

Oxidative Carbomethoxylation of Alkenes Using a Pd(II)/Molybdovanadophosphate (NPMoV) System under Carbon Monoxide and Air

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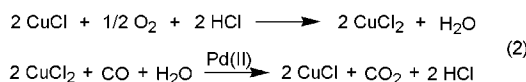
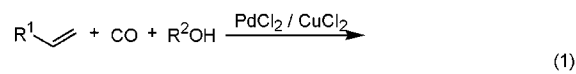
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Abstract: Oxidative carbomethoxylation of cyclopentene (**1**) under carbon monoxide and air by the use of a catalytic amount of Pd(OAc)₂ and molybdovanadophosphate (NPMoV) led to dimethyl *cis*-1,2-cyclopentenedicarboxylate (**2**) and dimethyl *cis*-1,3-cyclopentenedicarboxylate (**3**) in good yields. Total yields of **2** and **3** were found to be improved by adding a small amount of NH₄Cl. Several alkenes were similarly converted into the corresponding dimethyl dicarboxylates. The role of Cl⁻ in the present catalytic system is suggested.

Pd(II)-catalyzed carboalkoxylation of alkenes with CO in alcohol is known to produce α,β -unsaturated esters, β -alkoxy esters, and succinate derivatives (eq 1), and it is reported that the selectivity of these products was markedly influenced by the presence of a cocatalyst like a mercury salt¹ or a base² and the reaction conditions under a particular CO pressure.³ Similarly, cyclic alkenes such as cyclopentene, cycloheptene, cyclooctene, and norbornene also undergo carboalkoxylation by PdCl₂ to afford the corresponding 1,2- and 1,3-diesters.² However, these reactions call for the use of a stoichiometric amount of copper(II) chloride and sodium acetate. The Pd(II)-catalyzed carboalkoxylation of alkenes by using excess CuCl₂ as the reoxidant results in the formation of chlorinated byproducts and corrosion by the chloride anion. Another disadvantage in the reaction using the PdCl₂/CuCl₂/CO/O₂ system is that the CO is easily converted into CO₂ by the reaction with H₂O under the influence of CuCl₂ in the presence of PdCl₂ (eq 2).^{2,4} To overcome these drawbacks, several reoxidation systems other than the CuCl₂/O₂ were examined. Among them, the use of alkyl nitrites is thought to be a good method, and the carboalkoxylation of ethylene to succinate ester is currently carried out by this method on an industrial scale.⁵ The benzoquinone/Pd(II) system is also used as

an alternative redox couple in the carbomethoxylation.⁶ If the Pd(II)-catalyzed carbonylation can be performed in the absence of CuCl₂ using molecular oxygen as the terminal oxidant, such a system would be very attractive from environmental and industrial viewpoints. However, the carbonylation of alkenes with CO by Pd(II) using O₂ as the reoxidizing agent is usually difficult to carry out. Therefore, there has been little study on Pd(II)-catalyzed carbonylation using molecular oxygen as the terminal oxidant.⁷



Recently, we have reported that molybdovanadophosphate (NPMoV)/hydroquinone/O₂ is an efficient reoxidation system for the Pd(OAc)₂-catalyzed acetoxylation and acetalization of substituted alkenes.⁸ For example, cyclohexene and acrylonitrile are readily converted into 2-cyclohexenyl acetate and cyanoacetaldehyde diethylacetal, respectively, in quantitative yields under mild conditions. In addition, cyclotrimerization of internal and terminal alkynes was efficiently induced by the Pd(II)/chlorohydroquinone/NPMoV/O₂ to give polyalkylbenzenes in good yields.⁹ Thus, 4-octyne and *tert*-butylacetylene led to hexa-*n*-propylbenzene and 1,3,5-tri-*tert*-butylbenzene, respectively. Although the Wacker-type oxidation of cyclopentene to cyclopentanone has been very difficult to carry out so far, this transformation was successfully performed by Pd(OAc)₂ and NPMoV supported on activated carbon using molecular oxygen as the terminal oxidant.¹⁰ Moreover, we reported that the Pd(OAc)₂/chlorohydroquinone/NPMoV system catalyzes carbonylation of terminal alkynes in different ways by varying the solvent.¹¹ For instance, phenylacetylene was converted into methyl phenylpropionate in methanol and phenylmaleic anhydride in dioxane. This reaction provides a new carbonylation system catalyzed by Pd(OAc)₂ using NPMoV and molecular oxygen as the reoxidant. To extend our work on the Pd(OAc)₂/NPMoV/O₂ system in organic synthesis, we examined the carbomethoxylation of several alkenes with CO in methanol.

