Palladium(II)-Catalyzed Acetalization of Terminal Olefins Bearing Electron-Withdrawing Substituents with Optically Active Diols

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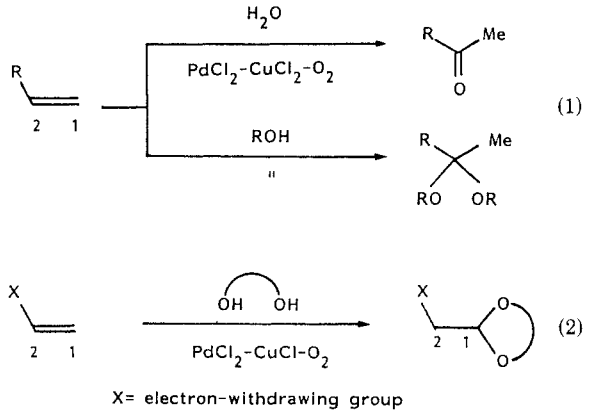
Terminal olefins bearing electron-withdrawing substituents such as CH_2=CHCOR (R = Ph, Me, *t*-Bu), CH_2=CHCOOMe, and CH_2=CHCN are regioselectively acetalized at the terminal carbon (C_1) by diols in the presence of $PdCl_2$ (0.1 equiv) and CuCl (1 equiv) in DME at 50 °C under an atmosphere of O_2 (1 atm). The use of optically active (*R,R*)-2,4-pentanediol (**4**) gives homochiral cyclic acetals of aldehyde precursors in good yields. The acetalization of CH_2=CHCOR is accompanied by the formation of Michael-type adducts such as **3a** (R = Ph). However, of importance is that their formation can be prevented by the use of Na_2HPO_4 as an additive. Although in an early stage of the reaction of CD_2=CHPh with **4**, a statistical *d* scrambling of the starting olefin occurs, no such scrambling is observed with CD_2=CHCOPh. Additionally, the acetalization of CD_2=CHCOPh with **4** results in 1,2 deuterium migration, together with 25% *d* loss. These results are accounted for by the reaction pathways involving oxypalladation, Pd-H elimination, and subsequent ring closure giving enol ether. A catalytic cycle involving the oxygenation of Pd-H species with molecular oxygen is proposed.

The Pd(II)-catalyzed oxidation of terminal olefins (R = alkyl) with water, which is well-known as the Wacker reaction, produces methyl ketones (eq 1).[1] A similar reaction in alcohols gives their acetals. These products arise via the attack of oxygen nucleophiles at the nonterminal olefinic carbon (C_2). If the attack at the terminal carbon (C_1) occurs selectively to give aldehydes or their precursors, the synthetic usefulness of the reactions will be certainly enhanced. However, there has been no systematic study from such a viewpoint.[2] We have recently found that terminal olefins bearing electron-withdrawing groups, upon treatment with diols in the presence of a Pd(II) catalyst, afford cyclic acetals via attack at the C_1 carbon (eq 2).[3] The use of optically active diols such as readily available (*R,R*)-2,4-pentanediol in the reaction provides a powerful strategy for preparing chiral cyclic acetals from olefins. Recently, such acetals have been extensively utilized as the chiral auxiliary in the field of asymmetric synthesis.[4]



X= electron-withdrawing group

Furthermore, cyclic acetals, which are usually prepared from aldehydes or ketones,[5] are able to be transformed into a variety of compounds such as esters[6] and ethers.[7] Considering this background, we describe the full detail of Pd(II)-catalyzed acetalization of terminal olefins with optically active diol **4** and its mechanistic aspects.

Results and Discussion

The Wacker oxidation of ethylene to acetaldehyde by $PdCl_2$, $CuCl_2$, and molecular oxygen has been carried out in aqueous medium containing HCl.[8] For the conversion of higher terminal olefins into methyl ketones, the original procedure was improved by utilizing aqueous dimethylformamide (DMF) as the solvent.[9] Copper(I) chloride has also been shown to be superior to $CuCl_2$ as the cocatalyst,[9c] since it minimizes undesired byproducts such as chlorinated compounds Under similar conditions, vinyl ketone **1b** (R = Me) was first allowed to react with 1 equiv of (*R,R*)-2,4-pentanediol (**4**)[10] in various solvents [$PdCl_2$/CuCl/substrate = 1/10/10, O_2 (1 atm, balloon), 50 °C, 20 h]. As the result, a fairly good yield (66%) of cyclic acetal **2b**, together with **3b** (12%), was obtained in dimethoxyethane (DME) (eq 3). DMF was not a good solvent for the reaction. The use of $CuCl_2$ in place of CuCl is not suitable, since **3a** (R = Ph) is formed in poor yield (17%) along with a variety of small amounts of byproducts.

In Table I are summarized the results of the acetalization of a series of vinyl ketones **1** with diols **4-6** under the above conditions. The C_1 carbon of terminal olefins is

(1) For comprehensive reviews, see: Tsuji, J. *Synthesis* **1984**, 369.

(2) Pd(II)-catalyzed acetalization of olefins, see: (a) Lloyd, W. G.; Luberoff, B. J. *J. Org. Chem.* **1969**, *34*, 3949. (b) Byrom, N. T.; Grigg, R.; Kongkathip, B.; Reimer, G.; Wade, A. R. *J. Chem. Soc., Perkin Trans. 1* **1984**, 1643. (c) Uchiumi, S.; Iwayama, A.; Abe, H.; Matsunaga, H. Jpn. Kokai Tokkyo Koho JP 56-5429, 1981. Uchiumi, S.; Iwayama, A.; Umezu, T. Ibid. JP 57-106635, 1982. (d) Matsumoto, M.; Kuroda, K. Ibid. JP 55-9029, 1980.

(3) Hosokawa, T.; Ohta, T.; Murahashi, S.-I. *J. Chem. Soc., Chem. Commun.* **1983**, 848.

(4) For recent reports in this area, see: (a) Elliott, J. D.; Steele, J.; Johnson, W. S. *Tetrahedron Lett.* **1985**, *26*, 2535. Johnson, W. S.; Edington, C.; Elliott, J. D.; Silverman, I. R. *J. Am. Chem. Soc.* **1984**, *106*, 7588 and preceeding papers in the series. (b) Mori, A.; Yamamoto, H. *J. Org. Chem.* **1985**, *50*, 5444; Maruoka, K.; Yamamoto, H. *Angew. Chem., Int. Ed. Engl.* **1985**, *24*, 668. (c) Ghribi, A.; Alexakis, A.; Normant, J. F. *Tetrahedron Lett.* **1984**, *25*, 3083.

(5) For recent reports on the acetalization of carbonyl compounds, see: (a) Meskens, F. A. J. *Synthesis* **1981**, 501. (b) Chan, T. H.; Brook, M. A.; Chaly, T. *Ibid.* **1983**, *203*. (c) Tsunoda, T.; Suzuki, M.; Noyori, R. *Tetrahedron Lett.* **1980**, *21*, 1357.

(6) (a) Deslongchamps, P.; Moreau, C.; Frêhel, D.: Chênevert, R. *Can. J. Chem.* **1975**, *53*, 1204. (b) Hosokawa, T.; Imada, Y.; Murahashi, S.-I. *J. Chem. Soc., Chem. Commun.* **1983**, 1245. (c) Sugai, S.; Kodama, T.; Akaboshi, S.; Ikegami, S. *Chem. Pharm. Bull.* **1984**, *32*, 99. (d) Mukaiyama, T.; Kato, J.; Miyoshi, N.; Iwasawa, N. *Chem. Lett.* **1985**, 1255.

(7) (a) Hosomi, A.; Endo, M.; Sakurai, H. *Chem. Lett.* **1976**, 941; **1978**, 499. (b) Ito, Y.; Imai, H.; Segoe, K.; Saegusa, T. *Ibid.* **1984**, 937. (c) Ghribi, A.; Alexakis, A.; Normant, J. F. *Tetrahedron. Lett.* **1984**, *25*, 3075. (d) Mioskowski, C.; Manna, S.; Falk, J. R. *Tetrahedron Lett.* **1984**, *25*, 519. (e) Borders, R. J.; Bryson, T. A. *Chem. Lett.* **1984**, 9.

(8) Smidt, J.; Hafner, W.; Jira, R.; Sieber, R.; Sedlmeier, J.; Sable, A. *Angew. Chem., Int. Ed. Engl.* **1962**, *1*, 80. For comprehensive reviews, see: (a) Maitlis, P. M. *The Organic Chemistry of Palladium*; Academic: New York, 1971; Vol. 2. (b) Henry, P. M. *Palladium Catalyzed Oxidation of Hydrocarbon*; Reidel: Dordrecht, Holland, 1980.

