Available online at www.sciencedirect.com

SCIENCE DIRECT®

Journal of Organometallic Chemistry 690 (2005) 4648–4655

Journal of Organo metallic Chemistry

www.elsevier.com/locate/jorganchem

Heck and Suzuki coupling reactions in water using poly(2-oxazoline)s functionalized with palladium carbene complexes as soluble, amphiphilic polymer supports

Daniel Schönfelder, Oskar Nuyken, Ralf Weberskirch *

TU München, Department Chemie, Lehrstuhl für Makromolekulare Stoffe, Lichtenbergstr. 4, D-85747 Garching, Germany

Received 27 April 2005; received in revised form 7 June 2005; accepted 11 July 2005
Available online 2 September 2005

Abstract

This paper describes the application of a novel class of amphiphilic, water-soluble diblock copolymers based on 2-oxazoline derivatives with pendant N-heterocyclic carbene/palladium catalysts in the hydrophobic block for Heck and Suzuki coupling in neat water. Heck coupling reaction of iodobenzene with styrene proceeded rapidly after optimization of various reaction parameters such as the base, the reaction temperature and the catalyst amount. High activities with turn over frequencies (*TOF*) of up to 2700 h^{-1} were observed at 110 °C. Furthermore, the Suzuki coupling reaction of phenylboronic acid was studied in detail with different haloarenes (iodobenzene and various bromoarenes). The observed catalytic activity is even higher and *TOF* numbers of up to 5200 h^{-1} were achieved at 80 °C. Therefore, the presented micellar catalytic system reveals turn over frequencies which are the highest ever reported for such transformations in neat water without the addition of an organic cosolvent.

Keywords: Green chemistry; Heck coupling; Suzuki coupling; Polymer support

1. Introduction

The palladium catalyzed C–C coupling reactions belong to the most powerful processes for carbon–carbon bond formation [1]. As most important representatives of this class of reactions *Heck* and *Suzuki* coupling have to be noted. In this context the Heck reaction is the transformation between an aryl halide and an olefin to form cinnamic acid and stilbene derivatives, respectively [2,3]. The corresponding reaction between an aryl halide and an arylboronic acid yields in a biphenyl derivative and is called *Suzuki* coupling [4–6]. Although homogeneous catalysts have many advantages, catalyst immobilization is a well known methodology to allow efficient catalyst separation and to obtain metal-free products. Well known materials for catalysts heterogenization are Pd/C [7–11], zeolites/silica [12–15], metal oxides [16–18] and polymer resins [19–23] that show remarkable activities in Heck and Suzuki reactions under rather mild reaction conditions.

With the increasing interest in *Green Chemistry Processing* the replacement of expensive, toxic and flammable organic solvents by water as the preferred solvent is highly desirable due to economically and safety related process engineering reasons [24–26]. Whereas most of the heterogenized catalysts mentioned above have been applied in organic solvents an increasing number of research groups have recently focused on the development of new polymeric support materials for catalysis in water based on polyethylene glycol [27,28] poly(acrylic acid)s [29] or poly(*N*-isopropylacrylamide) copolymers [30,31]. However, the transformation of hydrophobic substrates in pure aqueous media without the usage of

---

[*] Corresponding author.
E-mail address: ralf.weberskirch@ch.tum.de (R. Weberskirch).

0022-328X/$ - see front matter © 2005 Elsevier B.V. All rights reserved.
doi:10.1016/j.jorganchem.2005.07.053

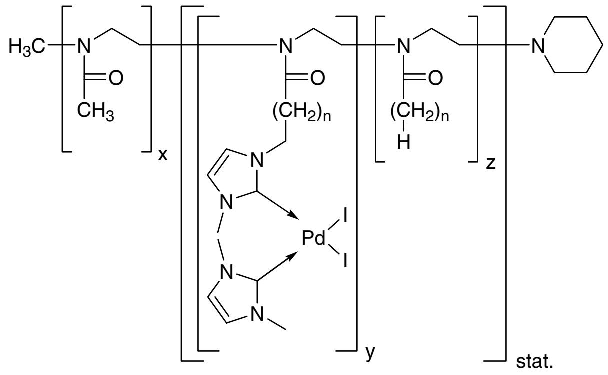
any organic cosolvent remains still a challenging task due to their limited water solubility. The most promising approach to increase the solubility of hydrophobic substrates in aqueous media is based on the use of amphiphilic polymer supports. Of particular interest is the work of Uozumi et al., who utilized commercially available poly(ethylene glycole) (PEG) modified poly(styrene) (PS) resins for catalyst immobilization in various transition-metal catalyzed reactions in neat water [32]. More recently, Yamada et al. described the preparation of a heterogeneous palladium catalyst by supramolecular self-assembling of $(NH_4)_2PdCl_4$ and poly[(*N*-isopropylacrylamide)-co-(4-diphenylstyrylphosphine)] [33,34]. However, typical limitations of cross-linked polymer materials, such as lowered reactivity and extended reaction times remain unsolved. In addition, fine tuning of the structure and composition of the polymer support to allow a better correlation with catalyst activity as an important feature of any support material is difficult to achieve with heterogeneous catalyst supports.

