Use of ferrocenyl chelated palladacycles as catalysts for the Heck reaction

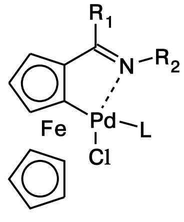
V. I. Sokolov, L. A. Bulygina, N. S. Khrushcheva, and N. S. Ikonnikov*

A. N. Nesmeyanov Institute of Organoelement Compounds, Russian Academy of Sciences,
28 ul. Vavilova, 119991 Moscow, Russian Federation.
Fax: +7 (499) 135 5085. E-mail: stemos@ineos.ac.ru

Two ferrocenyl palladacycles with bi- and tridentate (C,N) and (C,N,N) ligands were tested as possible catalysts for the Heck reaction. The latter complex efficiently catalyzed reactions of aryl halides with ethyl acrylate.

Key words: the Heck reaction, ferrocenyl palladacycles, catalysts.

Formation of new carbon—carbon bonds is an essential tool of organic synthesis. The most commonly used reactions of this type include the Heck and Suzuki—Miyaura reactions. Like many others, they are catalyzed by palladium complexes; both inorganic salts and other derivatives can serve as metal sources. Recently,[1—3] palladacycles **1** prepared by cyclopalladation of ferrocenylazomethines have been extensively tested as efficient catalysts for these reactions.



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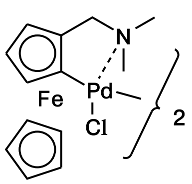
In the present communication, we studied structurally similar palladacycle **2** with a chelating ligand of the (C,N) type. In compound **2**, the electron donor is the N atom of the tertiary amino group rather than the imino N atom as in compound **1**. In our previous detailed investigations of the reactivities of such palladacycles, we have found that their stoichiometric reactions with enones afford vinylferrocenyl derivatives in high yields.[4,5] Recently, we have described the synthesis of fused bispalladacycle **3** with a chelating ligand of the (C,N,N) type. This complex is utterly inert to the reagents that successfully react with bicyclic palladium derivatives containing (C,N) ligands.[6]



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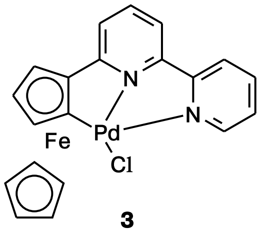
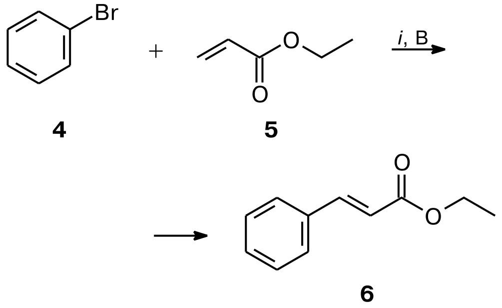


3

To find out how efficiently palladacycles **2** and **3** can catalyze the Heck reaction, we carried out two series of experiments involving a reaction of bromobenzene (**4**) with ethyl acrylate (**5**) in the presence of only one potential catalyst and different bases (Scheme 1, Table 1).

Scheme 1



B = Et_3N, K_2CO_3, K_3PO_4, Cs_2CO_3, AcOK

Reagents and conditions: *i.* **2** or **3**, DMF, 140 °C.

The Heck reactions were carried out under standard conditions (DMF, 140 °C) except that no inert atmosphere was employed. It turned out that both palladium complexes can catalyze the formation of ethyl cinnamate (**6**) (see Table 1); however, the yields of the product are mostly low. One could expect that the yield of the product would be increased in an inert atmosphere. To verify this assumption, we conducted one experiment under argon, achieving a 16% yield of ethyl cinnamate **6** (see Table 1, entry *2*).

The time of all the reactions was 7 h, whereupon the reaction mixtures were worked up and analyzed on a gas chromatograph to refine the yields of the products with allowance for the unreacted starting bromobenzene (**4**) (see Table 1). One can see in Table 1 that noticeable yields were obtained only in the presence of two bases (K_2CO_3

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Table 1. Catalytic reaction of bromobenzene (**4**) with ethyl acrylate (**5**) in the presence of bases*

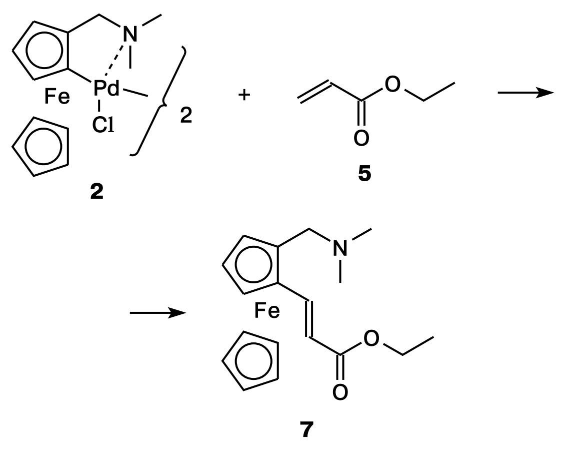
Entry	Base	Catalyst	Yield of **6** (%)	Unreacted C_6H_5Br (%)
1	Et_3N	**2**	1.3	3.8
2	K_2CO_3	**2**	3.3 (16)**	—
3	K_3PO_4	**2**	23.0	3.6
4	Cs_2CO_3	**2**	4.7	—
5	KOAc	**2**	3.5	<1.0
6	Et_3N	**3**	1.7	2.4
7	K_2CO_3	**3**	52.8	1.2
8	K_3PO_4	**3**	24.5	<1.0
9	Cs_2CO_3	**3**	4.8	3.2
10	KOAc	**3**	18.8	1.6

* The reaction time is 7 h; the reactions were not carried out in an inert atmosphere.