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Cyclopentene (**1**) was chosen as a model substrate and allowed to react with a mixed gas of CO and air in the presence of Pd(OAc)₂ and NPMoV under various conditions (Table 1). The reaction led to dimethyl *cis*-1,2-cyclopentanedicarboxylate (**2**) and dimethyl *cis*-1,3-cyclopentanedicarboxylate (**3**) as major products (eq 3).

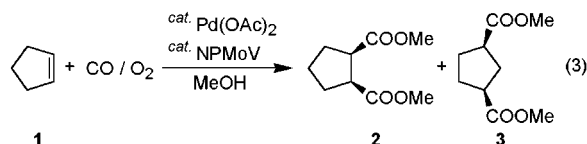


TABLE 1. Carbomethoxylation of Cyclopentene (1**) to Dimethyl *cis*-1,2-Cyclopentanedicarboxylate (**2**) and Dimethyl *cis*-1,3-Cyclopentanedicarboxylate (**3**) Using the Pd(II)/NPMoV Catalytic System under Various Reaction Conditions^a**

run	temp (°C)	time (h)	conv (%)	yield (%) ^b	ratio of 2/3
1	60	6	96	81	54/46
2 ^c	60	6	17	8	54/46
3 ^d	60	6	25	<1	
4 ^d	60	48	62	20	65/35
5 ^d	100	5	72	34	41/59
6 ^e	60	6	99	79	57/43
7 ^{d,f}	60	6	74	61	49/51
8 ^f	60	6	88	79	53/47
9 ^g	60	9	54	41	59/41
10 ^{d,g}	100	9	25	<1	
11 ^h	60	6	96	61	56/44
12	40	19	92	75	63/37
13	70	3	97	79	48/52
14	80	3	92	63	41/59
15	100	1	82	42	40/60

^a Compound **1** (2 mmol) was added to a solution of Pd(OAc)₂ (2.5 mol %), NPMoV (35 mg), NH₄Cl (3 mol %), and MeSO₃H (10 mol %) in MeOH (10 mL) and stirred under CO/air (5/5 atm). ^b Total yield of **2** and **3**. ^c In the absence of NPMoV. ^d In the absence of NH₄Cl. ^e NaCl was used instead of NH₄Cl. ^f PdCl₂ was used instead of Pd(OAc)₂. ^g In the absence of MeSO₃H. ^h Under CO/O₂ (5/1 atm).

The carbomethoxylation of **1** (2 mmol) under CO (5 atm)/air (5 atm) catalyzed by Pd(OAc)₂ (2.5 mol %) and NPMoV (35 mg) in the presence of NH₄Cl (3 mol %) in methanol (10 mL) acidified with MeSO₃H (10 mol %) at 60 °C for 6 h produced **2** and **3** in a ratio of 54:46 in 81% total yield and 96% conversion of **1** (run 1). A gap between the consumed cyclopentene and the resulting products was found to be due to the formation of oligomers derived from cyclopentene and CO. Indeed, a small amount of a tarry residue was left after removal of the solvent and the products. The geometry of the resulting diesters **2** and **3** was found to be of the *cis* configuration by comparing these spectral data with those reported previously.³ The *cis* geometry of dicarboxylic acid obtained by hydrolysis of **2** could be determined by a single-crystal X-ray analysis. The reaction course leading to *cis*-**2** is rationally explained by a reaction mechanism discussed below. The reaction in the absence of NPMoV under these conditions gave **2** (8%) in an amount comparable to that of the Pd(OAc)₂ present (run 2). In the absence of NH₄Cl under these conditions, the reaction was considerably retarded (runs 3 and 4). To improve the slow carbonylation in the absence of NH₄Cl at 60 °C, the reaction was run at 100 °C (run 5). The yields of **2** and **3** slightly increased, but the selectivity of the reaction was not

TABLE 2. Bismethoxycarbonylation of Cyclopentene (1**) to Dimethyl *cis*-1,2-Cyclopentanedicarboxylate (**2**) and Dimethyl *cis*-1,3-Cyclopentanedicarboxylate (**3**) Using the Pd(II)/NPMoV Catalytic System under Varying Pressure of CO/Air^a**

run	CO (atm)	air (atm)	time (h)	yield (%) ^b	ratio of 2/3
1	5	5	6	81	54/46
2	10	10	9	80	63/37
3	15	15	9	83	65/35
4	20	20	10	72	69/31
5	30	30	10	65	74/26
6	15	5	8	63	68/32
7	5	15	7	85	53/47

^a Compound **1** (2 mmol) was added to a solution of Pd(OAc)₂ (2.5 mol %), NPMoV (35 mg), NH₄Cl (3 mol %), and MeSO₃H (10 mol %) in MeOH (10 mL) and stirred under CO/air at 60 °C.

