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Selective Wacker-type oxidation of terminal alkenes and dienes using the Pd(II)/molybdovanadophosphate (NPMoV)/O_2 system

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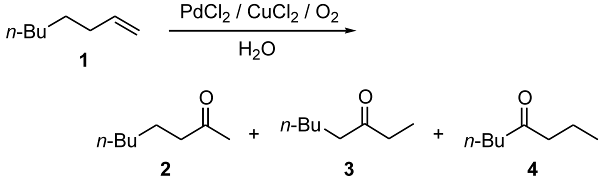
Abstract—Selective Wacker-type oxidation of long-chain terminal alkenes to methylketones was successfully achieved by using $Pd(OAc)_2$/molybdovanadophosphate (NPMoV)/O_2 system. The selectivity of the reaction increased by slow addition of the alkenes to the catalytic solution. The oxidation of α,ω-dienes was also examined, and the selectivity of the oxidation was found to depend on the chain length of the dienes used. © 2002 Elsevier Science Ltd. All rights reserved.

The oxidation of alkenes by the Wacker system consisting of $PdCl_2/CuCl_2/O_2$ to ketones is a well-established method and a very important reaction from synthetic and industrial viewpoints.[1] However, Wacker oxidation of long-chain terminal alkenes is usually difficult to carry out selectively, because the reaction is often accompanied by isomerization to internal alkenes whose subsequent oxidation affords a mixture of several isomerized ketones. For instance, the oxidation of 1-octene (**1**) by the Wacker system produces a mixture of three possible octanones (Eq. (1)).[2] In order to avoid the isomerization to internal alkenes, several methods have been proposed, e.g. the reaction using surfactants,[3] cyclodextrins[4] and the pyridine–O_2 system,[5] the improvement of reoxidants[6] and solvents,[7] and the use of water soluble Pd(II) complex[8] and supported catalysts.[9]



(1)

Previously, we reported that molybdovanadophosphate (NPMoV)/O_2 is an efficient reoxidation system for the $Pd(OAc)_2$-catalyzed oxidations of alkenes. For instance, acetoxylation of cycloalkenes and acetalization of substituted alkenes were successfully performed by this catalytic system under mild conditions.[10] In addition, the Wacker-type oxidation of cyclopentene to cyclopentanone, which has been very difficult to carry out so far, was aptly performed by $Pd(OAc)_2$ supported on activated carbon combined with the NPMoV/O_2 system.[11] More recently, we have reported carbomethoxylation of alkenes by $Pd(OAc)_2$/NPMoV/O_2 system.[12]

In continuation of our study to extend the Pd(II)/NPMoV/O_2 system in organic synthesis, our attention has been focused on the selective oxidation of higher terminal alkenes to the corresponding methyl ketones which is desired for a long time in industry.

The Wacker-type oxidation of 1-octene (**1**) was chosen as a model reaction and carried out under various reaction conditions using the Pd(II)/NPMoV/O_2 system. These results are summarized in Table 1. Compound **1** was allowed to react in the presence of $Pd(OAc)_2$, NPMoV[13] and $MeSO_3H$ in aqueous ethanol under oxygen atmosphere (1 atm) at 60°C for 6 h (standard conditions), giving 2-octanone (**2**) (21%) along with 3-octanone (**3**) (5%) and 4-octanone (**4**) (2%), and isomerized internal octenes were recovered (run 1). We showed that the catalytic activity of the $Pd(OAc)_2$/NPMoV/O_2 system was improved by adding of hydroquinone (HQ) in the acetoxylation and acetalization of alkenes.[10] In the present reaction, no pronounced effect of the HQ was observed, although the selectivity of **1** to **2** was somewhat improved (run 2). It was found that NH_4Cl serves as a good additive in the present reaction. When a small amount of NH_4Cl (5 mol%) was added to the catalytic system, **2** (43%) was obtained along with isomerized octanones, **3** (20%) and **4** (17%) (run 3). The yield of **2** was not altered by adding both HQ and NH_4Cl (run 4). Removing

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Table 1. Oxidation of 1-octene (**1**) to octanone using the Pd(II)/NPMoV/O_2 system under various reaction conditions[a]

