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Di(2-pyridyl)methylamine-palladium dichloride complex covalently anchored to a styrene-maleic anhydride co-polymer as recoverable catalyst for C-C cross-coupling reactions in water

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Abstract—A new polymer-supported di(2-pyridyl)methylamine–palladium dichloride complex covalently anchored to a styrene-alt-maleic anhydride co-polymer is prepared. This complex catalyzes Heck, Suzuki and Sonogashira cross-coupling reactions in neat water with similar efficiency than the monomeric complex. The turnover number (TON) of this polymer reaches up to 10^4 for Heck reactions, whereas for Suzuki and Sonogashira couplings TONs up to 10^5 are achieved. There is low leaching of palladium after filtration of the polymer and the activity remains almost constant after fourth and five reaction cycles especially in Sonogashira reactions. In the case of the Suzuki reaction Pd nanoparticles are dispersed into the polymer after the first cycle according to TEM images and 2.4% of Pd are found by ICP-OES in the corresponding filtrate. Alternatively, these palladium-catalyzed reactions can also be performed under microwave heating. These couplings take place with better efficiency with polymer-supported di(2-pyridyl)methylamine–palladium dichloride complex than with the polyurea-encapsulated Pd EnCat[™] 40.

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1. Introduction

Palladium-catalyzed cross-coupling reactions have become a major area of interest in organic chemistry.¹ From the environmental point of view several practical and economical aspects of these reactions have to be developed for their industrialization. The use of water as solvent has important advantages in large-scale processes due to nontoxic, nonflammable and inexpensive features.² Additionally, the recovery³ and recycling of the precious expensive catalyst and its complete removal from the products constitute essential problems to be solved.⁴ Several methodologies have been developed to remove and recover the catalyst from the reaction medium, the filtration of a heterogeneous catalyst being the most simple procedure. The palladium metal, salt or complex can be for instance encapsulated,⁵ incarcerated,⁶ or entrapped in sol-gels,⁷ inorganic supports,⁸ block co-polymer matrices,⁹ dendrimers,¹⁰ and PEGresins.¹¹ The preparation of covalently supported palladium catalysts either based on polymer or on silica gel-anchored ligands has experienced an important development in the last decade.¹² Some of these supported catalysts, derived

from palladium–phosphine complexes,¹⁴ palladacycles,¹⁵ and *N*-heterocyclic carbene complexes,¹⁶ have been used in aqueous media and in neat water,¹³ mainly in Heck and Suzuki reactions. The leaching of palladium from the solid support and the lower reactivity in comparison with related homogeneous catalysis are important problems when employing these type of strategies.

Dipyridyl- and dipyrimidyl-based ligands 1 and 2 showed excellent properties for palladium complexation and have proven to be efficient catalysts for C-C and C-N bond forming reactions.¹⁷ When this type of complexes were covalently anchored to a polymeric matrix resulting from a ROMP polymerization, the resulting PdCl₂ complexes 3 present similar or even higher catalytic activity than the monomeric ones and no leaching of palladium being observed in organic solvents. We have recently chosen dipyridyl-based ligands derived from di(2-pyridyl)methylamine in order to have a primary amino group, which could be more easily anchored to a polymeric support than the di(2-pyridyl)amine used by Buchmeiser et al.¹⁷ The corresponding PdCl₂ complexes 4 have shown as versatile catalysts for Heck, Suzuki, and Sonogashira reactions in organic and aqueous solvents.¹⁸ Herein we report the preparation of a novel polymer-supported di-(2-pirydyl)methylamine-based PdCl₂ complex covalently anchored to a poly(styrene-alt-maleic anhydride) resin 5.¹

Keywords: Heck reaction; Suzuki reaction; Sonogashira reaction; Supported-catalyst; Water.

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This polymer has been widely used by our group for the preparation of different polymer-supported *N*-hydroxysuccinimide-derived reagents presenting good mechanical stability and solubility (Fig. 1)²⁰



Figure 1.

