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Mild hydroarylation of alkynes with chelating dicarbene palladium(II) complex catalysts☆

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ABSTRACT

Chelating dicarbene palladium(II) complexes have been found to catalyse the hydroarylation of alkynes with excellent conversions and selectivities at low catalyst loading (0.1 mol.%). Products of formal *trans* hydroarylation of the triple bond are formed in high yields. Optimisation of the reaction parameters (nature of the solvent system, concentration of the reagents, reaction temperature) allows to further increase the selectivity of the reaction under mild reaction conditions.

1. Introduction

The development of C–H activation/functionalisation reactions into useful synthetic tools represents a formidable challenge in at least two respects, namely (i) the high average strength and low polarisability of a C–H bond, and (ii) the presence in the same molecule of many C–H bonds characterised by only slight differences in energy. Consequently, it is difficult to develop catalytic systems that are sufficiently active for practical use, and to control at the same time their selectivity in order to functionalise only a predetermined C–H bond in a target substrate. Nevertheless, research in this field has developed considerably in the course of the last 10–15 years [1,2], also as a result of some ground breaking discoveries mostly made at the beginning of the new century [3–8].

Among the different synthetic strategies proposed to functionalise C–H bonds, aromatic C–H bond functionalisation reactions can represent green and economical alternatives to more classical coupling reactions involving, e.g., aryl halides, such as Heck and cross-coupling reactions [9]. Several examples of such reactions have been reported in the recent literature [10–17]. They are based on: (i) chelate-assisted oxidative addition of the C–H bond to metal centres in low oxidation state [3,16–18], (ii) arene metallation by electrophilic metal centres which attack the aromatic ring *via* electrophilic aromatic substitution or *via* σ-bond metathesis [11,12,19], and finally (iii) Friedel–Crafts-type reactions promoted by metal centres that upon coordination activate electrophilically organic molecules toward attack at the aromatic ring [20,21].

Simple palladium(II) compounds such as $Pd(OAc)_2$ in a trifluoroacetic acid environment are for example known to promote the coupling reaction of arenes with alkynes [22–24]. In this case, products of formal *trans* hydroarylation of the triple bond are formed. The reaction is characterised by a high and quite unusual regio- and stereo-selectivity: in fact, it is remarkable that the thermodynamically less favoured *cis*-arylalkenes are the major products. There is at present some controversy about the reaction mechanism that fits best with these experimental findings. In fact, the initial (and purely speculative) mechanistic proposal made by Fujiwara and co-workers, invoking electrophilic arene metallation as the key reaction step with $Pd(OAc)_2$ as catalyst (left cycle in Scheme 1) [23] has been recently questioned by the valuable experimental work carried out by Tunge and Foresee as well as by the theoretical calculations of Soriano and Marco-Contelles, both favouring a Friedel–Crafts-type alkenylation (right cycle in Scheme 1) [25,26].

From the technological point of view, this reaction is arguably one of the most promising C–C coupling reactions *via* C–H activation/functionalisation, since it involves cheap, commercially available reagents and it requires neither directing groups on the arene nor oxidizing agents to regenerate the catalyst. However, its possible industrial utilization cannot leave apart a thorough optimisation of the catalyst and of the reaction conditions. In

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☆ Reactivity of chelating dicarbene metal complex catalysts, III; for Part II, see [A. Biffis, C. Tubaro, G. Buscemi, M. Basato, Adv. Synth. Catal. 350 (2008) 189.].

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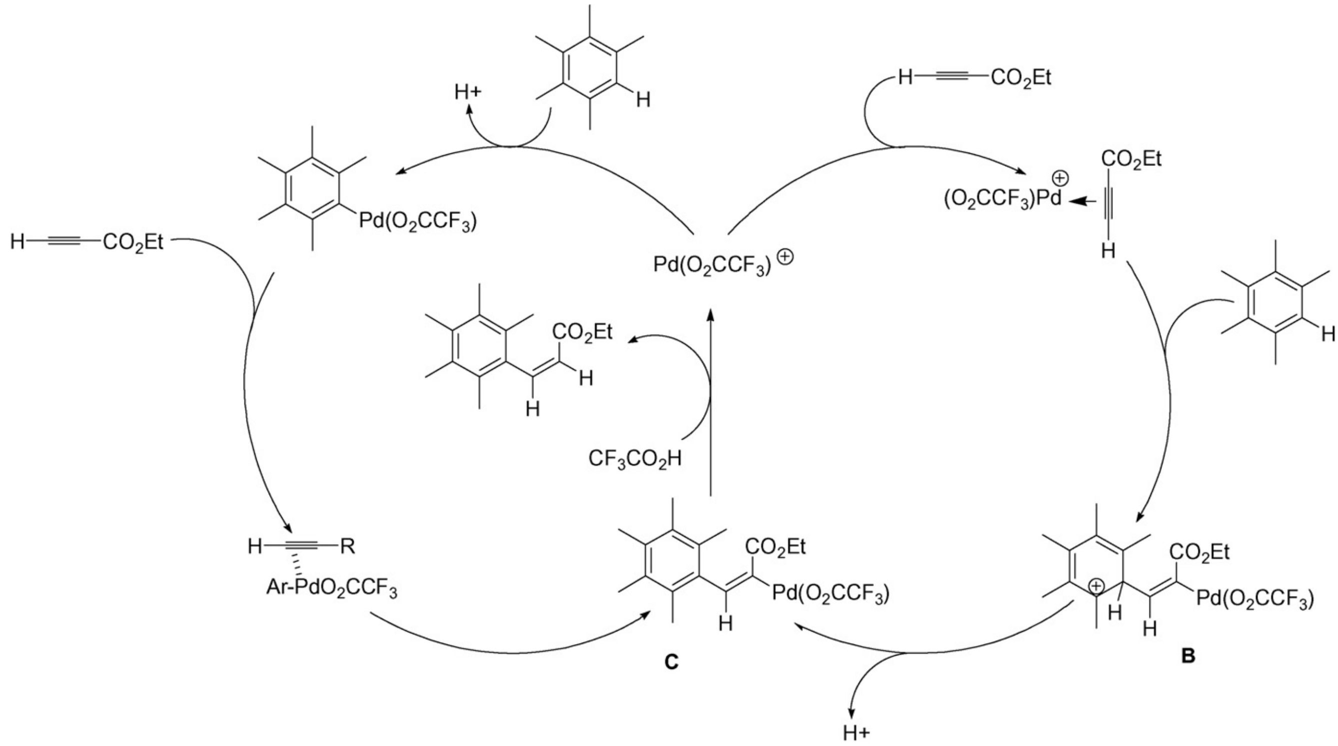

