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Catalysis of Pd(II)-Catalyzed Acetalization of Alkenes with Diols

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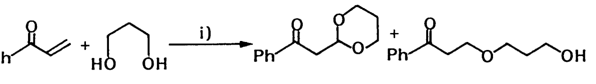
Alkenes bearing electron-withdrawing substituents are catalytically acetalized with 1,3-propanediol only by the use of $PdCl_2(MeCN)_2$ catalyst under O_2 atmosphere. When a combination of $BiCl_3$ and LiCl is used as co-catalyst, the acetalization proceeds effectively. These results indicate that a hydroperoxopalladium(II) species is most likely an active catalyst in the present reaction.

Pd(II)-catalyzed oxidation of alkenes with water (the Wacker oxidation), which has been widely used in organic syntheses,[1)] proceeds via nucleophilic attack of OH^- to coordinated alkenes followed by Pd–H elimination. Copper salts used as co-catalyst along with molecular oxygen is known to effect the catalytic cycle.[2)] The use of alcohols or diols, in place of water, induces acetalization of alkenes via similar processes.[3)] Synthetic utility of the acetalization has been demonstrated by a novel access of homochiral acetals from alkenes.[4,5)] Our systematic study of the reaction provides a new implication on the catalysis in which a hydroperoxopalladium(II) species derived from the oxygenation of Pd–H species with O_2 is the active catalyst. Efforts to reinforce this view led us to find that the acetalization proceeds catalytically even in the absence of a co-catalyst such as CuCl. In addition, a combination of $BiCl_3$ and LiCl serves as an efficient co-catalyst in place of CuCl. On the basis of these findings, we describe here the detail of the catalysis of the title reaction.

Results and Discussion

In contrast to the Wacker oxidation, alkenes bearing electron-withdrawing groups react smoothly with diols or alcohols. Phenyl vinyl ketone (**1**) was thus chosen as a typical substrate. $PdCl_2(MeCN)_2$ (10 mol%) catalyst was used in place of $PdCl_2$ because of higher solubility in 1,2-dimethoxyethane (DME). The acetalization of **1** with 1,3-propanediol (**2**) was performed in DME at 65 °C under O_2 atmosphere (1 atm) in the absence or presence of co-catalyst (Eq. 1).



1   2   3   4

i) $O_2/PdCl_2(MeCN)_2/DME$ (1)

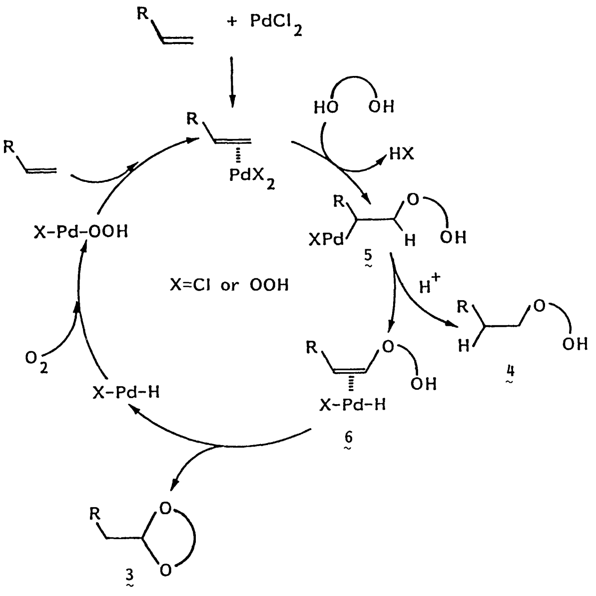
The results are given in Table 1. The catalytic acetalization evidently proceeds even in the absence of a co-catalyst. In order to obtain acetal **3** selectively, addition of Na_2HPO_4 (1.5 equiv per Pd) is required. In the absence of this base, simple addition of diol **2** to the olefin concurrently takes place to give **4** (Entry 1). The catalytic efficiency is obviously enhanced by employing CuCl as a co-catalyst (Entries 4 and 6); however, even in the absence of CuCl, use of a higher pressure of O_2 (10 atm) together with excess use of diol **2** (2 equiv per **1**) increases the catalytic turnover to give acetal **3** in 610% yield (based on Pd) (Entry 5). Catalytic acetalization does not take place in the absence of O_2.