In the past years, metal complexes of *N-heterocyclic carbenes* (NHC) have been reported as a class of moisture, temperature and air-stable catalysts with remarkable activity in various C–C coupling reactions [35–40]. Recently, we have introduced a new class of soluble, amphiphilic polymer supports based on poly(2-oxazoline)s which indicated remarkable activities in various transition-metal catalyzed reactions such as asymmetric hydrogenation, ATRP, and alkine polymerization [41–43]. Based on these design criteria we have prepared a soluble, amphiphilic block copolymer with pendent *N*-heterocyclic carbene (NHC)/palladium complexes in the hydrophobic block [44]. First results of these polymer bound catalysts in a micellar catalytic variant of Heck reaction of iodobenzene with styrene in water revealed turnover frequencies (*TOF*) up to 570 h^{-1} which are the highest ever reported for this reaction in neat water without addition of any organic cosolvent. The scope of this contribution is a detailed investigation of these polymers in Heck reaction and Suzuki coupling by varying several reaction parameters such as temperature, catalyst amount and amphiphilic structure as well as the substrate.

2. Results and discussion

2.1. Poly(2-oxazoline)s functionalized by a palladium carbene complex

Recently, we have reported on the synthesis of a new class of amphiphilic, water-soluble diblock copolymers based on 2-oxazoline derivatives with pendant NHC/Pd catalysts in the hydrophobic block [44]. The synthesis of these polymers is divided into two stages and already described in detail in our recent paper (i) the preparation of three 2-oxazoline monomers **M1**–**M3** functionalized with a heteroleptic NHC/Pd complex and (ii) the copolymerization of one of these monomers with 2-methyl-2-oxazoline and 2-alkyl-2-oxazoline monomers for building up the corresponding amphiphiles **P1**–**P3** [44]. The general formula of these polymers is depicted in Fig. 1.



P1: n = 4 (But) x = 28.4 y = 1.5 z = 2.9 $M_n = 3920\ g \cdot mol^{-1}$
P2: n = 6 (Hex) x = 29.9 y = 1.8 z = 3.2 $M_n = 4400\ g \cdot mol^{-1}$
P3: n = 8 (Oct) x = 30.4 y = 1.9 z = 3.4 $M_n = 4730\ g \cdot mol^{-1}$

Fig. 1. Structure and composition of the amphiphilic poly(2-oxazoline) block copolymers **P1**–**P3** functionalized with NHC/Pd catalyst complexes in the hydrophobic block [44].

2.2. Heck reaction

The Heck reaction of sp2-halides with alkenes is promoted by palladium catalysts and meanwhile one of the most important methods for C–C coupling in organic synthesis [45] in the synthesis of intermediates for pharmaceuticals [46] and also for the preparation of conducting polymers [47].

2.2.1. Heck reaction in aqueous media

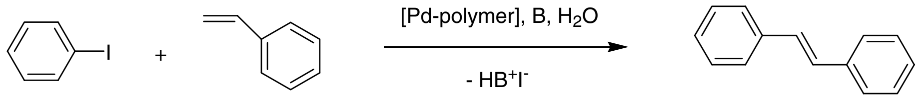
In the last years only a few reports have been presented that deal with Heck coupling in neat water without usage of any organic cosolvents. Jeffery for example studied intensively the transformation of iodobenzene with methyl acrylate in the presence of $Pd(OAc)_2/PPh_3$ in pure aqueous solution and explored in particular the beneficial effect of various tetrabutylammonia halides [48]. Another typical test reaction is the coupling of styrene with iodobenzene to give *trans*-stilbene. The transformation of these substrates in neat water is considerably more complicated due to the higher hydrophobicity and the accordingly lower water solubility of styrene (water solubility: 280 ppm) comparing to methyl acrylate (water solubility: 52 000 ppm) [49]. The first approach to react iodobenzene derivatives and various olefins under Heck coupling conditions in pure water was presented by Uozumi et al. [50]. They have used a palladium catalyst which is supported on a PS-PEG resin and obtained a yield of 92% of *trans*-stilbene after 14 h reaction time in case of styrene and iodobenzene as substrates. But unfortunately high catalyst amounts of 10 mol% were needed to achieve this result. The corresponding turnover frequency (*TOF*) as a measure of catalyst activity is less than 1 h^{-1}. Thus, the presented system shows excellent recyclability but poor activities.

2.2.2. Heck reaction in aqueous media using micellar catalysis

To solve this problem of low activities when transforming hydrophobic substrates in neat water, we have studied our amphiphilic polymers **P1**–**P3** in a micellar catalytic variant of the Heck coupling reaction of iodobenzene and styrene (Scheme 1). The course of the reaction was monitored by periodically taking samples and analyzing them by means of gas chromatography. The activity of the catalyst was determined from the point of inflection of substrate conversion. The primary product of this conversion is *trans*-stilbene **1**. Furthermore, the formation of the by-products *cis*-stilbene and 1,1-diphenylethene could be observed. In all coupling experiments the ratio of the three products *trans*-stilbene:1,1-diphenylethene:*cis*-stilbene was approximately 95:4:0.5.

In our first publication we have already studied the effect of spacer length on catalytic activity (see Table 1, exp. (**10**), (**11**), (**01**)) and have also demonstrated catalyst recycling and reusage in three consecutive cycles [44]. Herein we aimed to further optimize the reaction conditions and evaluated the dependence of the catalytic activity on characteristic system parameters, such as (i) *the base*, (ii) *the reaction temperature* and (iii) *the catalyst amount*. All Heck coupling reactions are summarized in Table 1. In Sections 2.2.2.1, 2.2.2.2, 2.2.2.3 these catalytic results are arranged according to the respective parameter.

2.2.2.1. Dependence on the base (B). In the first set of experiments the influence of the base on catalytic activity and induction time was studied. The transformations were conducted at 90 °C using the amphiphile **P3** with a palladium content of 0.67 mol%. Fig. 2 shows the kinetics of iodobenzene conversion as a function of different base used. We have used inorganic [*K_2CO_3* (**01/02**), *KOAc* (**03**)] and organic bases [*NEt_3* (**04**), *NBu_3* (**05**)] as well. As can be seen from the kinetics the investigated systems differ strongly in the duration of the induction period and formation of Pd(0) formation which is well



1

Scheme 1. Aqueous Heck coupling reaction of iodobenzene and styrene using the catalyst functionalized amphiphilic polymer **P1**–**P3** [Pd-polymer] and a base B (see Table 1, entries 1–11).

