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ALLYLIC ALKYLATIONS CATALYZED BY THE COUPLE PALLADIUM COMPLEXES-ALUMINA

D. FERROUD[a], J.P. GENET[a*] AND J. MUZART[b*]

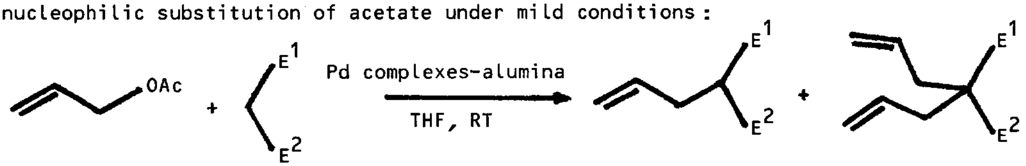
[a] *Laboratoire de Synthèse organique et organométallique, Laboratoire associé au C.N.R.S., Université Pierre et Marie Curie, 75005 PARIS*

[b] *Laboratoire de Photochimie, Unité de Recherche associée au CNRS, Université de Champagne-Ardenne, Moulin de la Housse, 51062 REIMS.*

Abstract :
Using both palladium complexes and alumina, nucleophilic substitutions of allyl acetate by various nucleophiles (pKa = 5-13) are realized with good yields at room temperature without preformation of the corresponding carbanions.

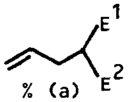
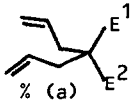
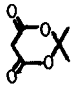
Formation of C-C bond through allylic exchange reactions with nucleophiles catalyzed by palladium is an important tool in organic synthesis (1). Intermolecular exchange was performed under neutral conditions when phenyl allyl ethers, allyl carbonates (2,3) or vinyl epoxides (4) were the starting materials, while the alkylation of allyl acetates generally required preformation of carbanions (1). As the latter substrate is much more common, it could be useful to suppress this preliminary step. This target has been realized in only a few cases with DBU (5,6) or Et_3N(7) as base. Meanwhile, one of us has described an easy aldolisation of carbonyl compounds using basic alumina as the enolisation reagent (8) ; furthermore, this reagent could also be employed to form carbanions of a variety of potential nucleophiles (9).

Following our interest for the C-C bond formation from π-allylpalladium complexes (3, 10,11),we have investigated the alkylation of allyl acetate by various nucleophiles catalyzed by palladium complexes and alumina. The simultaneous presence of these reagents has resulted in the nucleophilic substitution of acetate under mild conditions :



In addition to commercial basic alumina (table 1), we have also employed KF-alumina (table 2), which is known to allow the activation of acidic carbon compounds (12). As shown in the tables, yields and selectivities were very sensitive to the nature and quantities

Table 1 : Alkylation of allylacetate in the presence of commercial basic alumina (200 mg/mmol)

Run	$<^{E^1}_{E^2}$	Catalyst (mol. %)	Ligand (mol. %)	Time h.	 % (a)	 % (a)
1	$<^{NO_2}_{CO_2Et}$	Pd(dba)$_2$ (5)	PPh$_3$ (10)	7.5	89	-
2	$<^{NO_2}_{CO_2Et}$	Pd(dba)$_2$ (1)	PPh$_3$ (2)	22	74	22
3	$<^{NO_2}_{CO_2Me}$	Pd(dppe)$_2$ (5)	-	48	90	-
4	$<^{CO_2Et}_{CO_2Et}$	Pd(dba)$_2$ (5)	PPh$_3$ (10)	24	14	-
5	$<^{CO_2Et}_{CO_2Et}$	Pd(PPh$_3$)$_4$ (5)	PPh$_3$ (b) (10)	22	39	6
6 (c)	$<^{CO_2Et}_{CO_2Et}$	Pd(PPh$_3$)$_4$ (5)	PPh$_3$ (20)	40	70	15
7	$<^{CN}_{CO_2Et}$ (d)	Pd(PPh$_3$)$_4$ (5)	PPh$_3$ (15)	23	53	42
8	$<^{CN}_{CO_2Et}$	Pd(PPh$_3$)$_4$ (1)	PPh$_3$ (3)	23	19	56
9		Pd(dba)$_2$ (1)	PPh$_3$ (2)	19	-	76

a) all yields refer to isolated products.
b) similar results were obtained using more PPh$_3$ (20 mol. %)
c) 400 mg of alumina per mol. of allyl acetate were used.
d) using 4 eq. of E^1 CH_2E^2. Low yield of monoadduct was obtained in standard conditions.

