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Journal of Organometallic Chemistry 572 (1999) 141–145

Journal of Organo metallic Chemistry

Preliminary communication

Heck reaction catalyzed by phospha-palladacycles in non-aqueous ionic liquids[☆]

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Received 25 August 1998

Abstract

Phospha-palladacycles are among the most powerful palladium catalyst systems for the Heck reaction. We have shown the use of non-aqueous ionic liquids (NAILs) as an alternative to traditional molecular solvents for this reaction, with the phospha-palladacycle catalysts resulting in easy product separation, possible catalyst recycling and further increases in catalyst productivity. Preliminary results obtained with bromo- and chloro arenes are presented. © 1999 Elsevier Science S.A. All rights reserved.

Keywords: Palladium; Palladacycles; Catalysis; Heck reaction; Non-aqueous ionic liquids

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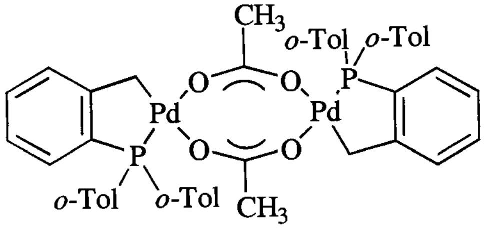
1. Introduction

Organopalladium catalyzed carbon–carbon bond forming reactions are versatile tools in synthetic chemistry [1]. In particular the vinylation of aryl halides—commonly called the Heck reaction—has received increased attention in the literature because of its enormous synthetic potential for generating carbon–carbon bonds and its tolerance towards a wide range of functional groups [2,3]. Attempts to achieve technical application of this reaction have failed in most cases due to the necessity of expensive aryl iodides or of high amounts of palladium catalyst. The former can be overcome by the use of more active catalysts being able to activate the more economic aryl bromides and chlorides whereas the latter can be overcome by recycling the catalyst.

We have introduced the cyclometallated complex *trans*-di(μ-acetato)-bis[*o*-(di-*o*-tolylphosphino)benzyl] dipalladium(II) **1** as an efficient catalyst for the Heck reaction with aryl bromides and electron-deficient aryl chlorides [4]. Although it is possible to retain complex **1** unchanged in yields up to 90 % after catalysis, this has never been a useful protocol for catalyst recycling because of the need for recrystallization and column chromatography.



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As the Heck reaction is normally performed in polar solvents like acetonitrile, DMF, DMAc or NMP [3] and since it was known that salt additives can activate

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[☆] Coordination chemistry and mechanism of metal-catalyzed *C–C* coupling reactions, Part 11; for Part 10 see R. Schmid, W.A. Herrmann, G. Frenking, Organometallics 16 (1997) 701.

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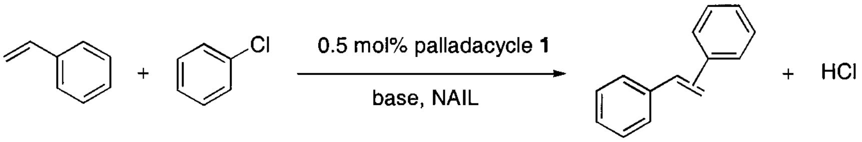
PII: S0022-328X(98)00941-3

Table 1
Heck reaction of chlorobenzene with styrene and 0.5 mol% palladacycle **1** as catalyst[a]