Table 1
Aqueous Heck coupling reactions

exp.[a]	P[b]	n_{Pd}/n_{PhI} (mol%)	*T* (°C)	Base B	*t* (h)	*x*[c] (%)	Yield **1**[d] (%)	*TOF* (h^{-1})
01	**P3**	0.67	90	K_2CO_3	1.5	97	>93	530
02	**P3**	0.67	90	K_2CO_3[e]	1.5	97	>93	200
03	**P3**	0.67	90	KOAc	3.0	93	27	110
04	**P3**	0.67	90	NEt_3	3.0	95	52	84
05	**P3**	0.67	90	NBu_3	5.0	93	5	88
06	**P3**	0.67	70	K_2CO_3	7.0	53	46	36
07	**P3**	0.67	110	K_2CO_3	0.5	96	>93	2700
08	**P3**[f]	0.10	90	K_2CO_3	6.0	94	>93	540
09	**P3**[f]	0.01	90	K_2CO_3	72.0	81	72	620
10	**P1**	0.67	90	K_2CO_3	2.0	96	>93	150
11	**P2**	0.67	90	K_2CO_3	1.5	97	>93	570
12	**P3**	0.67	90	K_2CO_3	3.0	97	2	n.d.
13	**P3**	0.67	110	K_2CO_3	3.0	95	4	n.d.
14	**P3**[f]	0.10	110	K_2CO_3	3.0	97	3	n.d.
15	**P3**[f]	0.10	110	K_2CO_3	3.0	97	5	n.d.

[a] Number of the experiment.

[b] P = polymer; the concentration of the polymeric amphiphile in water was $c_P = 0.57$ mM for all experiments, if not otherwise noted (see footnotef).

[c] Conversion of iodobenzene or various bromoarenes (see Scheme 2, exp. **12**–**15**).

[d] Yield of *trans*-stilbene (**1**).

[e] Additional 1.0 equiv. of tetrabutylammonia bromide NBu_4Br was added.

[f] The concentration of the polymeric amphiphile in water was $c_P = 0.17$ mM.

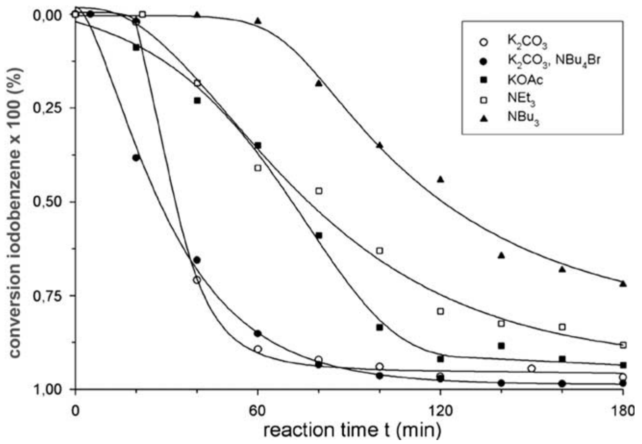


Fig. 2. Kinetic of the aqueous Heck coupling reaction of iodobenzene (PhI) and styrene in the presence of different *bases* (**01**–**05**; PhI:styrene:base = 1.0:1.25:1.5, $T = 90$ °C, $c_{P3} = 0.57$ mM, $n_{Pd}/n_{PhI} =$ 0.67 mol%).

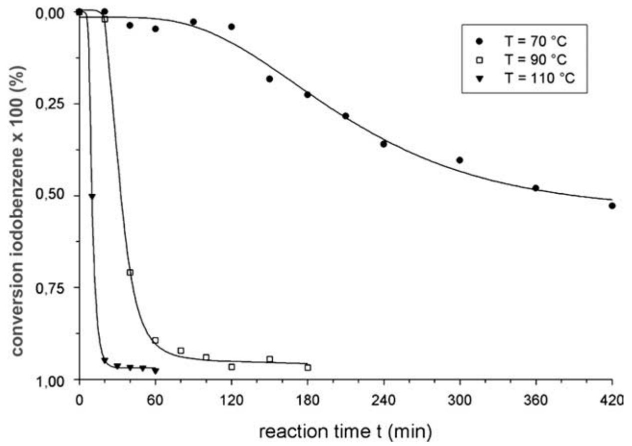


Fig. 3. Kinetic of the aqueous Heck coupling reaction of iodobenzene (PhI) and styrene in dependence on the *temperature T* (**06**, **01**, **07**; PhI:styrene:K_2CO_3 = 1.0:1.25:1.5, $c_{P3} = 0.57$ mM, $n_{Pd}/n_{PhI} =$ 0.67 mol%).

known to be the active species in heck reaction and also in their catalytic efficiency.

The highest activity was obtained by using *potassium carbonate* (**01**, $TOF = 530\ h^{-1}$) with an induction period of 15 min. The addition of *tetrabutylammonia bromide* does not cause an increase of the reaction rate (**02**). Rather, we have observed a decrease of the turnover frequency down to 200 h^{-1}. However, in this case the induction period was depleted down to 3 min. This can be ascribed to the fact, that tetrabutylammonia bromide is able to reduce Pd(II) to Pd(0), which is already described in the literature for the analogous catalyst complex with low molecular weight [51]. By using the bases *potassium acetate* (**03**, $TOF = 110\ h^{-1}$), *triethylamine* (**04**, $TOF = 84\ h^{-1}$) and *tributylamine* (**05**, $TOF = 88\ h^{-1}$) the catalytic activity decreased also. Moreover, the yield of *trans*-stilbene was far smaller, although the starting compounds were converted completely within a few hours. This fact was especially pronounced by using *tributylamine* as base. In this case mainly the dehalogenation of iodobenzene was observed and the yield of the coupling product was 5% only. The influence of the base on the catalytic activity of the system is very high and *potassium carbonate* exhibits the best results among those that have been investigated.