2. Results and discussion

2.1. Synthesis of the polymer-supported palladium complex

The polymer-supported ligand **7** was prepared by reaction of poly(styrene-alt-maleic anhydride) resin **5**¹⁹ with di-(2-pyridyl)methylamine (**6**)^{18b,21} in a mixture of acetone–water (1/2) under reflux for 1 day (Scheme 1). Elemental analyses of three different batches of supported-ligand **7** showed similar nitrogen content in the range of 10.38–11.40%, revealing a rather high ligand loading (average 2.6 mmol/g). For the preparation of the palladium complex **8** a 0.5 M methanolic solution of Na₂PdCl₄ (ca. 2 equiv) was mixed with the polymer **7** and stirred for 2 days at room temperature. Elemental analysis of the corresponding three different batches of complex **8** gave a 5.84–6.20% of N content. Inductive coupled plasma-optic emission



spectrometry (ICP-OES) revealed that resin **8** contained an average of 1.2 mmol/g of Pd, which supposes that ca. 46% of the di-(2-pyridyl)methylamine ligand participated in the formation of the PdCl₂ complex. The FT-IR spectra of polymeric ligand **7** and complex **8** are rather similar showing a sharp band at 1705 and 1712 cm⁻¹, respectively, for the imide carbonyls.²²

2.2. Use of the polymer-supported palladium complex 8 in cross-coupling reactions

The systematic study of the catalytic activity of the polymer-supported Pd-dipyridyl complex **8** for Heck, Suzuki, and Sonogashira reactions was investigated using water as solvent and compared with the same processes carried out with the monomeric complex **4b**.¹⁸ In addition, the stability, recovery and leaching of the heterogeneous catalyst were studied in all these processes under aqueous conditions. Recycling experiments have been also carried out with the commercially available polyurea-encapsulated [Pd EnCat 40^{m}]^{5,23} in order to compare with the results obtained with the polymeric complex **8**.

2.2.1. Heck reactions. Heck couplings were carried out with tert-butyl acrylate or styrenes as olefinic substrates and aryl halides. The reactions were performed in neat water as solvent with diisopropylamine as base in the presence of tetra-*n*-butylammonium bromide (TBAB, 0.5 equiv) (Scheme 2 and Table 1). The presence of TBAB in Pd-catalyzed cross-coupling reactions, especially in Heck reactions, increase the conversion rate by formation and stabilization of Pd colloids.²⁴ The arylation of *tert*-butyl acrylate and 4-chlorostyrene with 4-chloroiodobenzene in the presence of the polymeric complex 8 gave higher yields in similar or shorter reaction times than the monomeric 4b (Table 1, entries 1–6). The loading of both catalyst can be lowered down to 10^{-2} mol% of Pd but the temperature must be raised to 140 °C to get full conversion after more than 1 day reaction time (Table 1, entries 5 and 6). Similar processes with aryl bromides must to be performed at higher temperature and loading of catalyst (Table 1, entries 7–10). In the coupling between 4-chlorobromobenzene and tertbutyl acrylate quantitative yields were obtained at 160 °C with both catalysts (Table 1, entries 7 and 8). In case of the arylation of styrene with 4-bromoacetophenone the reaction was faster with the monomeric catalyst 4b (Table 1, entries 9 and 10). This reaction can be performed alternatively at 100 °C under microwave heating in 10 min in good yields (Table 1, entries 11 and 12). However, the vinylation of aryl chlorides under this reaction conditions failed.



Scheme 2.

Recycling and leaching experiments were assayed for the arylation of *tert*-butyl acrylate and 4-chlorostyrene with 4-chlorophenyl iodide using complex 8 (0.1 mol% Pd) at

Entry	Х	Y	R	Cat. (mol% Pd)	<i>T</i> (°C)	t	Yield (%) ^b
1	Ι	Cl	CO ₂ -t-Bu	8 (0.1)	100	14 h	99
2	Ι	Cl	CO ₂ -t-Bu	4b (0.1)	100	1 d	98
3	Ι	Cl	$4-ClC_6H_4$	8 (0.1)	100	2 d	99
4	Ι	Cl	$4-ClC_6H_4$	4b (0.1)	100	1 d	78
5	Ι	Cl	$4-ClC_6H_4$	8 (0.01)	140	38 h	97
6	Ι	Cl	$4-ClC_6H_4$	4b (0.01)	140	31 h	95
7	Br	Cl	CO ₂ - <i>t</i> -Bu	8 (0.1)	160	2 d	99
8	Br	Cl	CO ₂ -t-Bu	4b (0.1)	160	2 d	99
9	Br	CH ₃ CO	C_6H_5	8 (0.5)	100	6.5 h	85
10	Br	CH ₃ CO	C ₆ H ₅	4b (0.5)	100	4.5 h	99
11	Br	CH ₃ CO	C_6H_5	8 (0.1)	100 (MW)	10 min	80
12	Br	CH ₃ CO	C_6H_5	4b (0.1)	100 (MW)	10 min	96