^b Compound **1** was almost consumed every run. Total yield of **2** and **3**.

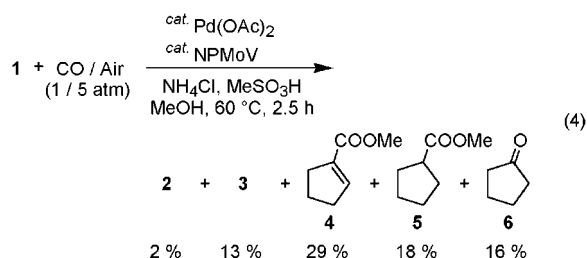
improved. When NaCl was used in place of NH₄Cl, the yields of **2** and **3** were almost the same as those in the reaction using NH₄Cl (run 6). These results show that the addition of a small amount of chloride ion markedly facilitates the present carbomethoxylation of **1**. The use of PdCl₂ in place of Pd(OAc)₂ without NH₄Cl resulted in **2** and **3** in moderate yields (run 7). Even in the use of the PdCl₂ catalyst, the addition of NH₄Cl to the catalytic system was effective in improving the yields of **2** and **3** (run 8). The reaction in the absence of MeSO₃H under these conditions resulted in the reduction of carbonylated products, **2** and **3** (run 9). No carbonylation took place in the absence of both NH₄Cl and MeSO₃H even at higher a temperature (100 °C) (run 10). In a previous paper, we showed that the catalytic potential of the NPMoV in the oxidation of isophorone with O₂ is considerably enhanced by the addition of an acidlike MeSO₃H to the catalytic system.¹² Bäckvall et al. described that the precipitation of Pd(0) is depressed by the addition of a small amount of a strong acid to the reaction system.¹³ Therefore, it is thought that the MeSO₃H has a similar effect in the present reaction. The reaction of **1** under CO (5 atm) and pure O₂ (1 atm) in place of air led to **2** and **3** in a somewhat lower yield (61%) (run 11). It is interesting to note that the carbomethoxylation at 40 °C gave **2** in preference to **3** in good yield (75%), although the reaction must be prolonged to 19 h (run 12). When the reaction temperature was raised to 70 °C, the carbomethoxylation was completed within 3 h to give **2** and **3** in 79% yield (run 13). Reactions at higher temperatures afforded **3** rather than **2** (runs 12–15).

The carbonylation of **1** under varying CO and air pressures is shown in Table 2. An approximately 1:1 mixture of **2** and **3** was obtained by the reaction of **1** under CO (5 atm) and air (5 atm) (run 1), and increasing the CO and air pressures caused an increase of the formation of **3** (runs 2–5). No significant influence on the yield of **2** and **3** was observed in the range of 5–15 atm of CO and air (runs 1–3), but the formation of **2** and **3** was gradually decreased in the reaction at over 20 atm of CO and air (runs 4 and 5). The reaction under CO (15 atm) and air (5 atm) resulted in a decrease of **2** and **3**

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
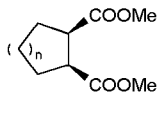
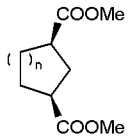




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(run 6), while the reaction at higher pressures of CO (5 atm) and air (15 atm) led to **2** and **3** in high yield (85%, run 7). It is interesting to note that the reaction at 1 atm of CO and 5 atm of air produced various carbonylated products such as monoesters, methyl 1-cyclopentenecarboxylate (**4**, 29%), methyl cyclopentane carboxylate (**5**, 18%), and cyclopentanone (16%) in addition to **2** (2%) and **3** (13%) (eq 4).



On the basis of these results, the carbonylation of several alkenes was attempted under CO (5 atm) and air (5–15 atm) (Table 3).

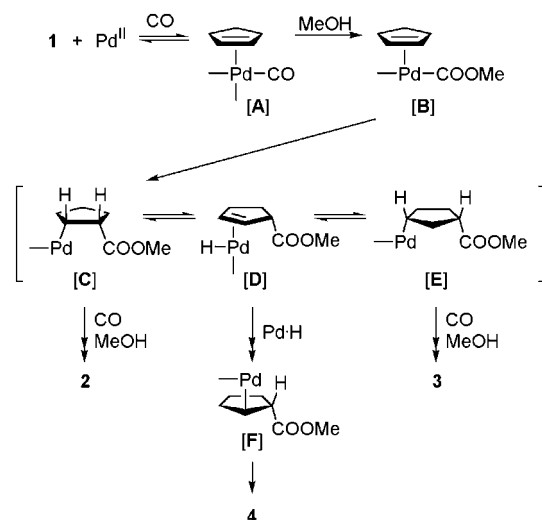
TABLE 3. Bismethoxycarbonylation of Various Alkenes Using the Pd(II)/NPMoV Catalytic System^a

