Carboxylation of anisole derivatives with CO and O_2 catalyzed by $Pd(OAc)_2$ and molybdovanadophosphates

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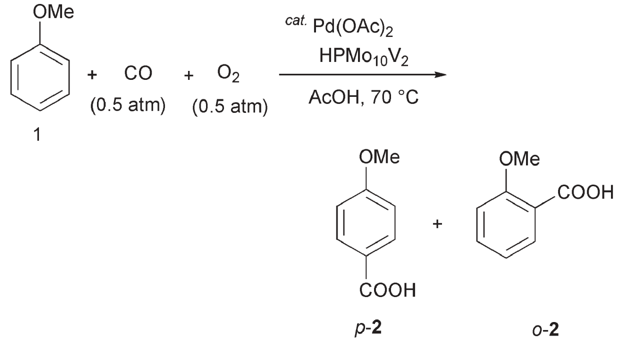
Anisole and its homologues were carboxylated under the influence of CO and O_2 catalyzed by $Pd(OAc)_2$ combined with molybdovanadophosphates (HPMoV) under mild conditions to give the corresponding carboxylic acids in fair to good yields; for instance, anisole underwent the carboxylation under a mixed gas of CO (0.5 atm) and O_2 (0.5 atm) in the presence of $Pd(OAc)_2$ (5 mol%) and $H_5PMo_{10}V_2O_{40}{\cdot}nH_2O$ (2 mol%) to form an isomeric mixture of anisic acids in good yield.

Benzenes react stoichiometrically with Pd(II) salts to undergo chlorination,[1] acetoxylation,[2] carbonylation,[3] carboxylation,[4] *etc.* The direct carboxylation of benzene with CO was first reported by Fujiwara *et al.* by the use of a stoichiometric amount of $Pd(OAc)_2$.[5] Thereafter, they reported the Pd-catalyzed carboxylation of benzene derivatives with CO using *t*-BuOOH[6] or $K_2S_2O_8$[7] as reoxidants in trifluoroacetic acid. Pd(II)-catalyzed carboxylation of hydrocarbons was reviewed by their group.[8] However, carboxylation using trifluoroacetic acid as a solvent is difficult to carry out on a large scale, since trifluoroacetic acid is an intractable compound. If molecular oxygen as an oxidant and acetic acid as a solvent can be used in place of $K_2S_2O_8$ and trifluoroacetic acid, respectively, in the carboxylation of benzene derivatives, such a method would provide an important practical synthetic route to the corresponding benzoic acids. Recently, we have found that $Pd(OAc)_2$ combined with molybdovanadophosphoric acids (HPMoV) is an efficient catalytic system for the direct activation of the C–H bond of arenes using molecular oxygen as the reoxidant. Thus, the Heck–Mizoroki reaction of benzene with acrylate was first achieved by using the $Pd(OAc)_2$/HPMoV/O_2 system.[9] We have now found that the $Pd(OAc)_2$/HPMoV system catalyzes efficiently the carboxylation of anisole derivatives under the influence of a mixed gas of CO and O_2 to give the corresponding anisic acids in fair to good yields (Scheme 1).

In order to confirm the optimum reaction conditions, anisole (**1**) was allowed to react under a mixed gas of CO and O_2 in the presence of catalytic amounts of $Pd(OAc)_2$ and HPMoV in acetic acid under various conditions (Table 1).

