-carbamates **4** highly depends on the kind of the substituents R^1 and R^2. As for R^1, the carbamate **4** with R^1 = Me or Ph did not provide aminocarbonylation product **5** in any detectable amounts under the conditions ever examined. The reaction was only successful for the carbamates with R^1 = tosyl. As for R^2, the carbamates **4** with R^2 = H, Me, and isobutyl underwent cyclization under acidic buffer conditions (condition A, see footnote 1, Table 2), although being very sluggish and requiring 80 - 90 h at 30 °C for completion (entries 1 - 3, Table 2). Under the similar conditions, however, the carbamates with R^2 = CH_2CH_2Ph (**4d**) and *tert*-butyl (**4e**) suffer from either decomposition or low conversion (entries 6 and 9, Table 2).

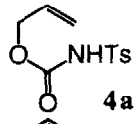
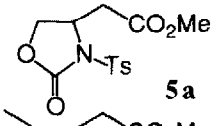
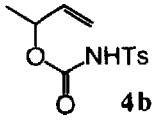
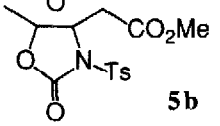
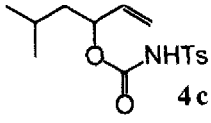
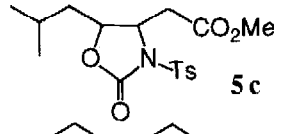
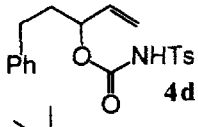
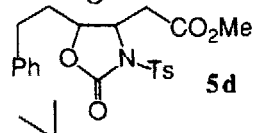
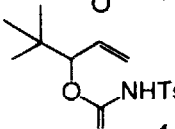
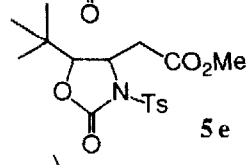
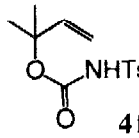
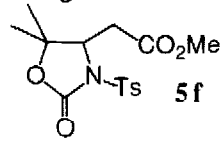
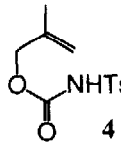
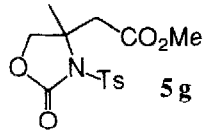
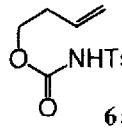
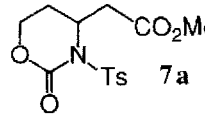
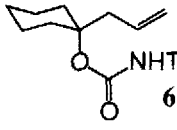
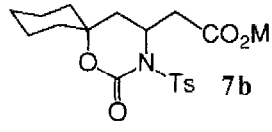
Table 1. Optimization of Reaction Conditions for the Palladium(II)-catalyzed Oxidative Aminocarbonylation of 4 (R^1 = toluenesulfonyl).

entry	carbamte **4** (R^2)	conditions[1]				% isolated yield[2] (% conversion)
		solvent	base	additive	temp., time	
1	**4b**: Me	MeOH-AcOH	AcONa	-----	30 °C, 87 h	**5b**: 89 (100)
2	**4d**: $PhCH_2CH_2$	MeOH-AcOH	AcONa	-----	30 °C, 72 h	**5d**: 10 (100)
3	**4d**: $PhCH_2CH_2$	MeOH-AcOH	AcONa	MOA	30 °C, 68 h	**5d**: 44 (100)
4	**4d**: $PhCH_2CH_2$	MeOH-AcOH	-----	-----	30 °C, 24h	**5d**: 0 (0)
5	**4d**: $PhCH_2CH_2$	MeOH	-----	-----	30 °C, 75 h	**5d**: ---- (100)[3]
6	**4d**: $PhCH_2CH_2$	MeOH	AcONa	-----	30 °C, 2 h	**5d**: 43 (48)[4]
7	**4d**: $PhCH_2CH_2$	MeOH	AcONa	MOA	30 °C, 8 h	**5d**: 100 (100)

1) Carbamate **4** (1 mmol), $PdCl_2$ (0.25 mmol), $CuCl_2$ (2.3 mmol), CO (1 atm) in MeOH-AcOH (2 mL-5 mL) or in MeOH alone (8 mL) in the presence or absence of AcONa (3 mmol) and MOA (methyl orthoacetate, 18 mmol).
2) Isolated yield based on conversion.
3) Complex mixture of products, containing less than 10% of **4d**.
4) No further reaction owing to precipitation of Pd-black.