Run	Substrate	Air / atm	Time / h	Conv. / %	Yield / %	
1		5	7	33	0	0
2		5	17	66	13	10
3		5	15	37	12	5
4		5	20	49	29	6
5		15	16	75	45	9
6		15	15	88	54	15
7 ^b		15	24	-	48	0

^a Substrate (2 mmol) was added to a solution of Pd(OAc)₂ (2.5 mol %), NPMoV (35 mg), NH₄Cl (3 mol %), and MeSO₃H (10 mol %) in MeOH (10 mL) and stirred under CO (5 atm)/air at 60 °C. ^b Ethylene (0.5 atm, ca. 1.5 mmol) was introduced into the autoclave containing the catalytic solution and stirred at 50 °C.

Although cyclohexene was not carbonylated at all, cycloheptene and cyclooctene were slightly carbonylated to form the corresponding diesters in low yields (runs 1–3). This tendency bears a close resemblance to the results reported by Stille et al. except for the result of the oligomerization of norbornene under our conditions.³ The carbomethoxylation of styrene gave dimethyl 2-phenylsuccinate in fair yield (45%) together with a small amount of acetophenone (run 5). The yield of the succinate derivative was improved by raising the pressure of air (runs 4 and 5). *p*-Methylstyrene was also carbonylated

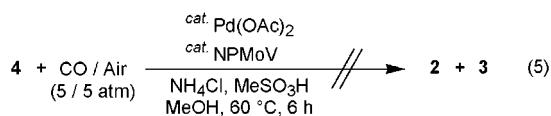
SCHEME 1



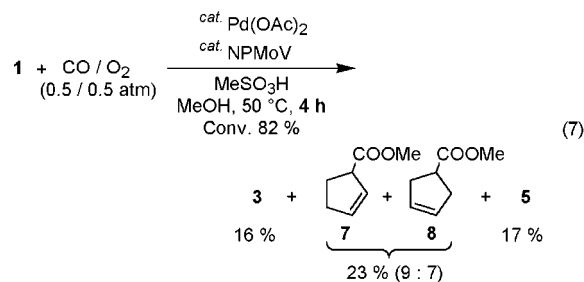
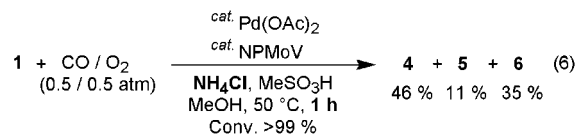
under these conditions to form the corresponding diester and ketone (run 6). Ethylene was selectively carbonylated into dimethyl succinate, and acetal based on the Wacker oxidation was not observed.

A plausible reaction path for the present carbomethoxylation is outlined in Scheme 1. The reaction is initiated by the coordination of cyclopentene **1** followed by CO to Pd(II) to form a Pd complex (**A**), which then reacts with methanol to form a carbomethoxypalladium complex (**B**). The cis addition of the palladium species to the coordinated cyclopentene double bond forms a σ -bonded palladium complex (**C**). It is probable that CO insertion into the complex **C** followed by methanolysis of the resulting palladium-acyl intermediate gives rise to dimethyl *cis*-1,2-cyclopentanecarboxylate **2**. On the other hand, β -hydrogen elimination from the complex **C** and recoordination of the Pd(II) species forms a σ -complex (**E**) through the formation of a π -complex (**D**). The complex **E** reacts with CO followed by methanolysis to afford dimethyl *cis*-1,3-cyclopentanecarboxylate **3**.

To obtain further information on the reaction course of the present carbomethoxylation, the carbomethoxylation of methyl 1-cyclopentenecarboxylate (**4**) was examined under CO (5 atm) and air (5 atm) at 60 °C for 6 h. However, the reaction was not induced at all and the starting **4** was recovered (eq 5). This shows that **4** is a stable compound and that **2** and **3** are not formed through **4**. Since β -hydrogen elimination is only capable of occurring when a palladium species and the hydrogen atom are located in the cis position, the formation of **4** from the complex **C** is impossible. For the formation of **4**, therefore, dissociation of the palladium-hydride species from the π -complex **D** and its recoordination from the opposite side is needed to form a σ -complex (**F**). The fact that the present carbonylation provides **2** and **3** having cis configurations shows that the reaction proceeds without dissociation of the Pd–H species from the complex **D**.