A search for another feature of the catalysis led us to find that a combination of $BiCl_3$ and LiCl acts as an efficient co-catalyst. The use of $BiCl_3$ alone gives both **3** and **4** even in the presence of Na_2HPO_4 (Entry 7). When $BiCl_3$ is combined with LiCl in a ratio of 1:1, the acetal **3** is exclusively formed in 850% yield (Entry 8). This system appears to be superior to CuCl as the

Table 1. Acetalization of Phenyl Vinyl Ketone (**1**) with 1,3-Propanediol[a)]

Entry	Diol (mmol)	Na_2HPO_4 (mmol)	O_2 (atm)	Co-catalyst[b)]	Yield/%[c)] **3**	**4**
1	1.2	0	1	—	220[d)]	300[d)]
2	1.2	0.15	1	—	490	—
3	1.2	0.20	1	—	300	—
4	2.0	0.15	1	—	520	—
5	2.0	0.15	10	—	610	—
6	2.0	0.15	1	CuCl	710	—
7	2.0	0.15	1	$BiCl_3$	610[d)]	320[d)]
8	2.0	0.15	1	$BiCl_3$/LiCl[e)]	850	—
9	2.0	0.15	1	$BiCl_3$/LiCl[e)]	6700[f)]	—

a) The reaction was performed by using **1** (1 mmol) and $PdCl_2(MeCN)_2$ (0.1 mmol) in DME (3 mL) at 65 °C for 48 h. b) The amount of co-catalyst, when used, was 0.2 mmol. c) Unless otherwise noted, yield based on Pd was determined by GLC using pentadecane as an internal standard. d) Isolated yield by preparative TLC. e) The ratio used was 1:1. f) 1 mol% of catalyst was used.



Scheme 1.

co-catalyst, and the catalytic turnover of 67 can be attained, when the concentration of catalyst is reduced to 1 mol% (Entry 9).

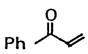
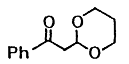
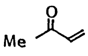
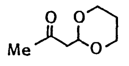
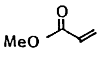
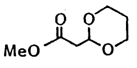
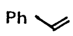
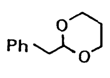
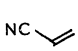
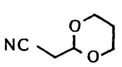
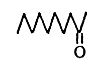
The reaction pathways of the acetalization can be envisioned as shown in Scheme 1. Coordination of the olefin to $PdCl_2$ followed by nucleophilic attack of diol with the loss of HCl gives oxypalladation intermediate **5**. Elimination of Pd–H species from **5** produces enol ether **6** which then cyclizes to acetal **3**. The resulting Pd–H species reacts with O_2 to give Pd–OOH species which acts as the active catalyst. Protonolysis of σ-bonded intermediate **5** with HCl leads to the prodcut **4**. If the PdHCl undergoes reductive elimination to give Pd(O) and HCl, the catalysis may be described as the conventional redox couples as shown in Eqs. 2 and 3.[1,2]

$$Pd^0 + 2CuX_2 \longrightarrow PdX_2 + 2CuX \qquad (2)$$

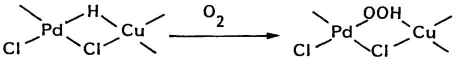
$$2CuX + 2HX + \tfrac{1}{2}O_2 \longrightarrow 2CuX_2 + H_2O \qquad (3)$$

This possibility is, however, ruled out as follows. In the presence of Na_2HPO_4, the catalytic acetalization takes place without forming by-product **4**, which indicates that HCl generated in situ is effectively captured by this base. Since the redox catalysis requires HCl in Eq. 3, the present reaction does not follow these equations. The validity of this argument is explicitly proven by the present result, because the catalytic acetalization occurs in the absence of copper salt. Further, the present result provides evidence that molecular oxygen directly participates into the catalysis. This allows us to consider that the oxygenation of Pd–H species with O_2 is crucial for the catalytic cycle.