In order to widen the structural flexibility, a variety of conditions have been screened taking **4d** as a probe. The results are summarized in Table 1. As apparent from this Table, basic buffer conditions B (entry 7, Table 1),[4] which differs from the conditions A (entry 2) in lacking AcOH and containing methyl orthoacetate, was most satisfactory. Methyl orthoacetate,[5] judging from two pairs of results (entries 2 and 3 and 6 and 7, Table 1), was very effective to improve the yields and seems to serve to suppress such $PdCl_2$-consuming side reactions as oxidations of methanol to formaldehyde and of carbon monoxide to dimethyl carbonate. Acceleration of reactions by an addition of sodium acetate (entries 6 vs. 5, Table 1) and by a deletion of acetic acid (entries 6 vs. 2 and 7 vs. 3) clearly indicates that the cyclization of *N*-tosyl carbamates **4** (pK_a = 4.2)[6] proceeds via dissociation of NH proton. This makes sharp contrast to the observations that **1** - **3** undergo cyclization under acidic conditions[4] via a non-dissociated NH form.[1]

Table 2. Palladium(II)-catalyzed Oxidative Aminocarbonylation of *N*-Toluenesulfonyl *O*-Allyl (4) and *O*-Homoallyl Carbamates (6)

entry	substrate **4** or **6**	conditions [1]	product **5** or **7**	% yield (% conversion) [2] [cis : trans ratio] [3]
1	 **4a**	A (88 h)	 **5a**	71 (100)
2	 **4b**	A (87 h)	 **5b**	89 (100) [1 : 7]
3	 **4c**	A (93 h)	 **5c**	91 (100) [1 : 10]
4		B (8 h)		95 (100)
5		B' (44 h)		87 (100)
6	 **4d**	A (72 h)	 **5d**	10 (100)
7		B (8 h)		100 (100) [1 : 3]
8		B' (25 h)		80 (90)
9	 **4e**	A (91 h)	 **5e**	0 (0)
10		B (16 h)		57 (50) [ca. 1 : 50]
11	 **4f**	A (94 h)	 **5f**	14 (100)
12		B (18 h)		86 (71)
13	 **4g**	A (90 h)	 **5g**	2 (50)
14		B (26 h)		25 (52)
15	 **6a**	A (88 h)	 **7a**	9 (100)
16		B (26 h)		0 (80)
17	 **6b**	A (90 h)	 **7b**	80 (100)

1) Conditions **A**: carbamate **4** or **6** (1 mmol), $PdCl_2$ (0.25 mmol), $CuCl_2$ (2.3 mmol), NaOAc (3.0 mmol), CO (1 atm, balloon) in MeOH-AcOH (2 mL-5 mL) at 30 °C; conditions **B**: carbamate (1 mmol), $PdCl_2$ (0.25 mmol), $CuCl_2$ (2.3 mmol), NaOAc (3 mmol), CO (1 atm), methyl orthoacetate (18 mmol) in MeOH (8 mL) at 30 °C; conditions **B'**: the same as the conditions **B** except for $PdCl_2$ (0.10 mmol).

2) Isolated yield based on conversion.

3) cis : trans Ratio determined by ^1H NMR.

The optimum conditions A and B thus decided were applied for the aminocarbonylation of *N*-tosyl carbamates possessing characteristics in their structural features. Some representative results for *O*-2-propenyl (**4**) and *O*-3-butenyl carbamates (**6**) are summarized in Table 2. In every case, the reaction was run until Pd-black precipitated.[7] A reduced amount of $PdCl_2$ (0.1 equivalents) may be applied (entries 5 and 8, Table 2).

