

REGIOSELECTIVE OXIDATION OF INTERNAL OLEFINS BEARING NEIGHBORING OXYGEN
FUNCTIONS BY MEANS OF PALLADIUM CATALYSTS. PREPARATION OF β -ALKOXY
OR ACETOXY KETONES FROM ALLYL AND HOMOALLYL ETHERS OR ESTERS

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Summary: A new preparative method of β - and γ -alkoxy (acetoxy) ketones, which are important precursors of vinyl ketones and 1,4-diketones, respectively, is presented. With $\text{PdCl}_2/\text{CuCl}/\text{O}_2$ or PdCl_2/p -benzoquinone catalyst system, internal olefins bearing allylic alkoxy or acetoxy group underwent regioselective oxidation to form the corresponding β -alkoxy or β -acetoxy ketones. Similarly, γ -acetoxy ketones were obtained from homoallyl acetates having internal olefins with high regioselectivity.

Industrial oxidation process of ethylene to acetaldehyde by means of palladium catalyst is well-known as the Wacker process.¹⁾ With appropriate catalyst system and solvent, such as $\text{PdCl}_2/\text{CuCl}/\text{O}_2$ in aqueous DMF, a wide variety of olefins are smoothly oxidized to the corresponding ketones or aldehydes.^{2,3)} Especially, terminal olefins are selectively oxidized to the corresponding methyl ketones under very mild conditions. Thus, this oxidation offers a very useful synthetic method of methyl ketones. On the other hand, oxidation of internal olefins has scarcely been studied, because it proceeds without regioselectivity. In the course of our studies on the oxidation of certain functionalized olefins with palladium catalysts, we have observed high regioselection in the oxidation of internal olefins bearing neighboring oxygen functions. As one example, we have reported the selective oxidation of α,β -unsaturated esters and ketones to give β -keto esters and 1,3-diketones, respectively.⁴⁾ In this paper, we wish to report the palladium catalyzed highly regioselective oxidation of allyl and homoallyl ethers or acetates. By this oxidation, β - and γ -alkoxy or acetoxy ketones, which are important precursors of vinyl ketones and 1,4-diketones, respectively, are easily prepared.



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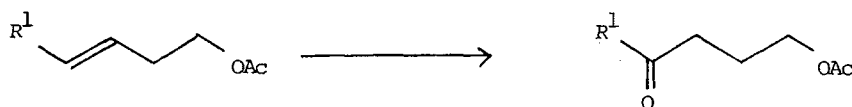
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As shown in Table 1, the oxidation of various allyl ethers and acetates with $\text{PdCl}_2/\text{CuCl}/\text{O}_2$ or $\text{PdCl}_2/p\text{-benzoquinone}$ catalyst system gave the corresponding β -alkoxy ketones regioselectively.⁵⁾ No α -alkoxy or acetoxy ketone was detected. In the oxidation of 2-octenyl acetate (1F), in addition to the normal oxidation, palladium catalyzed allylic rearrangement^{6,7)} and subsequent oxidation took place to give a small amount of 3-acetoxy-2-octanone as a by-product. Ethers of secondary allylic alcohols also underwent the regioselective oxidation to give the corresponding β -alkoxy ketones in 30 - 40% yields. But in this case too, by-products derived from the allylic rearrangement and subsequent oxidation were also detected.

Homoallyl acetates were oxidized to form the corresponding γ -acetoxy ketones with high regioselectivity. The results are shown in Table 2. In this oxidation, small amounts of β -acetoxy ketones were formed (10% or less).

In these palladium catalyzed reactions, oxygen atom was introduced at the carbon of the olefinic bond remote from the neighboring alkoxy or acetoxy group. The results suggest that there is definite influence of the alkoxy or acetoxy group, which may be explained by coordination of palladium with the oxygen function, to control the regioselection. The control by the neighboring oxygen functions is effective only in the oxidation of internal olefins. Terminal olefins bearing neighboring alkoxy or acetoxy group were oxidized to the corresponding methyl ketones, though the effect of the alkoxy or acetoxy group predicts the formation of the corresponding aldehydes. Typical examples are depicted below.

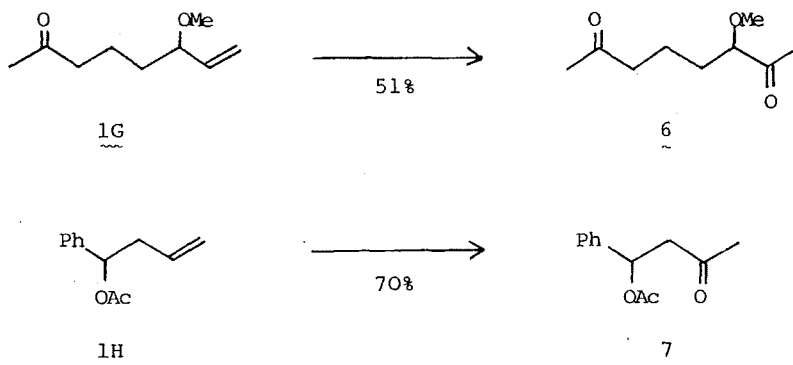



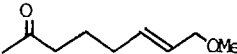
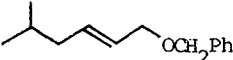