Table 2. Acetalization of Olefins with 1,3-Propanediol[a)]

Entry	Alkene	Product	Yield/%[b)] Co-catalyst —	BiCl3–LiCl	CuCl
1			520	850[c)]	710
2			360	680[c)]	690
3			120	670	640
4			10	350	400[d)] (800)[e)]
5			nd	150	nd
6			—	150	210[f)]

a) The reaction was performed by using olefin (1 mmol), diol (2 mmol), $PdCl_2(MeCN)_2$ (0.1 mmol), Na_2HPO_4 (0.1 mmol), and co-catalyst (0.2 mmol) in DME (13 mL) at 65 °C under O_2 (1 atm) for 48 h. b) Isolated yield based on Pd. c) Reaction time was 24 h. d) Acetophenone was formed in 250% yield. e) Without using Na_2HPO_4, and in this case, no acetophenone was formed. f) Accompanied by the formation of 3- and 4-decanones (110%), and the ratio of 2-, 3-, and 4-decanones was 64:17:19.



7 8

The role of copper salt as the co-catalyst is to form a bimetallic complex linked with chloride ligand. The bimetallic complex **7** prevents decomposition of Pd–H species and accelerates the oxygenation of Pd–H bond by O_2.[6)] Similar complexation of bismuth salt with palladium enhances the catalytic activity. Bismuth chloride itself reacts with diol **2** to liberate HCl in situ. Therefore, for the selective formation of acetal **3** in this system, it is required to suppress the liberation of HCl through coordination of LiCl to bismuth.

Given in Table 2 are the typical results of the acetalization of olefins with diol **2** in the presence or absence of co-catalyst under the conditions using Na_2HPO_4. In all cases, the reactivity of olefins decreases with decreasing electron-withdrawing ability of substituents on the olefin (PhCO>MeCO>MeCOO>Ph>alkyl), indicating that the nucleophilic attack of diol is also a crucial step for the acetalization.[7)] In the case of acrylonitrile, coordination of CN group retards the reaction. The use of Na_2HPO_4 was effective to exclude the formation of by-product (e.g. **4**) from vinyl ketones. However, for the acetalization of other

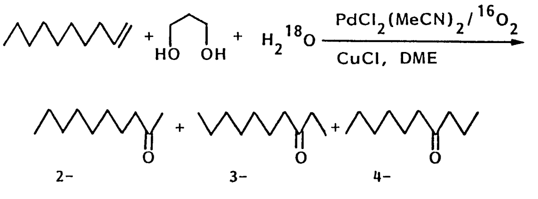
Table 3. Pd(II)-Catalyzed Reaction of 1-Decene with 1,3-Propanediol in the Presence of $H_2{}^{18}O$[a)]

Reaction time	Decanone				
h	Yield/%[b)]	Ratio 2- : 3- : 4-	^{18}O-Content/%[c)] 2-	 3-	 4-
1	190	56 : 20 : 24	51	57	62
24	630	34 : 26 : 40	31	35	36

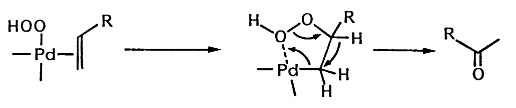
a) The reaction was performed by using 1-decene (1.0 mmol), $PdCl_2(MeCN)_2$ (0.1 mmol), CuCl (0.2 mmol), and $H_2{}^{18}O$ (1.0 mmol, CEA-ORIS, 98%) in DME (3 mL) at 65 °C. b) Yield based on Pd was determined by GLC using pentadecane as an internal standard. c) The ^{18}O-content was determined by GC-mass analysis.

olefins, addition of this base is not necessarily required, but it rather retards the reaction. For instance, in the absence of Na_2HPO_4, styrene reacts with diol **2** to give the corresponding acetal in 800% yield (Entry 4). This is certainly better result, when compared to that using Na_2HPO_4.