(9) (a) Clement, W. H.; Selwitz, C. M. *J. Org. Chem.* **1964**, *29*, 241. (b) McQuillin, F. J.; Parker, D. G. *J. Chem. Soc., Perkin Trans. 1* **1974**, 809. (c) Tsuji, J.; Nagashima, H.; Nemoto, H. *Org. Synth.* **1984**, *62*, 9.

(10) Tai, A.; Ito, K.; Harada, T. *Bull. Chem. Soc. Jpn.* **1981**, *54*, 223.

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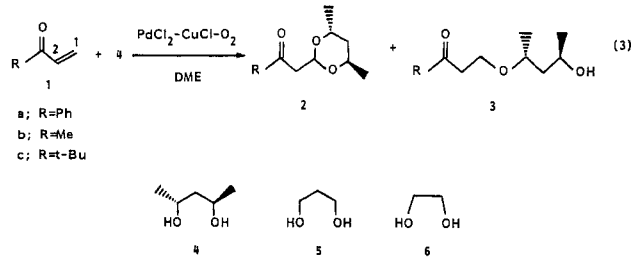
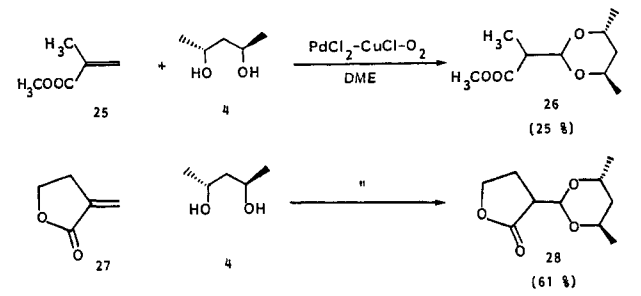


regioselectively acetalized. Neither acetalization of the carbonyl group in **1** nor racemization of the chiral carbon in **2** and **3** takes place during the reaction. Although the reactions are accompanied by the formation of Michael-type adducts **3**, **8**, and **10** as the byproducts, their formation is suppressed by using Na_2HPO_4 as an additive. This detail will be described later. When the reactivity among diols was compared, 1,3-diols seemed to be more reactive than 1,2-diols (entries 2, 8, and 12).

In Table II are given the results of the acetalization of other terminal olefins. Methyl acrylate is acetalized at the C_1 carbon selectively. Regardless of the structural variance in the diol, good yields of the acetals **12** and **13** are obtained (entries 1 and 2). Acrylonitrile, *o*-methylstyrene, and styrene are also acetalized at the C_1 carbon selectively[11] (entries 3–6). No Michael adducts were detected in these reactions. The reactivity of these olefins may correlate with the decrease in the π-electron density of olefins[12] as well as their coordination ability to Pd(II). In the case of CH_2=CHCN, competitive coordination of the CN group to Pd(II)[13] retards the reaction.

With terminal olefins bearing alkyl groups, oxygen nucleophiles preferentially attack at the C_2 carbon. Thus, in the case of allylbenzene and 1-decene, methyl ketones or the corresponding acetals are formed (entries 7 and 8). Such a preferential attack at the C_2 carbon has been utilized in the synthesis of natural and unnatural frontalines via intramolecular acetalization of an optically active diol.[14]

While no reaction takes place with CH_2=$CRCOCH_3$ (R = CH_3, Ph), methyl methacrylate gives a lower yield (25%) of acetal **26**[15] as a mixture of two diastereomers in 20% diastereomeric excess (de). However, less sterically hindered α-methylene-γ-butyrolactone affords a 61% yield of acetal **28** (4% de).



(11) The regioselectivity for the attack of oxygen nucleophiles to styrene has been shown to change with various conditions such as the ligand of Pd(II), see: Reference 8a, pp 90–91.

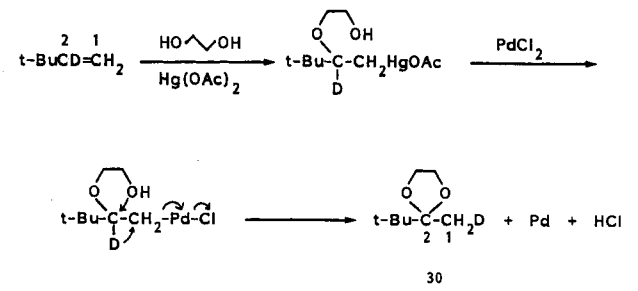
(12) The π-electron density of vinyl compounds is estimated by the ^{13}C NMR chemical shifts; see: Hatada, K.; Nagata, K.; Hasegawa, T.; Yuki, H. *Makromol. Chem.* **1977**, *178*, 2431 and references therein.

(13) Lenarda, M.; Nardin, G.; Pellizer, G.; Braye, E.; Graziani, M. *J. Chem. Soc., Chem. Commun.* **1985**, 1536.

(14) Hosokawa, T.; Makebe, Y.; Shinohara, T.; Murahashi, S.-I. *Chem. Lett.* **1985**, 1529.

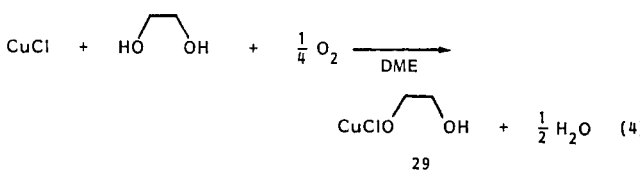
(15) The reaction is classified as the enantioface-differentiating Wacker-type reaction. For related reactions, see: (a) Hosokawa, T.; Uno, T.; Inui, S.; Murahashi, S.-I. *J. Am. Chem. Soc.* **1981**, *103*, 2318. (b) Bäckvall, J.-E.; Björkman, E. E.; Byström, E. S.; Solladié-Cavallo, A. *Tetrahedron Lett.* **1982**, *23*, 943. (c) Solladié-Cavallo, A.; Haesselein, J.-L. *Helv. Chim. Acta* **1983**, *66*, 1760.

Scheme I



Among the terminal olefins examined, only vinyl ketones produce the Michael adducts. Particularly, a relatively high amount of **3a**[16] is formed (entry 1, Table I). As already mentioned, the use of dibasic sodium phosphate (Na_2HPO_4, pH 8) as an additive prevents its formation. Considering that the additive may act as a proton scavenger, the effect of bases such as NaH_2PO_4 and K_2CO_3 on the reaction was examined. As shown in Table III, a good yield (84%) of the acetal **2a** was formed when the dibasic phosphate was used in a ratio of Na_2HPO_4/CuCl/$PdCl_2$ = 1/1/1 (entry 4), and no Michael adduct **3a** was formed. Under these conditions, even if the amount of $PdCl_2$ is decreased to 5 mol%, the acetal **2a** is obtained in 71% yield as the sole product.

We have already noted[17] that in the reaction of **1a** with **6** (entry 11, Table I) increasing the amount of CuCl relative to $PdCl_2$ also decreases the relative yield of the Michael adduct **10a**, e.g., **10a**/**9a** = 50/50 and 25/75 when CuCl/$PdCl_2$ = 1/1 and 50/1, respectively. When the alkoxide **29**, prepared from ethylene glycol and excess CuCl as shown in eq 4, was allowed to react with vinyl ketone **1a**, only the acetal **9a** was formed in 50% yield (see the Experimental Section). Therefore, the above phenomenon is ascribed to in situ formation of copper(II) alkoxide **29**, which acts as a base in the reaction.



Mechanistic Aspect. Hunt and Rodeheaver[18] have reported the acetalization of terminal olefins such as styrene and 1-hexene with ethylene glycol via oxymercuration of olefins, followed by transmetalation with $PdCl_2$. Although the reaction proceeds catalytically with respect to palladium in the presence of excess $CuCl_2$, it requires a stoichiometric amount of $Hg(OAc)_2$ for the oxymercuration step. Their study has shown that the acetal **30** (see Scheme I) that is formed in the reaction using 3,3-dimethyl-1-butene-2-d_1 retains 86% of the deuterium label at the C_1 carbon. On the basis of this result, concerted or stepwise palladium-assisted 1,2 migration of deuterium from C_2 to C_1 carbon has been proposed as the major reaction pathway as shown in Scheme I.