2.2.2.2. Dependence on the temperature (T). The temperature of a reaction is an important influencing factor especially for conversions with high activation energy, like Heck coupling. Due to this the reaction temperature was varied in the next set of experiments from 70 °C (**06**) to 90 °C (**01**) and finally up to 110 °C (**07**). The corresponding kinetic plots are represented in Fig. 3.

The turnover frequency reaches a value of 2700 h^{-1} at 110 °C (**07**) indicating excellent thermal stability and catalytic activity of the catalyst system. Beside the strong dependence of the catalytic reaction on the temperature, Fig. 3 shows also the influence of the temperature on the duration of the induction period. Within the investigated temperature range the induction period decreases from about 2 h (70 °C, **06**) down to 15 min (90 °C, **01**) reaching finally a duration of less than 3 min at 110 °C (**07**). Altogether a reaction temperature of about 110 °C can be considered as an optimal value with respect to a high reaction rate and a very short induction period.

2.2.2.3. Dependence on the catalyst amount (n_{Pd}/n_{PhI}). Beside the possibility to recycle a catalytic system the use of small catalyst amounts is another important aim in catalyst design. Both factors will reduce the economical costs of a catalytically synthesized product. Due to this fact in the next three experiments the catalyst amount n_{Pd}/n_{PhI} was varied from *0.67 mol%* (**01**) to *0.10 mol%* (**08**) and finally down to *0.01 mol%* (**09**). Thus, in relation to the starting compound iodobenzene only a small amount of 10^{-4} molar equivalents of the catalyst was used in experiment **09**. The obtained three kinetic plots are summarized in Fig. 4.

As can be seen from Fig. 4, the kinetic rate of the Heck reaction decreased when a smaller catalyst amount was used. Accordingly reaction time increased in the same way and the turnover frequencies of all three transformations are approximately the same (530–620 h^{-1}). Nevertheless, we have to emphasize that the Heck coupling reaction takes place in a unrestricted manner even at a catalyst amount of only 0.01 mol%, albeit the reaction time rises up to 72 h to reach a yield of 72% of *trans*-stilbene. Moreover, despite the longer reaction time no deactivation of the catalyst and no precipitation of palladium black was observed during this experiment just as in all other conducted coupling experiments using our micellar catalytic system.

However when studying bromoarenes as substrate with the optimized reaction conditions very low activities

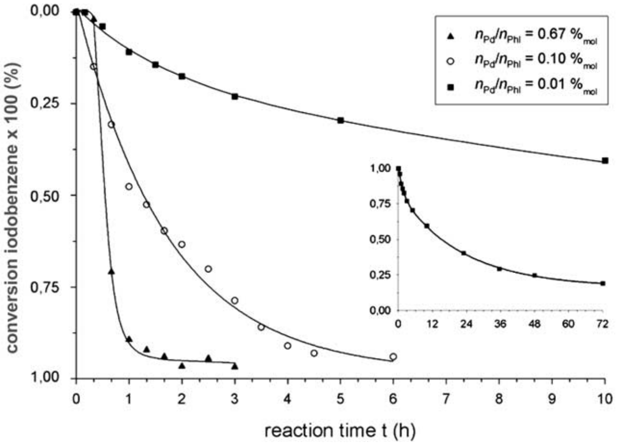


Fig. 4. Kinetic of the aqueous Heck coupling reaction of iodobenzene (PhI) and styrene in dependence on the *catalyst amount* n_{Pd}/n_{PhI}. The diagram at the right bottom corner represents the kinetic plot of experiment **09** (0.01 mol%) over the whole reaction period of 72 h (**08**, **01**, **09**; PhI:styrene:K_2CO_3 = 1.0:1.25:1.5, $T = 90$ °C, $c_{P3(01)}$ = 0.57 mM, $c_{P3(08/09)}$ = 0.17 mM).

were observed even at 110°C. Although bromobenzene (**12**, **13**, Table 1), 4-bromobenzaldehyde (**14**, Table 1) and 4-bromoacetophenone (**15**, Table 1) are still converted very fast, only about 2–5% of the *trans*-stilbene Heck products were formed. The major part of bromoearenes dehalogenated under the reaction conditions indicating clearly that the catalyst is most likely not active enough for the less active haloarenes.

Although the results are already very promising considering the pure aqueous reaction conditions they are still far away from results obtained with other supports...

2.3. Suzuki reaction

The Suzuki coupling of aryl halides with arylboronic acids is also promoted by palladium catalysts and nowadays a very important tool for building up biphenyl derivatives, which are required for a lot of pharmaceutical intermediates and fine chemicals.