Alkyl-substituted olefins such as 1-decene gave no acetal, but the corresponding ketone was obtained (Entry 6). This result deserves comments. As shown in Table 3, the reaction of 1-decene with 1,3-propanediol (**2**) in the presence of $H_2{}^{18}O$ (1 equiv) under the conditions using CuCl as a co-catalyst (Eq. 5) results in the predominant formation of 3- and 4-decanones which arise from isomerization of the C=C double bond to internal olefins followed by oxidation. This fact does not agree with inferior reactivity of internal olefins in the Wacker oxidation.[1,2)] The ^{18}O-content in each of the resulting decanones is not high (31—36%, 24 h), and thus neither nucleophilic attack of water ($H_2{}^{18}O$) on the olefin nor hydrolysis of the corresponding acetal merely accounts for these observations. Therefore, the reaction must involve O-atom transfer to olefin from Pd-OOH derived from Pd-H and molecular oxygen ($^{16}O_2$). The O-atom transfer most likely proceeds via pseudo-peroxypalladation[8,9)] as shown below.[10)]



(5)



In summary, Pd(II)-catalyzed acetalization of olefins with diols evidently involves a hydroperoxopalladium(II) species as an active catalyst. Involvement of this species appears to be common in oxidations of this type.

Experimental

Materials. Palladium(II) chloride and copper(I) chloride were purchased from Wako Pure Chemical Ind., Ltd. Bismuth chloride and lithium chloride were purchased from Nakarai Chemicals, Ltd. Disodium hydrogenphosphate (Na_2HPO_4) was commercially available and dried (80 °C/2 mmHg, 2 h; 1 mmHg≈133.322 Pa) prior to use. Bis(aceonitrile)dichloropalladium(II) [$PdCl_2(MeCN)_2$] was prepared from $PdCl_2$ and acetonitrile.[11)] 1,3-Propanediol was distilled over sodium. Phenyl vinyl ketone was prepared by the literature procedure.[12)] Methyl vinyl ketone, methyl acrylate, styrene, acrylonitrile, and 1-decene were all commercially available and distilled prior to use. 1,2-Dimethoxyethane (DME) was distilled over calcium hydride under argon.

Acetalization of Phenyl Vinyl Ketone (1) with 1,3-Propanediol. (i) In the Absence of Na_2HPO_4 and Cocatalyst. In a 25 mL round-bottom flask equipped with a rubber balloon filled with oxygen gas and a magnetic stirring bar were placed $PdCl_2(MeCN)_2$ (27 mg, 0.10 mmol) and dry DME (1.5 mL). To the flask was added a solution of phenyl vinyl ketone (**1**) (135 mg, 1.02 mmol) and 1,3-propanediol (**2**) (92 mg, 1.21 mmol) in dry DME (1.5 mL), and the resulting suspension was stirred at 65 °C for 48 h. The reaction mixture was then filtered through a pad of Florisil (2 g, 14 mm×20 mm, ether 100 mL). Removal of the solvent followed by preparative TLC (SiO, hexane: AcOEt= 7:3) gave **3** (46 mg, 22.3%) and **4** (63 mg, 30.2%). Spectral and analytical data of these products are as follows.

2-Benzoylmethyl-1,3-dioxane (3): R_f 0.43 (SiO_2, hexane: AcOEt=7:3); IR (neat) 1690 (C=O), 1140 and 1090 cm^{-1}; ^1H NMR ($CDCl_3$, 60 MHz) δ=1.15—1.52 (m, 1H, $-CH_2-$), 1.73—2.53 (m, 1H, $-CH_2-$), 3.28 (d, J=5.0 Hz, 2H, $C(O)-CH_2-$), 3.60—4.33 (m, 4H, $O-CH_2-$), 5.18 (t, J=5.0 Hz, 1H, O-CH-O), 7.53—7.63 (m, 3H, ArH), and 7.85—8.14 (m, 2H, ArH). Found: C, 69.66; H, 6.97%. Calcd for $C_{12}H_{14}O_3$: C, 69.88; H, 6.84%.

