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Palladium(II) chloride catalyzed selective acetylation of alcohols with vinyl acetate†

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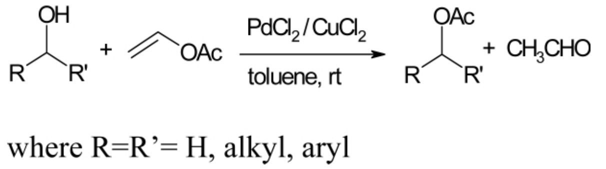
$PdCl_2$ can catalyze the acetylation of primary and secondary alcohols with vinyl acetate. The reaction is selective and mild with high yields. Tertiary alcohols, phenols and amines are unaffected under these reaction conditions.

The acetylation of alcohols is an important and frequently used transformation in organic synthesis.[1] Acetyl chloride[2] and acetic anhydride[3] are generally used as the acetylating agents in the presence of tributylphosphine[4] or pyridine derivatives.[5] Lewis acid catalysts such as $Sc(OTf)_3$,[6] TMSOTf,[7] $Cu(OTf)_2$,[8] $TaCl_4$,[9] $In(OTf)_3$,[10] $CoCl_2$,[11] yttria–zirconia based Lewis acids[12] have been reported to be efficient catalysts for acetylation of alcohols. Ishii and co-workers[13] have reported that Sm(II) complexes catalyze the acylation of alcohols with vinyl acetate.

Palladium chloride has long been used as a useful reagent for various organic reactions such as oxidation of olefins,[14] Cope rearrangement,[15] cyclization reaction,[16] deprotection of allyl ethers,[17] *etc.* Here we describe, for the first time, the palladium(II) chloride catalyzed acetylation of alcohols with vinyl acetate. It was reported that vinyl acetate reacts with lower aliphatic alcohols in the presence of palladium(II) catalyst to give vinyl ethers.[18] To our surprise, when a mixture of vinyl acetate, alcohol and catalytic amounts of $PdCl_2$ and $CuCl_2$ was allowed to stir in dry toluene at room temperature, acetate was obtained in high yields (Scheme 1). The reaction was generalized as shown by entries 1–16 of Table 1.‡

It was observed from Table 1 that reaction proceeds more rapidly with primary alcohols than secondary. Sterically hindered secondary alcohols like menthol need 2 mol% of the catalyst. Tertiary alcohols, phenols, thiols, aliphatic and aromatic amines are unaffected under these reaction conditions. With amines a palladium complex is formed. When acetic anhydride was used instead of vinyl acetate only a trace amount of the substrate **2** was converted to acetate after 3 hours. On the other hand, there were no reactions of ethyl acetate and acetic acid with **2** under the same reaction conditions. It was observed that $PdCl_2$ alone is not a good catalyst and the reaction is accelerated by the addition of $CuCl_2$. When $CuCl_2$ was used as a catalyst only a trace amount of acetate was formed after 12 h. This type of catalytic transesterification seems to be of interest, since acetylation of alcohols with acetyl chloride or acetic anhydride in the presence of base resulted in side products.[11] It is important to note that even 0.3 mol% palladium catalyst is enough for this transformation.

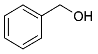
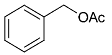
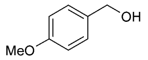
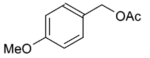
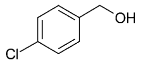
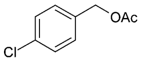
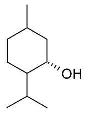
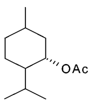
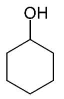
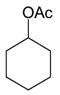
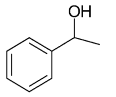
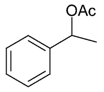
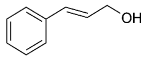
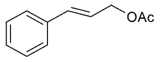
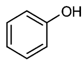
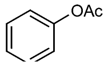
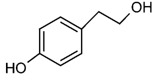
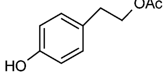
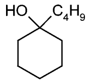
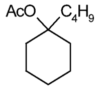
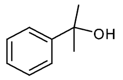
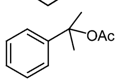
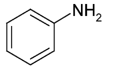
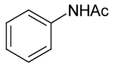


where R=R'= H, alkyl, aryl

Scheme 1

In conclusion, an efficient catalytic acetylation method using vinyl acetate as the acetylating agent under mild conditions has been developed. A variety of primary and secondary alcohols were acetylated in good yields under mild conditions. Groups such as methoxy, benzyloxy, thioether, thiol, chloro, and phenolic hydroxyl are unaffected under these reaction conditions. As the catalyst is heterogeneous, the work up process is very simple. The catalyst can be recovered by filtering the reaction mixture. The only byproduct acetaldehyde can be removed by evaporation along with the solvent. This catalytic acetylation of alcohols offers an additional

Table 1 Palladium catalyzed acetylation of alcohols with vinyl acaetate

No.	Substrate (**a**)	*t*/h	Product (**b**)	% Yield[a]
1		3.5		96
2		3		93
3		4		94
4	$PhCH_2O(CH_2)_4OH$	6	$PhCH_2O(CH_2)_4OAc$	82
5	$CH_3(CH_2)_8CH_2OH$	5.5	$CH_3(CH_2)_8CH_2OAc$	84
6		5		85[b]
7		3.5		89
8		9.5		92
9		4		96
10	$C_6H_{13}S(CH_2)_2OH$	5	$C_6H_{13}S(CH_2)_2OAc$	58
11	$HSCH_2CH_2OH$	3	$HSCH_2CH_2OAc$	95
12		9		0
13		4		86
14		9		0
15		9		0
16		9		0

[a] Yield refers to isolated yield. The compounds are characterized by ^1H NMR, elemental analysis and IR spectroscopy and comparison with the literature. [b] 2 mol% $PdCl_2$ was used.

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† Electronic supplementary information (ESI) available: ^1H, ^{13}C NMR and IR spectral data of **4b**, ^1H NMR, elemental analysis and IR spectral data of **5b**; ^1H and IR spectral data of **1b**, **2b**, **3b**, **6b**, **7b**, **8b**, **9b**, **11b** and **13b**. See http://www.rsc.org/suppdata/cc/b4/b401218f/

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method by use of vinyl acetate, instead of acetic anhydride or acetyl chloride, as acetylating agent under mild conditions.

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Notes and references

‡ Typical experimental procedures: A mixture of the substrate **2** (300 mg, 2.17 mmol), vinyl acetate (373 mg, 4.35 mmol), $PdCl_2$ (1.1 mg, 0.0065 mmol) and $CuCl_2$ (23 mg, 0.17 mmol) in dry toluene (1.0 mL) was stirred at room temperature for 3 h. The reaction was monitored by TLC using ethyl acetate and hexane as eluent. After completion of the reaction the catalyst was removed by fitration and the filtrate evaporated to dryness. Finally the product was purified by column chromatography to give 364 mg (93%) of the pure product. The compound was characterized by spectroscopic methods.

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