Run	Pd(II)	Additive	Isomerized octenes (%)[b]	**2**/**3**/**4**, Yield (%)
1	$Pd(OAc)_2$	–	47	21/5/2
2	$Pd(OAc)_2$	HQ	46	38/1/<1
3	$Pd(OAc)_2$	NH_4Cl	0	43/20/17
4	$Pd(OAc)_2$	HQ, NH_4Cl	2	42/19/8
5[c]	$Pd(OAc)_2$	NH_4Cl	62	17/5/3
6[d]	$Pd(OAc)_2$	NH_4Cl	41	30/8/5
7[e]	$Pd(OAc)_2$	NaCl	0	45/19/16
8	$PdCl_2$	–	0	36/22/19
9[f]	$Pd(OAc)_2$	–	3 (38)	16/10/2
10[f]	$Pd(OAc)_2$	NH_4Cl	0	40/22/16
11	5 wt% $Pd(OAc)_2/C$	–	33	40/2/<1
12	5 wt% $Pd(OAc)_2/C$	HQ	29	48/<1/0
13	5 wt% $Pd(OAc)_2/C$	NH_4Cl	51 (3)	20/2/1
14[g]	5 wt% $Pd(OAc)_2/C$	NH_4Cl	14 (5)	32/13/6
15[h]	5 wt% $Pd(OAc)_2/C$	NH_4Cl	0 (7)	83/<1/0
16[i]	5 wt% $Pd(OAc)_2/C$	NH_4Cl	9 (3)	73/<1/0
17[h]	$Pd(OAc)_2$	NH_4Cl	0	77/4/4

[a] Compound **1** (2 mmol) was added to a solution of Pd(II) (5 mol%), NPMoV (35 mg), HQ (20 mol%) or NH_4Cl (5 mol%) and $MeSO_3H$ (10 mol%) in EtOH:H_2O (19:1, 10 mL) and the mixture was stirred under O_2 (1 atm) at 60°C for 6 h.

[b] Number in parentheses shows the recovered octene without isomerization.

[c] In the absence of NPMoV.

[d] In the absence of $MeSO_3H$.

[e] NaCl (5 mol%) was added.

[f] 2-Octene (**5**) was used instead of **1**.

[g] 15 h.

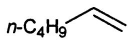
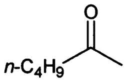
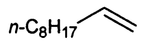
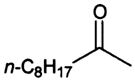
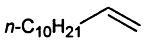
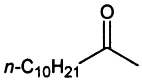
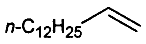
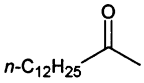
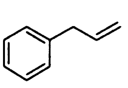
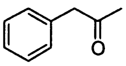
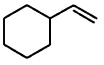
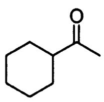
[h] A solution of **1** in EtOH: H_2O (19:1, 10 mL) was added by portions over a period of 5 h to a catalytic solution in EtOH:H_2O (19:1, 5 mL). The mixture was stirred for 0.5 h after completion of the addition.

[i] A solution of **1** in EtOH:H_2O (19:1, 5 mL) was added by portions over a period of 2.5 h to a catalytic solution in EtOH:H_2O (19:1, 5 mL). The mixture was stirred for 0.5 h after completion of the addition.

NPMoV from the catalytic system caused the decrease of the formation of octanones, **2**, **3** and **4**, and a large amount of isomerized octenes were recovered (run 5). The oxidation of **1** to octanones was depressed in the absence of $MeSO_3H$ (run 6). In a previous paper, we showed that the oxidation of isophorone with O_2 by NPMoV[14] and the acetalization of alkenes by $Pd(OAc)_2$/NPMoV[15] are considerably enhanced by adding $MeSO_3H$ to the catalytic system. In these reactions, the acid accelerates the reoxidation of the reduced $[NPMoV]_{red.}$ to the original oxidation state of NPMoV with O_2. Similar effect of rate enhancement by the addition of an acid is reported by several authors.[16] Bäckvall et al. reported that the presence of a small amount of a strong acid prevents the precipitation of the Pd(0) formed during the reaction.[6] Therefore, it is thought that the $MeSO_3H$ added has similar effects in the present reaction. NaCl was also effective as an additive to lead to almost the same results as run 3 using the NH_4Cl (run 7). The use of $PdCl_2$ in place of $Pd(OAc)_2$ resulted in the decrease of the selectivity to **2** (run 8). Internal alkene, 2-octene (**5**), was smoothly oxidized in the presence of the NH_4Cl to form octanones, **2** (40%), **3** (22%), **4** (16%) (run 10). These results indicate that a small amount of the chloride ion facilitates the smooth oxidation of internal alkenes. Furthermore, it is important to note that the product distribution of **2**, **3** and **4** by the oxidation of **5** was almost the same as that of **1** (runs 3 and 10). This fact suggests that the isomerization of terminal double bond to internal one occurs readily and reaches equilibrium between 1-, 2- and 3-octenes whose subsequent oxidations produce the corresponding octanones, **2**, **3** and **4**. The $Pd(OAc)_2/C$ catalyst, which was efficient for the oxidation of cyclopentene,[11] was also efficient for the present transformation (runs 11–16). In the oxidation of **1** by the $Pd(OAc)_2/C$, no additive effect of the NH_4Cl was observed (runs 13 and 14). It was found that the selectivity of **1** to **2** was considerably improved by slow addition of **1** to the catalytic solution. Thus, the selective oxidation of **1** by $Pd(OAc)_2/C$ in the presence of a small amount of NH_4Cl was achieved by adding **1** over a period of 5 h to form **2** in 83% yield with almost complete selectivity (run 15). However, the addition of **1** over a period of 2.5 h resulted in a slight decrease of **2** (73%) (run 16). Similar results were also obtained by non-supported $Pd(OAc)_2$ catalyst by adding **1** slowly (run 17).