The reaction of **1** under a 1 : 1 mixture of CO (0.5 atm) and O_2 (0.5 atm) in the presence of catalytic amounts of $Pd(OAc)_2$ (5 mol%) and $H_5PMo_{10}V_2O_{40}{\cdot}15.2H_2O$ ($HPMo_{10}V_2$) (2 mol%) in acetic acid at 70 °C for 15 h afforded a 74 : 26 isomeric mixture of *p*- and *o*-anisic acids (*p*- and *o*-**2**) in 88% conversion and 97% selectivity (Run 2).† This is the first successful direct carboxylation of benzene derivatives like **1** using CO and O_2 catalyzed by $Pd(OAc)_2$ and HPMoV. It is important to note that the carboxylation of **1** by the use of CO and O_2 can be achieved by the $Pd(OAc)_2$/HPMoV system, since the same reaction using $PdCl_2/CuCl_2$[5] under these conditions provided no carboxylated products at all (Run 10). The carboxylation was carried out under varying pressures of CO and O_2 (Runs 1 to 3). It was found that the carboxylation of **1** to **2** was considerably influenced by the partial pressures of CO and O_2. The best result was obtained when a 1 : 1 mixed gas of CO and O_2 was employed as shown in Run 2. The reaction under a 1 : 2 mixture of CO (0.33 atm) and O_2 (0.67 atm) resulted in the decrease of conversion of **1** and the selectivity of **2**, although the product ratio was almost the same (Run 1). Under a 2 : 1 mixture of CO (0.67 atm) and O_2 (0.33 atm), the conversion of **1** to **2** was considerably decreased (Run 3). When the amount of $Pd(OAc)_2$ was halved under these conditions, the conversion of **1** was decreased to 44%, but the selectivity to **2** was



Scheme 1

Table 1 Carboxylation of anisole (**1**) to anisic acid (**2**) with CO and O_2 by Pd(II) combined with $HPMo_{10}V_2$ under various conditions[a]

Run	Pd(II)	CO : O_2 (atm)	Solv.	Conv. (%)	Select.[b] (%)
1	$Pd(OAc)_2$	0.33 : 0.67	AcOH	80	88 (23 : 77)
2	$Pd(OAc)_2$	0.50 : 0.50	AcOH	88	97 (26 : 74)
3	$Pd(OAc)_2$	0.67 : 0.33	AcOH	17	20 (26 : 74)
4[c]	$Pd(OAc)_2$	0.50 : 0.50	AcOH	44	96 (26 : 74)
5[d]	$Pd(OAc)_2$	0.50 : 0.50	AcOH	83	99 (23 : 77)
6[e]	$Pd(OAc)_2$	0.50 : 0.50	AcOH	74	91 (23 : 77)
7	$Pd(OAc)_2$	0.50 : 0.50	EtCOOH	81	85 (23 : 77)
8	$Pd(OAc)_2$	0.50 : 0.50	CH_3CN	4	n.d.
9	$Pd(OAc)_2$	0.50 : 0.50	DMF	11	n.d.
10[f]	$PdCl_2$	0.50 : 0.50	AcOH	no reaction	
11	$Pd(SO_4)_2$	0.50 : 0.50	AcOH	no reaction	

[a] **1** (2 mmol) was allowed to react in the presence of $Pd(OAc)_2$ (0.1 mmol), $HPMo_{10}V_2$ (0.04 mmol) in solvent (7 mL) at 70 °C for 15 h. [b] Numbers in parentheses show the ratio of *o*-**2** and *p*-**2**. [c] $Pd(OAc)_2$ (0.05 mmol) was used. [d] At 80 °C. [e] At 90 °C. [f] $CuCl_2$ (0.04 mmol) was used instead of $HPMo_{10}V_2$.

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not changed (Run 4). The conversion of **1** to **2** was slightly decreased in the reaction at 80 °C, but the reaction at 90 °C under these conditions resulted in the decrease of the conversion of **1** (Runs 5 and 6). The formation of *m*-anisic acid was not observed at all in the present carboxylation.

The reaction was examined in several solvents such as propionic acid, CH_3CN and DMF. In a previous paper on the direct coupling of benzene with ethyl acrylate by $Pd(OAc)_2$ and HPMoV, propionic acid was a better solvent than acetic acid. However, the reaction in propionic acid resulted in a slight lowering of the conversion and selectivity (Run 7). It was found that CH_3CN and DMF were not suited for the present carboxylation (Runs 8 and 9). $PdCl_2$ and $PdSO_4$ combined with $HPMo_{10}V_2$ did not catalyze at all the present carboxylation (Runs 10 and 11).

We next tried the carboxylation of **1** by $Pd(OAc)_2$ combined with several heteropoly acids (Table 2).