Solvent (NAIL)		Base	Additive (mol%)	t (h)	Conversion (%)[b]	Yield (%)[c]	Isomer ratio (1,1:Z:E)
1[d]	$[NBu_4]Br$	Na[OAc]	–	16	28	26 (93)	7:2:91
2	$[NBu_4]Br$	Na[OAc]	$[PPh_4]Cl$ (6)	18	52	51 (98)	4:0:96
3	$[NBu_4]OAc$	–	$[PPh_4]Cl$ (6)	14	54	54 (99)	6:2:92
4	MPIMBr[e]	Na[OAc]	$[PPh_4]Cl$ (6)	19	22	22 (99)	8:10:82
5	TBHDP[e]	Na[OAc]	$[PPh_4]Cl$ (6)	16	20	19 (95)	9:2:89
6	TPMPC[e]	Na[OAc]	$[PPh_4]Cl$ (6)	16	24	21 (88)	10:3:87
7	[f]	Na[OAc]	$[PPh_4]Cl$ (6)	20	2	2 (99)	1:0:99
8	$[NBu_4]Br$	Et_3N	$[PPh_4]Cl$ (6)	16	46	46 (99)	15:0:85
9	$[NBu_4]Br$	K_2CO_3	$[PPh_4]Cl$ (6)	16	42	41 (98)	3:1:96
10	$[NBu_4]Br$	K_3PO_4	$[PPh_4]Cl$ (6)	16	40	38 (95)	3:0:97
11	$[NBu_4]Br$	Na[OAc]	–	17	44	36 (82)	10:2:88
12	$[NBu_4]Br$	Et_3N	–	16	44	32 (73)	11:1:88
13	$[NBu_4]Br$	Na[OAc]	$[PPh_4]Cl$ (6) DMG[e] (12)	24	43	43 (99)	6:2:92
14	$[NBu_4]Br$	Na[OAc]	$[PPh_4]Cl$ (20)	24	54	53 (98)	11:1:88
15	$[NBu_4]Br$	Na[OAc]	$[AsPh_4]Cl$ (6)	17	62	62 (99)	4:1:95
16	$[NBu_4]Br$	Na[OAc]	$[AsPh_4]Cl$ (20)	24	78	77 (99)	6:2:92

[a] One equivalent PhCl, 1.5 equivalents styrene, 1.2 equivalents base, 1 mol% Pd (0.5 mol% **1**); $T = 150°C$.

[b] GC conversion of chlorobenzene using diethyleneglycol-di-*n*-butylether as internal standard.

[c] GC yield based on PhCl; yield based on conversion of PhCl in brackets.

[d] 1 mol% $Pd(OAc)_2$ as catalyst.

[e] MPIMBr = 1-methyl-3-propylimidazolium bromide; DMG = *N*,*N*-dimethylglycine; TBHDP = tri-*n*-butyl-*n*-hexadecylphosphonium bromide; TPMPC = triphenylmethylphosphonium chloride; TPMPB = triphenylmethylphosphonium bromide.

[f] TPMPC/TPMPB (2:1) was used as solvent mixture.

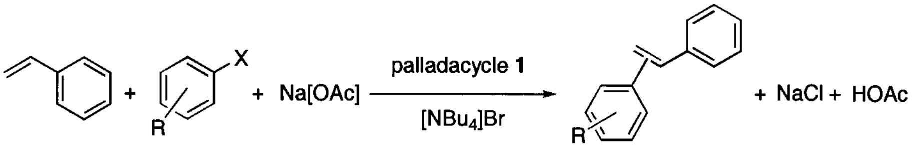
and stabilize the catalytically active palladium species [5], the use of non-aqueous ionic liquids (NAILs), i.e. molten salts, seemed to be a promising alternative to conventional molecular solvents [6]. The use of ionic liquids would have an advantage over conventional reaction conditions if the product could be distilled from the 'solvent' and the still active, stable catalyst thus giving the opportunity to recycle the whole catalyst–solvent system. This concept has already been tested for bromobenzene and butyl acrylate, but only with two different salts and catalysts [7]. Also, no details were given on the possibility of recycling the catalyst system in this report.

