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Palladium-catalysed synthesis of allyl acetates from allenes

Suren Husinec [a], Milka Jadranin [b], Rade Markovic [b], Milos Petkovic [c], Vladimir Savic [c,*], Nina Todorovic [b]

[a] Institute for Chemistry, Technology and Metallurgy (ICTM), Centre for Chemistry, PO Box 815, Njegoseva 12, 11000 Belgrade, Serbia
[b] Faculty of Chemistry, University of Belgrade, Studentski trg 12-16, 11000 Belgrade, Serbia
[c] Faculty of Pharmacy, University of Belgrade, Vojvode Stepe 450, 11221 Belgrade, Serbia

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ABSTRACT

Allyl acetates were synthesised from allenes utilising methodology based on the general reactivity of π-allyl palladium intermediates which participate efficiently in transformations involving nucleophiles. Reactions of allenes and aryl iodides in the presence of AcONa and $Pd(OAc)_2/PPh_3$ as the catalytic system afforded allyl acetates in moderate to good yields. Monosubstituted allenes, depending on their structure, produced either a separable mixture of two regioisomeric products or a single regioisomer. As allylic acetates can be easily hydrolysed, the methodology is applicable for the synthesis of allyl alcohols as well.

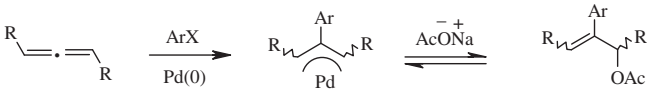
Allyl acetates are important compounds in organic synthesis and are widely used in C–C and C–X (X = heteroatom) bond formation. They have been extensively utilised in allylic alkylation employing, in particular, palladium catalysis,[1] but also other transition metals.[2] In these transformations, they undergo metal-promoted nucleophilic displacement with a range of C-, N-, S- and O-nucleophiles. This very useful methodology has been further expanded by umpolung using transmetallation of the intermediate π-allyl palladium species, thus allowing reactions with a range of electrophiles.[3] Related processes of allylic acetates can be effected by other transition metals, often with no need for transmetallation.[4] An additional important synthetic methodology employing allylic esters, including allyl acetates, is the Claisen-Ireland 3,3-sigmatropic rearrangement which produces γ-unsaturated carboxylic acids or derivatives.[5]

Most of the procedures for the preparation of allyl esters including allyl acetates are based on the acylation of allyl alcohols. Recently, the direct introduction of an acetoxy group, via Pd-activation of the C–H allylic position, emerged as an alternative synthetic pathway.[6] Substituted allyl acetates can be prepared from allyl acetate itself employing highly regioselective Pd-catalysed addition of boronic acids onto the double bond.[7] Dienes have also been shown to be suitable starting materials for the preparation of allyl acetate derivatives via halo-acetoxylation catalysed by palladium.[8]

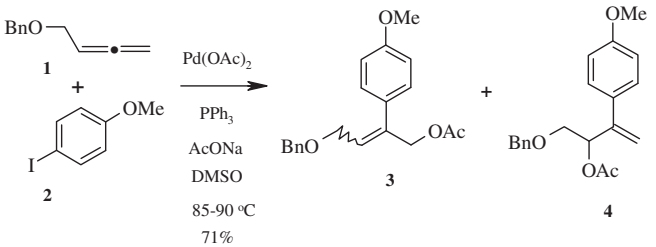
Our interest in the chemistry of allyl acetates led us to study the reactivity of allenes in the presence of nucleophilic acetates as a method for their synthesis. This approach is based on well-established nucleophilic substitution reactions involving π-allyl palladium species as outlined in Scheme 1.[9] Potential problems may arise from the fact that the last step is an equilibrium and thus may lead to side reactions of the π-allyl palladium intermediates. Intramolecular variations of this approach have been utilised for the preparation of lactones.[10]

Our initial experiment was carried out in DMSO as the solvent at 85–90 °C overnight (12 h) using allene **1**, an excess of *p*-methoxyiodobenzene **2** and $Pd(OAc)_2$ (10 mol %)/PPh_3 (20 mol %) as the catalytic system (Scheme 2). Five equivalents of AcONa were used in order to shift the equilibrium towards the product and also to address solubility issues.