2.3.1. Suzuki reaction in aqueous media

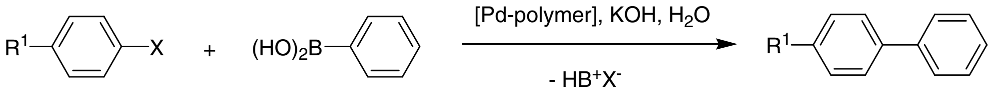
Uozumi and co-worker reported for the first time on the successful use of amphiphilic PEG-PS resin supported triphenyl phosphine palladium complexes in Suzuki coupling reactions in aqueous media under mild reaction conditions ($T = 25$ °C, $t = 24$ h) [52]. Also bromobenzene as substrate gave quantitative yield of the desried biphenyl compound with various phenyl boronic acid derivatives under the given reaction conditions ($T = 50$ °C, $t = 12$ h, 2 mol% Pd) [53]. Recently, Lee et al. have presented an NHC based palladium complex, which is supported by a PS resin, for the Suzuki coupling of iodobenzene and phenylboronic acid in water [53]. Beside the catalyst complexes some cationic imidazolium groups were attached to the outer sphere of the resin to reach an enhanced water solubility of the polymeric support. This system is outstandingly suited for the comparison with the system described in this contribution due to the general similarity. Using 1.2 mol% of the heterogenized catalyst the authors obtained a yield of 48% of biphenyl after 12 h reaction time at 50 °C. The corresponding turnover frequency is in the range of 10 h^{-1}. This disadvantage could only be eliminated by adding an organic cosolvent, like toxic *N*,*N*-dimethylformamide. Moreover, for the transformation of less active substrates, such as aryl bromides, the addition of an organic cosolvent is even coercively required.

2.3.2. Suzuki reaction in aqueous media using micellar catalysis

In analogy to the Heck coupling experiments we have tested our amphiphiles **P1**–**P3** also in a micellar catalytic variant of Suzuki reaction. Therefore, the conversions of iodobenzene and substituted bromobenzenes with phenylboronic acid to the corresponding biphenyl derivative **2** were explored (Scheme 2).

In the beginning, we have carried out a set of experiments to evaluate the dependence of the catalytic activity on characteristic parameters. Furthermore, different starting compounds were applied. All Suzuki experiments are summarized in Table 2 and discussed in Sections 2.3.2.1, 2.3.2.2, 2.3.2.3 with respect to the diversified parameters.

2.3.2.1. Dependence on the temperature (T). As visualized in Fig. 5 the catalyst shows also high activity in Suzuki coupling reaction and a pronounced dependency between reaction temperature and catalytic activity. Even at 50 °C the starting compounds were converted completely to the product biphenyl within 5 h (**1**). By increasing the reaction temperature up to 80 °C this yield can be reached already within 30 min (**2**). The corresponding turn over frequency is more than 1000 h^{-1}.



2

Scheme 2. Aqueous Suzuki coupling reaction of different halobenzenes with phenylboronic acid using the catalyst functionalized amphiphilic polymer **P1**–**P3** [Pd-polymer] and potassium hydroxide as base (see Table 2).

Table 2
Aqueous Suzuki coupling reactions

exp.[a]	P[b]	n_{Pd}/n_{PhI} (mol%)	T (°C)	R^1	X	t (min)	x[c] (%)	Yield **2**[d] (%)	TOF (h^{-1})
01	**P3**	1.00	50	H	I	240	98	91	110
02	**P3**	1.00	80	H	I	20	95	91	1200
03	**P1**	1.00	80	H	I	20	99	94	1200
04	**P2**	1.00	80	H	I	20	96	92	2600
05	**P1**	0.10	80	H	I	300	92	87	1100
06	**P2**	0.10	80	H	I	180	98	>95	3800
07	**P3**	0.10	80	H	I	180	98	>95	5200
08	**P2**[e]	0.67	110	H	Br	90	97	30	520
09	**P2**	0.10	110	CH_3CO	Br	300	97	84	560
10	**P3**	0.10	110	CHO	Br	300	98	90	2900

[a] Number of the experiment.

[b] P = polymer; the concentration of the polymeric amphiphile in water was $c_P = 0.17$ mM for all experiments, if not otherwise noted (see footnote[e]).

[c] Conversion of haloarene.

[d] Yield of biphenyl derivative (**2**).

[e] The concentration of the polymeric amphiphile in water was $c_P = 0.57$ mM.

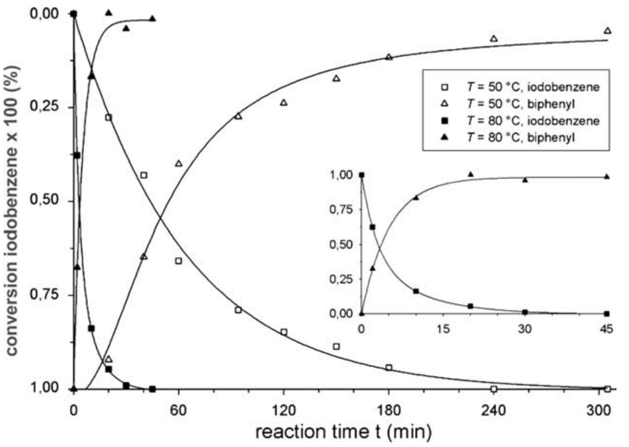


Fig. 5. Kinetic of the aqueous Suzuki coupling reaction of iodobenzene (PhI) and phenylboronic acid and biphenyl formation as a function of reaction *temperature T*. The diagram at the right bottom corner represents an enlargement of the kinetic plot of experiment **2** ($T = 80$ °C). (**1**, **2**; PhI:PhB$(OH)_2$:KOH = 1.0 : 1.5:2.0, $c_{P3} = 0.17$ mM, $n_{Pd}/n_{PhI} = 1.0$ mol%).