2. Results and discussion

The efficiency of various molten salts as solvent for the Heck reaction was tested by coupling chlorobenzene and styrene with 0.5 mol% palladacycle **1** (1 mol% Pd) [8]. In terms of productivity and stability of the catalyst, tetra-*n*-butylammonium bromide performed best as compared to other tested salts (Table 1). Tributylhexadecylphosphonium bromide was described as a superior reaction medium with bis(triphenylphosphine)palladium(II) dichloride as catalyst [7], but resulted in lower turnover numbers (TONs) with catalyst **1**. Sodium acetate, triethylamine, potassium carbonate and potassium phosphate were tested as base. Na[OAc] performed best, without exhibiting large differences in product yields compared to NEt_3 (Table 1, entries 2 and 8). Comparison of palladacycle **1** with palladium(II) acetate showed that it is necessary to use a phosphine-stabilized catalyst rather than a palladium salt (Table 1, entry 1). Not only a lower TON but also the formation of palladium black which could hamper recycling of the catalyst makes $Pd(OAc)_2$ no alternative to palladacycle **1**.

Using catalyst **1** does not lead to visible palladium black formation in most of the described media even in the reaction of chlorobenzene with styrene at 150°C. The addition of tetraphenylphosphonium chloride, $[PPh_4]Cl$, which had previously shown to be a superior additive for the Heck reaction [9], caused an increase in TON with chlorobenzene. The analogous arsonium salt, $[AsPh_4]Cl$, proved to be an even better additive in

Table 2
Heck reaction of aryl halides with olefins and palladacycle **1** as catalyst in $[NBu_4]Br$[a]



R	X	Pd [b] (mol%)	Additive (mol%)	*T* (°C)	*t* (h)	Conversion[c] (%)	Yield/isomer ratio (%)/(1,1:*Z*:*E*)[d]	TON (mol product·mol Pd^{-1})
4-$COCH_3$	Br	0.0001	–	120	60	>99	>99 (7:1:92)	1 000 000
4-H	Br	1	–	130	12	>99	>99 (6:1:93)	100
4-H	Br	0.1	–	120	16	>99	99 (5:1:94)	990
4-*n*-Bu	Br	0.1	–	130	15	99	99 (15:1:84)	990
4-OCH_3	Br	2	–	120	18	>99	99 (1:0:99)	50
2-thiophenyl	Br	0.1	$[AsPh_4]Cl$ (0.1)	130	16	93	92 (9:5:86)	920
4-NO_2	Cl	1	$[PPh_4]Cl$ (1)	150	16	>99	>99 (3:5:92)	100
4-$COCH_3$	Cl	0.1	$[AsPh_4]Cl$ (0.1)	150	15	99	99 (8:2:90)	990
4-CF_3	Cl	1	$[PPh_4]Cl$ (1)	150	15	99	98 (5:2:93)	98
4-H	Cl	2	$[AsPh_4]Cl$ (20)	150	16	97	96 (4:1:95)	48
4-H[e]	Cl	0.1	$[PPh_4]Cl$ (1)	150	66	39	39 (3:1:96)	390
4-OCH_3	Cl	4	$[PPh_4]Cl$ (2)	150	14	20	18 (22:2:76)	5
2-thiophenyl	Cl	1	$[AsPh_4]Cl$ (2)	160	16	58	51 (1:4:95)	51

[a] One equivalent ArX, 1.5 equivalents olefin, 1.2 equivalents Na[OAc], catalyst; $[NBu_4]Br$.

[b] Catalyst amounts given refer to Pd; for the amount of **1**, the value given has to be halved.

[c] GC conversion of aryl halide using diethyleneglycol-di-*n*-butylether as internal standard.

[d] GC yield based on ArX.

