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A FACILE SYNTHESIS OF γ,δ-UNSATURATED ESTERS BY THE Pd(II) CATALYZED CLAISEN REARRANGEMENT

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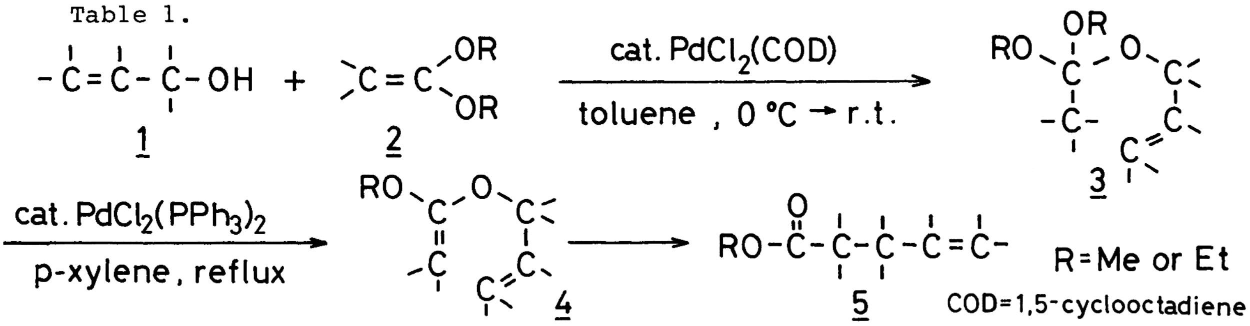
A mixed ortho ester is prepared under mild conditions from an allyl alcohol and a ketene acetal in the presence of $PdCl_2(COD)$. The ortho ester thus formed is successively treated with a catalytic amount of $PdCl_2(PPh_3)_2$ in refluxing p-xylene to afford a γ,δ-unsaturated ester in a high yield under neutral conditions.

The Claisen rearrangement provides a useful route to γ,δ-unsaturated carbonyl compounds from allyl alcohols, and is frequently employed as an important step in the synthesis of natural products. The synthesis of a γ,δ-unsaturated ester is often achieved by the ortho ester Claisen rearrangement.[1)] However, the synthetic procedure requires the addition of an acid catalyst such as propionic acid to the mixture of an allyl alcohol and an ortho ester. So it is desired to develop the new type of the ortho ester Claisen rearrangement, which proceeds under mild conditions, especially for the application to acid sensitive substrates. In this communication, we wish to describe a facile synthesis of γ,δ-unsaturated esters from allyl alcohols and ketene acetals under neutral conditions by the palladium promoted ortho ester Claisen rearrangement.

In the previous paper,[2)] we reported on the novel protective reagents for hydroxyl groups, and it was shown that $PdCl_2(COD)$ effectively catalyzed the addition of alcohols to vinyl ethers. So it could be expected that a mixed ortho ester ($\underline{3}$), the intermediate of the ortho ester Claisen rearrangement, was formed under mild conditions from an allyl alcohol ($\underline{1}$) and a ketene acetal ($\underline{2}$) using $PdCl_2(COD)$ as a catalyst. Thus, alcohols were treated with ketene acetals in the presence of $PdCl_2(COD)$, and several mixed ortho esters were obtained in 80-90% yields.

Next, we screened the reaction conditions for the preparation of a γ,δ-unsaturated ester ($\underline{5}$) from the mixed ortho ester ($\underline{3}$), and it was found that the desired ester was obtained in a good yield under neutral conditions, when the ortho ester ($\underline{3}$) was refluxed in the presence of a catalytic amount of $PdCl_2(PPh_3)_2$ in p-xylene. It was assumed that $PdCl_2(PPh_3)_2$ effectively promoted both the elimination of ethanol (or methanol) from the ortho ester ($\underline{3}$) and the rearrangement of the ketene acetal ($\underline{4}$) to the γ,δ-unsaturated ester ($\underline{5}$).[3)] Several γ,δ-unsaturated esters were prepared in good yields as summarized in Table 1. As shown in entry 4, the allyl alcohol having an acid-labile functional group gave the product in a high yield according to the present procedure.

Table 1.



Entry	Ketene acetal 2	Alcohol 1	Yield of 5/%
1	$CH_2=C(OEt)_2$	(E)-$PhCH=CHCH_2OH$	84
2		(Z)-$PhCO_2CH=CHCH_2OH$	88
3		(E)-$Ph(CH_2)_2CH(OH)CH=CHCH_3$	83
4		$Ph(CH_2)_2CH=C(OEt)CH_2OH$[a]	92
5	$CH_3CH=C(OMe)_2$	$PhCH(OH)CH=CH_2$	86

a) The addition of this alcohol to the ketene acetal proceeded in the absence of $PdCl_2(COD)$.

A typical procedure is described for the preparation of ethyl 3-phenyl-4-pentenoate (entry 1): Under an argon atmosphere, to a suspension of $PdCl_2(COD)$ (0.073 mmol) in toluene(1 ml) was added each toluene solution (2 ml) of cinnamyl alcohol (0.73 mmol) and 1,1-diethoxy-ethene (1.40 mmol) successively at 0 °C. The reaction mixture was allowed to warm to room temperature and stirred for 1 h. Several drops of pyridine were added, and the resulting mixture was diluted with dry ether. Insoluble materials were filtered off, and the solvent was evaporated to give the crude ortho ester. Then, a p-xylene solution (5 ml) of this crude product was added to a stirred suspension of $PdCl_2(PPh_3)_2$ (0.073 mmol) in p-xylene (3 ml), and stirring was continued for 4 h under reflux. After cooling, insoluble materials were filtered, and the solvent was removed. The residue was purified by preparative TLC to afford ethyl 3-phenyl-4-pentenoate (0.61 mmol, 84%).

It is noted that the present reaction provides a facile method for the synthesis of γ,δ-unsaturated esters in high yields under neutral conditions.

References

1) For example: W. S. Johnson, L. Werthemann, W. R. Bartlett, T. J. Brocksom, T. Li, D. J. Faulkner, and M. R. Petersen, J. Am. Chem. Soc., 92, 741 (1970).
2) T. Mukaiyama, M. Ohshima, and M. Murakami, Chem. Lett., 1984, 265; T. Mukaiyama, M. Ohshima, H. Nagaoka, and M. Murakami, ibid., 1984, 615.
3) When 3-phenyl-2-propenyl vinyl ether, a model intermediate of the present reaction, was refluxed in the presence of $PdCl_2(PPh_3)_2$ in p-xylene for 3 h, 3-phenyl-4-pentenal was obtained in 72% yield. On the other hand, the same reaction carried out in the absence of $PdCl_2(PPh_3)_2$ afforded the γ,δ-unsaturated aldehyde in 43% yield.

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