

Preliminary communication

“PALLADIUM COMPLEXES-KF/ALUMINA” CATALYSED EXCHANGE OF ALLYLIC GROUPS OF ESTERS WITH PHENOL

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Summary

In the presence of KF/alumina and catalytic amounts of palladium complexes, phenol reacts with allylic esters under mild conditions to give the corresponding allyl phenyl ethers.

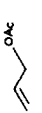
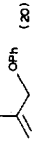
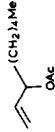
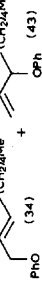
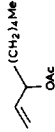
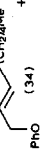
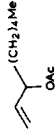
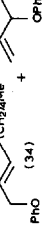
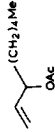
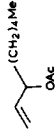
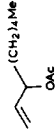
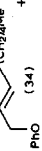
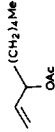
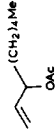
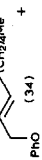
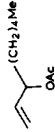
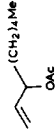
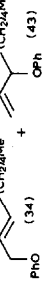
Carbon–carbon bond formation through nucleophilic addition of enolates to η^3 -allylpalladium complexes formed in situ from allyl acetates is an important procedure in organic synthesis [1]. Similar reactions under neutral conditions have been performed with allyl phenyl ethers [2], but the latter are generally obtained from allyl chlorides, which are less readily available than allyl alcohols. Therefore, methods of preparing allyl phenyl ethers from allyl alcohol derivatives such as allyl esters are of special value for syntheses, including those involving palladium catalysis.

We previously reported alkylations of allyl acetate promoted by the couple “palladium complexes-alumina” or by “Pd-KF/alumina” [3,4]. The recent report of the palladium catalysed allylic etherification by tin alkoxides [5] (Scheme 1, path A) prompted us to present the results of a study of the use of our system to induce exchange between acetate and phenoxy groups (Scheme 1, path B; Table 1).

The yields reported in Table 1 were not optimised, and although the efficiency of the exchange seems to be sensitive to substitution in the allylic entity (compare runs 1 and 2), a substantial improvement was achieved by modification of the reaction conditions (runs 12 and 13). No exchange was observed in the absence of the palladium complex (run 7), and there was only a very low degree of conversion when KF/alumina was omitted (run 5). Activation of the alumina by KF [6] led to a basic support much more efficient than the original alumina [7] (runs 3 and 6).

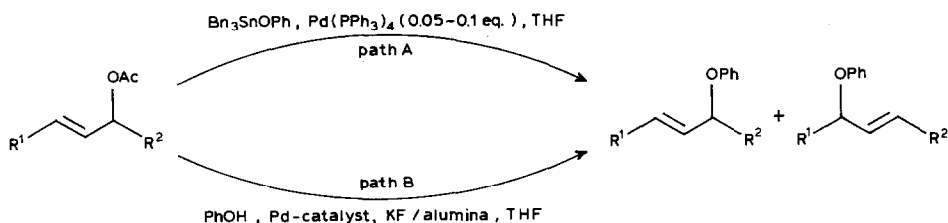
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TABLE 1
EXCHANGE OF ALLYLIC GROUPS ^a

Run	Starting ester	PhOH (equiv.)	Catalyst (equiv.)	Ligand (equiv.)	Al ₂ O ₃ /KF (mg/ mmole of acetate)	Time	Conversion (%)	Phenoxy compounds (yields %) ^b
1		1.5	Pd(dba) ₂ (0.05)	dppe (0.05)	500	24 h	c	 (84)
2		1.5	Pd(dba) ₂ (0.05)	dppe (0.05)	500	6 days	c	 (20)
3		1.5	Pd(dba) ₂ (0.05)	dppe (0.05)	500	20 h	100	 (34) +  (43)
4		1.5	Pd(dba) ₂ (0.01)	dppe (0.01)	500	7 days	100	 (80)
5		1.5	Pd(dba) ₂ (0.03)	dppe (0.03)	—	21 h	≈ 5	 (3)
6		1.5	Pd(dba) ₂ (0.03)	dppe (0.03)	500 ^d	20 h	≈ 80	 (7)
7		1.5	—	—	500	20 h	≈ 0	
8		1.5	Pd(dba) ₂ (0.05)	dppe (0.05)	500	24 h	93	 (38) +  (45)
9		1.1	Pd(dba) ₂ (0.05)	dppe (0.05)	200	20 h	67	 (23)
10		1.5	Pd(dba) ₂ (0.05)	dppe (0.05)	500	24 h	95	 (94)
11		1.5	Pd(dba) ₂ (0.05)	dppe (0.05)	500	6 days	66	 (11)
12		1.5	Pd(dba) ₂ (0.03)	dppe (0.03)	500	21 days	≈ 0	 (14)

13		1.1	$\text{Pd}(\text{dppe})_2$ (0.05)	dppe (0.1)	500	2 h ^e	100	
14		1.1	$\text{Pd}(\text{dppe})_2$ (0.05)	—	500	24 h	65	
15		1.1	$\text{Pd}(\text{dppe})_2$ (0.05)	dppe (0.1)	500	3.5 h	95	
16		1.1	—	—	500	48 h	< 5 ^c	
17		1.1	$\text{Pd}(\text{PPh}_3)_4$ (0.03)	PPh_3 (0.05)	500	48 h		
18		1.1	$\text{Pd}(\text{dppe})_2$ (0.05)	—	500	48 h ^e	0	
19		1.1	$\text{Pd}(\text{dba})_2$ (0.03)	PPh_3 (0.15)	500	10 h ^f	75	
20		1.1	$\text{Pd}(\text{dba})_2$ (0.03)	dppe (0.06)	500	48 h	70	

^a Reaction was carried out under argon in THF at room temperature with use of KF-alumina prepared as described previously [3]. ^b Isolated yields based on the quantity of starting ester introduced. ^c Not determined. ^d Predried commercial basic alumina (Merck, aluminium oxide 60, 70–230 mesh, activity 1) was used instead of KF/alumina. ^e Reaction at 40 °C. ^f Reaction at 60 °C.