The expected product, comprising a separable mixture of compounds **3** and **4**, was isolated in 71% combined yield in the ratio 2.7:1. The major product **3** was isolated as a 1.4:1 mixture of *E*- and *Z*-isomers.



Scheme 1.



Scheme 2.

* Corresponding author. Tel.: +381 11 3951 243; fax: +381 11 3972 840.
E-mail address: vladimir.savic@pharmacy.bg.ac.rs (V. Savic).

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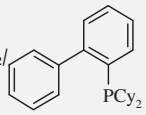
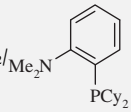
Table 1
Variation of the reaction conditions[a]

Entry	Catalyst	T (°C)	Solvent	Yield[b] (%)
a	$Pd(OAc)_2/PPh_3$	55–60	DMSO	47
b	$Pd(OAc)_2/PPh_3$	rt	DMSO	40
c	$Pd(OAc)_2/PPh_3$	85–90	DMF	37
d	$Pd(OAc)_2/PPh_3$	Reflux	MeCN	—
e	$Pd(OAc)_2/PPh_3$	85–90	1,4-Dioxane	—
f	$Pd(OAc)_2$/ 	85–90	DMSO	45
g	$Pd(OAc)_2$/ 	85–90	DMSO	40
h	$Pd(OAc)_2$/BINAP	85–90	DMSO	47

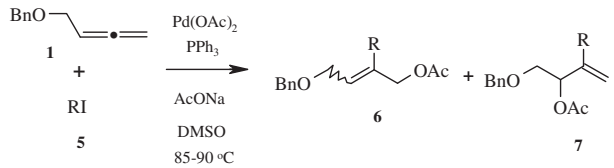
[a] Reaction conditions: allene **1** (0.4 mmol), *p*-$MeOC_6H_4I$ (0.6 mmol), AcONa (2.0 mmol), $Pd(OAc)_2$ (0.04 mmol), ligand (0.08 mmol), solvent (6 mL), 12 h.
[b] Isolated combined yield after column chromatography.

We attempted to optimise the reaction conditions further by exploring the effect of various parameters on the reaction and the results are summarised in Table 1. Performing the reaction with allene **1** and iodide **2** under the conditions described, but at lower temperatures (Table 1, entries a and b), afforded significantly lower yields of the products. Replacing DMSO with solvents such as DMF, MeCN or 1,4-dioxane (Table 1, entries c, d and e) had a remarkable effect. While in DMF the yield of the combined products decreased to 37%, reactions carried out in MeCN and 1,4-dioxane did not afford the products at all. This suggests that the solubility of AcONa is essential for the reaction to proceed and the best results were obtained using DMSO. We also screened several ligands (Table 1, entries f, g and h) varying their steric properties and the coordination mode under the optimal conditions. They generally afforded lower yields than with Ph_3P. This brief study showed that the initial conditions, described in Scheme 2, are superior and were used for further investigations.

Reaction of a range of aryl iodides with allene **1** afforded the expected allylic acetates in moderate to good yields (Scheme 3, Table 2). Aryl iodides with electron-donating substituents (Table 2, entries a–d) were shown to be slightly more reactive than iodides with electron-accepting moieties (Table 2, entries f and g). As expected, the major product in all cases was obtained via nucleophilic attack of the acetate on the less substituted terminus of the π-allyl palladium intermediate. The ratio of products **6** and **7** seemed to be influenced by the aryl substituent.