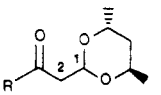
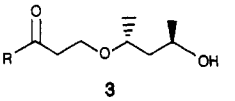
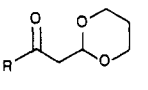
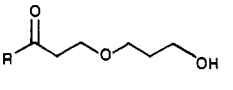
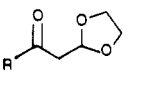
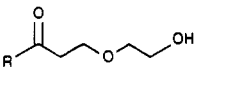
Hunt's acetalization is one of the reactions that is closely related to the present study, but it is not certain whether their mechanism is actually operative in the present sys-

(16) In the earlier experiments,[3] CuCl left standing for several months in the laboratory was used. In these cases, the yield of **3a** was less than 5%. However, when CuCl of a commercial reagent grade (Tokyo Kasei) was used as received, a relatively high yield of **3a** (33%) was formed, and the results were reproducible.

(17) For detailed results, see: Reference 3.

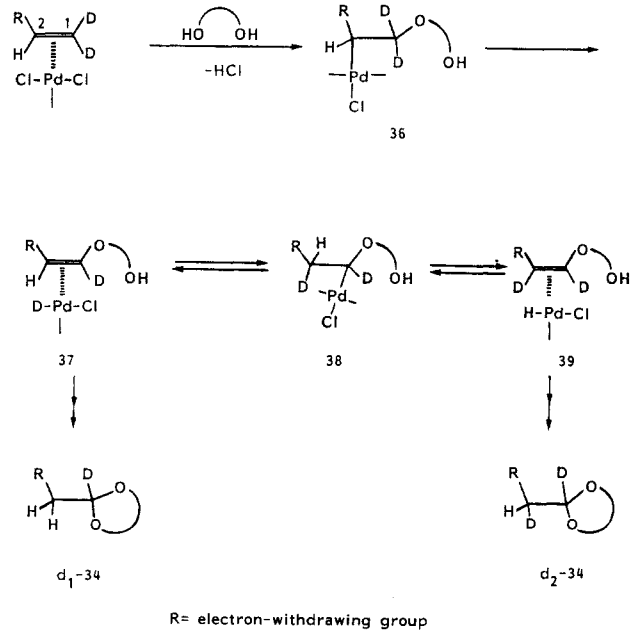
(18) Hunt, D. F.; Rodeheaver, G. T. *Tetrahedron Lett.* **1972**, 3595.

Table I. Acetalization of Vinyl Ketones 1 with Diols 4-6[a]

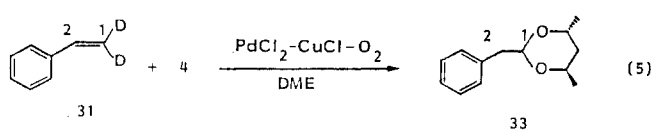
entry	vinyl ketone RCOCH=CH$_2$ no.	R	diol	additive[b]	isolated yield, % acetal	Michael adduct
					 2	 3
1	1a	Ph	4		2a (41)	3a (33)
2	1a	Ph		Na_2HPO_4	2a (75)	3a (0)
3	1b	Me			2b (66)	3b (12)
4	1b	Me		Na_2HPO_4	2b (69)	3b (0)
5	1c	*t*-Bu			2c (63)	3c (8)
6	1c	*t*-Bu		Na_2HPO_4	2c (64)	3c (0)
					 7	 8
7	1a	Ph	5		7a (42)	8a (14)
8	1a	Ph		Na_2HPO_4	7a (82)	8a (0)
9	1b	Me			7b (45)	8b (~5)
10	1c	*t*-Bu			7c (52)	8c (nd)[c]
					 9	 10
11	1a	Ph	6		9a (20)	10a (10)
12	1a	Ph		Na_2HPO_4	9a (55)	10a (0)
13	1b	Me			9b (33)	10b (~5)
14	1c	*t*-Bu			9c (38)	10c (~5)

[a] Reaction conditions: vinyl ketone (2 mmol), diol (2 mmol), $PdCl_2$ (0.2 mmol), CuCl (2 mmol), DME (2 mL), 50 °C, O_2 (1 atm). [b] In this case, the reaction was performed by using 1 mmol of vinyl ketone 1 in a ratio of 1/diol/$PdCl_2$/CuCl/Na_2HPO_4 = 10/10/1/1/1 in DME (1.5 mL) under otherwise the same conditions as above. [c] Note determined in this case.

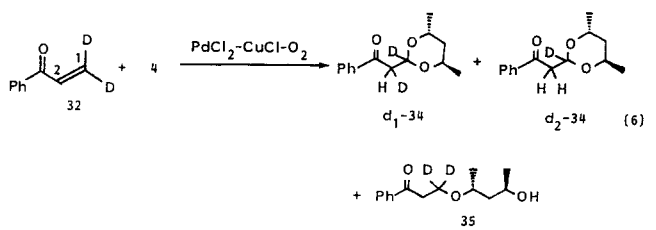
Scheme II



tem. Accordingly, we have studied the acetalization of CD_2=CHPh (**31**) and CD_2=CHCOPh (**32**) with (*R,R*)-2,4-pentanediol (**4**). NMR analysis of the acetal **33** derived from CD_2=CHPh (eq 5) has shown that its C_1 and C_2

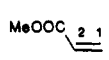
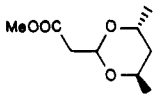
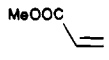
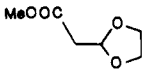
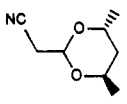
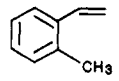
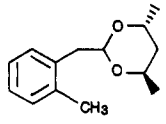
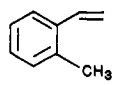
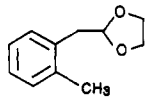
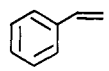
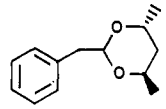
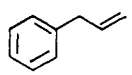
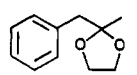
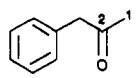
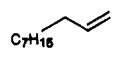
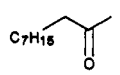


carbons bear 1.20 and 0.80 deuterium, respectively. However, the value of deuterium distribution itself is not meaningful, because at the early stage of the reaction a statistical distribution of deuterium takes place on the C_1 and C_2 carbon of the starting styrene-d_2. Nevertheless, the facile H–D scrambling in the styrene-d_2 is of importance, since it strongly suggests that the present reaction involves a Pd–H(D) species (vide infra). In the case of CD_2=CHCOPh (**32**), no deuterium scrambling of the starting olefin occurs during the course of the reaction. The product acetal **34** obtained retains 75% of the deuterium label, and the *d* contents of the C_1 and C_2 carbons are approximately 1.00 and 0.50, respectively. This means that 1,2 deuterium migration from C_1 to C_2 carbon takes place together with 25% of *d* loss. In other words, the acetals-d_2 and -d_1 **34** are formed in a ratio of 1/1 (eq 6). In the Michael adduct **35** formed together, neither deuterium migration nor loss was detected. These results can be best accounted for by the reaction pathways involving a Pd–H intermediate as shown in Scheme II.



Coordination of the olefin to $PdCl_2$ followed by oxypalladation with the loss of HCl gives the σ-bonded palladium(II) intermediate **36**, where the oxygen nucleophile prefers to attack the more electron-deficient carbon atom (C_1) of the olefin. The polarity of the double bond[12] in-

Table II. Acetalization of Various Terminal Olefins[a]

entry	olefin	diol	acetal	isolated yield, %
1	 11	4	 12	79
2	 11	6	 13	72
3	 14	4	 15	45
4	 16	4	 17	84
5	 16	6	 18	77
6	 19	4	 20	79
7	 21	6	 22	14
			 23	40
8	 24	4		43[b]

[a] Reaction conditions, see: footnote *a*, Table I. [b] The reaction was carried out in the presence of Na_2HPO_4 (0.1 equiv).

duced by an electron-withdrawing substituent is, thus, one of the factors governing the C_1 attack in the present reaction. Elimination of deuterium from the C_1 carbon of **36** leads to (π-olefin)Pd–D species **37**, which is in equilibrium with (π-olefin)Pd–H **39** via an addition–elimination sequence. Ring closure of the resulting enol ether, assisted by either palladium(II) or a proton, produces the corresponding acetals-d_1 and -d_2 **34**. As shown below, treatment of the enol ether **40** with HCl or $PdCl_2(CH_3CN)_2$ in the presence of NEt_3 in DME gives the acetal **41** (see the Experimental Section), which supports the ring-closure pathway proposed.