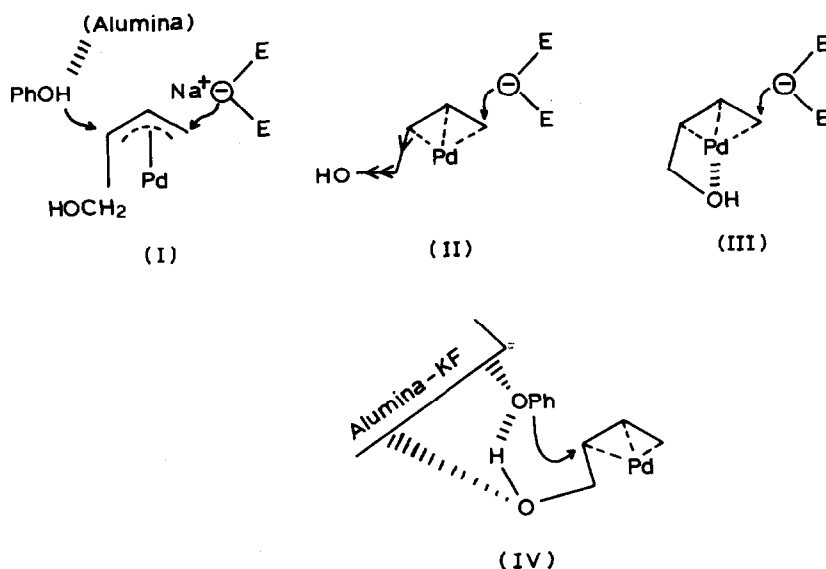
SCHEME 1.

Decrease in the quantity of the catalyst to 1 mole% did not greatly lower the yield of the phenoxy compound (run 4).

Reaction of a compound bearing both a hydroxy and an acetoxy group in allylic positions led to the selective exchange of the acetoxy group (run 14). With related compounds bearing chloro and acetoxy groups there was regioselective replacement of the chloro group (runs 15 and 17); it is of interest that in the absence of any palladium catalyst there was only a small amount of exchange of this chloro group at room temperature (run 16).

Regioselective formation of 1-hydroxy-2-phenoxybut-3-ene from *Z*-1-hydroxy-4-acetoxybut-2-ene (run 14) is surprising, since palladium catalysed substitution of the same compound by soft carbon nucleophiles [8] leads to the opposite regioselectivity [9,10]. In other words, a phenoxy entity generated from phenol and KF/alumina attacks the η^3 -allylpalladium intermediate on the carbon close to the hydroxy group, whereas stabilised enolates attack at the other end (I) (Scheme 2). An electronic effect of the hydroxy group [9,10] (II) and/or its intramolecular association with the palladium atom of the η^3 -allyl intermediate [8] (III) have been suggested to explain the regiospecificity observed in the case of stabilised enolates. From the present work it appears that the use of KF/alumina as base markedly influences the course of the reaction. There may be strong intramolecular interactions between the hydroxyl group in the starting material, the active sites of alumina, and phenol; they would prevent the hydroxypalladium intramolecular association in the η^3 -allyl intermediate and determine the regioselectivity of the addition (IV). Such an explanation is attractive, since the palladium-catalysed addition of phenol to 1,2-epoxycyclopent-3-ene, which is performed under neutral conditions, gives *cis*-1-hydroxy-4-phenoxy-cyclopent-2-ene [11]. The selective substitution of the chloro group and the regioselectivity observed with chloro acetates (runs 15 and 17) were expected in the light of the high reactivity of allyl halides compared with allyl acetates [11] and the inductive effect of the acetoxy group [10]. With derivatives of carveol, allyl acetate showed a low reactivity (run 18); switching to allyl benzoate produced the expected exchange (runs 19 and 20) with stereocontrol corresponding to a *trans* nucleophilic attack of the allylic ligand coordinated to the palladium atom [13], a racemic compound being obtained.

Comparison of the exchanges described in this paper with those obtained with organotin alkoxides [5] leads to the following conclusions. In the case of cinnamyl acetate which is the only common example, both procedures gave similar high yields. In the case of allyl acetates not bearing other functional groups, a low regioselectivity of the nucleophilic attack towards one of the two ends of the allyl



SCHEME 2

moiety was observed in both cases *. In the case of cyclic unsaturated esters, our method led to a higher stereoselectivity. Moreover, our procedure avoids the needs to use tin derivatives, and KF/alumina is easy to prepare and to handle.

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* In response to a referee's comment, we have checked that both the 1- and 3-phenoxy compounds isolated in run 3 remained unchanged when kept under our experimental conditions. However, when the mixture was heated at 60 °C, the 1-phenoxy isomer was obtained from the 3-phenoxy compound, as was expected since heating is required to form η^3 -allylpalladium complexes from allyl phenyl ethers [2,14]. Thus, the mixture of products isolated from 3-acetoxy-eicos-1-ene was that obtained under kinetic control at room temperature.

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