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

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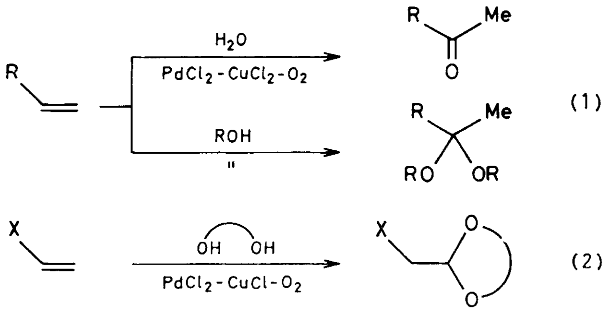
Treatment of terminal olefins bearing electron-withdrawing groups with (*R*,*R*)-pentane-2,4-diol (**2**) in the presence of $PdCl_2$–CuCl–O_2 in 1,2-dimethoxyethane gives cyclic acetals such as (**3**) and (**12b**) *via* attack at the terminal carbon atom; the corresponding acetals are similarly formed 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.

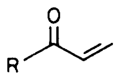
The reaction of the vinyl ketones (**1a**—**c**) (1 M) with 1 equiv. of the optically active (*R*,*R*)-pentane-2,4-diol (**2**)[3] in the presence of $PdCl_2$ and CuCl in DME (1,2-dimethoxyethane) at 50 °C for 20 h under O_2 (1 atm) [(**1**) : Pd : Cu, 10 : 1 : 10], gave the cyclic acetals (**3a**—**c**) 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 $PdCl_2$ (Table 1). Similar trends were observed with the diol (**2**). The use of $CuCl_2$ (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 $PdCl_2$–CuCl–O_2 in dimethylformamide[4] or with Na_2PdCl_4–Bu^tOOH in AcOH[5] affords various products.

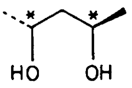


X = electron-withdrawing group.

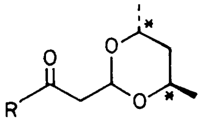
The olefins (**11**) bearing a CO_2Me group are also acetalized at the terminal carbon atom selectively. Thus, (**11a**) reacts with the diol (**2**) to give the acetal (**12a**) in 79% yield.§ Methyl



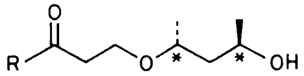
(**1**)



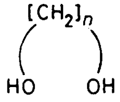
(**2**)



(**3**)

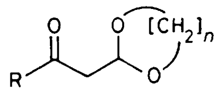


(**4**)



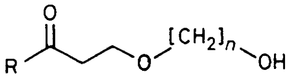
(**5**); *n* = 3

(**8**); *n* = 2



(**6**); *n* = 3

(**9**); *n* = 2



(**7**); *n* = 3

(**10**); *n* = 2

a; R = Ph
b; R = Me
c; R = Bu^t

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. (SiO_2, eluant n-hexane–EtOAc, 9 : 1), and based on (**1a**) used.

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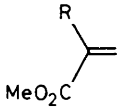
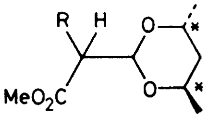
† Grigg *et al.* cyclised vicinal dihydroxy terminal olefins to form bicyclic acetals by $PdCl_2$–$CuCl_2$–O_2 and synthesized *endo*-brevicomin and related compounds (N. T. Byrom, R. Grigg, and B. Kongkathip, *J. Chem. Soc., Chem. Commun.*, 1976, 216). However, these reactions occur *via* an attack of diols on the non-terminal olefinic carbon atom.

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

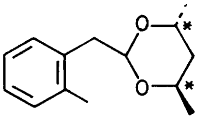
§ For the effective conversion of (**11**) into (**12**), pretreatment of the diol (**2**) with $PdCl_2$–CuCl in DME under N_2 was required.



(11)



(12)



(14)

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-withdrawing 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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