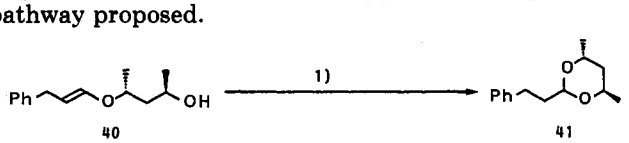
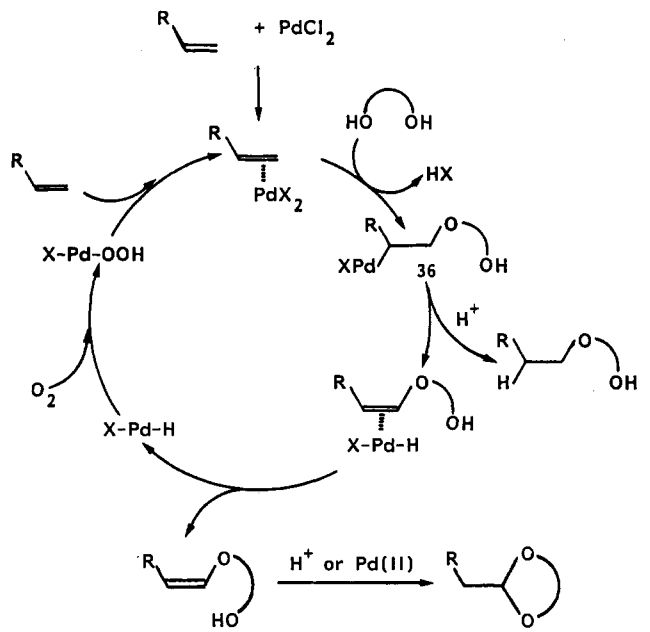


Table III. Pd(II)-Catalyzed Reaction of Phenyl Vinyl Ketone (1a) with (*R*,*R*)-2,4-Pentanediol (4) in the Presence of Base[a]

entry	cocatalyst (equiv)[c]	base (equiv)[c]	yield,[b] % acetal **2a**	yield,[b] % Michael adduct **3a**
1	CuCl (10)		41[e]	33[e]
2	CuCl (10)	Na_2HPO_4 (3)	58	0
3	CuCl (1)	Na_2HPO_4 (2)	73	0
4	CuCl (1)	Na_2HPO_4 (1)	84	0
5	CuCl (1)	Na_2HPO_4 (0.5)	67	20
6	CuCl (1)	NaH_2PO_4 (1)	64	16
7	CuCl (10)	NEt_3 (2)	22	0
8	CuCl (10)	Proton Sponge[d] (2)	27	2–5
9	CuCl (10)	K_2CO_3 (3)	34	0
10	$CuCO_3$·Cu(O-H)$_2$·H_2O (10)		33	2

[a] Reaction conditions: **1a** (1 mmol), **4** (1 mmol), $PdCl_2$ (0.1 mmol), DME (1.5 mL), 50 °C, O_2 (1 atm), 20 h. [b] GLC yield (pentadecane as the internal standard). [c] Equivalents per $PdCl_2$ used. [d] *N,N,N′,N′*-Tetramethyl-1,8-naphthalenediamine. [e] Isolated yield.

Scheme III



In the catalytic cycle depicted in Scheme III, protonation of the σ-bonded Pd(II) intermediate **36** with HCl[19] leads to the Michael adduct.[20] When the substituent R is a highly electron-withdrawing group such as PhCO, the Pd–C bond in **36** must be destabilized, being susceptible to heterolytic cleavage. Hence, only vinyl ketones give the Michael adducts. The Pd–H species generated via **36** will react with O_2 to give Pd–OOH,[21] thereby completing the catalytic cycle as shown in Scheme III. If the PdHCl decomposes to Pd(0) and HCl, the catalysis is described as the conventional redox couples shown in eq 7 and 8.

(19) Protonolysis of a σ bond of palladium(II) species has been recently proposed in the Pd(II)-catalyzed conjugated addition of aryl iodides with α,β-unsaturated ketones; see: Cacchi, S.; Arcadi, A. *J. Org. Chem.* **1983**, *48*, 4236.

(20) The Michael adduct is not a precursor of the acetal, since the treatment of **3b** (R = Me) with $PdCl_2$–CuCl–O_2 under the normal conditions gives only a trace amount of acetal **2b**.

(21) The oxygenation of Pd–H by O_2 has been already proposed; see: (a) Reference 15a and other references cited therein. (b) Muzart, J.; Pete, J. P. *J. Mol. Catal.* **1982**, *15*, 373.

However, such discrete processes seem to be unlikely, because if no formation of the Michael adduct in the presence of base means the capture of HCl, then eq 8 requiring HCl is not justified.

$$Pd(0) + 2CuCl_2 \rightarrow PdCl_2 + 2CuCl \quad (7)$$

$$2CuCl + 2HCl + {}^1/_2O_2 \rightarrow 2CuCl_2 + H_2O \quad (8)$$

Experimental Section

General Procedures. NMR spectra were recorded on a 60-MHz Model JNM-MH-60 (JEOL), PMX-60 SI (JEOL), or a 100-MHz Model JMN-FX-100 (JEOL) spectrometer. IR spectra were recorded on a Hitachi 215 spectrometer. GLC analyses were carried out on a JEOL Model JGC-20-KFP flame-ionization chromatograph using a 1 m × 1 mm 10% PEG 20 M on 80–120-mesh Uniport HP with injection temperature 200 °C and column temperature 100–230 °C. Mass spectra were obtained on a Hatachi RSM-4 mass spectrometer. Elemental analyses were determined on a Yanagimoto MT-2 CHN recorder.

Materials. Commercially available (*R,R*)-2,4-pentanediol was used as received. Its optical purity was 96.9% [$[\alpha]^{25}_D$ +52.3° (*c* 10, EtOH)]. 1,3-Propanediol and ethylene glycol were distilled over Na. Methyl vinyl ketone, methyl acrylate, acrylonitrile, methyl methacrylate, *o*-methylstyrene, styrene, and allylbenzene were all commercially available and distilled prior to use. Phenyl vinyl ketone[22] and *tert*-butyl vinyl ketone[23] were prepared according to the literature procedures. Palladium(II) chloride and copper(I) chloride were purchased from Wako Pure Chemical Ind., Ltd. Dimethoxyethane (DME) was dried over CaH and distilled.

Acetalization of Vinyl Ketones 1: General Procedure. In a 25-mL flask fitted with a rubber balloon filled with oxygen and containing a Teflon-coated magnetic stirring bar were placed $PdCl_2$ (0.035 g, 0.2 mmol) and CuCl (0.198 g, 2 mmol). Into the flask was added a solution of vinyl ketone **1** (2 mmol) and diol (2 mmol) in DME (2 mL), and the resulting suspended solution was stirred for 20 h at 50 °C under an oxygen atmosphere. After the reaction mixture was cooled to room temperature, ether (20 mL) was added into the mixture. The resulting insoluble materials were removed by filtration, and the filtrate was concentrated under reduced pressure. The products were separated by means of Florisil column chromatography (2 g, hexane–ether) and purified by Kugelrohr distillation or by preparative TLC. The yields of acetals and Michael adducts are summarized in Table I.

When other solvents in place of DME were used, the isolated yields of **2b** (R = Me) were 43 (THF), 40 (acetone), 24 (benzene), 17 (DMF), 13 (dioxane), and 10% (diglyme). The reaction conditions using Na_2HPO_4 are described in footnote *b* in Table I.

Acetal 2a: R_f 0.60; bp 119–121 °C (1 mmHg); IR (neat) 1700 (C=O), 1220, 1140, 1023 cm^{-1}; ^1H NMR ($CDCl_3$, 60 MHz) δ 1.20–1.45 (m, 1 H, CH_2), 1.18 (d, *J* = 6.0 Hz, 3 H, CH_3), 1.38 (d, *J* = 6.2 Hz, 3 H, CH_3), 1.60–2.11 (m, 1 H, CH_2), 3.22 (d, *J* = 5.2 Hz, 2 H, $C(O)CH_2$), 3.73–4.45 (m, 2 H, OCH), 5.47 (t, *J* = 5.2 Hz, 1 H, –OCHO–), 7.23–7.53 (m, 3 H, ArH), 7.75–8.00 (m, 2 H, ArH). Anal. Calcd for $C_{14}H_{18}O_3$: C, 71.77; H, 7.74. Found: C, 71.28; H, 7.74.

Acetal 2b: bp 92–95 °C (1 mmHg; Kugelrohr); IR (neat) 1725 (C=O), 1137, 1062, 1000 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.17 (d, *J* = 6.0 Hz, 3 H, CH_3), 1.24–1.38 (m, 1 H, CH_2), 1.36 (d, *J* = 6.6 Hz, 3 H, CH_3), 1.64–1.94 (m, 1 H, CH_2), 2.16 (s, 3 H, $C(O)CH_3$), 2.62 (d, *J* = 5.6 Hz, 2 H, $C(O)CH_2$), 3.76–4.36 (m, 2 H, OCH), 5.20 (t, *J* = 5.6 Hz, 1 H, –OCHO–). Anal. Calcd for $C_9H_{16}O_3$: C, 62.76; H, 9.36. Found: C, 62.39; H, 9.34.