Table 1. Heck reactions with polymeric 8 and monomeric 4b di(2-pyridyl)methylamine-based PdCl₂ complexes^a

^a Reaction conditions: aryl halide (1 mmol), alkene (1.5 mmol), *i*-Pr₂NH (3 mmol), TBAB (0.5 mmol), Pd complex and H₂O (2 mL). ^b Determined by GLC using decane as internal standard.

80 °C instead under reflux in order to prevent degradation of the polymer (Table 2, entries 1 and 2). The same catalyst batch was isolated by filtration (G-5) from the reaction medium and reused in 4 consecutive coupling reactions and only extended reaction time was observed after the first run in the case of tert-butyl acrylate (Table 2, entry 1). When the polyurea-encapsulated [Pd EnCat 40[™]]^{5,23} (0.1 mol% Pd) was used as catalyst for the coupling between 4-chloroiodobenzene and 4-chlorostyrene, a similar behaviour than complex 8 was observed after three cycles (Table 2, compare entries 2 and 3). Catalytic cycles for the arylation of tert-butyl acrylate and styrene with 4-bromoacetophenone were also carried out with complex 8 (1 and 0.5 mol% of Pd, respectively) at 100 °C (Table 2, entries 4 and 5). In the case of tert-butyl acrylate the reaction time increased after the first run and it was maintained in the next three consecutive cycles. In all cases, yields remained almost constant, however, in the arylation of styrene the yield decreased after the third run. Apparently, no leaching of Pd was observed because filtrates did not show catalytic activity in any case. When the arylation of styrene with 4-bromoacetophenone was performed under microwave heating degradation of the polymer and leaching of palladium was observed.

2.2.2. Suzuki reactions. The cross-coupling between phenylboronic acid and aryl bromides such as 4-bromoacetophenone and 4-bromophenol were carried out with K₂CO₃ as base under water reflux and in aqueous MeOH either at 60 °C or at room temperature using KOH as base (Scheme 3 and Table 3). The cross-coupling of 4-bromoacetophenone with phenylboronic acid under water reflux took place with similar TON using the polymeric 8 and the monomeric **4b** catalysts either with 0.1 or 0.001 mol% loading of Pd and slightly higher TOF (TON \times h⁻¹) of 10⁵ (h^{-1}) with the polymeric complex (Table 3, entries 1–4). The same results were obtained with both complexes when couplings were performed in aqueous MeOH at 60 °C (Table 3, entries 5 and 6). In the case of the cross-coupling of 4-bromophenol with phenylboronic acid, no differences were observed with both complexes 8 and 4b under the three essayed reaction conditions (Table 3, entries 7-12). When 4-chloroacetophenone was coupled with phenylboronic acid under water reflux with K₂CO₃ as base, TBAB (0.5 equiv) was added (Table 3, entries 13-16). In this case a higher Pd loading had to be used for the polymeric complex 8 (4.5 mol% Pd) than for the momomeric **4b** (0.1 mol% Pd). Under microwave heating 56 and 88% yield were obtained for the same catalyst loading (0.1 mol% Pd) when the

