

Palladium(II)-catalysed Acetalization of Terminal Olefins Bearing Electron-withdrawing Substituents with 1,3- and 1,2-Diols

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Treatment of terminal olefins bearing electron-withdrawing groups with (*R,R*)-pentane-2,4-diol (**2**) in the presence of PdCl₂-CuCl-O₂ in 1,2-dimethoxyethane gives cyclic acetals such as (**3**) and (**12b**) *via* attack at the terminal carbon atom; the corresponding acetals are similarly formed from propane-1,3-diol (**5**) and ethylene glycol (**8**).

The palladium(II)-catalysed oxidation of terminal olefins in water, the Wacker process, produces methyl ketones, and a similar reaction in alcohols gives their acetals. These products arise *via* the attack of oxygen nucleophiles at the non-terminal olefinic carbon atom [reaction (1)]. Although these reactions have been widely studied,¹ acetalization at the terminal carbon atom [reaction (2)] is extremely rare,² and studies to increase its synthetic utility have not been performed.† We now report that this type of acetalization proceeds generally with terminal olefins bearing electron-withdrawing substituents. Also described is the synthesis of cyclic acetals which appear to be precursors of a variety of chiral aldehydes.

The reaction of the vinyl ketones (**1a**–**c**) (1 M) with 1 equiv. of the optically active (*R,R*)-pentane-2,4-diol (**2**)³ in the presence of PdCl₂ and CuCl in DME (1,2-dimethoxyethane) at 50 °C for 20 h under O₂ (1 atm) [(1):Pd:Cu, 10:1:10], gave the cyclic acetals (**3a**–**c**) in good yield‡ [(**3a**), 86%; (**3b**), 57%; (**3c**), 63%], together with *ca.* 5% of the open chain alcohols (**4**) which could easily be separated by Florisil column chromatography. Neither acetalization of the ketone group in (**1**) nor racemization of the chiral carbon in (**3**) occurred. In other solvents such as dimethylformamide and diglyme, the reaction between (**1a**) and (**2**) gave (**3a**) in low yields (*ca.* 20%).

Propane-1,3-diol (**5**) similarly gave the corresponding acetals (**6**) in moderate yields [(**6a**), 59%; (**6b**), 45%; (**6c**), 52%], together with 5% of the by-products (**7**). The five-membered acetals (**9**) were also formed from ethylene glycol, but in low yields [(**9a**), 20%; (**9b**), 33%; (**9c**), 36%]. The by-products (**10**) were formed in relatively high yields (10%),

and by-product formation increased further on decreasing the amount of CuCl used relative to PdCl₂ (Table 1). Similar trends were observed with the diol (**2**). The use of CuCl₂ (Cu: Pd, 10:1) in place of CuCl gave at least seven products. All these results indicate that the efficient synthesis of cyclic acetals such as (**3**) requires the use of excess of CuCl with 1,3-diols in DME. It is noteworthy that products derived from attack of the diols at the non-terminal olefinic carbon atom of (**1**) are not formed in any case, and that there is no synthetic advantage in the usual Wacker reaction of vinyl ketones (**1**) since the reaction of (**1a**) with water either with PdCl₂-CuCl-O₂ in dimethylformamide⁴ or with Na₂PdCl₄-Bu^tOOH in AcOH⁵ affords various products.

The olefins (**11**) bearing a CO₂Me group are also acetalized at the terminal carbon atom selectively. Thus, (**11a**) reacts with the diol (**2**) to give the acetal (**12a**) in 79% yield.§ Methyl

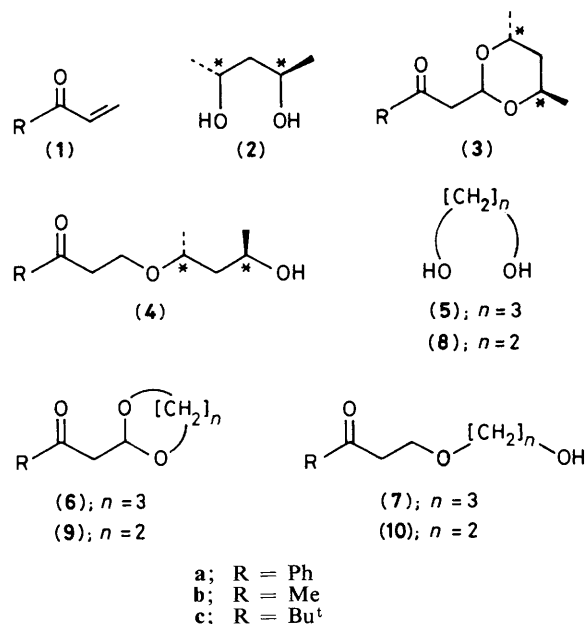
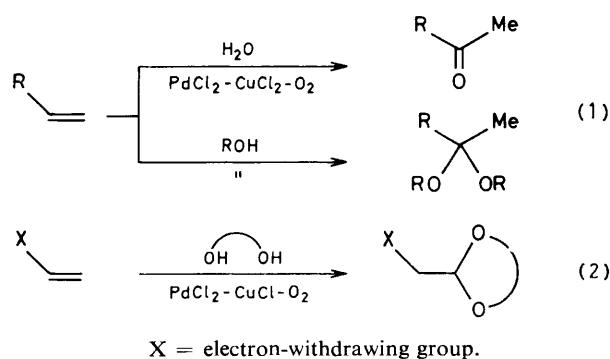