3-(3-Hydroxypropoxy)-1-phenyl-1-propanone (4): R_f 0.11 (SiO_2, hexane: AcOEt=7:3); IR (neat) 3400 (OH), 1673, (C=O), 1210, 1075, and 1000 cm^{-1}; ^1H NMR ($CDCl_3$, 60 MHz) δ=1.61—2.02 (tt, J=5.0 and 5.0 Hz, 2H, $-CH_2-$), 2.87 (bs, 1H, OH), 3.18 (t, J=5.0 Hz, 2H, $C(O)-CH_2-$), 3.58 (t, J=5.0 Hz, 2H, $O-CH_2-$), 3.66 (t, J=5.0 Hz, 2H, $O-CH_2-$), 3.83 (t, J=5.0 Hz, 2H, $O-CH_2-$), 7.33—7.65 (m, 3H, ArH), and 7.86—8.12 (m, 2H, ArH). Found: C, 68.95; H, 7.76%. Calcd for $C_{12}H_{16}O_3$: C, 69.21; H, 7.74%.

(ii) In the Presence of Na_2HPO_4. The reaction was performed by the same procedure as above, except that Na_2HPO_4 (22 mg, 0.155 mmol) was added to the flask prior to addition of substrates. Similarly, $BiCl_3$ (65 mg, 0.2 mmol), LiCl (9 mg, 0.2 mmol), or CuCl (20 mg, 0.2 mmol), when used, was added into the flask in advance. Product yields were determined by GLC using pentadecane as an internal standard. Details are given in Table 1.

Acetalization of Olefins with 1,3-Propanediol. As outlined above, methyl vinyl ketone, methyl acrylate, styrene, and acrylonitrile were allowed to react with 1,3-propanediol, and products were isolated by column chromatography (Florisil or SiO_2) or Kugelrohr distillation. Results are given in Table 2, and spectral and analytical data of products are as follows.

2-(2-Oxopropyl)-1,3-dioxane (from Methyl Vinyl Ketone): R_f 0.42 (SiO_2, hexane:AcOEt=7:3); IR (neat) 1720 (C=O), 1135, 1080, 1060, 1050, and 1015 cm^{-1}; ^1H NMR ($CDCl_3$, 60 MHz) δ=1.16—1.55 (m, 1H, $-CH_2-$), 1.75—2.45 (m, 1H, $-CH_2-$), 2.17 (s, 3H, $-CH_3$), 2.68 (d, J=5.4 Hz, 2H, C(O)-CH-), 3.50—4.27 (m, 4H, O-CH_2-), 4.91 (t, J=5.4 Hz, 1H, O-CH-O); MS m/z 144 (M^+).

2-Methoxycarbonylmethyl-1,3-dioxane (from Methyl Acrylate): R_f 0.70 (SiO_2, hexane:AcOEt=7:3); IR (neat) 1740 (C=O), 1195, 1140, 1080, 1035, and 1000 cm^{-1}; ^1H NMR ($CDCl_3$, 60 MHz) δ=1.13—1.57 (m, 1H, $-CH_2-$), 1.70—2.33 (m, 1H, $-CH_2-$), 2.64 (d, J=5.8 Hz, 2H, C(O)-CH_2-), 3.53—4.32 (m, 4H, O-CH_2-), 3.60 (s, 3H, C(O)O-CH_3), 4.96 (t, J=5.8 Hz, 1H, O-CH-O). Fond: C, 52.37; H, 7.50%. Calcd for $C_7H_{12}O_4$: C, 52.49; H, 7.55%.

