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Acetalization of Alkenes Catalyzed by $Pd(OAc)_2$/NPMoV Supported on Activated Carbon under a Dioxygen Atmosphere

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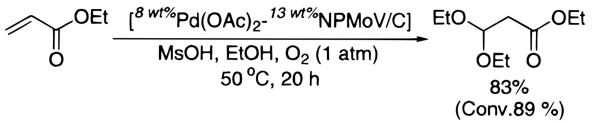
ABSTRACT



The acetalization of terminal alkenes such as ethyl acrylate and acrylonitrile with alcohols under O_2 was efficiently achieved by $Pd(OAc)_2$ supported on activated carbon combined with molybdovanadophosphate (NPMoV). For example, ethyl acrylate was subjected to acetalization with EtOH acidified by CH_3SO_3H under O_2 (1 atm) in the presence of [$^{8\ wt\%}Pd(OAc)_2/C$] and NPMoV to form ethyl 3,3-diethoxypropionate in quantitative yield.

The reaction of terminal alkenes with water by $PdCl_2/CuCl_2/O_2$, which leads to methyl ketones, is well-known as the Wacker oxidation.[1] The reaction of alkenes bearing an electron-withdrawing substituent such as acrylate and acrylonitrile in alcohols by the Wacker system produces the corresponding acetals which are very important precursors in pharmaceutical chemistry.[2] Hosokawa et al. have reported in detail the acetalization reactions by the use of a Pd(II) species.[3] The acetalization by Pd(II) using alkyl nitrites as oxidants is industrialized by Ube Industries, Ltd.[4] More recently, the acetalization of acrylates with methanol by $PdCl_2/CuCl_2$ (or CuCl)/O_2 in supercritical CO_2 has been presented.[5] In these acetalizations, the $CuCl_2/O_2$ system is used as a convenient reoxidation reagent of the Pd(0) reduced in the course of the reaction. However, the catalytic system involving a chloride ion has two major disadvantages: (i) the formation of chlorinated byproducts and (ii) corrosion of the reactor. Therefore, it is very important to develop Pd(II)-catalyzed acetalization by a chloride-free reoxidation system. In a previous paper, we showed that $Pd(OAc)_2$ and molybdovanadophosphate (NPMoV) supported on activated carbon promoted efficiently the oxidation of cyclopentene to cyclopetanone which so far has been difficult to carry out by a chloride-free Wacker system.[6]

To extend our work on the chloride-free Wacker system, we examined the acetalization of alkenes to acetals by $Pd(OAc)_2$ and NPMoV supported on activated carbon (hereafter abbreviated to Pd(II)−NPMoV/C)[7] using dioxygen as the ultimate oxidant.

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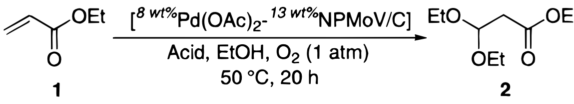
A typical reaction was carried out as follows: To a suspended solution of [$^{8\text{wt}\%}$Pd(OAc)$_2$−$^{13\text{wt}\%}$NPMoV/C] (50 mg) were added ethyl acrylate (**1**) (2 mmol) and CH_3SO_3H (6 mg), and the mixture was stirred under dioxygen atmosphere (1 atm) at 50 °C for 20 h (standard conditions). Products were isolated by column chromatography on silica gel with hexane/ethyl acetate eluent.