Acetal 2c: bp 110–120 °C (1 mmHg; Kugelrohr); IR (neat) 1718 (C=O), 1165, 1045, 1003, 930 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.12 (s, 9 H, *t*-Bu), 1.15 (d, *J* = 6.4 Hz, 3 H, CH_3), 1.20–1.39 (m, 1 H, CH_2), 1.37 (d, *J* = 7.0 Hz, 3 H, CH_3), 1.62–1.93 (m, 1 H, CH_2), 2.70 (d, *J* = 5.0 Hz, 2 H, $C(O)CH_2$), 3.77–4.35 (m, 2 H, OCH), 5.20 (t, *J* = 5.0 Hz, 1 H, –OCHO–). Anal. Calcd for $C_{12}H_{22}O_3$: C, 67.25; H, 10.35. Found: C, 66.95; H, 10.24.

Acetal 7a: 3.58–4.40 0.47; IR (neat) 1698 (C=O), 1335, 1220, 1132, 1090, 1020, 982, 931, 838, 756, 694 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.15–1.52 (m, 1 H, CH_2), 1.72–2.52 (m, 1 H, CH_2), 3.28 (d, *J* = 5.0 Hz, 2 H, $C(O)CH_2$), 3.58–4.40 (m, 4 H, OCH_2), 5.20 (t, *J* = 5.0 Hz, 1 H, –OCHO–), 7.33–7.63 (m, 3 H, ArH), 7.86–8.13 (m, 2 H, ArH). Anal. Calcd for $C_{12}H_{14}O_3$: C, 69.88; H, 6.84. Found: C, 69.56; H, 6.92.

Acetal 7b: bp 90 °C (3 mmHg; Kugelrohr); IR (neat) 1720 (C=O), 1140, 1090, 980, 940 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.09–1.54 (m, 1 H, CH_2), 1.67–2.49 (m, 1 H, CH_2), 2.17 (s, 3 H, CH_3), 2.69 (d, *J* = 5.0 Hz, 2 H, $C(O)CH_2$), 3.50–4.27 (m, 4 H, OCH_2), 4.90 (t, *J* = 5.0 Hz, 1 H, –OCHO–); mass spectrum, *m/e* 144 (M^+).

Acetal 7c: bp 91–92 °C (1 mmHg; Kugelrohr); IR (neat) 1713 (C=O), 1138, 1062, 1000, 932 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.07 (s, 9 H, *t*-Bu), 1.33–1.63 (m, 1 H, CH_2), 1.73–2.48 (m, 1 H, CH_2), 2.77 (d, *J* = 5.2 Hz, 2 H, $C(O)CH_2$), 3.50–4.24 (m, 4 H, OCH_2), 4.98 (t, *J* = 5.2 Hz, 1 H, –OCHO–); mass spectrum, *m/e* 186 (M^+).

Acetal 9a: R_f 0.40 (SiO_2, hexane/ethyl acetate = 7/3); IR (neat) 1685 (C=O), 1215, 1125, 990, 842, 748, 680 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.32 (d, *J* = 5.2 Hz, 2 H, $C(O)CH_2$), 3.78–4.07 (m, 4 H, CH_2), 5.40 (t, *J* = 5.2 Hz, 1 H, –OCHO–), 7.27–7.57 (m, 3 H, ArH), 7.77–8.07 (m, 2 H, ArH); mass spectrum, *m/e* 192 (M^+). Anal. Calcd for $C_{11}H_{12}O_3$: C, 68.74; H, 6.29. Found: C, 68.76; H, 6.33.

Acetal 9b: R_f 0.36; bp 108 °C (3 mmHg; Kugelrohr); IR (neat) 1718 (C=O), 1130, 1047, 945 cm^{-1}; ^1H NMR (CCl_4) δ 2.19 (s, 3 H, CH_3), 2.78 (d, *J* = 5.0 Hz, 2 H, $C(O)CH_2$), 3.76–4.06 (m, 4 H, CH_2), 5.18 (t, *J* = 5.0 Hz, 1 H, –OCHO–), mass spectrum, $C_6H_{10}O_3$ *m/e* 130 (M^+).

Acetal 9c: bp 112 °C (3 mmHg; Kugelrohr); IR (neat) 1715 (C=O), 1135, 1045, 1008, 980 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.13 (s, 9 H, *t*-Bu), 2.85 (d, *J* = 5.0 Hz, 2 H, $C(O)CH_2$), 3.73–4.05 (m, 4 H, CH_2), 5.23 (t, *J* = 5.0 Hz, 1 H, –OCHO–). Anal. Calcd for $C_9H_{16}O_3$: C, 62.76; H, 9.36. Found: C, 62.30; H, 9.43.

Michael Adduct 3a: R_f 0.23; bp 150–152 °C (2 mmHg; Kugelrohr); IR (neat) 3430 (OH), 1685 (C=O), 1212, 1160, 1113, 1005, 748, 688 cm^{-1}; ^1H NMR (CCl_4) δ 1.05 (d, *J* = 6.0 Hz, 3 H, CH_3), 1.12 (d, *J* = 6.0 Hz, 3 H, CH_3), 1.42 (dd, *J* = 6.2, 5.8 Hz, 2 H, CH_2), 2.78 (br, 1 H, OH), 2.96–3.18 (m, 2 H, $C(O)CH_2$), 3.38–4.11 (m, 4 H, OCH, OCH_2), 7.18–7.51 (m, 3 H, ArH), 7.78–8.10 (m, 2 H, ArH). Anal. Calcd for $C_{14}H_{20}O_3$: 71.16; H, 8.53. Found: C, 71.01; H, 8.43.

Michael Adduct 3b: R_f 0.24 (SiO_2, hexane/ethyl acetate = 6.5/3.5); IR (neat) 1720 (C=O), 1380, 1240, 1160, 1120, 1080, 1050, 840 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.16 (d, *J* = 6.0 Hz, 6 H, CH_3), 1.55 (dd, *J* = 6.4, 5.2 Hz, 2 H, CH_2), 2.18 (s, 3 H, $C(O)CH_3$), 2.67 (t, *J* = 6.0 Hz, 2 H, $C(O)CH_2$), 2.93 (br, 1 H, OH), 3.47–4.28 (m, 4 H, OCH, OCH_2); mass spectrum, *m/e* 174 (M^+). Anal. Calcd for $C_9H_{18}O_3$: C, 62.04; H, 10.41. Found: C, 61.54; H, 10.27.

Michael Adduct 3c: IR (neat) 3400 (OH), 1710 (C=O), 1160, 1122, 1105, 1080, 1055 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.16 (s, 9 H, *tert*-Bu), 1.16 (d, *J* = 6.8 Hz, 3 H, CH_3), 1.18 (d, *J* = 6.0 Hz, 3 H, CH_3), 1.44–1.62 (m, 2 H, CH_2), 2.62–2.86 (m, 3 H, $C(O)CH_2$, OH), 3.48–4.06 (m, 4 H, OCH_2, OCH). Anal. Calcd for $C_{12}H_{24}O_3$: C, 66.63; H, 11.18. Found: C, 66.38; H, 11.16.

Michael Adduct 8a: R_f 0.12 (SiO_2, hexane/ethyl acetate = 6.5/3.5); IR (neat) 3400 (OH), 1673 (C=O), 1210, 1075, 1000, 970, 938, 858, 748, 686 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.61–2.02 (m, 2 H, CH_2), 2.47 (br, 1 H, OH), 3.23 (t, *J* = 6.0 Hz, 2 H, $C(O)CH_2$), 3.56–4.00 (m, 6 H, OCH_2), 7.33–7.65 (m, 3 H, ArH), 7.86–8.12 (m, 2 H, ArH); mass spectrum, *m/e* 209 ($M^+ + 1$).

Michael Adduct 8b: R_f 0.15 (SiO_2, hexane/ethyl acetate = 6.5/3.5); IR (neat) 3420 (OH), 1720 (C=O), 1370, 1250, 1180, 970 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.59–1.99 (m, 2 H, CH_2), 2.17 (s, 3 H, CH_3), 2.67 (t, *J* = 6.0 Hz, 2 H, $C(O)CH_2$), 2.75 (br, 1 H, OH), 3.46–3.93 (m, 6 H, OCH_2); mass spectrum, *m/e* 147 ($M^+ + 1$).