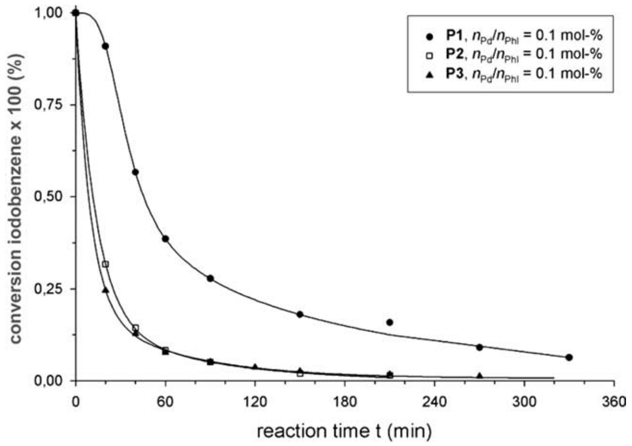


Fig. 6. Kinetic of the aqueous Suzuki coupling reaction of iodobenzene (PhI) and phenylboronic acid in dependence on the *amphiphilic structure* **P1**–**P3** at a *catalyst amount* of $n_{Pd}/n_{PhI} = 0.1$ mol% (**5**–**7**; PhI:PhB$(OH)_2$: KOH = 1.0:1.5:2.0, $T = 80$ °C, $c_P = 0.17$ mM).

*2.3.2.2. Dependence on the catalyst amount (n_{Pd}/n_{PhI}) and the amphiphilic structure (**P1**–**P3**).* In the next set of experiments (**02**–**04**, Table 2) the amphiphiles **P1**–**P3** were used at a constant catalyst amount of *1.0 mol%*. All reactions were characterized by a quantitative conversion of iodobenzene and a yield of biphenyl of more than 91% after less than 30 min. Unfortunately, the kinetic rates were too fast to identify reliably potential differences in the catalytic activities of the respective polymers. As a consequence, we have repeated the experiments using a smaller catalyst amount of *0.1 mol%* (**5**–**7**). By this means the reaction time decreased as expected by a factor of 10 so that even small differences of polymer activities could be detected (Fig. 6). In accordance to the Heck coupling experiments the catalytic activity of polymer **P1** is smaller than the activity of the both other amphiphiles **P2** and **P3** again. More precisely, the turn over frequency in experiment **5** (**P1**) is by a factor of 3.5 and 4.7 lower than the corresponding value of reaction **6** (**P2**) and **7** (**P3**) respectively. We attribute this smaller activity of amphiphile **P1** to the effect of spacer length mentioned before [44].

In addition, it should be stressed here that the activity of our micellar catalytic system is in case of Suzuki coupling even higher than in Heck reaction and the achieved turn over frequencies are up to 5200 h^{-1} (**7**) thus being a multiple higher than the activity of the also Pd/NHC based system of Lee and co-worker [31].

2.3.2.3. Using different halobenzenes as starting compounds. In the last set of experiments we have used different halobenzenes as starting compounds. In detail we have tested 4-bromoacetophenone (**9**) and 4-bromobenzaldehyde (**10**) as activated bromobenzenes and

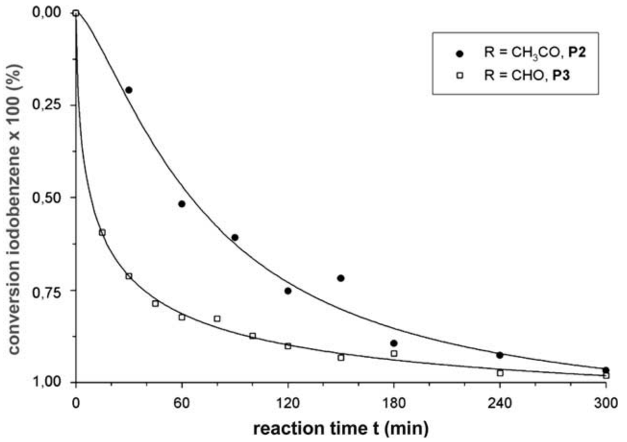


Fig. 7. Kinetic of the aqueous Suzuki coupling reaction of 4-bromobenzophenone (**9**) and 4-bromobenzaldehyde (**10**) with phenylboronic acid (**9**, **10**; RPhBr:PhB(OH)$_2$:KOH = 1.0:1.5:2.0, T = 110 °C, $c_P = 0.17$ mM, $n_{Pd}/n_{RPhBr} = 0.1$ mol%).

bromobenzene (**8**) as a non-activated one. The catalytic activity of our system for the transformation of activated bromobenzenes is with turn over frequencies of 560 h^{-1} (**9**) and 2900 h^{-1} (**10**) just a little bit lower than the activities for the conversions of iodobenzene (see Fig. 7).

An interesting difference between these both transformations is the lack of an induction period in case of 4-bromobenzaldehyde and the resulting extensive advantage in the conversion-time dependence of the corresponding reaction. This fact can be attributed to the reducing character of the formyl group and is already described for the analogous palladium complexes with low molecular weight [54].

Furthermore, we succeeded to convert the non-activated bromobenzene in a fast reaction too (**8**, TOF = 520 h^{-1}) using our micellar catalytic system (see Fig. 8). But unfortunately, even at a quantitative degree of conversion of bromobenzene the yield of biphenyl as coupling product was comparatively small at T = 90 °C with 6% yield of the biphenyl product. Only when we increased the reaction temperature to 110 °C biphenyl yield could be increased to 30% and the remaining portion of bromobenzene was dehalogenated to benzene (**8**). We assume, that the limited activity of the catalyst is the reason for this since also under homogenous conditions high temperature with T = 140 °C are required for this substrate. New NHC /Pd catalysts with bulky substituents however seem to be more promising to enhance the catalytic activity of our micellar catalytic system [55]. The preparation of these amphiphiles should be feasible in an analogous manner as the described one.