Scheme 1. Possible mechanistic pathways of the Fujiwara reaction; the actual catalytically active species $Pd(O_2CCF_3)^+$ is supposedly generated in situ from $Pd(OAc)_2$ and CF_3COOH.

particular, the original Fujiwara reaction protocol implies the use of 1–5 mol.% palladium, which heavily affects the cost of the process. Other metal centres such as platinum(II) [27–29], gold(I) and gold(III) [30,31] have been successfully employed as alternative catalyst, but their efficiency appears to be lower than that of palladium(II). Furthermore, use of less-noble, electrophilic metal centres has been also reported; however, their applicability appears to be currently limited to arylacetylenes [32–34].

A viable solution could be the use of palladium(II) complexes with suitable ligands, which should increase the stability of the catalyst under reaction conditions without negatively affecting its reactivity. *N*-Heterocyclic carbene ligands [35–39] appear particularly suited to this purpose, in that it is known that their palladium(II) complexes possess a high thermal and hydrolytic stability, even under strongly acidic conditions [40,41]. Indeed, very recently our group [42] as well as others [43] have reported on palladium(II) complexes with chelating dicarbene ligands or monocarbene ligands, respectively, that are active in the Fujiwara reaction in the absence of other promoters, and exhibit a superior performance in comparison to that of simple $Pd(OAc)_2$. In this contribution, we pursue further our work on chelating dicarbene palladium(II) complexes and investigate on the most suitable conditions for carrying out the hydroarylation reaction.

2. Experimental

2.1. General remarks

All manipulations were carried out using standard Schlenk techniques under an atmosphere of argon. The reagents were purchased by Aldrich as high-purity products and generally used as received. Complexes (**1**) [44], (**2**) [45,46], (**3**) [47], (**4**) [48], (**5**) [48], (**6**) [49], (**7**) [42], (**8**) [50] were prepared by literature procedures. All solvents were used as received as technical grade solvents. NMR spectra were recorded on a Bruker Avance 300 MHz (300.1 MHz for ^1H and 75.5 for ^{13}C).

2.1.1. General procedure for the catalytic tests

General procedure for the catalytic tests reported in Tables 1 and 2. The arene (5.3 mmol) and the palladium(II) complex (0.0265 or 0.00265 mmol) were placed in a 50 mL round bottomed flask, previously evacuated and filled with argon. Trifluoroacetic acid (4 mL) and 1,2-dichloroethane (1 mL) were then added and the resulting solution was stirred at room temperature for 5 min. Finally the alkyne (2.65 mmol) was added and the reaction mixture was heated at 80 °C and further stirred for 20 h (or 5 h for the tests reported in Table 2). Portions of the solution (0.2 mL) were drawn off from the reaction mixture and analysed by ^1H NMR or GC–MS. For the catalytic tests reported in Figs. 2 and 4 the molar amounts of the various reagents were slightly changed as indicated in the figure captions.

Table 1
Conversion (%) for the reaction of pentamethylbenzene and ethyl propiolate catalysed by different dicarbene palladium(II) complexes (1 mol.% catalyst, reaction time 20 h)

Complex	Conversion (%)[a]	Yield (%)[b]		
		a	**b**	**c**
1	98	49(33)	10(6)	–
2	98	54(28)	9(3)	2
3	96	45(17)	7(3)	12
4	100	84(9)	6(1)	–
6	100	73(15)	5(1)	3
8	92	84	8	–

Reaction conditions: see Section 2.

[a] Conversion and yields determined by GC–MS and/or ^1H NMR.

[b] In parentheses the yield in the hydrolysed product.