Table 1. Product distribution in the reaction of phenyl vinyl ketone (**1a**) and ethylene glycol (**8**).

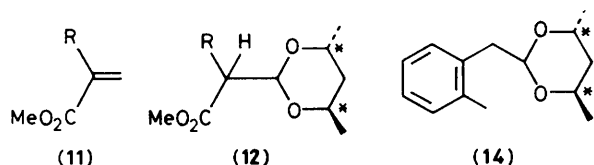
Molar ratio CuCl: PdCl ₂	Product yield (%) ^a (9a)	(10a)
50:1	20	7
10:1	20	10
1:1	17	15
0	7	15

^a Isolated yield following preparative t.l.c. (SiO₂, eluant n-hexane-EtOAc, 9:1), and based on (**1a**) used.

† Grigg *et al.* cyclised vicinal dihydroxy terminal olefins to form bicyclic acetals by PdCl₂-CuCl₂-O₂ and synthesized *endo*-brevicomin and related compounds (N. T. Byrom, R. Grigg, and B. Kongkathip, *J. Chem. Soc., Chem. Commun.*, 1976, 216). However, these reactions occur *via* an attack of diols on the non-terminal olefinic carbon atom.

‡ The products were isolated by Florisil column chromatography followed by kugelrohr distillation.

§ For the effective conversion of (**11**) into (**12**), pretreatment of the diol (**2**) with PdCl₂-CuCl in DME under N₂ was required.



a; R = H

b; R = Me

methacrylate (**11b**), although its reaction is slow, gives a 24% yield of (**12b**) (50% conversion) as a mixture of two diastereoisomers in 20% diastereoisomer excess. This reaction may be classified as the *enantio-face-differentiating* Wacker-type reaction.

o-Methylstyrene (**13**) is similarly acetalized by the diol (**2**) at the terminal carbon atom exclusively to give (**14**) in 84% isolated yield. The use of ethylene glycol produces the corresponding acetal in 77% yield. Since the usual Wacker reaction of (**13**) gives *o*-methylacetophenone *via* attack at the non-terminal olefinic carbon atom, the regioselectivity for the attack of oxygen nucleophiles is completely reversed between water and diol in this reaction.

Regioselective acetalization at the terminal carbon atom, however, occurs only with olefins bearing electron-with-

drawing groups, since the treatment of allylbenzene with ethylene glycol gives methyl benzyl ketone (40%) and its acetal (14%); oct-1-ene affords methyl hexyl ketone along with two other unidentified products.

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References

- (a) P. M. Henry, 'Palladium Catalyzed Oxidation of Hydrocarbons,' Reidel, Holland, 1980; (b) J. Tsuji, 'Organic Synthesis with Palladium Compounds,' Springer-Verlag, Berlin, 1980; P. M. Maitlis, 'The Organic Chemistry of Palladium,' Academic Press, New York, 1971, Vol. 2.
- W. G. Lloyd and B. Luberoft, *J. Org. Chem.*, 1969, **34**, 3949; also see ref. 1(a), pp. 133—140.
- K. Ito, T. Harada, T. Tai, and Y. Izumi, *Chem. Lett.*, 1979, 1049; A. Tai, K. Ito, and T. Harada, *Bull. Chem. Soc. Jpn.*, 1981, **54**, 223.
- F. J. McQuillin and D. J. Parker, *J. Chem. Soc., Perkin Trans. 1*, 1974, 809; J. Tsuji, I. Shimizu, and K. Yamamoto, *Tetrahedron Lett.*, 1976, 2976.
- J. Tsuji, H. Nagashima, and K. Hori, *Chem. Lett.*, 1980, 257.