The yield of compound **6 in an argon atmosphere is given in parentheses.

and K_3PO_4) used in the Heck reaction. In addition, unlike palladacycle **3**, the stability of which under various, including very drastic, conditions is well studied,[6] dimer **2** was always used in reactions with vinyl ketones under milder conditions[4,5] (Scheme 2).

Scheme 2



Reagents and conditions: PhMe, Et_3N, 110 °C.

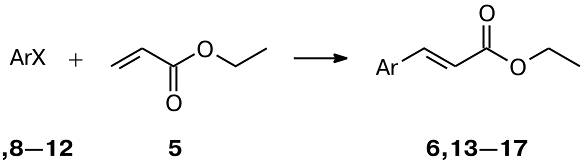
To study the stability of dimer **2** and its derivatives in our experiments, we heated compound **2** with an excess of ethyl acrylate in DMF in the presence of K_2CO_3 or K_3PO_4 at 140 °C for 7 h. However, the expected product **7** was not detected even in trace amounts, while the starting dimer **2** decomposed completely even at 100 °C (TLC, ethyl acetate as an eluent). Apparently, the Pd atom in dimer **2** is rapidly replaced by ethyl acrylate in DMF and the product decomposes on further heating. It should be noted that visual resinification of the reaction mixture in the presence of K_3PO_4 was slower than that in the presence of K_2CO_3, which may account for the highest yield with K_3PO_4 as a base (see Table 1, entries *1* and *2*).

To confirm the stability of palladacycle **3** under our experimental conditions, we heated it with a threefold excess of ethyl acrylate and K_2CO_3 in DMF at 140 °C for 12 h. According to TLC data, the final reaction mixture contained only the starting compound **3**.

Therefore, dimer **2** is an inefficient catalyst for the Heck reaction under our experimental conditions. At the same time, compound **3** is a promising catalyst, which motivated us to examine its properties in more detail, primarily in the presence of K_2CO_3 since this base provided the highest yield of ethyl cinnamate **6** in our preliminary experiments.

A further series of experiments was intended to study reactions of various aryl halides with ethyl acrylate (**5**) in the presence of K_2CO_3 (DMF, 140 °C) under argon (Scheme 3, Table 2).

Scheme 3



Reagents and conditions: **3**, K_2CO_3, DMF, 140 °C.

Compound	Ar	X	Compound	Ar	X
4,6	C_6H_5	Br	**10,15**	4-MeC_6H_4	I
8,13	C_6H_5	I	**11,16**	4-$MeOC_6H_4$	Br
9,14	4-MeC_6H_4	Br	**12,17**	1-Naphthyl	Br

It can be seen in Table 2 that the yields of ethyl cinnamates are sufficiently high, the conversion of the starting aryl halides being complete in 10 h. The exception is 1-bromonaphthalene (**12**) (Table 2, entry *6*), which was the sole reagent that was consumed incompletely over that period of time. This is probably due to mutual steric hindrances of the catalyst and aryl halide.

To sum up, we demonstrated that ferrocenyl palladacycle **3** is an efficient catalyst for the Heck reaction. For the ferrocenyl palladacycles under study, two alternative catalysis pathways can take place: associative, without cleavage of the carbon—palladium σ-bond, and dissociative, when this bond breaks down and the catalytically active species contains no palladium—carbon bond. The dissociative mechanism for palladacycle **3** can confidently be discarded. The sole possibility for the metal atom in complex **3** to participate in catalysis is its outer-sphere coordination with aryl halide and/or the vinyl group of acrylate, which initiates the associative mechanism with an increase in its coordination number to 5—6.

Table 2. Reactions of aryl halides **4** and **8—12** with ethyl acrylate (**5**) in the presence of palladacycle **3** and K_2CO_3 under argon*

Entry	ArX	Product	Yield (%)
1	C_6H_5Br (**4**)	**6**	41
2	C_6H_5I (**8**)	**13**	77
3	4-MeC_6H_4Br (**9**)	**14**	90
4	4-MeC_6H_4I (**10**)	**15**	63
5	4-$MeOC_6H_4Br$ (**11**)	**16**	46
6	1-Bromonaphthalene (**12**)	**17**	18

* The reaction time is 10 h.

Experimental

^{1}H NMR spectra were recorded on a Bruker instrument (300 MHz). Reaction products were analyzed on a Khromos GKh-1000 chromatograph (flame ionization detector, quartz capillary column 25 m×0.25 mm, phase SE-30, film 0.2 μm, column temperature 80 °C, programmed temperature rise to 220 °C at a heating rate of 40 deg min^{-1}, nitrogen as a carrier gas). Catalysts **2** (see Ref. 7) and **3** (see Ref. 6) were prepared as described earlier.

Catalytic reactions of ethyl acrylate (5) with aryl halides 4 and 8—12 (general procedure). A mixture of an aryl halide (1 equiv., 0.04—0.06 mol), ethyl acrylate (**5**) (1.5 equiv.), a base (2 equiv.), and a catalyst (0.002 equiv.) in DMF (6—10 mL) was heated with stirring at 140 °C for 7—10 h (see Tables 1, 2). The reaction mixture was diluted with water, and the product was extracted with AcOEt. The extract was dried with Na_2SO_4 and concentrated. The residue was dissolved in AcOEt—hexane (1 : 3), passed through a short column with silica gel, and concentrated. For the reactions of ethyl acrylate (**5**) with bromobenzene (**4**) (see Table 1) and 1-bromonaphthalene (**12**) (see Table 2, entry *6*), the yields of the products were determined by gas chromatography. Since all the compounds obtained have been described earlier, we characterized them by comparing their ^{1}H NMR spectra with the literature data.

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