The acetalization of **1** in ethanol acidified with CH_3SO_3H or *p*-toluenesulfonic acid under standard conditions gave ethyl 3,3-diethoxypropionate in good yield (83%) (Table 1, entries 1 and 3). However, a very low yield of **2** was obtained in the absence of CH_3SO_3H (entry 2). Similar effects by acids have been observed in the NPMoV-catalyzed oxidation of isophorone.[9] Among the activated carbons examined, Kurare BP-25 (I) was found to give the best results (entries 4−6). By nonsupported Pd(OAc)$_2$ combined with NPMoV, **2** was obtained in moderate selectivity (71%) at 97% conversion (entry 7). The benefit in the reaction using heterogeneous catalytic system is that the catalyst is easily separable by filtration from the reaction mixture. The acetalization of **1** was examined by use of the catalyst recovered from run 1. It was found that the recovered [$^{8\text{wt}\%}$Pd(OAc)$_2$−$^{13\text{wt}\%}$NPMoV] catalyst was considerably deactivated (entry 8). From the ICP analysis, leaching of the metal species (Pd = 0.01×10^{-2} mmol (0.6%), Mo = 0.01×10^{-2} mmol (0.7%), and V = 1.53×10^{-2} mmol (55%)) from the catalyst was observed. In particular, a large amount of vanadium ion was found to be leached into the solution. Thus, from recovered catalyst, reoxidation to Pd(II) of the Pd(0) reduced during the reaction was difficult. Hence, when a small amount of NPMoV was added to the recovered catalyst [$^{8\text{wt}\%}$Pd(OAc)$_2$−$^{13\text{wt}\%}$NPMoV/C], the acetalization was found to proceed in quantitative yield (>99%) after 5 h (entry 9). It is interesting to note that the acetalization of **1** was performed by the use of [$^{8\text{wt}\%}$Pd(OAc)$_2$/C] combined with NPMoV in place of the [$^{8\text{wt}\%}$Pd(II)−$^{13\text{wt}\%}$NPMoV/C] to give **2** in quantitative yield (entry 10).

Table 1. Acetalization of Ethyl Acrylate (**1**) to Ethyl 3,3-Diethoxypropionate (**2**)[a]



entry	acid	activated carbon	convn (%)	yield (%)
1	CH_3SO_3H	Kurare BP-25 (I)	89	83
2[b]		I	15	9
3[c]	*p*-TsOH	I	84	84
4[d]	CH_3SO_3H	Darco	56	11
5[e]	CH_3SO_3H	Shirasagi	37	34
6[f]	CH_3SO_3H	Kurare coal GLC	63	54
7[g]	CH_3SO_3H	I	97	71
8[h]	CH_3SO_3H	I	60	35
9[i]	CH_3SO_3H	I	>99	>99
10[j]	CH_3SO_3H	I	99	99

[a] **1** (2 mmol) was allowed to react with O_2 (1 atm) in the presence of catalyst (50 mg) and CH_3SO_3H (6 mg) in EtOH (3 mL) at 50 °C for 20 h. [b] In the absence of CH_3SO_3H. [c] *p*-Toluenesulfonic acid (11 mg) was used instead of CH_3SO_3H. [d] Darco was used as activated carbon. [e] Shirasagi was used as activated carbon. [f] Kurare coal GLC was used as activated carbon. [g] Pd(OAc)$_2$ (4.1 mg) and NPMoV (6.3 mg) were used instead of [$^{8\text{wt}\%}$Pd(OAc)$_2$−$^{13\text{wt}\%}$NPMoV/C]. [h] Recovered catalyst from run 1 was used. [i] NPMoV (6.3 mg) was added to the recovered catalyst from run 1. The reaction was carried out at 50 °C for 5 h. [j] The reaction was carried out by using [$^{8\text{wt}\%}$Pd(OAc)$_2$/C] (50 mg) and NPMoV (6.3 mg).

Table 2 shows the acetalization of **1** by [Pd(OAc)$_2$/C] and [Pd(0)/C][10] in the presence of NPMoV. **1** was smoothly acetalized by [$^{8\text{wt}\%}$Pd(OAc)$_2$/C] and NPMoV in EtOH at 50 °C for 8 h to form **2** in good yield (92%). The combined catalyst of [$^{10\text{wt}\%}$Pd(0)/C] with NPMoV was found to catalyze efficiently the acetalization of **1** to **2**. This fact shows that Pd(0)/C is readily oxidized to Pd(II)/C by NPMoV under dioxygen.

Table 2. Recycles of Pd(OAc)$_2$/C and Pd(0)/C Combined with NPMoV in the Acetalization of **1** to **2**[a]

	[$^{8\text{wt}\%}$Pd(OAc)$_2$/C]		[$^{10\text{wt}\%}$Pd(0)/C][b]	
no. of recovery	convn (%)	yield (%)	convn (%)	yield (%)
0	92	92	>99	95
1	85	85	>99	92
2	85	85	>99	92
3	86	86	92	92
4	49	48	89	89
5	33	22	89	69

[a] **1** (3 mmol) was allowed to react with O_2 (1 atm) in the presence of catalyst (50 mg) and NPMoV (6.3 mg) acidified by CH_3SO_3H (6 mg) in EtOH (3 mL) at 50 °C for 8 h. [b] 12 h.