Table 1. Oxidation of Allyl Ethers and Acetates

$\begin{array}{c} \text{R}^1 \\ \diagdown \\ \text{CH} \\ \diagup \\ \text{CH}_2\text{OR}^2 \\ \text{1A} - \text{1F} \end{array} \longrightarrow \begin{array}{c} \text{R}^1 \\ \diagdown \\ \text{C}=\text{O} \\ \diagup \\ \text{CH}_2\text{OR}^2 \\ \text{2A} - \text{2F} \end{array}$					
Temp (°C)	Time (h)	Yields (%)	Temp (°C)	Time (h)	Yields (%)
A. 	50 r.t. b)	6 6	67 54	D. 	50 12 60
B. 	50	8	65	E. 	50 24 64
C. 	50	48	76	F. 	50 12 42

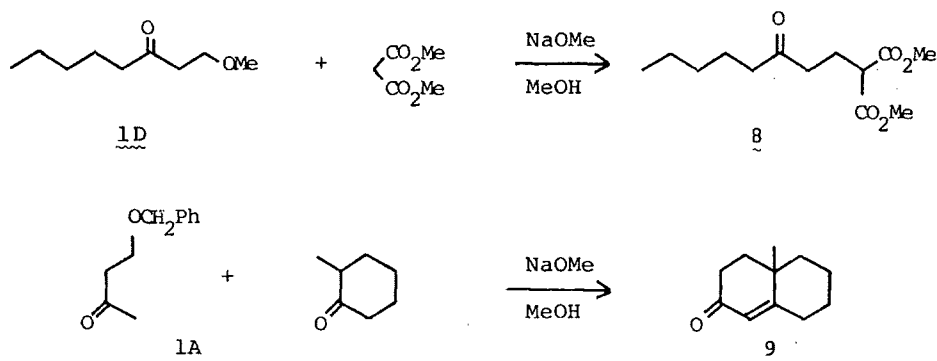
a) Unless otherwise noted, the oxidation was carried out in the presence of PdCl_2 (10 mol%) and CuCl (100 mol%) in aqueous DMF ($\text{DMF} : \text{H}_2\text{O} = 7 : 1$) under oxygen atmosphere. b) The oxidation was carried out with PdCl_2 (10 mol%)/*p*-benzoquinone (100 mol%) in aqueous THF ($\text{THF} : \text{H}_2\text{O} = 7 : 1$).

Table 2. Oxidation of Homoallyl Acetates

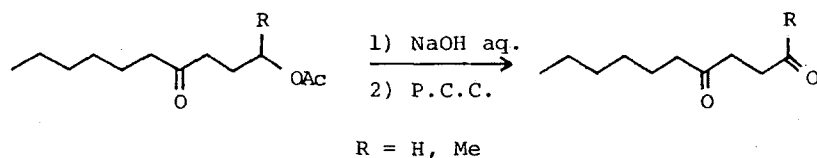
$\begin{array}{c} \text{R}^1 \\ \diagdown \\ \text{CH} \\ \diagup \\ \text{CH}_2\text{CH}_2\text{OAc} \\ \text{3A} - \text{3D} \end{array} \longrightarrow \begin{array}{c} \text{R}^1 \\ \diagdown \\ \text{C}=\text{O} \\ \diagup \\ \text{CH}_2\text{CH}_2\text{OAc} \\ \text{4A} - \text{4D} \end{array} + \begin{array}{c} \text{R}^1 \\ \diagdown \\ \text{CH} \\ \diagup \\ \text{C}=\text{O} \\ \diagup \\ \text{CH}_2\text{CH}_2\text{OAc} \\ \text{5A} - \text{5D} \end{array}$					
Yields (%)	Ratio (4 : 5)	Yields (%)	Ratio (4 : 5)		
A.	80	91 : 9	C.	72	90 : 10
B.	73	88 : 12	D.	42 ^{b)}	100 : 0

a) All reactions were carried out in the presence of PdCl_2 (10 mol%) and CuCl (100 mol%) in aqueous DMF at 50°C under oxygen atmosphere. The ratio between 4 and 5 was determined by GLC. b) 20 mol% of PdCl_2 was used.

β -Alkoxy ketones and γ -acetoxy ketones prepared by the oxidation of allyl ethers and homoallyl acetates, respectively, are synthetically useful intermediates. In the presence of excess sodium methoxide in methanol, β -alkoxy ketone 1D was allowed to react with dimethyl malonate to give the Michael adduct 8 in 72% yield. Similarly, the reaction of 1A with 2-methylcyclohexanone afforded methyl-octalone 9 in 42% yield. Thus, allyl ethers can be regarded as "masked vinyl ketones" by means of this palladium catalyzed oxidation.



1,4-Diketones or γ -keto aldehydes were prepared from γ -acetoxy ketones by saponification of the acetate with aqueous NaOH, followed by oxidation with pyridinium chlorochromate.



References and Notes

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- 4) J. Tsuji, H. Nagashima, and K. Hori, *Chem. Lett.*, **1980**, 257.
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