Table 2. Heck reactions with polymer 8 and Pd EnCat TM 40 over 3 or 4 cyc	les ^a
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Entry	ArX	Alkene	Cat. (mol% Pd)	T (°C)	Cycle 1		Cycle 2		Cycle 3		Cycle 4	
			((-)	<i>t</i> (h)	Yield (%) ^b						
1	CI-	CH ₂ =CHCO ₂ - <i>t</i> -Bu	8 (0.1) ^c	80	7	99	24	99	38	89	38	92
2	CI	4-CIC ₆ H ₄ CH=CH ₂	8 (0.1) ^c	80	24	99	24	99	24	99		
3	CI	4-ClC ₆ H ₄ CH=CH ₂	Pd EnCat (0.1) ^d	100	15	99	15	91	23	95		
4	CH ₃ CO-Br	CH ₂ =CHCO ₂ -t-Bu	8 (1) ^d	100	6	99	21	85	22	88	22	82
5	CH ₃ CO-Br	C ₆ H ₅ CH=CH ₂	8 (0.5) ^e	100	6	85	22	91	40	59		

^a Reaction conditions: aryl halide (1 equiv), alkene (1.5 equiv), *i*-Pr₂NH (3 equiv), TBAB (0.5 equiv), Pd complex and H₂O (2 mL/equiv).

^b Determined by GLC using decane as internal standard.

^c Scale (3 mmol).

^d Scale (1 mmol).

^e Scale (2 mmol).



Scheme 3.

Table 3. Suzuki reactions with polymeric 8 and monomeric 4b di(2-pyridyl)methylamine-based PdCl₂ complexes^a

Entry	Х	Y	Cat. (mol% Pd)	Solvent	Base	<i>T</i> (°C)	t	Yield (%) ^b
1	Br	CH ₃ CO	8 (0.1)	H ₂ O	K ₂ CO ₃	100	1 h	99
2	Br	CH ₃ CO	4b (0.1)	H ₂ O	K_2CO_3	100	30 min	98
3	Br	CH ₃ CO	8 (0.001)	H_2O	K_2CO_3	100	1 h	99
4	Br	CH ₃ CO	4b (0.001)	H_2O	K_2CO_3	100	75 min	99
5	Br	CH ₃ CO	8 (0.1)	MeOH/H ₂ O ^c	KOH	60	1 h	99
6	Br	CH ₃ CO	4b (0.1)	MeOH/H ₂ O ^c	KOH	60	30 min	99
7	Br	HO	8 (0.1)	H_2O	K_2CO_3	100	30 min	88 (82)
8	Br	HO	4b (0.1)	H_2O	K_2CO_3	100	40 min	99 (87)
9	Br	HO	8 (0.1)	MeOH/H ₂ O ^c	KOH	60	30 min	94
10	Br	HO	4b (0.1)	MeOH/H ₂ O ^c	KOH	60	30 min	99
11	Br	HO	8 (0.1)	MeOH/H ₂ O ^c	KOH	Room temperature	6 d	86
12	Br	HO	4b (0.1)	MeOH/H ₂ O ^c	KOH	Room temperature	5 d	75
13	Cl	CH ₃ CO	8 (4.5)	H ₂ O	$K_2CO_3^d$	100	7 h	99
14	Cl	CH ₃ CO	4b (0.1)	H_2O	$K_2 CO_3^d$	100	6 h	68
15	Cl	CH ₃ CO	8 (0.1)	H_2O	$K_2 CO_3^d$	120 (MW)	5 min	56
16	Cl	CH ₃ CO	4b (0.1)	H ₂ O	$K_2 CO_3^{d}$	120 (MW)	5 min	88

^a Reaction conditions: aryl halide (1 mmol), PhB(OH)₂ (1.5 mmol), base (2 mmol), Pd complex, and H₂O (2 mL).

^b Determined by GLC using decane as internal standard. In parenthesis isolated yield after flash chromatography.

^c Volume ratio 2/3.

^d TBAB (0.5 mmol) was added.

reaction was carried out with complex **8** at 100 $^{\circ}$ C and monomeric complex **4b** at 120 $^{\circ}$ C, respectively (Table 3, entries 15 and 16).