On the basis of these results, the conversion of several terminal alkenes to methylketones was examined (Table 2).[17] Several long-chain terminal alkenes were selectively oxidized to the corresponding methyl ketones in satisfactory yields without formation of isomerized ketones (runs 1–4). In the case of allylbenzene, the oxidation took place with somewhat difficulty, and 1-propenylbenzene was recovered, but not allylbenzene (run 5). Vinylcyclohexane was oxidized to the corre-

Table 2. Oxidation of various terminal alkenes using the $Pd(OAc)_2$/NPMoV catalytic system under dioxygen[a]

Run	Alkene	Recovered alkenes / %[b]	Ketone	Yield / %[c]
1[d]		-		77 (<1)
2		7		82 (<1)
3		18		74 (1)
4		5		88 (1)
5		53		35 (0)
6		9		80 (0)

[a] Reaction conditions are shown in Ref. 17.

[b] Recovered alkenes consisted of a mixture of internal alkenes.

[c] Number of parentheses shows the isomerized ketones.

[d] The amount of recovered hexenes was difficult to estimate owing to overlapping peaks.

sponding ketone and almost no internal alkenes were recovered (run 6).

It is well-known that the isomerization of alkenes is easily promoted by Pd–hydride species.[18] In addition, we suggested that the chloride ion facilitates the formation of Pd–hydride species in a previous paper on carbomethoxylation of alkenes by the same catalytic system.[12] In the present work, the fact that the isomerization of terminal alkenes to internal ones is depressed by slow addition of the alkenes to the catalytic solution shows that the generation of a Pd–hydride may be suppressed during the reaction. An alkene presented in excess in the reaction system may prevented the reoxidation of the Pd–hydride to Pd(II) which can induce the Wacker oxidation.

We next examined the oxidation of several dienes using the $Pd(OAc)_2/NPMoV/O_2$ system under similar conditions (Table 3).[19] 7-Methyl-1,6-octadiene (**6**) having both terminal and internal carbon–carbon double bonds was converted into mono ketone, 7-methyl-6-octen-2-one (**7**), in moderate conversion (50%) and yield (34%) (run 1). When HQ (20 mol%) was added to this reaction system, the selectivity of the reaction was considerably improved to give **7** in 92% yield. Similarly, the oxidation of dihydromyrcene produced 3,7-dimethyl-6-octen-2-one in satisfactory yield (87%) (run 4). α,ω-Dienes consisted of 7 or 8 carbon atoms were found to be oxidized to the corresponding diketones in moderate yields (runs 5 and 6), but 1,13-tetradecadiene afforded a complex mixture of isomeric dienes, mono ketones and diketones (run 7). The oxidation of dienes proceeded more selectively by adding of NaCl rather than NH_4Cl (runs 2, 4, 5 and 6).

In conclusion, the selective Wacker-type oxidation of terminal alkenes to methylketones using the NPMoV/O_2 reoxidation system in the presence of a small amount of chloride ion was successfully achieved by adding alkenes slowly to the catalytic solution under mild conditions. In addition, some dienes were selectively oxidized to the corresponding methylketones or diketones by the $Pd(OAc)_2/NPMoV/O_2$ system, and the selectivity of the oxidation of dienes was dependent upon the chain length of the starting dienes.

Acknowledgements

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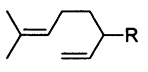
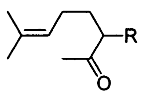
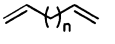
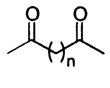
Table 3. Oxidation of various dienes using the Pd(II)/NPMoV catalytic system under dioxygen[a]

Run	Diene	Ketone	Time / h	Conv. / %[b]	Yield / %[b]
					
1[c]	R = H		2	50	34
2	R = H		2	>99 (>99)	92 (97)
3[d]	R = H		2	40	20
4	R = Me		5	>99 (>99)	82 (87)
					
5	n = 3		5	>99 (85)	59 (69)
6	n = 4		5	>99 (91)	41 (58)
7[e]	n = 10		5	>99	mixture

[a] Reaction conditions are shown in Ref. 19.