Michael Adduct 8c: IR (neat) 3450 (OH), 1710 (C=O), 1125, 1110, 1055, 995 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.12 (s, 9 H, *t*-Bu), 1.59–1.97 (m, 2 H, CH_2), 2.17 (br, 1 H, OH), 2.73 (d, *J* = 6.0 Hz, 2 H, $C(O)CH_2$), 3.50–3.83 (m, 6 H, OCH_2); mass spectrum, *m/e* 189 ($M^+ + 1$). Anal. Calcd for $C_{10}H_{20}O_3$: C, 63.79; H, 10.71. Found: C, 63.39; H, 10.58.

Michael Adduct 10a: R_f 0.26 (SiO_2, hexane/ethyl acetate = 7/3); IR (neat) 3400 (OH), 1672 (C=O), 1360, 1215, 1116, 1042, 980, 885, 745 cm^{-1}; ^1H NMR (CCl_4) δ 2.39 (br, 1 H, OH), 3.24 (t, *J* = 6.0 Hz, 2 H, $C(O)CH_2$), 3.46–3.79 (m, 4 H, OCH_2CH_2O), 3.93

(22) (a) Farberov, M. I.; Mironov, G. S. *Dokl. Akad. Nauk SSSR* **1963**, *148*, 1095; *Chem. Abstr.* **1963**, *59*, 5062f. (b) Mironov, G. S.; Farberov, M. I.; Orlova, I. M. *Zh. Prikl. Khim. (Leningrad)* **1963**, *36*, 654.

(23) Overberger, C. G.; Schiller, A. M. *J. Polym. Sci., Part C* **1963**, 325.

(t, J = 6.0 Hz, 2 H, CH_2), 7.29–7.59 (m, 3 H, ArH), 7.81–8.08 (m, 2 H, ArH); mass spectrum, m/e 195 (M^+).

Michael Adduct 10b: IR (neat) 3440 (OH), 1712 (C=O), 1120, 1062, 890 cm^{-1}; ^1H NMR (CCl_4) δ 2.12 (s, 3 H, CH_3), 2.60 (t, J = 6.0 Hz, 2 H, $C(O)CH_2$), 2.67 (br, 1 H, OH), 3.33–3.84 (m, 6 H, OCH_2).

Michael Adduct 10c: R_f 0.25 (SiO_2, hexane/ethyl acetate = 7/3); IR (neat) 3420 (OH), 1708 (C=O), 1120, 1052, 988, 882 cm^{-1}; ^1HNMR ($CDCl_3$) δ 1.13 (s, 9 H, t-Bu), 2.03 (br, 1 H, OH), 2.77 (t, J = 6 Hz, 2 H, $C(O)CH_2$), 3.43–3.87 (m, 6 H, CH_2); mass spectrum, m/e 175 (M^+ + 1).

Acetalization of Methyl Acrylate (11). The reaction with (*R,R*)-2,4-pentanediol (**4**) (0.208 g, 2 mmol) was performed by the same procedure as above. After the usual workup, Kugelrohr distillation [bp 100–102 °C (3 mmHg)] gave 2-(carbomethoxymethyl)-4,6-dimethyl-1,3-dioxane (**12**; 0.297 g, 79%). No Michael adduct was detected in this reaction. **12**: IR (neat) 1740 (C=O), 1190, 1135, 1030, 930 cm^{-1}; ^1H NMR (CCl_4) δ 1.13–1.43 (m, 1 H, CH_2), 1.14 (d, J = 6.0 Hz, 3 H, CH_3), 1.35 (d, J = 6.4 Hz, 3 H, CH_3), 1.50–2.07 (m, 1 H, CH_2), 2.43 (d, J = 5.8 Hz, 2 H, $C(O)CH_2$), 3.62 (s, 3 H, OCH_3), 3.64–4.40 (m, 2 H, OCH), 5.14 (t, J = 5.8 Hz, 1 H, –OCHO–). Anal. Calcd for $C_9H_{16}O_4$: C, 57.43; H, 8.57. Found: C, 57.16; H, 8.65.

The acetalization of **11** with ethylene glycol (0.124 g, 2 mmol) gave 2-(carbomethoxymethyl)-1,3-dioxolane (**13**; 0.211 g, 72%): bp 94–96 °C gave (4 mmHg; Kugelrohr); IR (neat) 1735 (C=O), 1130, 1055, 1010, 945 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.68 (d, J = 5.0 Hz, 2 H, $C(O)CH_2$), 3.69 (s, 3 H, CH_3), 3.78–4.08 (m, 4 H, OCH_2CH_2O), 5.27 (t, J = 5.0 Hz, 1 H, –OCHO–). Anal. Calcd for $C_6H_{10}O_4$: C, 49.31; H, 6.90. Found: C, 48.76; H, 6.98.

Acetalization of Acrylonitrile (14) with 4. The reaction was performed by using 2 mmol of **14** (0.106 g). After the usual workup, column chromatography (Al_2O_3, 12 g, CH_2Cl_2) gave 2-(cyanomethyl)-4,6-dimethyl-1,3-dioxane (**15**; 0.138 g, 45%): IR (neat) 2267 (C≡N), 1245, 1152, 1138, 1105, 1035, 998, 938, 898, 838, 802 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.21–1.47 (m, 1 H, CH_2), 1.22 (d, J = 6.0 Hz, 3 H, CH_3), 1.37 (d, J = 6.8 Hz, 3 H, CH_3), 1.64–2.16 (m, 1 H, CH_2), 2.59 (d, J = 5.0 Hz, 2 H, CH_2CN), 3.87–4.54 (m, 2 H, OCH), 5.07 (t, J = 5.0 Hz, 1 H, –OCHO–). Anal. Calcd for $C_8H_{13}NO_2$: C, 61.91; H, 9.03. Found: C, 61.49; H, 8.44.

Acetalization of *o*-Methylstyrene (16). The reaction with **4** was performed by using 2 mmol of **16** (0.236 g). After the usual workup, Kugelrohr distillation [bp 133–136 °C (1 mmHg)] gave 2-[(*o*-methylphenyl)methyl]-4,6-dimethyl-1,3-dioxane (**17**; 0.370 g, 84%): IR (neat) 1608, 1138, 1102, 1010, 925, 740 cm^{-1}; ^1H NMR (CCl_4) δ 1.01–1.38 (m, 1 H, CH_2), 1.14 (d, J = 6.6 Hz, 3 H, CH_3), 1.26 (d, J = 7.0 Hz, 3 H, CH_3), 1.52–2.09 (m, 1 H, CH_2), 2.29 (s, 3 H, CH_3Ar), 2.75 (d, J = 5.0 Hz, 2 H, CH_2Ar), 3.63–4.43 (m, 2 H, OCH), 4.84 (t, J = 5.0 Hz, 1 H, –OCHO–), 6.90–7.25 (m, 4 H, ArH). Anal. Calcd for $C_{14}H_{20}O_2$: C, 76.32; H, 9.15. Found: C, 75.89; H, 9.24.

The acetalization of **16** with ethylene glycol (0.248 g, 4 mmol) gave 2-[(*o*-methylphenyl)methyl]-1,3-dioxolane (**18**; 0.550 g, 77%): bp 115–118 °C (2 mmHg; Kugelrohr); IR (neat) 1140, 1045, 990, 912, 725 cm^{-1}; ^1H NMR (CCl_4) δ 2.32 (s, 3 H, CH_3), 2.88 (d, J = 4.2 Hz, 2 H, CH_2Ar), 3.63–3.87 (m, 4 H, OCH_2CH_2O), 4.92 (t, J = 4.2 Hz, 1 H, –OCHO–), 6.90–7.20 (m, 4 H, ArH). Anal. Calcd for $C_{11}H_{14}O_2$: C, 74.13; H, 7.92. Found: C, 73.95; H, 7.91.

Acetalization of Styrene (19) with 4. The reaction was performed by using 2 mmol of **19** (0.208 g). After the usual workup, preparative TLC (SiO_2, hexane/ethyl acetate = 7.5/2.5, R_f 0.74) gave 2-benzyl-4,6-dimethyl-1,3-dioxane (**20**; 0.326 g, 79%): bp 90–95 °C (4 mmHg; Kugelrohr); IR (neat) 1338, 1321, 1240, 1218, 1132, 1102, 1075, 1027, 1000, 925, 755, 695 cm^{-1}; ^1H NMR (CCl_4, 60 MHz) δ 1.12–1.35 (m, 1 H, CH_2), 1.13 (d, J = 6.0 Hz, 3 H, CH_3), 1.24 (d, J = 6.4 Hz, 3 H, CH_3), 1.47–2.03 (m, 2 H, CH_2), 2.74 (d, J = 5.0 Hz, 2 H, CH_2Ar), 3.52–4.42 (m, 2 H, OCH), 4.84 (t, J = 5.0 Hz, 1 H, –OCHO–), 7.09 (s, 5 H, ArH).