In the absence of HPMoV as a co-catalyst under the same conditions, no reaction took place using $Pd(OAc)_2$ (Run 1). The carboxylation of **1** by $Pd(OAc)_2$ was found to be considerably affected by the vanadium content in HPMoV used (Runs 2 to 7). No reaction was promoted by $Pd(OAc)_2$ combined with $H_3PMo_{12}O_{40}$ ($HPMo_{12}$) not containing vanadium (Run 2). The carboxylation of **1** was promoted by $Pd(OAc)_2$ combined with $H_4PMo_{11}V_1O_{40}{\cdot}nH_2O$ ($HPMo_{11}V_1$) and $H_6PMo_9V_3O_{40}{\cdot}nH_2O$ ($HPMo_9V_3$) containing vanadium[10] to give **2** in 19% and 43% yields, respectively (Runs 3 and 4). Although the reaction was examined using molybdotungstophosphoric acids ($HPMo_{11}W_1$ and $HPMo_{10}W_2$) and vanadotungstophosphoric acid ($HPW_{10}V_2$) under these conditions, no carboxylation was observed (Runs 6 to 8). These results show that vanadium in heteropolyoxometalates is an essential component to catalyze the present carboxylation of **1**. Among heteropoly acids examined, $HPMo_{10}V_2$ was the best combination with $Pd(OAc)_2$. Although several vanadium compounds such as V_2O_5 and $VO(acac)_2$ were employed instead of HPMoV, no carboxylation took place (Runs 9 and 10)

On the basis of these results, the carboxylation of several anisole derivatives was carried out by the use of $Pd(OAc)_2$ and $HPMo_{10}V_2$ in acetic acid at 70 °C for 15 h (Table 3).

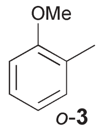
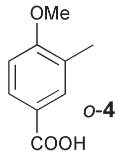
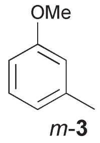
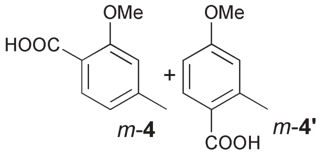
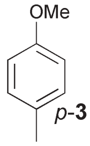
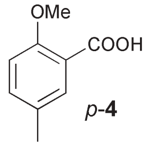
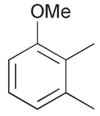
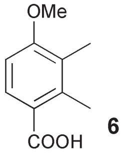
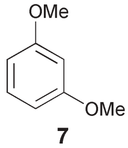
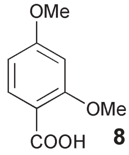
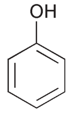
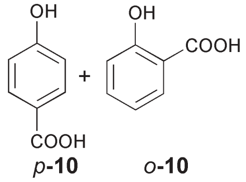
In order to obtain information on the reaction path, the carboxylation of **1** was compared with that of *o*-, *m*- and *p*-methylanisoles (*o*-, *m*-, and *p*-**3**). The reactivity in the carboxylation was found to decrease in the order of *o*-**3**, *m*-**3**, and *p*-**3**. The selectivity in the carboxylation could be satisfactorily explained by the electronic effect of the methoxy substituent. For instance, the carboxylation of *m*-**3** took place at the 4-position possessing the highest electron density. The low reactivity of *p*-**3** is due to the occupation of its *para*-position by the methyl group. Additionally, *p*-hydroxybenzoic acid (*p*-**10**) and *o*-hydroxybenzoic acid (*o*-**10**) were obtained in 59% selectivity at 90% conversion in the reaction of phenol (**9**) (Run 6). Unfortunately, however, benzene is inert for the present carboxylation, giving a small amount of benzoic acid (< 5%).