[b] Parentheses show the results by adding NaCl in place of NH_4Cl.

[c] In the absence of HQ.

[d] In the absence of NH_4Cl.

[e] A complex mixture of isomeric dienes, mono ketones and diketones was formed.

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13. Preparation of molybdovanadophosphate (NPMoV): To a solution of $NaVO_3$ (7.32 g, 60 mmol) in water (38 mL) was added $Na_2MoO_4{\cdot}2H_2O$ (8.22 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 as a brown precipitate. The NPMoV was purified by the recrystallization from water, and dried in vacuo with heating at about 90°C. The resulting NPMoV was a complex mixture of molybdovanadophosphate partly substituted by ammonium cation having an average atomic ratio of N/P/Mo/V = 5.0/1.0/4.0/7.8.[10] The average composition of the NPMoV is shown as $(NH_4)_5H_6PMo_4V_{7.8}O_{40}{\cdot}nH_2O$.
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17. A typical procedure for oxidation of terminal alkene: A solution of 5 wt% $Pd(OAc)_2/C$ (0.1 mmol), NPMoV (35 mg), NH_4Cl (0.1 mmol) and $MeSO_3H$ (0.2 mmol) in $EtOH:H_2O$ (19:1, 5 mL) was placed in a two-necked flask (30 mL) equipped with a balloon filled with O_2 and a dropping funnel. Then an $EtOH:H_2O$ (19:1, 10 mL) solution of alkene (2 mmol) in a dropping funnel was

added to the catalytic solution over a period of 5 h. The mixture was stirred for 0.5 h after completion of the addition. Products were separated by column chromatography over silica gel by hexane–ethyl acetate (gradient up to 9:1) to give ketone, which was characterized by ^{1}H and ^{13}C NMR. All yields were determined by GLC analyses using undecane as an internal standard. 5 wt% $Pd(OAc)_2$/C was prepared as follows: Activated carbon (Kurare BP-25) was grind up using the tumbling ball mill and then passed through a sieve (Opening: 75 μm, Wire diameter: 0.052 mm, Meshes: 200). The obtained activated carbon powder (6.65 g) was added to a solution of $Pd(OAc)_2$ (350 mg) in excess acetone. After stirring overnight at rt, 5 wt% $Pd(OAc)_2$/C was filtered off and dried in vacuo with heating at about 60°C. 5 wt% $Pd(OAc)_2$/C was obtained in quantitative yield.

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19. A typical procedure for oxidation of diene: A solution of diene (2 mmol), $Pd(OAc)_2$ (0.1 mmol), NPMoV (35 mg), HQ (0.4 mmol), NH_4Cl (0.4 mmol) and $MeSO_3H$ (0.2 mmol) in EtOH:H_2O (19:1, 10 mL) was placed in a round-bottomed flask (30 mL) equipped with a balloon filled with O_2. The mixture was stirred for 5 h. Products were separated by column chromatography over silica gel by hexane–ethyl acetate (gradient up to 15:1) to give ketone or diketone, which was characterized by ^{1}H and ^{13}C NMR. All yields were determined by GLC analyses using tridecane as an internal standard. Spectral data for 7-methyl-6-octen-2-one: ^{1}H NMR ($CDCl_3$/TMS) δ 1.59 (s, 3H), 1.63 (m, 2H), 1.69 (s, 3H), 1.98 (q-like, 2H, $J=7.3$ Hz), 2.13 (s, 3H), 2.41 (t, 2H, $J=7.4$ Hz), 5.07 (tt-like, 1H, $J=1.4$, 7.1 Hz); ^{13}C NMR ($CDCl_3$/TMS) δ 17.6, 23.8, 25.6, 27.1, 29.7, 43.0, 123.6, 132.2, 209.1; for 3,7-dimethyl-6-octen-2-one: ^{1}H NMR ($CDCl_3$/TMS) δ 1.01 (d, 3H, $J=6.9$ Hz), 1.22–1.35 (m, 1H), 1.52 (s, 3H), 1.57–1.70 (m, 1H), 1.61 (s, 3H), 1.88 (q-like, 2H, $J=7.6$ Hz), 2.06 (s, 3H), 2.44 (qt, 1H, $J=6.9$, 6.9 Hz), 5.00 (tt-like, 1H, $J=1.3$, 7.1 Hz); ^{13}C NMR ($CDCl_3$/TMS) δ 16.1, 17.6, 25.6, 25.6, 27.9, 32.9, 46.6, 123.7, 132.2, 212.8.