Table 3 shows the acetalization of various olefins by the [$^{8\text{wt}\%}$Pd(OAc)$_2$/C−NPMoV] system. The reaction of methyl acrylate and **1** in methanol gave the corresponding acetals in almost quantitative yields (entries 1 and 2). The acetal-

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(7) Activated carbons available from a commercial source: Kurare BP-25 (2420 cm^2/g), Kurare coal GLC (1570 cm^2/g), Shirasagi (1200 cm^2/g), and Darco (650 cm^2/g). Molybdovanadophosphate (NPMoV) was prepared according to the literature procedure.[8] To a solution of $NaVO_2$ (7.32 g, 60 mmol) in water (38 mL) was added $Na_2MoO_4 \cdot 5H_2O$ (18.22 g, 34 mmol) in water (12 mL). To the resulting solution was added 85% H_3PO_4 (7.6 g, 66 mmol) in water (10 mL), and the mixture was heated to 95 °C under stirring for 1 h. After cooling to 0 °C, a saturated aqueous ammonium chloride (150 mL) was added to the solution to give NPMoV which was purified by recrystallization from water and dried in vacuo with heating at about 90 °C. The preparation of [Pd(OAc)$_2$−NPMoV/C] is as follows: Pd(OAc)$_2$ (268 mg) was dissolved in excess acetone and then activated carbon (3 g) was added. After stirring overnight at room temperature, [Pd(OAc)$_2$/C] was obtained in quantitative yield. To the suspended water of the [Pd(OAc)$_2$/C] (3.27 g) was added NPMoV (471 mg), and the resulting solution was vigorously stirred for 3 h at room temperature. [Pd(OAc)$_2$−NPMoV/C] was filtered off, washed with water, and dried in vacuo with heating at about 90 °C to give [Pd(OAc)$_2$−NPMoV/C] in almost quantitative yield.

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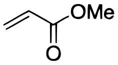
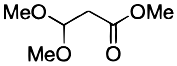
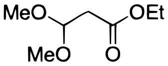
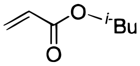
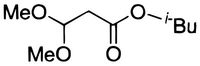
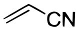
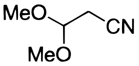
(9) Hanyu, A.; Sakurai, Y.; Sakaguchi, S.; Fujibayashi, S.; Ishii, Y. *Tetrahedron Lett.* **1997**, *38*, 5659.

(10) [$^{10\text{wt}\%}$Pd(0)/C] catalyst was purchased from N.E.CHEMCAT.

Table 3. Acetalization of Alkenes with Dioxygen Catalyed by $Pd(OAc)_2/C-NPMoV$ System[a]

entry	Substrate	Product	Conv.(%)	Yield (%)
1			97	95
2[b]	**1**		98	96
3[b]			99	99
4[c]			—	12 (96)

[a] Substrate (2 mmol) was allowed to react with O_2 (1 atm) in the presence of [$^{8wt\%}Pd(OAc)_2/C$] (50 mg) and NPMoV (6.3 mg) acidified by CH_3SO_3H (6 mg) in MeOH (3 mL) at 50 °C for 8 h. [b] Reaction was carried out for 20 h. [c] Number in parentheses shows the result of the reaction was performed using [$^{8wt\%}Pd(OAc)_2/C$] (200 mg) and NPMoV (44 mg) acidified by CH_3SO_3H (20 mg) in MeOH (10 mL) at 60 °C for 20 h.

ization of isobutyl acrylate afforded isobutyl 3,3-diethoxypropionate in good yield (99%) (entry 3). These acetals are useful precursors for the preparation of various heterocyclic compounds.[11] Acrylonitrile in methanol is converted into cyanoacetaldehyde dimethylacetal which is a precursor of vitamine B_1 (entry 4).

In conclusion, the acetalization of alkenes bearing an electron-withdrawing substituent was achieved by the chloride-free $Pd(OAc)_2-NPMoV$ system under dioxygen in mild conditions. From an industrial point of view, it is very important that the acetalization of acrylate and acrylonitrile is performed by a chloride-free palladium system.

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Supporting Information Available: General experimental details spectra for compounds prepared. This material is available free of charge via the Internet at http://pubs.acs.org.

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