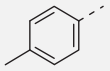
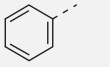
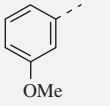
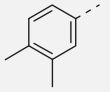
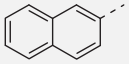
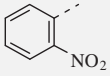
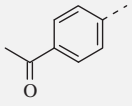
We also briefly investigated the reactivity of amido allene **8**. Under the typical conditions, compound **8** reacted with several aryl iodides producing allylic acetates in good yields (Scheme 4, Table 3). Surprisingly, allene **8** did not afford the internal acetate related to compound **7**. This regioselectivity may be attributed to steric hindrance caused by the sulfonamide moiety.

Using the above-mentioned method, allylic acetates can be prepared from allenes in good yields, but, since they can be easily hydrolysed, this method may also be useful for the preparation

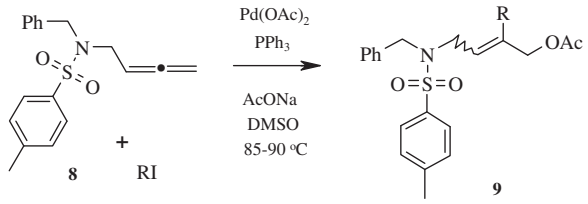


Scheme 3.

Table 2
Synthesis of allyl acetates from allene **1**[a]

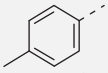
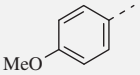
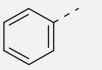
Entry	R	Ratio **6**:**7**[c]	Yield[b] (%)
a		2.6 (1.4:1):1	64
b		3 (1.2:1):1	64
c		1.4 (1.8:1):1	63
d		1.7 (1.8:1):1	66
e		6.5 (0.8:1):1	60
f		5.2 (0.8:1):1	50
g		2.7 (0.9:1):1	31

[a] Reaction conditions: allene **1** (0.4 mmol), ArI (0.6 mmol), AcONa (2.0 mmol), $Pd(OAc)_2$ (0.04 mmol), PPh_3 (0.08 mmol), DMSO (6 mL), 12 h, 85–90 °C.
[b] Isolated combined yield after column chromatography.
[c] The *E*:*Z* ratio of compound **6** is given in parenthesis.



Scheme 4.

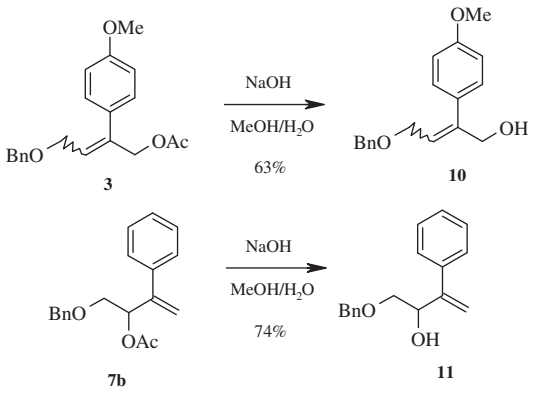
Table 3
Synthesis of allyl acetates from allene **8**[a]

Entry	R	Ratio *Z*/*E*	Yield[b] (%)
a		1:1	64
b		1.1:1	68
c		1:1	63

[a] Reaction conditions: allene **8** (0.4 mmol), ArI (0.6 mmol), AcONa (2.0 mmol), $Pd(OAc)_2$ (0.04 mmol), PPh_3 (0.08 mmol), DMSO (6 mL), 12 h, 85–90 °C.
[b] Isolated yield after column chromatography.

of allyl alcohols (Scheme 5), which are compounds of great importance in organic synthesis. Hydrolysis of acetates, such as **3** and **7b**, afforded the expected alcohols in good yields. The *Z*/*E* ratio of the starting material **3** did not change during the hydrolyses.

In summary, we have described a procedure for the preparation of allylic acetates from allenes. Under the optimised conditions employing $Pd(OAc)_2/PPh_3$ as the catalytic system, allenes react with aryl iodides in the presence of AcONa to afford the corresponding allyl acetates in moderate to good yields. This method



Scheme 5.

can be used for the preparation of allyl alcohols since the acetates can be hydrolysed efficiently.

Acknowledgements

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