The recovery of the polymeric complex 8 was studied for the cross-coupling of phenylboronic acid with 4-bromoacetophenone and 4-bromophenol under different reaction

Table 4. Suzuki cross-coupling reactions between phenylboronic acid and aryl halides with polymer 8 and Pd EnCatTM 40 over 2, 3, 4 or 5 cycles^a

Entry	ArX	Cat. (mol% Pd)	T (°C)	Cycle	Cycle 1		Cycle 2		Cycle 3		Cycle 4		Cycle 5	
		(1101% 14)	(0)	<i>t</i> (h)	Yield (%) ^b									
1	CH ₃ CO-	8 (0.1) ^c	100 ^d	1.5	99	2	99	2.5	93					
2	CH ₃ CO-	Pd EnCat (0.1) ^c	100 ^d	2	88	2	80							
3 ^e	CH ₃ CO-	8 (0.1)	$60^{\rm f}$	1	99	1.5	99	2	99	2.5	99			
4 ^g	CH ₃ CO-	8 (0.1)	$60^{\rm f}$	7	80	7	98	7	97	7	94			
5	HOBr	8 (0.1) ^h	$60^{\rm f}$	0.5	94	2	73	3	93	3	92			
6	CH3CO-CI	8 (4.4) ^{i,j}	130 ^d	3	76	14	41	14	39	15	49	15	47	

^a Reaction conditions: aryl halide (1 equiv), PhB(OH)₂ (1.5 equiv), base (2 equiv), Pd complex, and H₂O (2 mL/equiv).

^b Determined by GLC using decane as internal standard.

^c Scale (2 mmol).

^d In H₂O and K_2CO_3 as base.

^e The cycles were performed in situ without filtration of the polymer 8.

^f In MeOH/H₂O and KOH as base.

^g The catalyst was recovered by filtration from the previous cycles of entry 3 and the new 4 cycles were performed in situ without filtration of the polymer 8. ^h Scale (3 mmol).

ⁱ Scale (1 mmol).

^j In H₂O, K₂CO₃ as base and in the presence of TBAB.



Figure 2. TEM images of the catalyst 8 before (left) and after (right) the first cycle of the Suzuki reaction (Table 4, entry 1).

conditions (Table 4). Slight variations were observed in the case of 4-bromoacetophenone under water reflux conditions when the catalyst was filtered off after three catalytic cycles (Table 4, entry 1). However, comparative recycling studies using Pd EnCat 40 (0.1 mol% Pd) in the cross coupling between phenylboronic acid and 4-bromoacetophenone under water reflux revealed lower yields, longer reaction times, and only 30% yield being obtained in the second run with total deactivation of the catalyst (Table 4, entry 2). Transmission electron microscopy (TEM) analysis of the polymer 8 before and after the 1st Suzuki coupling between 4-bromoacetophenone and phenylboronic acid in the absence of TBAB (Table 4, entry 1) showed the formation of some Pd nanoparticles (7-10 nm) in the surface of the polymer (Fig. 2). The filtrate of this reaction was analyzed by ICP-OES giving a low Pd leaching (2.4%).

For the recycling experiments in aqueous MeOH at 60 °C fourth consecutive cycles were performed in the same flask just adding all reagents with similar quantitative yields in 1–2.5 h (Table 4, entry 3). Then the polymer was filtered off and again fourth cycles were carried out in situ observing in this case that the reaction needed longer reaction times, 7 h in order to obtain 80–98% yield in each run (Table 4, entry 4).

The recycling experiments for the cross-coupling of 4-bromophenol and phenylboronic acid were studied using KOH as base in aqueous MeOH at 60 °C. Under this reaction conditions the reaction time increased from 0.5 to 3 h in the third run and remained constant for the fourth cycle (Table 4, entry 5). The catalytic cycles in the case of 4-chloroacetophenone were performed in water at 130 °C using K₂CO₃ as base and TBAB as additive to give in 3 h 76% yield. However, a lower conversion was observed in the second cycle in a longer reaction time. Similar results, around 39–49% yield in 14–15 h, were observed in four consecutive cycles (Table 4, entry 6). In all recycling experiments the filtrate showed no catalytic activity.