O-(2-Methyl-2-propenyl) carbamate (**4g**) was very reluctant (entries 13 and 14, Table 2), and *O*-(3-methyl-2-propenyl) carbamate was unreactive toward cyclization and gave only a mixture of decomposition products (conditions B for 28 h, 79% conversion).

Like many other precedents,[1b,8] the cyclization giving six-membered nitrogen heterocycles met difficulties. *O*-(3-Butenyl) (**6a**, entries 15 and 16, Table 2), *O*-(1-methyl-3-butenyl) and *O*-[1-(2-phenylethyl)-3-butenyl] carbamates gave the expected six-membered products in similarly poor yields. Among these, the reaction of **6b** (entry 17, Table 2) was exceptional, which provided **7b** in good yield.

Although the aminocarbonylation of **4** and **6** could be realized, there still remain problems in its limited scope and low turn-over numbers of the catalyst. Further improvement and application to the syntheses of physiologically interesting γ- and δ-hydroxy β-amino acids (e.g., negamycin[9] and γ-hydroxy β-lysine)[10] and β-lactams are continuing subjects of our concern.[11]

References and Notes

(1) (a) Tamaru, Y.; Yoshida, Z. *J. Organometal. Chem.* **1987**, *334*, 213. (b) Tamaru, Y.; Hojo, M.; Higashimura, H.; Yoshida, Z. *J. Am. Chem. Soc.* **1988**, *110*, 3993 and references cited therein. (c) Tamaru, Y.; Hojo, M.; Yoshida, Z. *J. Org. Chem.* **1988**, *53*, 5731.

(2) The terms *exo* and *endo* are meant to refer to the relative positions between an olefin and functional groups (urea and carbamate), i.e., *exo*-urea **1**, on cyclization, leaves an urea group outside the ring, while *endo*-urea **2** inside.

(3) Lathbury, D.; Vernon, P.; Gallagher, T. *Tetrahedron Lett.* **1986**, *27*, 6009.

(4) Two moles of HCl are produced in every one cycle of conversion of $PdCl_2$ to Pd(0).

(5) Tamaru, Y.; Hojo, M.; Yoshida, Z. *J. Org. Chem.* **1991**, *56*, 1099.

(6) Taylor, L. D.; MacDonald, R. J.; Rubin, E. L. *J. Polym. Sci. Part A-1*, **1971**, *9*, 3059.

(7) A typical procedure (entry 7, Table 2): a flask containing a mixture of **4d** (1 mmol), $PdCl_2$ (0.25 mmol), $CuCl_2$ (2.3 mmol), and NaOAc (3 mmol) was purged with CO (a balloon) and into this was added dry methanol (8 mL) and $MeC(OMe)_3$ (18 mmol) via syringes. Homogeneous green solution was stirred at 30 °C until Pd-black began to precipitate (8 h) and then transferred into ethyl acetate (30 mL). The mixture was washed with 1 : 1 mixture of 10%-NH_4OH and 10%-$NH_4^+Cl^-$ twice and then with water. The organic layer was dried over $MgSO_4$ and evaporated to leave oil, which was purified by column chromatography over silica gel (benzene-ethyl acetate 70 : 1) to give **5d** as a mixture of *cis* : *trans* = 1 : 3; 100% isolated yield; mp 125 - 126°C (benzene); IR (KBr) 1795 (s), 1725 (s) cm^{-1}. *Anal.* C, H, N, S.

(8) (a) Hegedus, L. S.; McKearin, J. M. *J. Am. Chem. Soc.* **1982**, *104*, 2444. (b) Kimura, M.; Yoshida, Z.; Tanaka, S.; Fugami, K.; Tamaru, Y. *Tetrahedron Lett.* **1990**, *34*, 4887.

(9) (a) Wang, Y.-F.; Izawa, T.; Kobayashi, S.; Ohno, M. *J. Am. Chem. Soc.* **1982**, *104*, 6465. (b) Iida, H.; Kasahara, K.; Kibayashi, C. *J. Am. Chem. Soc.* **1986**, *108*, 4647.

(10) Wakamiya, T.; Shiba, T.; Kaneko, T. *Bull. Chem. Soc. Jpn.* **1972**, *45*, 3668.

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