Pergamon

Tetrahedron Letters 39 (1998) 9439–9442

TETRAHEDRON
LETTERS

Palladium(0)-Catalyzed Substitution of Allylic Substrates in Perfluorinated Solvents

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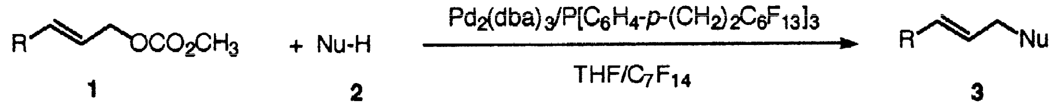
Received 14 September 1998; accepted 13 October 1998

Abstract

Palladium(0)-catalyzed alkylation reactions of allylic substrates can be performed using the new concept of fluorous biphasic system, allowing a very easy recycling of the catalyst.

Key words: allylic substitution; palladium(0); perfluorinated solvent; perfluorinated ligands; recycling.

Homogeneous transition metal catalysis is now a well established and powerful tool in organic synthesis. However, one of the greatest drawbacks of this methodology is the need for sometimes labour and cost intensive separation procedures to isolate the organic products from the homogeneous dissolved catalyst. There is a great demand for efficient methodologies to recover and recycle the often toxic and expensive metal catalysts [1]. A very elegant approach to solve this problem is the use of a biphasic system, consisting usually of water and an organic solvent; in this case the catalyst is soluble only in water and the product(s) are preferable miscible with the organic phase [2]. A new biphasic system called Fluorous Biphasic System (FBS) was recently developed by Horvàth and Ràbai [3,4]; this approach uses a perfluorinated liquid and an organic solvent, the catalyst being soluble preferably in the perfluorophase due to the presence of perfluorinated ligands. Several catalytic reactions have been achieved in FBSs: hydroformylation of higher olefins [3], hydroboration of alkenes [5], oxidation of hydrocarbons [6-8], aldehydes [7] and sulfides [7], epoxidation of alkenes even in an enantioselective manner [9], and palladium cross-coupling of organozinc bromides with aryl iodides [10]. Our continuing interest in the area of palladium-catalyzed reaction in aqueous two-phase systems [11] prompted us to examine also the new FBS concept in palladium chemistry. In the present communication we report some preliminary results on the palladium-catalyzed allylic nucleophilic substitution reaction in perfluorinated solvents according to Eq. 1.



Eq. 1

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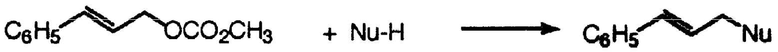
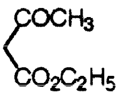
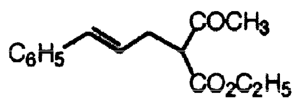
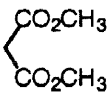
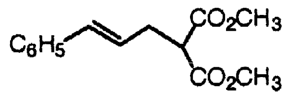
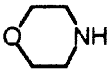
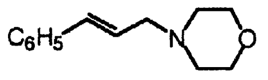
PII: S0040-4039(98)02188-1

Table 1. Palladium(0)-Catalyzed Reaction of Cinnamyl Methyl Carbonate with Various Nucleophiles[a]



Entry[b]	Nu-H	% Pd	T °C/mn	Product(s)	Yield %[c]
1a		5	50/15		100 (70)
1b	"	"	"	"	100 (78)
1c-g	"	"	"	"	100
1h	"	"	"	"	43
2a		2.5	50/15		100 (67)
2b	"	"	"	"	100
2c-e	"	"	"	"	100
3a-b		1.25	50/15		100
3c	"	"	"	"	100 (78)
3d	"	"	25/80	"	100 (85)
3e	"	"	50/15	"	100
3f	"	"	"	"	80
3g	"	"	"	"	39

[a] The reaction was performed in 3mL of THF and 3 mL of C_7F_{14}; [1] = 0.33 mM; [1] : [nucleophile] = 1:1.5; [Pd] : [phosphane] = 1:3; the products were fully caracterized by ^1H and ^{13}C NMR.

[b] Entry a corresponds to the 1st cycle; b: 1st recycling; c: 2nd recycling and so on.

[c] Determined by g.c.; isolated yields are given in parentheses and are not optimized.

