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A New Aerobic Oxidation System Using Pd-Cu Catalysts in the Presence of CO

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Oxidation of benzylic ethers, tosylamides, and 9,10-dihydroanthracene could be performed efficiently under O_2 and CO atmosphere in the presence of $PdCl_2$-$CuCl_2$ catalysts to give the corresponding esters (lactones), amides and anthraquinone, respectively.

The selective, oxidative functionalization of C-H bonds in organic substrates is one of the most challenging problems in organic synthesis, and many metal-mediated methods for oxidation of C-H bond using various oxidants were reported.[1)] Clearly, molecular oxygen (O_2) is the most desirable oxidant because of its ready availability.[2)] Herein we report a novel and simple oxidation system using O_2 as an oxidant.

We have recently described the selective mono- and bis-alkoxycarbonylation of olefins catalyzed by Pd in the presence of $CuCl_2$ or CuCl, respectively.[3)] During the course of our systematic study on the carbonylation reaction with Pd-Cu catalysts, the carbonylation of 4-phenyl-1-butene was tried using $PdCl_2$ and $CuCl_2$ in THF and H_2O under O_2 and CO atmosphere at 25 °C. Unexpectedly, γ-butyrolactone was obtained in 1950% yield based on $PdCl_2$, besides the monocarbonylated products, *i.e.*, 2-methyl-4-phenylbutanoic acid and 5-phenylpentanoic acid in total yield of 58%. Thus, this carbonylation system appears to work also as an oxidation system for ethers such as THF. Therefore, we examined the catalytic ability of Pd-Cu combined system for oxidation under O_2 and CO atmosphere.[4,5)]

First, *o*-xylylene oxide (**1**) was chosen as a substrate for oxidation reaction; *i.e.*, a mixture of *o*-xylylene oxide (0.5 mmol), Pd salt (0.01 mmol), and Cu salt (0.15 mmol) was stirred in acetone (3 ml) and H_2O (0.1 ml) at room temperature under mixed atmosphere of O_2 and CO (1:1, 1 atm). The results were summarized in Table 1. As the Pd catalysts examined with the combined use of $CuCl_2$, $PdCl_2$ has proved to be most effective among Pd-C, $Pd(OAc)_2$, $PdCl_2$, $PdCl_2(CH_3CN)_2$, and $PdCl_2(PPh_3)_2$, to give phthalide (**2**) in 43% (2150% based on $PdCl_2$) yield (Entries 1-5). The effect of Cu salts was also examined for the oxidation catalyzed by $PdCl_2$. $CuCl_2$ was found to be the most effective among $Cu(OAc)_2 \cdot H_2O$, CuO, $CuCl_2$, CuCl, and CuI (Entries 3, 6-9). The effect of the molar quantities of $CuCl_2$ was examined and the use of excess $CuCl_2$ resulted in decreasing the yield (Entries 3, 11-13). In order to obtain reasonable amount of **2**, each of $PdCl_2$, $CuCl_2$, O_2, CO, and H_2O appeared to be necessary (Entries 10, 14-17). When the reaction was performed at higher temperature, the oxidation product was obtained in poor yield (Entry 18). As a solvent, THF, *t*-BuOH, and AcOMe were also usable (Entries 19-21). However, DMF, which was the common solvent in Wacker reaction,[6)] was not suitable (Entry 22). In order to enhance the rate of oxidation, the oxidation was then carried out under pressurized conditions, *i.e.*, *o*-xylylene oxide was treated with $PdCl_2$ and $CuCl_2$ in acetone-

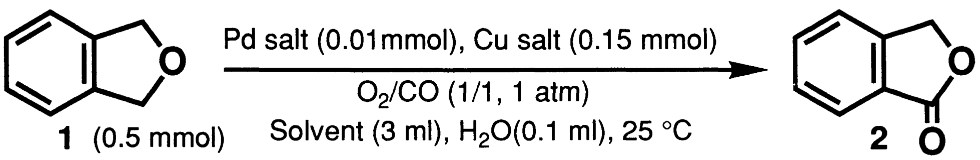


Table 1. Oxidation of *o*-xylylene oxide (**1**) by Pd-Cu catalysts under mixed atmosphere of O_2 and CO