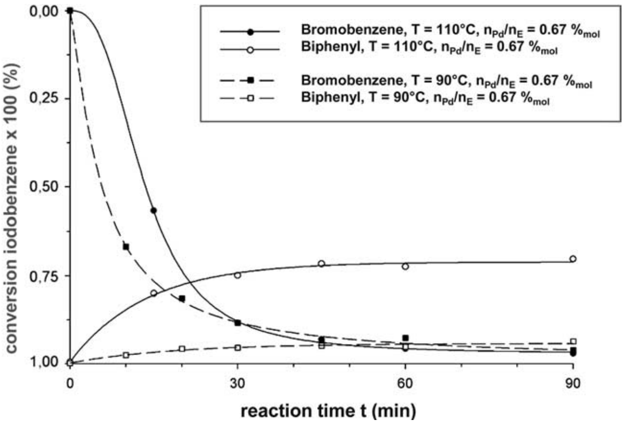


Fig. 8. Kinetic of the aqueous Suzuki coupling reaction of bromobenzene with phenylboronic acid and biphenyl formation (**8**; PhBr:PhB(OH)$_2$:KOH = 1.0:1.5:2.0, T = 110 °C, $c_P = 0.57$ mM, $n_{Pd}/n_{PhBr} = 0.67$ mol%).

3. Conclusion

In this contribution we have demonstrated the applicability of polymeric amphiphiles with pendant carbene/palladium complexes in Heck and Suzuki coupling reactions in water as solvent and investigated the effect of several reaction parameters such as temperature, catalyst amount, amphiphile structure and starting compounds on catalytic activity. The polymer supported catalyst indicated excellent activities in the Heck reaction of iodobenzene with styrene with TOF numbers up to 2700 h^{-1} at 110 °C. In the Suzuki reaction of iodobenzene with phenylboronic acid the polymer catalyst showed highest activities with TOF numbers up to 5200 h^{-1}. In addition also 4-bromobenzophenone and 4-bromobenzaldehyde could be successfully converted with phenylboronic acid. In summary, the successful catalyst immobilization on defined amphiphilic block copolymers in combination with easy catalyst handling and high activity makes these polymer supports very attractive for the preparation of various biaryl and stilbene derivatives under environmental benign reaction condition in the future.

4. Experimental

4.1. Measurements

Gas chromatographic analyses were performed on a Varian CP-3380, capillary column CP-Sil 8 CB, length: 25 m, with helium in combination with a flame ionization detector FID/1177.

4.2. Materials

All chemicals and solvents were purchased from Aldrich Chemical Co. and Fluka. The solvents were distilled under argon and additional degassed twice before use. Furthermore, they were stored under argon atmosphere.

4.3. Poymeric macroligands *P1–P3*

Synthesis and characterization of the amphiphilic, water-soluble block copolymers **P1**–**P3** with pendant NHC/palladium catalysts in the side chain has been reported in a recent publication [44].

4.4. Micellar catalysis

Catalysis experiments: All catalysis experiments were carried out under argon in 50 mL reaction tubes. In 10 mL of degassed water a portion of the polymer (**P1**–**P3**) was dissolved so that the concentration of the polymer is about 0.1–0.6 mM. The first starting compound, a base and tetradecane as internal standard were added in the respective ratio (*Heck*:haloarene:styrene: base = 1.0:1.25:1.5, *Suzuki*:haloarene:phenylboronic acid:base = 1.0:1.5:2.0). The mixture was stirred and heated to the reaction temperature. Then the catalysis was started by adding the second starting compound. The course of the reaction was monitored by periodically taking samples and analyzing them by means of gas chromatographic analysis.