2.2.3. Sonogashira reactions. For the alkynylation of aryl iodides and bromides, a Sonogashira-Cassar-Heck copperfree protocol, set up recently by our group using complex **4b** and $PdCl_2$ as catalysts was used.^{18c} The cross-coupling of activated and deactivated iodides and bromides with phenylacetylene and triisopropylsilylacetylene was performed with pyrrolidine (2 equiv) as base and TBAB as additive under water reflux (Scheme 4 and Table 5). For aryl iodides 0.1 mol % of Pd was employed with the polymeric 8 and the monomeric 4b catalysts, whereas for aryl bromides a higher loading (0.2 mol% of Pd) gave better conversions. It is worthy to note that in general better efficiency, concerning yield and reaction rate, was observed for the polymeric than for the monomeric complex. In addition, the formation of secondary products from dimerization of the alkyne decreased when the polymer was used as catalyst. The Pd loading could be decreased to 10^{-3} mol% in the cross-coupling of phenylacetylene and 4-chloroiodobenzene but longer reaction times were necessary in order to get full conversion (Table 5, entries 1 and 3). Under these low Pd loading the polymer 8 showed a higher efficiency (TOF $3225 h^{-1}$) than when using the monomer **4b** (TOF: $730 h^{-1}$) (Table 5, entries 3 and 4). Under microwave heating the coupling between phenylacetylene and 4-chlorobromobenzene gave variable yields in the case of polymer 8 (between 13 and 47%) and lower than the monomer 4b (Table 5, entries 11 and 12).

$$R^{1}-X + R^{2} - H \xrightarrow{\text{cat.}} R^{2} - R^{1}$$

$$Pyrrolidine, TBAB \\ H_{2}O \text{ reflux}$$

$$\begin{bmatrix} X = I, Br \\ R^{1} = 4-CIC_{6}H_{4}, 4-MeOC_{6}H_{4}, 4-AcC_{6}H_{4}, Thienyl \\ R^{2} = Ph, TIPS \end{bmatrix}$$

Scheme 4.

For the recycling studies of the polymer, alkynylation of 4-chloroiodobenzene with phenylacetylene was performed during 5 runs without appreciable lost of catalytic activity

Table 5. Sonogashira reactions with	polymeric 8 and	d monomeric 4b di-	(2-pyridyl)methy	vlamine-based PdCl ₂	complexes
			\ F2 ~ 2 / · · .		

Entry	R^1X	\mathbb{R}^2	Cat. (mol% Pd)	t	Yield (%) ^b
1	CII	Ph	8 (0.1)	1 h	99
2	CI	Ph	4b (0.1)	1 h	99
3	CI	Ph	8 (0.001)	31 h	99
4	CI	Ph	4b (0.001)	4 d	70
5	CH ₃ O-	Ph	8 (0.1)	1 h	96
6	CH ₃ O-	Ph	4b (0.1)	2 h	91
7	CI	TIPS	8 (0.1)	3 h	99
8	CI	TIPS	4b (0.1)	6 h	94
9	CH ₃ COBr	Ph	8 (0.2)	1.5 h	99
10	CH ₃ CO-Br	Ph	4b (0.2)	2 h	86
11	Cl	Ph	8 (0.1)	10 min ^c	47
12	Cl	Ph	4b (0.1)	10 min ^d	66
13	Cl	TIPS	8 (0.2)	14 h	99
14	Cl	TIPS	4b (0.2)	22 h	87
15	SBr	Ph	8 (0.2)	1 h	92
16	SBr	Ph	4b (0.2)	2 h	90

^a Reaction conditions: aryl halide (1 mmol), alkyne (1.2 mmol), pyrrolidine (2 mmol), TBAB (0.5 mmol), Pd complex, and H₂O (2.5 mL) reflux.
 ^b Determined by GLC using decane as internal standard.
 ^c The reaction was carried out under microwave heating at 100 °C (0.5 mmol scale).
 ^d The reaction was carried out under microwave heating at 120 °C (0.5 mmol scale)

Table 6.	Sonogashira	reactions b	between p	ohenylacet	ylene and	l aryl	halides	with p	olymer 8	and Pd	EnCat ^{1M}	40 over	4 or 5	cycles	;²
	U U				•									~	