Table 2 Carboxylation of anisole (**1**) to anisic acid (**2**) with CO and O_2 catalyzed by $Pd(OAc)_2$ and heteropoly acids[a]

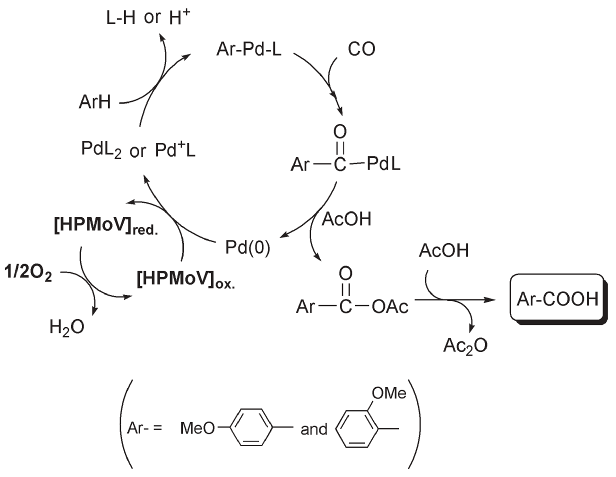
Run	HPA	Conv. (%)	Select. (%)
1	—	no reaction	
2	$HPMo_{12}$	2	—
3	$HPMo_{11}V_1$	30	64
4	$HPMo_9V_3$	53	81
5	$HPMo_8V_4$	27	57
6	$HPMo_{11}W_1$	1	—
7	$HPMo_{10}W_2$	2	—
8	$HPW_{10}V_2$	no reaction	
9	V_2O_5	no reaction	
10	$VO(acac)_2$	no reaction	

[a] **1** (2 mmol) was allowed to react under CO (0.5 atm) and O_2 (0.5 atm) by $Pd(OAc)_2$ (0.1 mmol) and HPA (0.04 mmol) in AcOH (7 mL) at 70 °C for 15 h.

Table 3 Carboxylation of various anisoles and phenol with CO and O_2 by the $Pd(OAc)_2$/$HPMo_{10}V_2$ system[a]

Run	Substrate	Products	Conv. (%)	Select. (%)
1	 *o*-**3**	 *o*-**4**	90	73
2[b]	 *m*-**3**	 *m*-**4** + *m*-**4′**	82	72
3	 *p*-**3**	 *p*-**4**	49	64
4	 **5**	 **6**	90	75
5	 **7**	 **8**	89	92
6[c]	 **9**	 *p*-**10** *o*-**10**	90	59

[a] Substrate (2 mmol) was allowed to react under CO (0.5 atm) and O_2 (0.5 atm) by $Pd(OAc)_2$ (0.1 mmol) and $HPMo_{10}V_2$ (0.04 mmol) in AcOH (7 mL) at 70 °C for 15 h. [b] *m*-**4** : *m*-**4′** = *ca.* 50 : 50. [c] In AcOH (4 mL) at 60 °C; *p*-**10** : *o*-**10** = *ca.* 90 : 10.



Scheme 2

The carboxylation is rationally explained by a similar reaction path proposed by Fujiwara[7b] (Scheme 2). The *ortho–para* orientation of the carboxylation of **1** by the present reaction system suggests that the reaction involves the electrophilic substitution of aromatic C–H bonds by Pd(II)‡ followed by the CO insertion of the Ar–Pd(II) species leading to an aroylpalladium species (**A**). The subsequent reductive elimination of Pd(0) and acetic anhydride from **A** leads to anisic acid. The Pd(0) is reoxidized by the action of HPMoV and O_2 to the parent Pd(II) species.

In conclusion, we have developed Pd-catalyzed direct carboxylation of anisole derivatives using CO and O_2 under mild conditions.

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Notes and references

† Representative procedure: To an AcOH solution (7 mL) of $Pd(OAc)_2$ (0.1 mmol) and $H_5PMo_{10}V_2O_{40}\cdot 15.2H_2O$ (0.04 mmol) was added **1** (2 mmol). Then, the reaction mixture was stirred at 70 °C for 15 h under a 1 : 1 mixed gas (1 atm) of CO and O_2. After the reaction, the GC and GC-MS analyses were performed. The conversions and yields of products were estimated from the peak areas based on the internal standard technique using GC.

‡ Although we could not determine the real active Pd(II) species at this stage, a PdL_2 or a cationic Pd^+L (L: OAc) may be formed under these reaction conditions.

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