Available online at www.sciencedirect.com
ScienceDirect
Tetrahedron 63 (2007) 9642–9651
Tetrahedron

Microwave-assisted Suzuki–Miyaura and Heck–Mizoroki cross-coupling reactions of aryl chlorides and bromides in water using stable benzothiazole-based palladium(II) precatalysts

Kamal M. Dawood*

Department of Chemistry, Faculty of Science, Cairo University, Giza 12613, Egypt

Received 5 May 2007; revised 24 June 2007; accepted 12 July 2007
Available online 19 July 2007

Abstract—The catalytic activity of benzothiazole-based Pd(II)-complexes was evaluated in Suzuki–Miyaura and Heck–Mizoroki C–C cross-coupling reactions of aryl chlorides and bromides with olefins and arylboronic acids both under thermal as well as microwave irradiation conditions in water. The factors affecting the optimization of such reactions as well as the reusability of the Pd-precatalysts are studied.

1. Introduction

Modern synthetic chemistry is sustained by the use of transition metal catalysts as powerful tools for carbon–carbon bond-forming processes.[1] The formation of carbon–carbon bonds is a fundamental reaction in organic synthesis, the efficiency of which has interested organic chemists for a long time ago.[2] Biaryls are versatile intermediates in organic synthesis and are recurring functional groups in many natural products, bioactive compounds, and liquid crystal materials.[3,4] As a result, considerable effort has been directed toward the development of efficient and selective methods for the synthesis of biaryls.[5–7] The palladium-catalyzed Suzuki–Miyaura cross-coupling reaction represents one of the most widely used processes for the synthesis of biaryls.[8–11] Modern techniques are focused on the design of new methodologies able to make the already known chemical transformations simpler, faster, cheaper and in general, more efficient processes.[12] Solid-phase organotransition metal complexes having high activity and selectivity, particularly those based on palladium, offer several significant practical advantages in synthetic and industrial chemistry; among those, the ease of separation of the catalyst from the desired reaction products and the ease of recovery and re-use of the catalyst are most important.[13] In addition, microwave irradiation methodology assists in achieving rapid incorporation of organic synthesis into broad industrial diversities.[14] The combination of immobilized homogenous catalysts and microwave assistance is of particular importance. In addition, organic reactions that can proceed well in aqueous media offer advantages over those occurring in organic solvents.[15] Homogenous oxime-palladacycles **1**, **2**, and the immobilized one **3** (Fig. 1) recently appeared in the literature with high activity and often they are air stable.[16–19] In continuation of our recent publications concerning the use of the immobilized Pd-catalyst **4** under microwave irradiation conditions in Suzuki–Miyaura, Heck–Mizoroki and Sonogashira cross-coupling reactions in aqueous media,[20] we report herein the development of new homogenous benzothiazole-oxime Pd(II) precatalyst **5** as well as its immobilized form **6** anchored to a glass/polymer composite material shaped as Raschig rings, which is a material with relevance in industrial applications, in order to evaluate their suitability in Suzuki–Miyaura and Heck–Mizoroki cross-coupling reactions of aryl bromides and chlorides under thermal as well as microwave irradiation conditions in water.

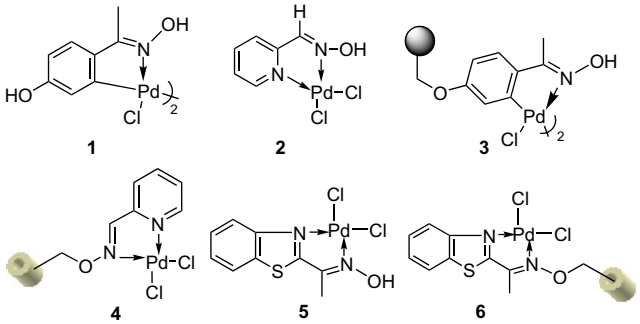
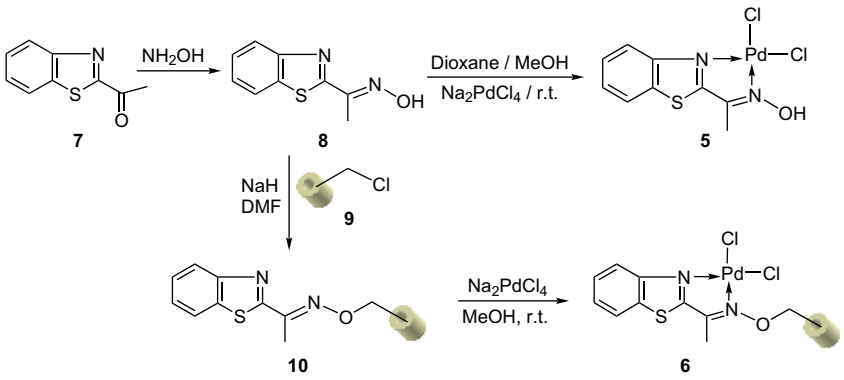


Figure 1.

