Journal of Organometallic Chemistry 555 (1998) 141–144

Preliminary communication

A survey of reaction conditions for palladium-catalyzed processes

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Received 26 September 1997; received in revised form 20 November 1997

Abstract

Various reaction conditions and catalysts including cyclometallated Pd^{II}-complexes and palladium on activated carbon have been tested for Pd-catalyzed reactions that are assumed to proceed via Pd^{IV}-intermediates or via ligand exchange reactions between Pd^{II}-intermediates. © 1998 Elsevier Science S.A. All rights reserved.

Keywords: Heck reaction; Palladium catalysis; Ullmann reaction

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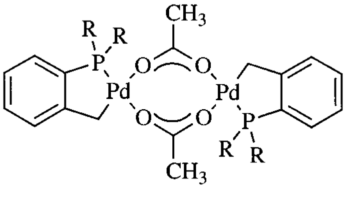
Recently, some palladium-catalyzed reactions have been developed that are assumed to involve Pd^{IV}-intermediates [1,2]. Originally these processes were found to proceed under Jeffery-conditions [3] (a catalytic amount of palladium acetate, K_2CO_3, tetra-*n*-butyl ammonium bromide [4], DMF), without any neutral ligand except for the solvent DMF. Now we have tested several reaction conditions and palladium catalysts in order to study their influence on the chemoselectivity of these reactions. Palladium on carbon was applied as an example for a heterogenous catalyst. Another focus of interest was the influence of phosphane ligands. Particularly interesting was the question, how the cyclometallated complex **1** introduced as a catalyst by Herrmann et al. [5] would perform: In 1983 Spencer reported that tris-*ortho*-tolyl phosphane is a superior ligand for the Heck reaction, achieving turnover numbers up to 130 000 [6]. Heck and coworkers [7] found that under the typical reaction conditions this ligand leads to the formation of cylometallated complexes of type **1** (with bromide and iodide as bridging ligands), but stated that these Pd^{II}-complexes are not the active catalyst. In contrast, in a series of publications Herrmann et al. [5] reported that the complex **1** is more active than the in situ formed system, achieving turnover numbers up to 1 000 000 and allowing the Heck reaction to be carried out with notoriously sluggish aryl chlorides. The extraordinary activity of the dimer **1** or of the corresponding mono-nuclear monomer is explained by its increased stability against P–C bond scission. According to Hartwig [8] the Pd^{II}-complex **1** is reduced to Pd^0-species under various reaction conditions and in the case of the Stille reaction there is evidence that a Pd^0-species is the active catalyst. However, in the case of the Heck reaction Herrmann and coworkers could not detect such a Pd^0-species by NMR experiments. This surprising result leads to the conclusion that either an extremely active Pd^0-catalyst in very low concentration is present or different mechanisms such as Pd^{II}–Pd^{IV}-cycles have to be taken into consideration even for the Heck reaction.



1 (R = *o*-tolyl)

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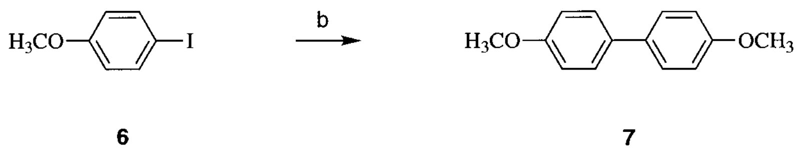
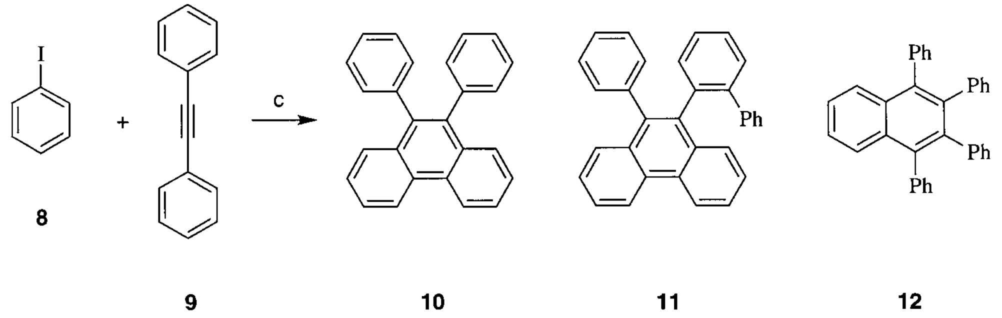
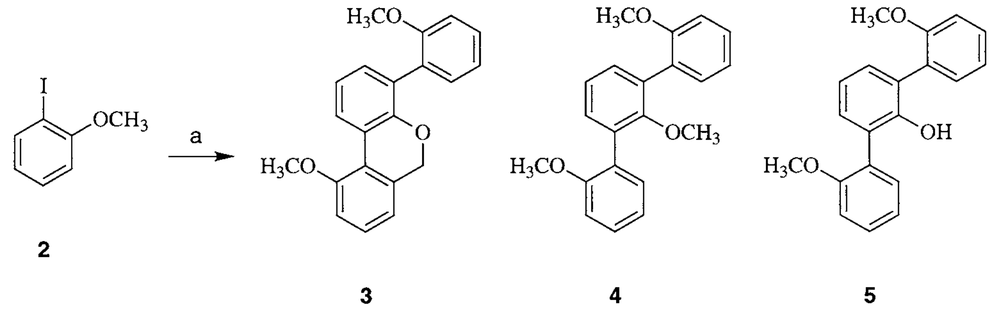
PII S0022-328X(98)00384-2