2-Benzyl-1,3-dioxane (from Styrene): Kugelrohr distillation; 89—92 °C/1 mmHg; IR (neat) 1080 and 1015 cm^{-1}; ^1H NMR ($CDCl_3$, 60 MHz) δ=1.07—1.52 (m, 1H, $-CH_2-$), 1.65—2.48 (m, 1H, $-CH_2-$), 2.89 (d, J=5.4 Hz, 2H, Ph-CH_2-), 3.42—4.28 (m, 4H, O-CH_2-), 4.65 (t, J=5.4 Hz, 1H, O-CH-O), 7.21 (s, 5H, ArH). Found: C, 73.96; H, 7.97%. Calcd for $C_{10}H_{14}O_2$: C, 74.13; H, 7.92%.

2-Cyanomethyl-1,3-dioxane (from Acrylonitrile): IR (neat) 2270 (CN), 1130 and 1030 cm^{-1}; ^1H NMR ($CDCl_3$, 60 MHz), δ=1.10—1.70 (m, 1H, $-CH_2-$), 1.70—2.43 (m, 1H, $-CH_2-$), 2.55 (d, J=5.0 Hz, 2H, NC-CH_2-), 3.45—4.30 (m, 4H, O-CH_2-), 4.67 (t, J=5.0 Hz, 1H, O-CH-O).

Ketonization of 1-Decene with 1,3-Propanediol. The reaction was performed by using $PdCl_2(MeCN)_2$ (130 mg, 0.50 mmol), $BiCl_3$ (316 mg, 1.00 mmol), LiCl (43 mg, 1.01 mmol), Na_2HPO_4 (110 mg, 0.77 mmol), 1-decene (705 mg, 5.02 mmol), 1,3-propanediol (763 mg, 10.0 mmol), and dry DME (10 mL) at 65 °C for 48 h. Florisil column chromatography (20 g, 28 mm×80 mm) with elution of hexane-CH_2Cl_2 (1:1) gave 2-decanone (121 mg, 15%).

The reaction using CuCl was performed in 1 mmol scale; 1-decene (140 mg, 1.0 mmol), 1,3-propanediol (152 mg, 2.00 mmol), $PdCl_2(MeCN)_2$ (26 mg, 0.10 mmol), CuCl (20 mg, 0.20 mmol), Na_2HPO_4 (22 mg, 0.15 mmol), and dry DME (3 mL). SiO_2 column chromatography (6 g, 18 mm×50 mm) gave a mixture of 2-, 3-, and 4-decanones (50 mg, 32%) in a ratio of 64:17:19. The ratio was determined by GLC (Shimadzu Model GC-MINI 2 flame ionization chromatography) using glass capillary column (25 m×0.25 mm PEG-20 M, chemical bonded column).

Ketonization of 1-Decene with 1,3-Propanediol in the Presence of $H_2{}^{18}O$. In a 25 mL side-arm round-bottom flask equipped with a rubber balloon filled with oxygen gas and a magnetic stirring bar were placed $PdCl_2(MeCN)_2$ (27 mg, 0.10 mmol), CuCl (20 mg), and dry DME (1 mL). To the flask was subsequently added a solution of 1,3-propanediol (152 mg, 2.0 mmol) in dry DME (1 mL), $H_2{}^{18}O$ (20 µl, 1.0 mmol, CEA-ORIS, 98%), and a solution of 1-decene (140 mg, 1.0 mmol) and pentadecane (38.51 mg, internal standard for GLC) in DME (1 mL). The resulting suspension was stirred at 65 °C, and aliquot samples were analyzed by GLC (Shimadzu Model GC-8A, 1 m SE-30 column) and GC-mass (JEOL Model MS-GCG 06, 30 m× 0.25 mm DB-1 capillary column, J&W Scientific Inc.). Details are given in Table 3.

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7) The catalytic efficiency increases with increasing the O_2 pressure, but the effect is not remarkable. Thus, under the present conditions, nucleophilic attack of diol must be a turnover limiting step.

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