It is interesting to note that the reaction of **1** under low pressures of CO (0.5 atm) and O₂ (0.5 atm) proceeded despite the presence or absence of NH₄Cl. The reaction in the presence of NH₄Cl was completed within 1 h to give **4** as a main product, while in the absence of NH₄Cl a longer reaction time was needed and a regioisomeric mixture of methyl 2-cyclopentenecarboxylate (**7**) and methyl 3-cyclopentenecarboxylate (**8**) was formed in place of **4** (eqs 6 and 7). This observation suggests that the isomerization of **7** and **8** to **4** did not take place in the absence of NH₄Cl though **4** is thermodynamically more stable than **7** and **8**. Therefore, the formation of **7** and **8** may be explained by the β -elimination of Pd–H from the complexes **C** and **E** before the coordination of CO to **C** or **E**. In the case of the presence of NH₄Cl in the reaction system, the resulting **7** and **8** seem to be isomerized to the stable **4**. The formation of the saturated monoester **5** under a low pressure of CO strongly suggests that the Pd–H species is generated in the course of the reaction. Thus, it is probable that the CO insertion into a σ -complex derived from hydropalladation of the Pd–H to **1** followed by methanolysis of the resulting palladium-acyl intermediate leads to **5**. In the reaction without NH₄Cl under a low pressure of CO, the formation of **3**, **7**, and **8** may indicate that the complex **E** is more stable than the complex **C** and that the β -elimination of Pd–H from the complex **E** occurs in preference to that from the complex **C**. On the basis of these facts, the Cl[–] ion is thought to facilitate the formation of the Pd–H species.



In conclusion, the carbomethoxylation of alkenes with CO in methanol using air as the terminal oxidant was successfully achieved by using Pd(OAc)₂ combined with

NPMoV in the presence of a very small amount of the Cl[–] ion under mild conditions.

Experimental Section

General. All solvents and reagents were purchased from commercial sources and used without further purification unless otherwise noted. ¹H and ¹³C NMR were measured at 270 and 67.5 MHz, respectively, in CDCl₃ with Me₄Si as the internal standard. Infrared (IR) spectra were measured using a NaCl plate or the KBr method. GLC analyses were performed with a flame ionization detector using a 25 m (0.22 mm i.d., 0.25 μ m film thickness) fused silica capillary column (BP1). All yields were determined by GLC analyses using undecane as the internal standard.

Typical Procedure for the Carbomethoxylation of Cyclopentene (1). A solution of Pd(OAc)₂ (2.5 mol %), NPMoV (35 mg),^{8,14} NH₄Cl (3 mol %), MeSO₃H (10 mol %), and cyclopentene (**1**) (2 mmol) in MeOH (10 mL) was placed in a stainless autoclave (50 mL). The autoclave was pressurized with 5 atm of air and then with 5 atm of CO at room temperature. The reaction mixture was allowed to react under stirring at 60 °C until the CO and O₂ uptake had not been observed (6 h). After the reaction, the solvent was removed under reduced pressure and the residue was dissolved in diisopropyl ether. The solution was filtered, washed with diluted NaHCO₃, and dried over anhydrous MgSO₄. After removal of diisopropyl ether under reduced pressure, the residual liquid was separated by HPLC that was performed on GPC columns to give dimethyl *cis*-1,2-cyclopentanedicarboxylate (**2**) and dimethyl *cis*-1,3-cyclopentanedicarboxylate (**3**) as a clear liquid, respectively, in 81% total yield. The biscarbomethoxylated products from cycloalkene³ and styrene^{6a} and compounds **5**,¹⁵ **7**,¹⁶ and **8**¹⁷ were previously reported. Other products were commercially available and identified through comparison of the isolated product with an authentic sample.

Dimethyl 2-*p*-Tolylsuccinate: ¹H NMR (270 MHz, CDCl₃) δ 7.17–7.10 (m, 4H), 4.08–4.03 (m, 1H), 3.66 (s, 6H), 3.20–3.14 (m, 1H), 2.68–2.60 (m, 1H), 2.31 (s, 3H); ¹³C NMR (67.5 MHz, CDCl₃) δ 173.3, 171.7, 137.1, 134.5, 129.4, 127.4, 52.2, 51.7, 46.6, 37.6, 21.0.

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Supporting Information Available: Preparation of NP-MoV and an X-ray structure for *cis*-1,2-cyclopentanedicarboxylic acid. This material is available free of charge via the Internet at <http://pubs.acs.org>.

JO0255779

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