References

[1] R.A. Sheldon, H. van Bekkum, Fine Chemicals through Heterogeneous Catalysis, Wiley–VCH, Weinheim, 2001.
[2] R.F. Heck, J.P. Nolley Jr., J. Org. Chem. 37 (1972) 2320.
[3] R.F. Heck, Acc. Chem. Res. 12 (1979) 146.
[4] N. Miyaura, A. Suzuki, Chem. Commun. (1979) 866.
[5] N. Miyaura, T. Yanagi, A. Suzuki, Synth. Commun. 11 (1982) 513.
[6] N. Miyaura, A. Suzuki, Chem. Rev. 95 (1995) 2457.
[7] F.Y. Zhao, M. Shirai, Y. Ikushima, M. Arai, J. Mol. Catal. A 180 (2002) 211.
[8] M. Gruber, S. Chouzier, K. Koehler, L. Djakovitch, Appl. Catal. A 265 (2004) 161.
[9] K. Koehler, R.G. Heidenreich, J.G.E. Krauter, M. Pietsch, Chem. Eur. J. 8 (2002) 622.
[10] D.A. Conlon, B. Pipik, S. Ferdinand, C.R. LeBlond, J.R. Sowa, B. Izzo, P. Collins, J.M. Williams, Y.J. Shi, Y.K. Sun, Adv. Synth. Catal. 345 (2003) 931.
[11] C.R. LeBlond, A.T. Andrews, Y.K. Sun, J.R. Sowa, Org. Lett. 3 (2001) 1555.
[12] C. Baleizao, A. Corma, H. Garcia, A. Leyva, Chem. Commun. 5 (2003) 606.
[13] A. Corma, H. Garcia, A. Leyva, A. Primo, Appl. Catal. A 257 (2004) 77.
[14] M. Dams, L. Drijkoningen, B. Pauwels, G. vam Tendeloo, D.E. De Vos, P.A. Jacobs, J. Catal. 209 (2002) 225.
[15] L. Djakovitch, K. Koehler, J. Am. Chem. Soc. 123 (2001) 5990.
[16] M. Wagner, K. Kohler, L. Djakovitch, S. Weinkauf, V. Hagne, M. Muhler, Top. Catal. 13 (2000) 319.
[17] B.M. Choudary, K. Jyothi, M. Roy, M.L. Kantam, B. Sreedhar, Adv. Synth. Catal. 346 (2004) 1471.
[18] S.S. Prockl, W. Kleist, M.A. Gruber, K. Kohler, Angew. Chem. Int. Ed. 43 (2004) 1881.
[19] M.R. Buchmeiser, K. Wurst, J. Am. Chem. Soc 121 (1999) 11101.
[20] C.A. Lin, F.T. Luo, Tetrahedron Lett. 44 (2003) 7565.
[21] M.M. Dell'Anna, P. Mastrorilli, F. Muscio, C.F. Nobile, G.P. Suranna, Eur. J. Inorg. Chem. 5 (2002) 1094.
[22] M.M. Dell'Anna, P. Mastrorilli, F. Muscio, C.F. Nobile, G.P. Scranna, Eur. J. Inorg. Chem. 5 (2002) 1094.
[23] A. Datta, K. Ebert, H. Plenio, Organometallics 22 (2003) 4685.
[24] P.T. Anastas, J.C. Warner, Green Chemistry: Theory and Practice, Oxford University Press, Oxford, 1998.
[25] P. Tundo, P. Anastas, D.S. Black, J. Breen, T. Collins, S. Memoli, J. Miyamoto, M. Polyakoff, W. Tumas, Pure Appl. Chem. 72 (2000) 1207.
[26] B. Cornils, W.A. Herrmann, Aqueous Phase Organometallic Catalysis – Concept and Application, Wiley–VCH, Weinheim, 1998.
[27] F. Sieber, P. Wentworth, K.D. Janda, J. Combinat. Chem. 1 (1999) 540.
[28] P. Wentworth, K.D. Janda, Chem. Commun. 19 (1999) 1917.
[29] T. Malmström, C. Andersson, Chem. Commun. 10 (1996) 1135.
[30] D.E. Bergbreiter, B.L. Case, Y.S. Liu, J.W. Caraway, Macromolecules 31 (1998) 6053.
[31] P.L. Osburn, D.E. Bergbreiter, Prog. Polym. Sci. 26 (2001) 2015.
[32] For a recent review see: Y. Uozumi, Top. Curr. Chem. 242 (2004) 77, and references therein.
[33] Y.M.A. Yamada, H. Takahashi, S. Ikegami, Tetrahedron Lett. 44 (2003) 2379.
[34] Y.M.A. Yamada, K. Takeda, H. Takahashi, S. Ikegami, Tetrahedron 60 (2004) 4097.
[35] C.W.K. Gstottmayr, V.P.W. Bohm, E. Herdtweck, M. Grosche, W.A. Herrmann, Angew. Chem. Int. Ed. 41 (2002) 1363.
[36] H.M. Lee, C.Y. Lu, C.Y. Chen, W.L. Chen, H.C. Lin, P.L. Chiu, P.Y. Chen, Tetrahedron 60 (2004) 5807.
[37] A.R. Kovacevic, B.M. Zeglis, J.W. Faller, R.H. Crabtree, Organometallics 23 (2004) 2461.
[38] M.T. Zarka, M. Bortenschlager, K. Wurst, O. Nuyken, R. Weberskirch, Organometallics 23 (2004) 4817.
[39] N. Hadej, E.A.B. Kantchey, C.J. O'Brien, M.G. Organ, Org. Lett. 10 (2005) 1991.
[40] M. Shi, H.X. Qian, Tetrahedron 61 (2005) 4949.
[41] J.O. Krause, M.T. Zarka, U. Anders, R. Weberskirch, O. Nuyken, M.R. Buchmeiser, Angew. Chem. Int. Ed. 42 (2003) 5965.
[42] T. Kotre, O. Nuyken, R. Weberskirch, Macromol. Rapid. Commun. 23 (2002) 871.
[43] M.T. Zarka, O. Nuyken, R. Weberskirch, Chem. Eur J. 9 (2003) 3228.
[44] D. Schönfelder, O. Nuyken, R. Weberskirch, Macromolecules 38 (2005) 254.
[45] I.P. Beletskaya, A.V. Cheprakov, Chem. Rev. 100 (2000) 3009.
[46] J. Li, L.M. Zheng, I. King, T.W. Doyle, S.H. Chen, Curr. Med. Chem. 8 (2001) 121.
[47] A.D. Schlüter, G. Wegner, Acta Polym. 44 (1993) 59.
[48] T. Jeffery, Tetrahedron Lett. 35 (1994) 3051.
[49] H. Zhao, M.-Z. Cai, C.-Y. Peng, C.-S. Song, J. Chem. Res. (S) (2002) 28.
[50] Y. Uozumi, T. Kimura, Synlett 12 (2002) 2045.
[51] W.A. Herrmann, M. Elison, J. Fischer, C. Köcher, G.R.J. Artus, Angew. Chem., Int. Ed. Engl. 34 (1995) 2371.
[52] Y. Uozumi, H. Danjo, T. Hayashi, J. Org. Chem. 64 (1999) 3384.
[53] Y. Uozumi, Y. Nakai, Org. Lett. 4 (2002) 2997.
[54] J.-W. Byun, Y.-S. Lee, Tetrahedron Lett. 45 (2004) 1837.
[55] C.W. Gstöttmayr, V.P.W. Böhm, E. Herdtweck, M. Grosche, W.A. Herrmann, Angew. Chem. Int. Ed. 41 (2002) 1363.