Keywords: Pd(II) precatalysts; Microwave irradiation; Suzuki–Miyaura; Heck–Mizoroki cross-coupling reactions.
* Fax: +20 2 5727556; e-mail: dr_dawood@yahoo.com

0040–4020/$ - see front matter © 2007 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tet.2007.07.029



Scheme 1. New benzothiazole-oxime-based palladium(II) precataylsts.

2. Results and discussion

2.1. Preparation of Pd-precatalysts 5 and 6

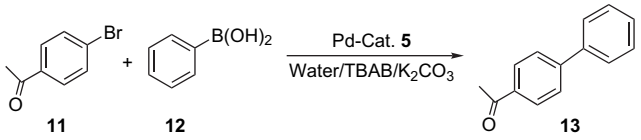
Benzothiazole-oxime-based Pd(II) precatalyst **5** was prepared by dissolving the 2-acetylbenzothiazole-oxime (**8**) in dioxane followed by the addition of an equimolar amount of sodium tetrachloropalladate in methanol at room temperature (Scheme 1). The immolilized Pd-precatalyst **6** was obtained via coupling of 2-acetylbenzothiazole-oxime (**8**) with the polymer matrix **9** by heating it at 80 °C in DMF in the presence of sodium hydride. Finally, the heterogenous precatalyst **6** was obtained by treatment of **10** with a solution of sodium tetrachloropalladate in methanol at room temperature. The synthesis of benzothiazole-oxime-based Pd(II) precatalysts **5** and **6** directly from 2-acetylbenzothiazole-oxime (**8**) in methanol under mild conditions has made these important precursors for C–C cross-coupling reactions. The elucidation of structure **5** and N–Pd bonding instead of S–Pd bonding in the complexe **5**, and consequently the analogous heterogeneous catalyst **6**, was based on spectral data as well as in comparison with related reported literature data.[21,22]

2.2. Precatalysts 5 and 6 in Suzuki–Miyaura cross-coupling reactions of activated and deactivated aryl bromides

The search for coupling catalyst systems exhibiting high efficiency (i.e., high turnover frequency (TOF)) and greater stability (i.e., high turnover number (TON)) has recently been receiving much interest.[23] Firstly, we studied the factors affecting the optimization of the catalytic activity of the Pd-precatalyst **5**. Thus, the effect of concentration of palladium precatalyst **5** on the coupling reaction between phenylboronic acid and *p*-bromoacetophenone under thermal conditions in water at 100 °C was evaluated as shown in Table 1. At first, the reaction was conducted using 1 mol % of the precatalyst **5** with a molar ratio of *p*-bromoacetophenone/phenylboronic acid/tetrabutylammonium bromide/potassium carbonate: 1:1.2:0.6:2, to give 98% isolated yield of 4-acetyl-1,1′-biphenyl. In the second experiment, we used 0.5 mol % of the catalyst to give full conversion in 99% isolated yield. The reaction was repeated with different catalytic mol % as shown in Table 1. Full conversion was obtained even in the presence of 0.0007 mol % of the catalyst **5** using *p*-bromoacetophenone (60 mmol), phenylboronic acid (72 mmol), tetrabutylammoium bromide (36 mmol), potassium carbonate (120 mmol), and water (100 mL) to give 4-acetyl-1,1′-biphenyl in 100% (GC-yield) with a turnover number (TON) 133,000 and turnover frequency (TOF) 53,500 h^{-1}, revealing the high activity of the catalytic system. Finally, we repeated the same experiment with the same mmol scale as above using 0.0005 mol % of the catalyst **5** to give 62% GC-yield with TON 124,000 and turnover frequency (TOF) 49,600 h^{-1}. As can be readily seen from the data in Table 1, the Pd-prectalayst **5** shows excellent catalytic activity, giving rise to extremely high TONs.