[e] With 2-ethylhexyl acrylate as the olefin.

molten $[NBu_4]Br$ although a darkening of the solution was observed in contrast to the addition of $[PPh_4]Cl$. Thus, chlorobenzene could be coupled with styrene in almost quantitative yield by 2 mol% palladium (Table 2). These observations indicate that $[PPh_4]Cl$ constitutes a stabilizing and activating additive whereas $[AsPh_4]Cl$ activates the catalyst but does not stabilize it. The dark solution obtained could also indicate the formation of palladium(0) aggregates implying that the reaction took place at the surface of palladium clusters, a hypothesis which is currently under investigation. Nevertheless until now, colloidal palladium was not capable of efficiently coupling chlorobenzene [10], thus suggesting that at least with PhCl the reaction is not mediated by palladium clusters. Using $[PPh_4]Cl$ and $[AsPh_4]Cl$ additives in the Heck reaction increases selectivity towards vinylation, i.e. less dehalogenation and biaryl formation occurs. Unfortunately, at the same time the reaction suffers from the formation of scrambled by-products in $< 1-15\%$ yield with activated aryl chlorides and from 20 up to 50% yield in the case of deactivated aryl chlorides depending on the substrates, the additive concentration and the reaction conditions. The isomer distributions of 1,1-diphenylethylene, (*Z*)-stilbene and (*E*)-stilbene are in the expected ratios with the (*E*)-isomer always being formed as the main product. The addition of *N*,*N*-dimethylglycine (DMG) had no further influence on the isomer distribution in contrast to literature reports [9].

The reaction of aryl bromides and aryl chlorides with styrene was also tested under the best conditions found for the reaction of chlorobenzene (Table 2). Activated aryl bromides like 4-bromoacetophenone react at low catalyst concentrations quantitatively. Thus, TONs of 1 000 000 [(mol product)·(mol palladium)$^{-1}$] have been achieved for the reaction of 4-bromoacetophenone with styrene. Deactivated aryl bromides like 4-bromoanisole require higher catalyst concentrations for quantitative yields. Activated aryl chlorides could be coupled quantitatively with good TONs of up to 1000. In these cases the use of NAILs proved to be much more effective than molecular solvents [4]. Nevertheless, deactivated aryl chlorides like 4-chloroanisole still leave room for further improvement.

The stability of catalyst **1** in molten $[NBu_4]Br$ suggested a possible recycling procedure [11]. The catalytic activity of complex **1** after recycling was tested by reacting bromobenzene with styrene and 1 mol% of palladium in $[NBu_4]Br$. Recycling of the solvent and the catalyst **1** was achieved by distillation of the reactants and products from solvent and catalyst in vacuo. Only NaBr as a stoichiometric salt by-product was left in the solvent–catalyst system. After the fourth run visible palladium black formation occurred and after the sixth