Acetalization of Allylbenzene (21) with 6. The reaction was performed by using 2 mmol of **21** (0.236 g). After the usual workup, preparative TLC (SiO_2, hexane/ethyl acetate = 12/1) gave phenylacetone (**23**; 0.107 g, 40%; R_f 0.27) and 2-benzyl-2-methyl-1,3-dioxolane (**22**; 0.050 g, 14%; R_f 0.41). **22**: IR (neat) 1715, 1678, 1220, 1125, 1045, 950, 830, 748, 698 cm^{-1}; ^1H NMR (CCl_4) δ 1.22 (s, 3 H, CH_3), 2.84 (s, 2 H, CH_2), 3.51–3.85 (m, 4 H, OCH_2CH_2O), 7.14 (s, 5 H, ArH). Anal. Calcd for $C_{11}H_{14}O_2$: C, 74.13; H, 7.92. Found: C, 73.90; H, 7.73.

Phenylacetone (**23**) was identified by comparing its spectral data with that of the authentic sample.

Reaction of 1-Decene (24) with 4. The reaction was performed by using 1 mmol of **24** (0.141 g, 1 mmol) in the presence of $PdCl_2$ (0.018 g, 0.1 mmol), CuCl (0.010 g, 0.1 mmol), and Na_2HPO_4 (0.015 g, 0.1 mmol). After the usual workup, SiO_2 column chromatography (10 g, CH_2Cl_2) gave 2-decanone (43%) and two unidentified products.

Acetalization of Methyl Methacrylate (25) with 4. Into a 20-mL round-bottomed flask were placed CuCl (0.198 g, 2 mmol), $PdCl_2$ (0.035 g, 0.2 mmol), (*R,R*)-2,4-pentanediol (**4**; 0.208 g, 2 mmol), and DME (2 mL). After the mixture was stirred at 50 °C for 30 min under an atmosphere of oxygen (1 atm, balloon), methyl methacrylate (0.21 mL, 2 mmol) was added into the flask, and stirring was continued for 48 h. At that time, conversion of the diol **2** was 64% (GLC). After the usual workup, Florisil column chromatography (1 g) with ether gave an oily material from which the product **26** (0.115 g, 28%) was isolated by using a short column of Al_2O_3 (1 g, pentane 100 mL). **26**: IR (neat) 1745 (C=O), 1380, 1340, 1200, 1150, 1105, 1065, 1010, 905, 805, 765 cm^{-1}; ^1H NMR (as a 63/37 mixture of two diastereomers in $CDCl_3$) δ 1.13–1.41 (m, 9 H, CH_3), 1.18–1.52 (m, 1 H, CH_2), 1.57–2.12 (m, 1 H, CH_2), 2.38–2.92 (m, 1 H, OCH), 3.69 (s, 3 H, OCH_3), 3.74–4.58 (m, 2 H, OCH), 5.02 (d, J = 6.0 Hz, 0.37 H, –OCHO–), 5.06 (d, J = 6.4 Hz, 0.63 H, –OCHO–). From the relative intensity of the signals at δ 5.02 and 5.06, the diastereomeric excess of this compound was determined to be 26%; mass spectrum m/e 201 (M^+ – 1).

In some of the experiments, we have experienced that no reaction takes place under the usual conditions. For effective conversion of **25** into **26**, pretreatment of the diol **4** with $PdCl_2$–CuCl in DME seems to be required. When the reaction temperature was raised to 65 °C, the reaction occurred smoothly but was less selective (16% de).

Acetalization of α-Methylene-γ-butyrolactone (27) with 4. The reaction was performed by using 1 mmol of **27** (0.990 g). After the usual workup, Kugelrohr distillation [120–125 °C (3 mmHg)] have (3*R*,5*R*)-2-(3,5-dimethyl-2,6-dioxanyl)-4-butanolide (**28**; 0.124 g, 61g): IR (neat) 1770 (C=O), 1135, 1100, 1030, 1000, 960, 910 cm^{-1}; ^1H NMR (as a 52/48 mixture of two diastereomers in $CDCl_3$) δ 1.17 (dd, J = 6.4, 6.0 Hz, 3 H, CH_3), 1.23–1.40 (m, 1 H, CH_2), 1.36 (dd, J = 6.4, 6.4 Hz, 3 H, CH_3), 1.64–1.95 (m, 1 H, CH_2), 2.08–2.91 (m, 3 H, $C(O)CHCH_2$), 3.80–4.47 (m, 4 H, OCH_2, OCH), 5.25 (d, J = 3.0 Hz, 0.52 H, –OCHO–), 5.28 (d, J = 2.0 Hz, 0.48 H, –OCHO–). From the relative intensity of the signals at δ 5.25 and 5.28, the diastereomeric excess of this compound was determined to be 4%. Anal. Calcd for $C_{10}H_{16}O_4$: C, 59.98: H, 8.05. Found: C, 59.89; H, 8.05.

Preparation of Copper(II) Alkoxide 29. CuCl (0.495 g, 5 mmol) was placed in a 100-mL flask equipped with an O_2 buret. Ethylene glycol (3.103 g, 50 mmol) and DME (20 mL) were added to the flask, and the mixture was stirred at 50 °C under oxygen. Oxygen consumption was measured with the O_2 buret. After 24 h, 30.1 mL (1.3 mmol) of oxygen consumption was observed, and the resulting green precipitate was collected by filtration with Willstätter nail and washed with ether. The yield was 0.774 g (97%). The copper(II) alkoxide **29** is slightly hygroscopic. **29**: mp 155–156 °C dec; IR (KBr) 3300–3100 (OH), 1220, 1033, 1015, 881, 855 cm^{-1}. Anal. Calcd for $C_2H_5O_2ClCu$: C, 15.01; H, 3.15; Cl, 22.15. Found: C, 14.82; H, 3.12; Cl, 21.90.

Acetalization of Vinyl Ketone 1 with Copper(II) Alkoxide 29. The reaction was performed by using $PdCl_2$ (0.035 g, 0.2 mmol), CuCl (0.198 g, 2 mmol), copper alkoxide **29** (0.320 g, 2 mmol), and phenyl vinyl ketone (**1a**) in DME (2 mL). After 20 h, the usual workup followed by Kugelrohr distillation gave only acetal **9a** (0.192 g, 50%).

The same reaction of *tert*-butyl vinyl ketone (**1c**) with **29** gave the acetal **9c** as a sole product (0.151 g, 44%).

Synthesis of Styrene-d_2 (31). Acetophenone-d_3 (99% d content) was first prepared by the following procedure. A solution of acetophenone (5 g, 42 mmol) in benzene (17 mL) was stirred in the presence of D_2O (15 mL), K_2CO_3 (6.330 g, 46 mmol), and n-Bu_4NHSO_4 (0.566 g, 1.67 mmol) at 50 °C for 42 h under an atmosphere of argon. The organic layer was separated and washed with 1 N HCl (15 mL × 2), H_2O (15 mL × 2), and brine (15 mL) and dried over anhydrous magnesium sulfate. Filtration followed

by removal of the solvent afforded acetophenone-d_3 (4.735 g, 92%). At this stage, the d content was 90%. Repetition of this procedure by three times gave acetophenone-d_3 (70% total yield; 99% d content): IR (neat) 2260 (CD), 1600 (C=O), 1582, 1312, 1270, 1108, 981, 745, 684 cm^{-1}; ^1H NMR δ 6.59 (m, 1 H, PhCH), 7.04–7.35 (m, 5 H, ArH).

The acetophenone-d_3 (3.442 g, 0.28 mmol) thus prepared was allowed to react with $LiAlH_4$ (0.320 g, 8.43 mmol) in anhydrous ether (12 mL) at room temperature to give 1-phenylethanol-d_3 (99% yield). This compound was then converted into styrene-d_2 by the method of Overberger and Saunders.[24] The d content of **31** determined by ^1H NMR was 99%. **31**: IR (neat) 2235 (CD), 1600, 1572, 1497, 1447, 1122, 1080, 1041, 1015, 941, 905, 762, 723, 693 cm^{-1}; ^1H NMR (CCl_4) δ 6.52–7.33 (m, 1 H, =CH), 7.07–7.50 (m, 5 H, ArH).