The Pd-catalyzed domino process condensating three equivalents of *ortho*-iodoanisol **2** to give the substituted dibenzopyrane **3** [9] is best explained by assuming Pd^{IV}-intermediates, especially for the CH-activation at the methoxy group. Presumably the catalytic active palladium has to adopt oxidation states ranging from Pd^{0} to Pd^{IV} and therefore an apparent Pd^{II}-catalyst such as **1** should not be suitable. Therefore we anticipated that **1** should either fail to catalyze the reaction or at least should result in a special product distribution. However, as it turned out **1** behaves similar to palladium acetate combined with two equivalents of triphenyl phospane (Table 1, entries 7 and 10): this result suggests that the Pd^{II}-complex **1** is not the catalytic active species in this case. Additional information derived from Table 1: tetraalkyl ammonium halides are crucial for achieving high yields of **3** (entry 2); water disturbs the domino process and at the same time favours the formation of the hydrolysis product **4** [9] (entries 3 and 4). An excess of either phenanthroline or triphenyl phospane completely inhibits the domino process (entries 6 and 8). Since a higher concentration of these stabilizing ligands obviously prevents the formation of Pd-aggregates and in all other experiments including entries 10 and 11 a typical black solution had been formed, this type of reaction might actually take place at the surface of palladium clusters [10], a hypothesis that is currently under investigation. In comparison, the heterogeneous reaction with palladium on carbon as catalyst is indeed successful (entry 9).







Also for Pd-catalyzed Ullmann reactions [11] such as the reductive coupling of **6** and for annelation reactions of iodobenzene (**8**) with tolane (**9**) [12] Pd^{IV}-intermediates and alternatively ligand exchange reactions [13] between Pd^{II}-species have been suggested to explain the formation of the biaryl bonds. For both processes the cyclometallated complex **1** proved to be suitable (Table 2, entries 14 and 15; Table 3, entries 22 and 23). Considering the difficulties to develop a mechanistic rationale for these reactions starting from an apparent Pd^{II}-catalyst such as **1** or its monomer it is more likely that a catalytic active Pd^{0}-species is formed in situ under the reaction conditions [14]. Pd-clusters or other Pd-aggregates are ruled out for entries 22 and 23 since

Table 1
CH-activation at the methoxy group of **2**; a: 2 mmol of **2**, 5 mol-% $Pd(OAc)_2$ (or 15 mol-% Pd on carbon or 2 mol-% **1**), 2 mmol n-Bu_4NBr, 8 mmol K_2CO_3, 10 ml dimethyl formamide (DMF) or dimethyl acetamide (DMA), 3 d, 100°C; isolated yields are given

Entry	Pd-cat	Variations	Solvent	Yield (%)		
				3	**4**	**5**
1	$Pd(OAc)_2$		DMF	90	–	–
2	$Pd(OAc)_2$	Without n-Bu_4NBr	DMF	47	3	16
3	$Pd(OAc)_2$	+5 vol-% H_2O	DMF	25	32	17
4	$Pd(OAc)_2$	+10 vol-% H_2O	DMF	1	15	–
5	$Pd(OAc)_2$	+5 mol-% phenanthroline	DMF	64	7	12
6	$Pd(OAc)_2$	+10 mol-% phenanthroline	DMF	–	–	–
7	$Pd(OAc)_2$	+10 mol-% PPh_3	DMF	57	7	–
8	$Pd(OAc)_2$	+50 mol-% PPh_3	DMF	–	–	–
9	Pd on C		DMF	61	10	27
10	**1**		DMF	57	28	9
11	**1**		DMA	72	17	–

Table 2
Pd-catalyzed Ullmann coupling reaction of **6**; b: 2 mmol of **6**, 5 mol-% $Pd(OAc)_2$ (or 5 mol-% Pd on carbon or 2 mol-% **1**), 2 mmol n-Bu_4NBr, 8 mmol K_2CO_3, 10 ml DMF or DMA, 4-15 h, 135°C; isolated yields are given

Entry	Pd-cat	Variations (h)	Solvent	Yield [%]: **7**
12	$Pd(OAc)_2$	15 h	DMF	80
13	Pd on C	15 h	DMF	60
14	**1**	15 h	DMF	67
15	**1**	4 h	DMA	47

the typical darkening of the reaction mixture did not appear in these two cases. Most interestingly the change of the solvent from DMF to DMA had a significant influence on the product distribution. Whereas with DMF the 1:2-product **12** is slightly favoured, DMA leads mainly to the 2:1-product **10**. Clearly the choice of the solvent for palladium catalyzed processes deserves more attention, because its influence on the selectivity can surpass that of additional phosphane or other ligands.

Table 3
Annelation reaction of **8** with **9**; b: 4 mmol of **8**, 1 mmol of **9**, 5 mol-% of $Pd(OAc)_2$ and $Pd(PPh_3)_4$ (or 15 mol-% Pd on carbon or 2 mol-% **1**), 2 mmol n-Bu_4NBr, 8 mmol K_2CO_3, 10 ml DMF or DMA, 3 d, 100°C; d: triphenylethene was found as a byproduct in this case with 16% yield

Entry	Pd-cat	Variations	Solvent	Yield [%]		
				10	**11**	**12**
16	$Pd(OAc)_2$		DMF	77	4	21
17	$Pd(OAc)_2$	without n-Bu_4NBr	DMF	51	2	4
18[d]	$Pd(OAc)_2$	+20 vol-% H_2O	DMF	14	2	35
19	$Pd(OAc)_2$	+10 mol-% PPh_3	DMF	86	3	4
20	$Pd(PPh_3)_4$		DMF	61	33	<3
21	Pd on C		DMF	37	12	10
22	**1**		DMF	35	12	42
23	**1**		DMA	67	25	5

Acknowledgements

Financial support of the Fonds der Chemischen Industrie and a donation of palladium acetate by the Degussa AG is gratefully acknowledged.

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