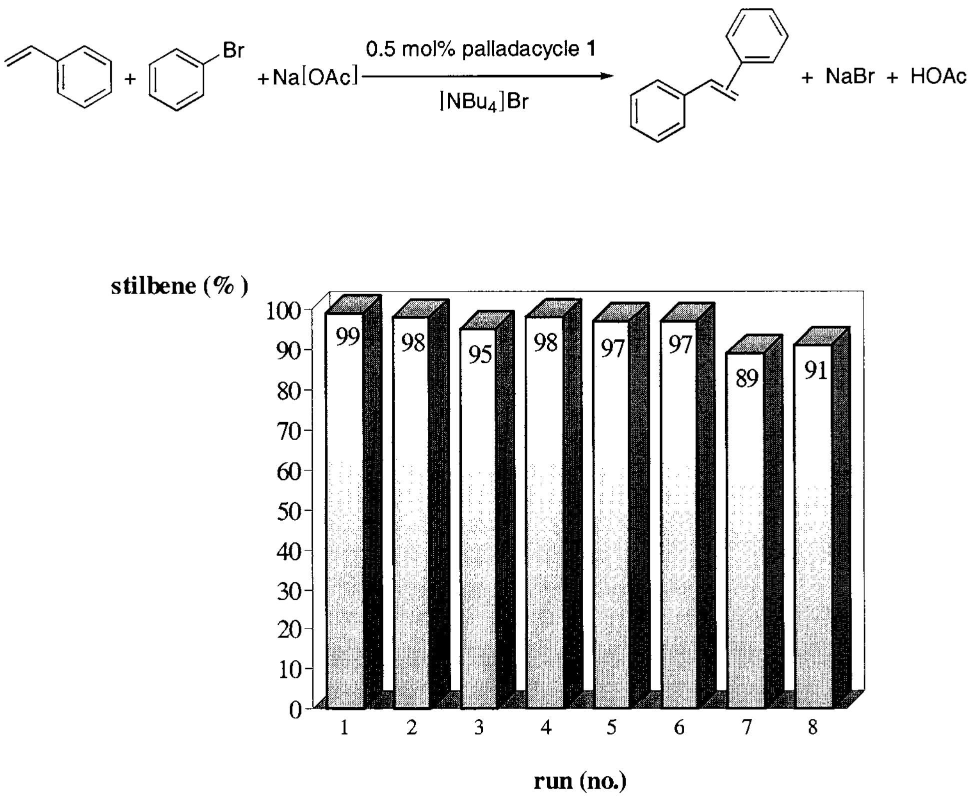


Fig. 1. Heck reaction of bromobenzene with styrene and 0.5 mol% palladacycle **1** as catalyst (above). Recycling of solvent and catalyst (below). Conditions: 1 equivalent PhBr (382 mg), 1.5 equivalents styrene (380 mg), 1.2 equivalents Na[OAc] (239 mg), 0.5 mol% **1**; 3.0 g [NBu$_4$]Br; $T = 130$°C; $t = 12$ h. Isolated yields of analytically pure stilbene by distillation.

run the melt became more viscous but catalysis could still be performed with excellent yields in further runs. Decomposition of the catalyst and the formation of palladium black could have been caused by either a long term, intrinsic catalyst instability or by a NaBr by-product promoted catalyst destabilisation. Further investigations are in progress. A graphical comparison of the catalytic activity of complex **1** over consecutive runs is shown in Fig. 1.

3. Conclusions

Molten salts as media for the Heck reaction have various advantages. As certain salt additives stabilize and activate the catalyst, the use of these additives as 'solvents' increases the stabilization and activation to a further extent. Inhibition of catalysis by the blocking of essential coordination sites on the palladium center has not been observed. Although NAIL protocols are homogeneous one-phase reaction conditions, catalyst recycling is possible like in two-phase- or in heterogeneous catalysis. Thus, the advantages of homogeneous catalysis like high selectivity and activity of the catalysts as well as the possibility of recycling can be used at the same time. Furthermore, NAIL protocols require less solvent due to the good solubility of Na[OAc] base and salt additives. Thus, the price for the solvent per reaction is comparable to NMP or DMAc.

Comparison of the yields obtained with palladacycle **1** in [NBu$_4$]Br with those obtained in DMAc shows that aryl bromides can be coupled with the same high TONs. In the case of aryl chlorides even an enhancement in activity was observed most probably due to increased thermal stability of the catalytically active species at elevated temperatures of 150°C and higher.

Further investigations concerning comparisons with other established palladium catalysts, activation of aryl chlorides and the detection of the catalytically active species are currently in progress.

Acknowledgements

This research was supported by the German Science Foundation (DFG), Degussa AG (palladium salt grants) and the Fonds der Chemischen Industrie (studentship for VPWB). We would like to thank Dr M.G. Gardiner for stimulating and helpful discussion.

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[8] General experimental procedure: 1.5 g of salt are stirred in vacuo at 130°C or 10 K over its melting point for 1 h in order to remove water and oxygen. After cooling to room temperature 1.0 mmol aryl halide, 1.5 mmol olefin, 1.2 mmol base, 0.05 g diethyleneglycol-di-*n*-butylether (GC standard) and catalyst **1** are added (all have been previously degassed) under an inert reaction atmosphere. After completion of the reaction the mixture was diluted with water, the products extracted with CH_2Cl_2 and filtered. Yields were determined by GC/MS.

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[11] For the experiments concerning recycling, the reactants and products were distilled from the catalyst and the solvent at 130°C/10^{-2} mbar. Yields given are of the isolated, analytically pure product isomers.