Preparation of Vinyl-d_2 Phenyl Ketone (32). In a 10-mL autoclave containing a Teflon-coated magnetic stirring bar were placed acetophenone (2.884 g, 24 mmol), diethylamine hydrochloride (3.068 g, 28 mmol), formaldehyde-d_2 (30% in D_2O, 2.990 g, 28 mmol), and a drop of DCl. After the mixture was heated at 100 °C with stirring for 3 h, the resulting mixture was dissolved into 130 mL of water and azeotropically distilled at 125 °C. The condensate oil was taken up with ether. The aqueous layer was extracted with ether (15 mL × 5). The combined ether extracts were dried over anhydrous $MgSO_4$ and concentrated. Chromatographic separation (SiO_2, 20 g, 1.8 × 19.2 cm; CH_2Cl_2/hexane = 1/9, 700 mL) gave pure **32** (0.690 g, 21%): ^1H NMR (CCl_4) δ 7.00–7.10 (m, 1 H, CH=CD_2), 7.26–7.56 (m, 3 H, ArH), 7.79–7.91 (m, 2 H, ArH). Further elution gave a 1/3 mixture (0.265 g) of **32** and acetophenone.

Acetalization of Styrene-d_2 (31) with 4. The reaction was performed according to the general procedure. After 7.5 h of stirring at 50 °C, 18% of styrene-d_2 was consumed (GLC). Usual workup followed by preparative TLC gave unreacted styrene (R_f 0.92) and acetal **33** (R_f 0.53; 0.044 g, 11%). NMR analysis of **33** has shown that the d contents of the C_1 and C_2 carbons are 0.8 and 1.2, respectively. **33**: ^1H NMR ($CDCl_3$, 100 MHz) δ 1.16–1.32 (m, 1 H, CH_2), 1.20 (d, J = 6.6 Hz, 3 H, CH_3), 1.28 (d, J = 6.9 Hz, 3 H, CH_3), 1.88–1.99 (m, 1 H, CH_2), 2.72–2.90 (m, 0.8 H, PhCHD), 3.73–4.41 (m, 2 H, OCH), 4.92–5.03 (m, 0.2 H, –OCDO–), 7.22 (s, 5 H, ArH). In the recovered styrene, the d contents of C_1 and C_2 carbons are 1.3 and 0.7, respectively: ^1H NMR (CCl_4, 100 MHz) δ 5.06–5.18 (m, 0.32 H), 5.52–5.89 (m, 0.32 H), 6.44–6.69 (m, 0.32 H), 7.04–7.35 (m, 5 H, ArH).

When the reaction was carried out for 20 h under otherwise the same conditions, ~99% of the styrene was consumed. After the usual workup, the acetal **33** was obtained in 61% isolated yield, and its d content was nearly identical with that of the acetal obtianed from the above reaction.

Acetalization of Vinyl-d_2 Phenyl Ketone (32) with 4. The reaction was performed by using **32** (0.269 g, 2 mmol), (*R*,*R*)-2,4-pentanediol (**4**; 0.208 g, 2 mmol), $PdCl_2$ (0.035 g, 0.2 mmol), and CuCl (0.198 g, 2 mmol) in DME (2 mL). After 20 h, ~99% of the diol was consumed (GLC), and the acetal **34** and Michael adduct **35** were formed in 32 and 39% yields (pentadecane as the internal standard), respectively. After the usual workup, preparative TLC (SiO_2, hexane/ethyl acetate = 7/1) gave **34** (R_f 0.55; 0.127 g, 27%) and **35** (R_f 0.22; 0.119 g, 25%). The NMR analysis of **34** has shown that the d contents of C_1 and C_2 carbon are 1.00 and 0.50, respectively, with 25% of d loss. **34**: ^1H NMR ($CDCl_3$, 100 MHz) δ 1.24–1.44 (m, 1 H, CH_2), 1.18 (d, J = 6.4 Hz, 3 H, CH_3), 1.37 (d, J = 7.0 Hz, 3 H, CH_3), 1.64–1.99 (m, 1 H, CH_2), 3.22 (s, 1.5 H, PhCOCHD), 3.81–4.41 (m, 2 H, -OCH), 7.22–7.61 (m, 3 H, ArH), 7.66–8.02 (m, 2 H, ArH). No peak corresponding to the C_1 proton was observed.

The ^1H NMR data of **35** ($CDCl_3$, 100 MHz) were as follows: δ 1.15 (d, J = 6.0 Hz, 3 H, CH_3), 1.19 (d, J = 6.0 Hz, 3 H, CH_3), 1.46–1.62 (m, 2 H, CH_2), 2.90 (br, 1 H, OH), 3.19 (d, J = 3.8 Hz, 2 H, $C(O)CH_2$), 3.61–4.28 (m, 2 H, OCH), 7.28–7.61 (m, 3 H, ArH), 7.73–8.00 (m, 2 H, ArH).

The same reaction was performed, monitoring the progress of the reaction by GLC. When the conversion of diol reached ~50%, the reaction was stopped, and unreacted phenyl vinyl ketone was recovered by preparative TLC (SiO_2). Neither d loss nor d scrambling was observed in the recovered olefin by ^1H NMR.

Preparation of (2*R*,4*R*)-4-Methyl-8-phenyl-5-oxa-6-octen-2-ol (40).[25] Into an ethereal solution (5 mL) of (4*R*,6*R*)-2-vinyl-4,6-dimethyl-1,3-dioxane (0.214 g, 1.5 mmol), which was prepared from acrolein and (*R*,*R*)-2,4-pentanediol, was added PhLi (0.585 M in ether, 4.62 mL, 2.7 mmol) at −78 °C under N_2, and the mixture was warmed to room temperature and stirred for 21 h. Into the resulting mixture was added water (2 mL), and the product was extracted with ether (10 mL × 3). The aqueous layer was neutralized with 2 N HCl, and the solution was again extracted with ether (10 mL × 3). The combined organic layer was dried over $MgSO_4$ and concentrated. Preparative TLC (Al_2O_3, hexane/ethyl acetate = 9/1) gave 0.083 g (32% yield) of **40**: R_f 0.19; IR (neat) 3370 (OH), 1675 (C=O), 1655, 1610, 1500, 1455, 1380, 1160, 930, 830, 745, 698 cm^{-1}; ^1H NMR (CCl_4) δ 1.08 (d, J = 6.0 Hz, 3 H, CH_3), 1.15 (d, J = 6.0 Hz, 3 H, CH_3), 1.31–1.59 (m, 2 H, CH_2), 2.80 (br, 1 H, OH), 3.18 (d, J = 7.0 Hz, 2 H, $PhCH_2$), 3.73–4.20 (m, 2 H, OCH), 4.95 (dt, J = 7.0, 12.2 Hz, 2 H, $PhCH_2$), 6.10 (d, J = 12.2 Hz, 1 H, HC=C), 7.13 (s, 5 H, ArH).

(4*R*,6*R*)-4,6-Dimethyl-2-(2-phenylethyl)-1,3-dioxane (41). In a 20-mL round-bottomed flask was placed DME (1 mL) into which dry hydrogen chloride was bubbled for 3 min, and then a solution of **40** (0.041 g, 0.18 mmol) in DME (0.5 mL) was added. After the solution was stirred for 3 h at 50 °C, the reaction mixture was concentrated under reduced pressure to leave 0.037 g (93% yield) of **41** as a single product (GLC analysis). **41**: IR (neat) 1610, 1500, 1455, 1380, 1145, 1035, 750, 695 cm^{-1}; ^1H NMR (CCl_4) δ 1.13–1.35 (m, 1 H, CH_2), 1.15 (d, J = 6.4 Hz, 3 H, CH_3), 1.26 (d, J = 7.0 Hz, 3 H, CH_3), 1.52–2.03 (m, 3 H, CH_2, $PhCCH_2$), 2.66 (dd, J = 11.0, 9.0 Hz, 2 H, CH_2), 3.64–4.49 (m, 2 H, OCH), 4.72 (t, J = 5.0 Hz, 1 H, –OCHO–), 7.13 (s, 5 H, ArH). Anal. Calcd for $C_{14}H_{20}O_2$; C, 76.32; H, 9.15. Found: C, 76.03; H, 9.20.

Compound **41** was also obtained in ~90% yield by the reaction of **40** (0.041 g, 0.18 mmol), $PdCl_2(CH_3CN)_2$ (0.041 g, 0.18 mmol), and Et_3N (0.040 g, 0.39 mmol) in DME (1.2 mL) at 50 °C for 4 h.

(24) Overberger, G. H.; Saunders, J. H. *Organic Syntheses*; Wiley: New York, 1955; Collect. Vol. 3, p 204.

(25) For a related reaction, see: Bailey, W. F.; Zartun, D. L. *J. Chem. Soc., Chem. Commun.* **1984**, 34.