	•			•	-	•				•		
Entry	ArX	Cat. (mol% Pd)	Cycle	Cycle 1		Cycle 2		Cycle 3		Cycle 4		5
			<i>t</i> (h)	Yield (%) ^b								
1	CI	8 (0.1) ^c	1	99	1	99	1	99	1	99	1	99
2	CI	Pd EnCat (0.1) ^c	1.5	99	1.5	99	8	27				
3 ^d	CI	8 (0.1) ^c	1	99	1	99	1	99	1	99	1	99
4 ^e	CI	8 (0.1) ^c	1	99	1	99	1	99	1	99	1	99
5	CH ₃ O-	8 (0.1) ^c	1	96	1	92	1	92	1	94	1	92
6	CH ₃ COBr	8 (0.2) ^f	1.5	99	1.5	99	2	88	2.5	91	2.5	93

 ^a Reaction conditions: aryl halide (1 mmol), alkyne (1.2 mmol), pyrrolidine (2 mmol), TBAB (0.5 mmol), Pd complex, and H₂O (2.5 mL) reflux.
 ^b Determined by GLC using decane as internal standard.
 ^c Scale (3 mmol).
 ^d The cycles were performed in situ without filtration of the polymer 8.
 ^e The catalyst was recovered by filtration from the previous cycles of entry 3 and the new 5 cycles were performed in situ without filtration of the polymer 8. ^f Scale (2 mmol).

(Table 6, entry 1). However, when recycling studies were performed with Pd EnCat 40 (0.1 mol% Pd) for the same cross-coupling under the same reaction conditions the catalytic activity was kept only during the two first cycles (Table 6, entry 2). In the case of 4-chloroiodobenzene the coupling was performed in situ during four quantitative cycles of 1 h by adding the reagents (except TBAB) to the flask. Then the polymer was filtered off and four more quantitative cycles were performed again during 1 h without loss of the catalytic activity (Table 6, entries 3 and 4). The alkynylation of the deactivated 4-iodoanisol with phenylacetylene gave practically the same yields in 1 h after five cycles (Table 6, entry 5). Even in the coupling of 4-bromoacetophenone and phenylacetylene good catalytic activity of the polymer was observed after five consecutive runs (Table 6, entry 6).

3. Conclusions

In conclusion, we have found that the new polymersupported di(2-pyridyl)methylamine–palladium dichloride complex covalently anchored to a styrene-alt-maleic anhydride co-polymer showed similar catalytic activity than the monomeric palladium complex for Heck, Suzuki and Sonogashira reactions in water. This polymer maintains in general their efficiency especially in Sonogashira reactions through five recycle runs even better than the encapsulated Pd EnCat 40. The formation of Pd nanoparticles have been detected in the surface of the polymer by TEM analysis after a Suzuki reaction and 2.4% of Pd leaching was detected in the corresponding filtrate. On the other hand, the polymer cannot be recycled after microwave heating. In general, no appreciable catalytic activity was detected from the filtrates during recycling processes.

4. Experimental

4.1. General

The reagents and solvents were obtained from commercial sources and were generally used without further purification. Flash chromatography was performed on silica gel 60 (0.040–0.063 mm, Merck). Thin-layer chromatography was performed on Polygram[®] SIL G/UV₂₅₄ plates. Gas chromatographic analyses were performed on a HP-6890 instrument equipped with a WCOT HP-1 fused silica capillary column. IR data were collected on a Nicolet Impact-400D-FT spectrophotometer in cm^{-1} . ICP-OES analyses were performed with a Perkin-Elmer Optima 4300. TEM analyses were performed with a JEOL JSM-840 and examples were dried, sonicated in hexane and supported on a carbon-coated copper grid. Elemental analyses were carried out by the corresponding services at the University of Alicante. The amounts of catalysts were weighed up in an electronic microscale (Sartorius, XM1000P) with precision of 1 µg. Microwave reactions were performed with a CEM Discover Synthesis Unit in glass vessels (10 mL) sealed with a septum under magnetic stirring at the temperature indicated on Tables 1, 3, and 5. All products have been previously described.18