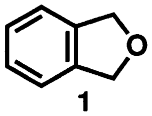
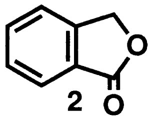
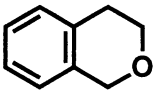
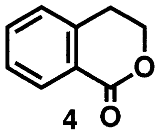
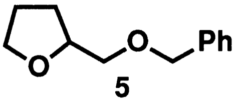
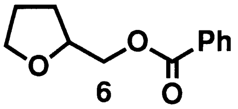
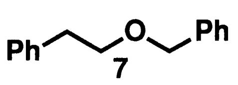
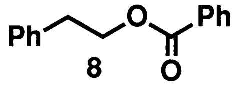
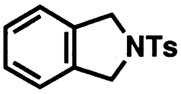
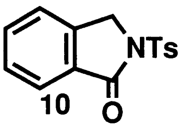
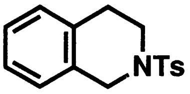
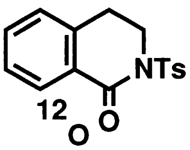
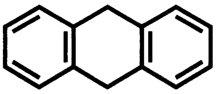
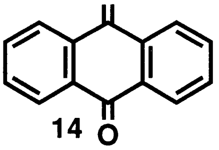
Entry	Pd salt	Cu salt	Solvent	Time/day	Yield/%	Yield based on Pd/%	Recovery/%
1	Pd-C	$CuCl_2$	acetone	6	33	1650	30
2	$Pd(OAc)_2$	$CuCl_2$		6	34	1700	62
3	$PdCl_2$	$CuCl_2$		5	43	2150	52
4	$PdCl_2(CH_3CN)_2$	$CuCl_2$		6	30	1500	30
5	$PdCl_2(PPh_3)_2$	$CuCl_2$		5	34	1700	43
6	$PdCl_2$	$Cu(OAc)_2{\cdot}H_2O$		6	3	150	73
7	$PdCl_2$	CuO		4	trace	---	58
8	$PdCl_2$	CuCl		6	31	1550	35
9	$PdCl_2$	CuI		5	12	600	42
10	$PdCl_2$	------		5	12	600	57
11	$PdCl_2$	$CuCl_2$ (0.05)[a]		5	37	1850	30
12	$PdCl_2$	$CuCl_2$ (0.5)[a]		5	16	800	53
13	$PdCl_2$	$CuCl_2$ (1.5)[a]		5	10	500	53
14	------	$CuCl_2$		6	7	350	67
15[b]	$PdCl_2$	$CuCl_2$		4	trace	---	67
16[c]	$PdCl_2$	$CuCl_2$		4	trace	---	63
17[d]	$PdCl_2$	$CuCl_2$		6	15	750	53
18[e]	$PdCl_2$	$CuCl_2$		4	9	450	60
19	$PdCl_2$	$CuCl_2$	THF	6	24	1200	58
20	$PdCl_2$	$CuCl_2$	*t*-BuOH	5	37	1850	48
21	$PdCl_2$	$CuCl_2$	AcOMe	7	24	1200	43
22	$PdCl_2$	$CuCl_2$	DMF	7	3	150	50
23[f]	$PdCl_2$	$CuCl_2$	acetone	2	86	4300	trace

a) The number in parenthesis is the molar quantities of used $CuCl_2$ (mmol). b) The reaction was carried out without O_2. c) The reaction was carried out without CO. d) The reaction was carried out without H_2O. e) The reaction was carried out at 50 °C. f) The reaction was carried out under 30 atm of gaseous mixture of O_2 and CO (1:1).

H_2O under 30 atm of gaseous mixture of O_2 and CO (1:1) for 2 days to afford phthalide (**2**) in enhanced yield, 86% (4300% based on $PdCl_2$) (Entry 23).

Next, several substrates were subjected to the oxidation reaction using $PdCl_2$-$CuCl_2$ catalyzed system under O_2 and CO atmosphere (Table 2). Isochroman (**3**), benzyl tetrahydrofurfuryl ether (**5**), and benzyl phenethyl ether (**7**) were selectively oxidized at benzylic positions to afford the corresponding lactone **4**, and benzoic acid esters **6**, **8**, respectively. Instead of ethers, nitrogen compounds were subjected to the oxidation.

Table 2. Oxidation by $PdCl_2$-$CuCl_2$ catalysts under mixed atmosphere of O_2 and CO (1:1)[a]

Substrate	Total pressure /atm	Solvent	Time/day	Products	Yield/%	Yield based on Pd/%	Recovery /%
 1	30	Acetone	2	 2	86	4300	trace
 3	60	Acetone	3	 4	66[b]	3300	28
	60	*t*-BuOH	3		72[c]	3600	7
 5	60	Acetone	5	 6	23	1150	31
 7	60	Acetone	2	 8	16	800	77
 9	60	Acetone	4	 10	73	3650	8
 11	60	Acetone +*t*-BuOH	3	 12	21	1050	78
 13	60	Acetone	3	 14	54	2700	trace

a) The reaction was performed on 0.5 mmol scale in the presence of $PdCl_2$ (0.01 mmol) and $CuCl_2$ (0.15 mmol) in solvent (3 ml) and H_2O (0.1 ml) under O_2 and CO atmosphere. b) 4-Isochromanone was obtained in 5% yield. c) Trace amount of 4-isochromanone was obtained.

