

A NOVEL SYNTHETIC METHOD FOR γ -ACETOXY-(*E*)- α,β -UNSATURATED ESTERS BY THE PALLADIUM CATALYZED REGIO- AND STEREOSELECTIVE ACETOXYLATION OF β,γ -UNSATURATED ESTERS

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Summary: A new synthetic method for γ -acetoxy- α,β -unsaturated esters by the acetoxylation of β,γ -unsaturated esters catalyzed by PdCl_2 in the presence of KOAc and pentyl nitrite in acetic acid is presented. The reaction takes place at γ -position of the esters regioselectively with double bond migration to α,β -position. The *E* configuration of the double bond was confirmed by NMR analysis. Preliminary investigation to synthesize pyrenophorin and pyrenophorol using this reaction is described.

In our continuous studies on the oxidation of olefins using Pd(II) salts, we have reported the oxidation of 1-olefins to methyl ketones¹⁾ and its application to natural products synthesis.²⁾ We also found that certain functional groups near an internal double bond show a remarkable neighbouring effect on the regioselectivity in the oxidation. Thus, α,β -unsaturated esters and ketones were oxidized to β -keto esters and 1,3-diketones, respectively,³⁾ whereas allyl and homoallyl ethers were converted to β -alkoxy ketones and γ -alkoxy ketones, respectively.⁴⁾ Interestingly, the oxidation of β,γ -unsaturated esters and ketones using $\text{PdCl}_2\text{-CuCl-O}_2$ system afforded γ -keto esters and 1,4-diketones respectively in 20-40% yields with concomitant formation of a small amount of π -allylpalladium chloride complexes. No β -keto carbonyl compound was formed, and hence this reaction seemed to proceed *via* π -allylpalladium intermediate. While the reaction of ethylene with acetic acid using palladium catalyst gives vinyl acetate,⁵⁾ the oxidation of higher olefins under the same conditions gives a complex mixture of allyl acetates and homoallyl acetates *via* π -allyl intermediate.⁶⁾ We paid our attention to a possibility of acetoxylation of β,γ -unsaturated esters, and found that β,γ -unsaturated esters **1** were oxidized regioselectively to give γ -acetoxy- α,β -unsaturated esters **3** with PdCl_2 catalyst in the presence of KOAc and pentyl nitrite.

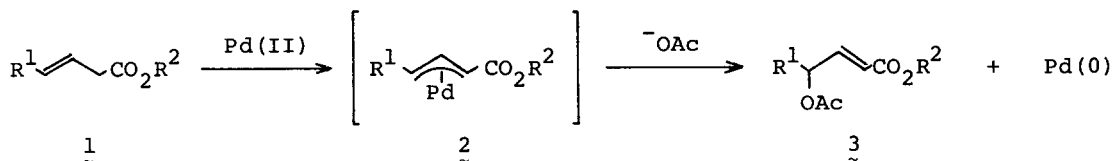


Table Acetoxylation of β,γ -Unsaturated Esters

	Products	Isolated Yield(%)
		52
		52
		54
		45
		47

The best results were obtained using 10 mol% of PdCl_2 , 150 mol% of pentyl nitrite and 200 mol% of KOAc . The reaction was carried out at 60°C under oxygen atmosphere for several hours. Moderate yields of the desired esters are mainly attributed to isomerization of the β,γ -double bond to α,β -position without being oxidized. It was confirmed that no reaction took place with α,β -unsaturated esters. In this reaction, pentyl nitrite is the reoxidant of $\text{Pd}(0)$. The use of conventional reoxidants such as CuCl_2 and *p*-benzoquinone gave the same products in lower yields even at elevated temperatures, and considerable amounts of α,β - γ,δ -diene esters were obtained.⁷⁾ The reaction of β,γ -unsaturated ketones did not give satisfactory result, because the double bond migration occurred predominantly. Results of the oxidation of β,γ -unsaturated esters are summarized in the Table. Preparation of methyl 3-acetoxy-(*E*)-2-decenoate is typical: A mixture of PdCl_2 (35 mg, 0.2 mmol), KOAc (392 mg, 4 mmol), pentyl nitrite (351 mg, 3 mmol), and methyl 3-decenoate (368 mg, 2 mmol) in acetic acid (4 ml) was heated at 60°C with stirring under oxygen atmosphere for 5 h. After usual work-up, the residue was purified by column chromatography (silica gel, hexane-ether) to give methyl 4-acetoxy-(*E*)-2-decenoate (255 mg, 52%): IR (neat) 1728, 1660, 1236, and 1022 cm^{-1} ; NMR (CCl_4 , TMS) δ 2.0 (s, 3H), 3.7 (s, 3H), 5.0-5.5 (m, 1H), 5.9 (dd, 1H, $J = 16$ and 1 Hz), 6.8 (dd, 1H, $J = 16$ and 6 Hz).