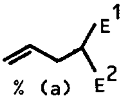
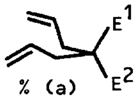
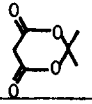
of both alumina and palladium complex ; for example :

- with diethylmalonate as nucleophile, switching from Pd(dba)$_2$ (run 4) to Pd(PPh$_3$)$_4$ (run 5) led to a better yield which was further significantly improved by using a larger quantity of basic alumina (run 6) or KF-alumina (runs 17 and 18).
- alkylation with α-methyl nitroacetate afforded a substantial proportion of the diadduct when 10 mol.% of Pd(dppe)$_2$ were present (run 11), while a specific monoalkylation was obtained in using 5 mol.% of the same catalyst (run 12). Interestingly, decreasing the amount of the palladium complex to 1 mol.% resulted also in a satisfactory yield in a reasonable period of time (run 13).

Meldrum's acid needs special comments. The preformed carbanion of this compound was reputed to be unreactive towards π-allylpalladium complexes (13) while, under our conditions, Meldrum's acid was a good nucleophile with exclusive formation of the diadduct (runs 9 and 20).

Furthermore, we have also to point out that the alkylations described here, were not accompagnied by decarboalkoxylation as could be happening when using DBU (5) instead of alumina, and were not observed when palladium was omitted from the reaction medium. The scope of this new process for alkylation catalyzed by transition metal is under investigation.

Table 2 : Alkylation of allylacetate in the presence of KF-alumina (200 mg/mmol)

Run	$<^{E^1}_{E_2}$	Catalyst (mol. %)	Ligand (mol. %)	Time h.	 % (a)	 % (a)
10	$<^{NO_2}_{CO_2Et}$	Pd(dba)$_2$ (10)	PPh$_3$ (20)	3.5	35	-
11	$<^{NO_2}_{CO_2Me}$	Pd(dppe)$_2$ (10)	-	2	59	40
12	$<^{NO_2}_{CO_2Me}$	Pd(dppe)$_2$ [b,c] (5)	-	4	95	-
13	$<^{NO_2}_{CO_2Me}$	Pd(PPh$_3$)$_4$ (1)	-	4	90	-
14	$<^{NO_2}_{CO_2Me}$	Pd(OAc)$_2$ (5)	dppe (0,5)	72	-	80
15	$<^{CN}_{SO_2p.tol}$	$\langle$(Pd(dppe)$^+$BF$_4^-$ (5)	-	1	50	25
16	$<^{CN}_{SO_2p.tol}$	$\langle$(Pd(dppe)$^+$BF$_4^-$ [d] (1)		1.5	75	5
17	$<^{CO_2Et}_{CO_2Et}$	Pd(dba)$_2$ (5)	PPh$_3$ (10)	3.5	54	-
18	$<^{CO_2Et}_{CO_2Et}$	Pd(dppe)$_2$ (5)	dppe (10)	4.5	75	-
19	$<^{CN}_{CO_2Et}$	$\langle$(Pd (dppe)$^+$)BF$_4^-$ [b] (5)		2	80	5
20		Pd(dba)$_2$ (1)	PPh$_3$ (3)	8	-	82

a) all yields refer to isolated products .
b) similar results were observed when using (Pd PPh$_3$)$_4$ as catalyst .
c) similar results were observed when using [(η^3-C$_3$H$_5$)Pd(dppe)]$^+$BF$_4^-$ as catalyst .
d) similar results were observed when using Pd(dppe)$_2$ as catalyst.

Procedure :

In a typical small scale experiment, allyl acetate (1 mmol.) and nucleophile (1 mmol.) were successively added to a THF solution (1.5-3 ml) of palladium complex (0.01-0.1 mmol.) (14) sometimes containing the extra ligand. Then, alumina (200 mg) (15) was introduced ; magnetic stirring was maintained under an argon atmosphere at room temperature. The following simple work-up was usually carried out : the slurry was diluted with ethyl acetate (20-30 ml); after efficient stirring during 15-20 mn, the mixture was passed through a short pad of Celite. Products were isolated by flash-chromatography (16). Aqueous work-up was also used, specially when products were purified by distillation.

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- Commercial basic alumina was a gift from Merck : catalogue n° 1067, aluminium oxide 60, 70-230 mesh, activity 1.
- KF-alumina was prepared from an aqueous slurry of the preceeding alumina (20 g in 200 ml of H$_2$O) containing KF (15 g). The mixture was stirred during four hours at room temperature ; the water was removed in a rotavapor and the residue was dried overnight *in vacuo* (80°C/1 torr).

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