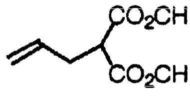
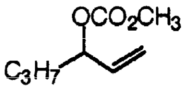
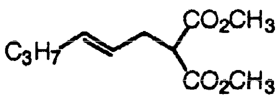
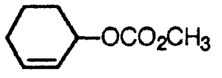
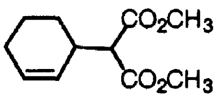
[d] 76% yield in pure product was obtained for the 3rd cycle.

Aryl phosphorus ligands bearing a $-(CH_2)(CF_2)_nF$ (n = 6,8) substituent have been introduced by some of us recently for catalysis in supercritical carbon dioxide as a reaction medium [12,13]. The ethyl-spaced perfluoroalkyl chain can be introduced into the aryl moiety in very flexible synthesis [14]. In case of the phosphane $P[C_6H_4\text{-}p\text{-}(CH_2)_2C_6F_{13}]_3$, it has been demonstrated that the specific substitution pattern provides efficient protection of the catalytic active center from steric or electronic influences of the perfluoroalkyl solubilizers. It was suggested on basis of this observation that the ligand should be useful also in FBS catalysis [12]. We now found that a fluorous phase soluble palladium catalyst could be indeed prepared *in situ* by treating $Pd_2(dba)_3$ (dba = dibenzylidene acetone) by the perfluorinated phosphane in perfluoromethylcyclohexane. A THF solution of the allylic substrate **1** and the nucleophile **2** was added and the solution was stirred at the indicated temperature. The reaction mixture was cooled to 0 °C. At this temperature, the tetrahydrofuran phase containing the coupling product **3** was easily separated by simple decantation, whereas the palladium catalyst remained in the fluorous phase and could be reused several times. Some substitutions using cinnamyl methyl carbonate as the allylic substrate and various nucleophiles are summarized in Table 1.

When cinnamyl methyl carbonate and ethyl acetoacetate were reacted in the presence of the phosphane/palladium catalyst (5 mol % based on palladium) at 50 °C, the transformation was almost quantitative after 15 min. The non-optimized isolated yields for the 1st and the 2nd cycles were 70 and 78%, respectively. We observed a decrease in the conversion only for the 8th recycling. The same trends were observed with dimethyl malonate (entries 2a-e) and morpholine (entries 3a-g). Up to 5 quantitative recyclings were readily performed in the latter case using palladium loadings as low as 1 mol%.

The condensation between dimethyl malonate and various allylic carbonates was studied under standard set of reaction conditions and the results are shown in Table 2. Allyl methyl carbonate, (2-vinyl)butyl ethyl carbonate and cyclohex-2-enyl methyl carbonate reacted with dimethyl malonate to give quantitatively the corresponding alkylated product(s). In each case 3 recyclings of the catalyst were performed without any decrease in conversion. It is noteworthy that the reaction could be performed at 25 °C in the case of allyl methyl carbonate.

Table 2. Palladium(0)-Catalyzed Reaction of Allylic Carbonates with Dimethyl Malonate[a]

Entry[b]	Allylic Carbonate	% Pd	T °C/mn	Product(s)	Yield %[c]
1a		2	25/30		100 (89)
1b-c	"	"	"	"	100
2a		2	50/15		100 (45)[d]
2b-c	"	"	"	"	100
3a		2	50/180		100 (68)
3b-c	"	"	"	"	100
3d	"	"	"	"	27

[a] The reaction was performed in 3mL of THF and 3 mL of C_7F_{14}; [1] = 0.33 mM; [1] : [nucleophile] = 1:1.5; [Pd] : [phosphane] = 1:3; the products were fully caracterized by ^1H and ^{13}C NMR.

[b] Entry a corresponds to the 1st cycle; b: 1st recycling; c: 2nd recycling and so on.

[c] Determined by g.c.; isolated yields are given in parentheses and are not optimized.

[d] Trace amounts of the *E* isomer and the *iso* product were also detected by NMR.

In conclusion we have shown that palladium(0)-catalyzed alkylation reaction can be performed very effectively using the new concept of fluorous biphasic catalysis, and that recycling of the catalyst is possible in a very simple and straightforward manner. Further extension in the area of palladium catalysis is under work and will be reported in due course.

Acknowledgements. This work was supported by the MESR and the CNRS (Programme Catalyse et Catalyseurs pour l'Industrie et l'Environnement and a fellowship to G. P.), the Max-Planck-Society and the Deutsche Forschungsgemeinschaft (Gerhard-Hess-Award to W.L.). W.L. wishes to thank Clariant GmbH, Werk Gendorf, for generous donation of perfluorinated starting materials

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