N-(*p*-Tosyl)dihydroisoindole (**9**) and *N*-(*p*-tosyl)tetrahydroisoquinoline (**11**) were oxidized to give the corresponding *N*-tosyl lactams **10** and **12**. Especially, 5-membered one **9** was effectively oxidized. Furthermore, aromatic hydrocarbon 9,10-dihydroanthracene (**13**) was found to be oxidized to anthraquinone (**14**).

Although the precise mechanism of the present oxidation reaction is still an open question, one possible reaction pathway is shown in Scheme 1. Cu salt reacts with CO and H_2O successively to give CuCOOH species. The transfer of hydroxycarbonyl group to Pd is followed by the loss of CO_2 to give PdH species. Then, the O atom would be transferred to a substrate from PdOOH species derived from PdH species and O_2.[7]

In summary, a unique aerobic oxidation reaction was achieved utilizing $PdCl_2$ and $CuCl_2$ as catalysts in the presence of CO. The present oxidation system does not require an organic coreductant, such as aldehyde. The study of the scope and the limitation of this oxidation is currently underway in our laboratory.

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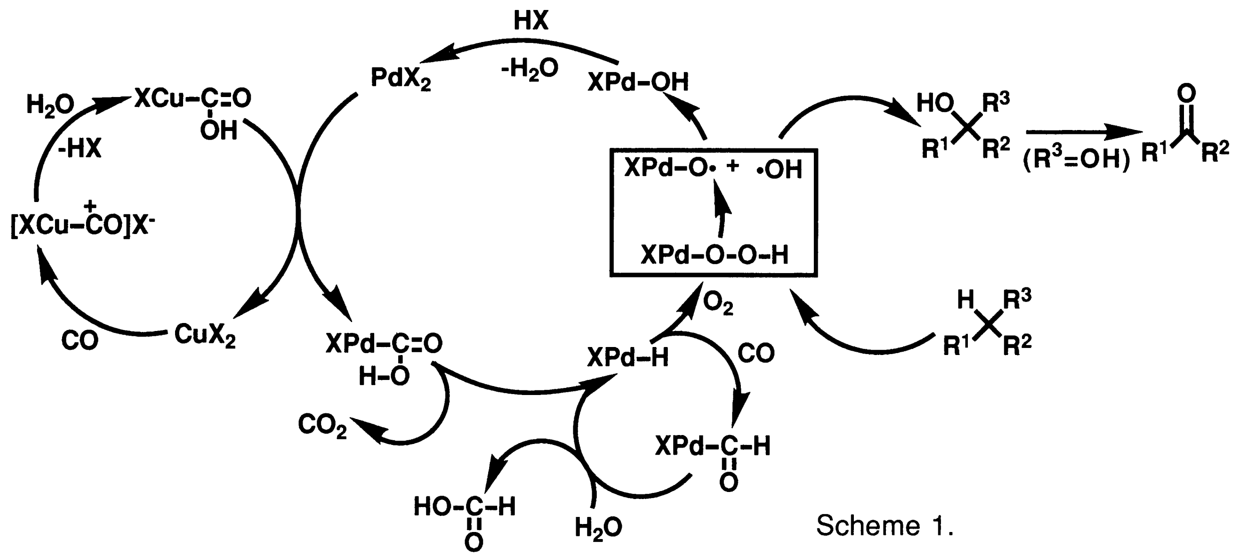

Scheme 1.

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5) The reaction of hydrocarbons with CO and $K_2S_2O_8$ catalyzed by $Pd(OAc)_2$ and $Cu(OAc)_2$ was recently reported to give the corresponding carboxylic acids: K. Nakata, J. Watanabe, K. Takaki, and Y. Fujiwara, *Chem. Lett.*, **1991**, 1437; T. Nishiguchi, K. Nakata, K. Takaki, and Y. Fujiwara, *ibid.*, **1992**, 1141; T. Miyata, K. Nakata, Y. Yamaoka, Y. Taniguchi, K. Takaki, and Y. Fujiwara, *ibid.*, **1993**, 1005.

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7) The formation of formic acid and acetic acid was confirmed by GC analysis. The latter acid seemed to be formed by oxidation of acetone used as a solvent. The generation of CO_2 was also confirmed. Furthermore, in the oxidation reaction of **1**, 1-hydroxy-1,3-dihydroisobenzofuran was scarcely detected. This fact suggested that the oxidation of the lactol derivative seemed to be faster than that of the ether **1**.

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