4.2. Synthesis of polymer-supported complex 8

A mixture of di(2-pyridyl)methanamine (300 mg, 1.6 mmol)^{18c} and poly(styrene-alt-maleic anhydride) resin (195 mg) was stirred under reflux during 24 h in H₂O/ acetone (3 mL, 2/1). The solution was cooled to room temperature and water was added to precipitate the polymer. The solid was filtered, washed with H₂O and MeOH and dried under vacuum to yield 288 mg of a pale brown precipitate of polymer 7. The average loading of amine (2.61 mmol/g) was determined by means of the nitrogen content from combustion analysis from three different batches. Without further purification, the modified polymer 7 (82 mg) was stirred for 2 days in MeOH (1 mL) with a 0.5 M methanolic solution of Na₂PdCl₄ (0.8 mL, 0.4 mmol). The mixture was filtered off (G-5) and washed with MeOH. The product was dried under reduced pressure and placed into an oven (130 °C) overnight to yield 130 mg of a brown solid. For the ICP-OES analysis, the resin was decomposed with HNO₃ giving 1.21 mmol/g of Pd.

4.3. General procedure for the Heck reactions

A suspension of aryl halide (1 mmol), alkene (1.5 mmol), diisopropylamine (0.420 mL, 3 mmol), tetra-*n*-butylammonium bromide (161 mg, 0.5 mmol), Pd complex (see Tables 1 and 2) and H₂O (2 mL) was stirred at the temperature indicated on Tables 1 and 2 in air, and the reaction progress was analyzed by GLC. After the reaction was completed and cooled to room temperature, the mixture was filtered off through a glass filter (G-5). The filtrate was extracted with ethyl acetate $(3 \times 15 \text{ mL})$ and the organic layer was dried over MgSO₄, evaporated (15 mmHg) and the resulting residue purified by flash chromatography.

4.4. General procedure for the Suzuki reactions in water

A solution of aryl halide (1 mmol), phenylboronic acid (183 mg, 1.5 mmol), potassium carbonate (276 mg, 2 mmol) tetra-*n*-butylammonium bromide (161 mg, 0.5 mmol, only for aryl chlorides), Pd complex (see Tables 3 and 4) in H₂O (2 mL) was stirred under reflux in air, and the reaction progress was analyzed by GLC. After the reaction was completed and cooled to room temperature, the mixture was filtered off through a glass filter (G-5). The filtrate was extracted with ethyl acetate (3×10 mL), the organic phases were dried over MgSO₄, and evaporated (15 mmHg). The subsequent residue was purified by recrystallization or by flash chromatography on silica gel to give pure products.

4.5. General procedure for the Suzuki reactions in methanol/water

A mixture of aryl halide (1 mmol), phenylboronic acid (183 mg, 1.5 mmol), potassium hydroxide (112 mg, 2 mmol), Pd complex (see Tables 3 and 4) and methanol/ water: 2/3 (2.5 mL) was stirred at room temperature or at 60 °C (see Tables 3 and 4) and the reaction progress was analyzed by GC. After the reaction was completed and cooled to room temperature, the mixture was filtered off through a glass filter (G-5). When the product was not soluble in the solvent mixture the solid was dissolved in ethyl acetate. The filtrate was extracted with ethyl acetate

 $(3 \times 10 \text{ mL})$, the organic phases were dried over MgSO₄, evaporated (15 mmHg) and the crude product purified by recrystallization (MeOH/H₂O:2:3) or flash chromatography on silica gel.

4.6. General procedure for the Sonogashira reactions

A 10 mL round-bottom flask was charged with palladium catalyst (see Tables 5 and 6), aryl halide (1 mmol), alkyne (1.5 mmol), pyrrolidine (0.164 mL, 2 mmol), tetrabutyl-ammonium bromide (161 mg, 0.5 mmol) and water (2.5 mL). The mixture was stirred under reflux during the reaction time indicated in Tables 5 and 6. The reaction progress was analyzed by GLC. After the reaction was completed and cooled to room temperature, the mixture was filtered off through a glass filter (G-5). The filtrate was extracted with EtOAc (3×15 mL), washed with 2 M HCl, dried over MgSO₄, concentrated in vacuo and the residue purified by flash chromatography on silica gel.

4.7. General procedure for recycling reactions

When the corresponding Heck, Suzuki or Sonogashira reaction was finished the suspension was cooled down to room temperature and filtered off (G-5). The polymer was washed with water and ethyl acetate, dried under vacuum and reused.

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