Deactivated aryl bromides are important for measuring the high catalytic activity of catalytic systems.[24] Thus, we studied the Suzuki–Miyaura cross-coupling reaction of 4-bromoanisole under different concentrations of the precatalysts **5** and **6** and the results are shown in Table 2, runs 1–5. The precatalyst **5** was found to be highly active and resulted in full conversion into **16** even at 0.001 mol % and 20 mmol scale of coupling partners with high turnover number (TON) 100,000 and turnover frequency (TOF) 25,000 h^{-1} (run 5, Table 2). When the above reaction was repeated under microwave irradiation at 160 °C (250 W) full conversion (97% isolated yield) after 10 min was obtained with TON 2000 and TOF 12,000 h^{-1}. 4-Bromotoluene (**15**) was similarly coupled with phenylboronic acid using 0.5 and 0.05 mol % of the precatalyst **5** resulting in the formation of

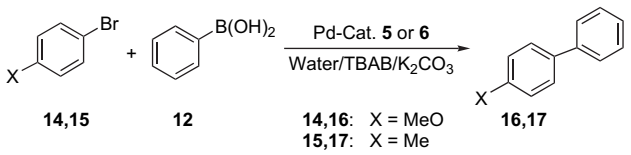
Table 1. Effect of Pd concentration on the reactivity of the catalyst **5** in Suzuki–Miyaura cross-coupling of 4-bromoacetophenone **11**



Entry	mmol scale of **11**	mol % of cat. **5**	Time (h)	Yield,[a] %	TON	TOF [h^{-1}]
1	1	1	2	100 (98)	100	50
2	1	0.5	2	100 (99)	200	100
3	1	0.1	2	100 (96)	1000	500
4	5	0.05	2	100 (98)	2000	1000
5	10	0.01	2	100	10,000	5000
6	20	5×10^{-3}	2.5	100	20,000	8000
7	40	1×10^{-3}	2.5	100	100,000	40,000
8	60	7×10^{-4}	2.5	100	133,000	53,500
9	60	5×10^{-4}	2.5	62	124,000	49,600

[a] Conditions: Bromide/boronic acid/K_2CO_3/TBAB/water (mL): 1:1.2:2:0.6:2, heating at 100 °C. The values in parentheses are the isolated yields.

Table 2. Suzuki–Miyaura cross-coupling of deactivated aryl bromides



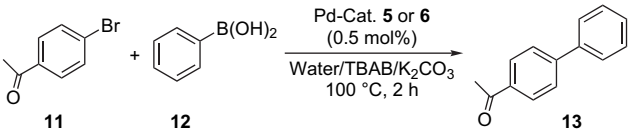
Run	Aryl bromide	Pd-cat/mol %	Time (h)	Product: Yield,[a] %	TON	TOF [h^{-1}]
1	**14**	**5**/0.5	4	**16**: 100 (99)	200	50
2	**14**	**6**/0.5	4	**16**: 100 (99)	200	50
3	**14**	**5**/0.05[b]	4	**16**: 100	2000	500
4	**14**	**5**/0.005	4	**16**: 100	20,000	5000
5	**14**	**5**/0.001	4	**16**: 100 (97)	100,000	25,000
6	**15**	**5**/0.5	6	**17**: 100 (91)	182	32
7	**15**	**5**/0.05[c]	6	**17**: 100 (95)	1900	330
8	**15**	**6**/0.5	6	**17**: 81	162	27

[a] Conditions: Bromide/boronic acid/K_2CO_3/TBAB/water (mL): 1:1.2:2:0.6:2, thermal heating at 100 °C. The values in parentheses are the isolated yields.
[b] Under microwave irradiation (160 °C and 250 W) full conversion (97% isolated yield) after 10 min was obtained with TON 2000 and TOF 12,000 h^{-1}.
[c] Under microwave irradiation (160 °C and 250 W) full conversion (94% isolated yield) after 10 min was obtained with TON 1880 and TOF 11,300 h^{-1}.

4-methyl-1,1′-biphenyl (**17**) with full conversion in all cases (91% and 95% isolated yields, respectively) after 6 h of thermal heating (runs 6 and 7, Table 2). When the above reaction was repeated under microwave irradiation at 160 °C (250 W) full conversion (94% isolated yield) after 10 min was obtained with TON 1880 and TOF 11,300 h^{-1}. The use of 0.5 mol % of precatalyst **6** resulted in 81% conversion into **17** after 6 h of thermal heating (run 8, Table 2).

The longevity effect of the Pd-precatalysts **5** and **6** was tested in the model Suzuki–Miyaura cross-coupling reaction using *p*-bromoacetophenone (5 mmol) and phenylboronic acid (6 mmol) as coupling partners (Table 3). The reaction was conducted in the presence of Pd-precatalyst **5** or **6** (0.5 mol %) in water at 100 °C under air using potassium carbonate (10 mmol) as base and TBAB (3 mmol) as phase transfer agent. Under these conditions, the reaction was completed within 2 h (run 1, Table 3). At this point, fresh portions of the coupling partners and the base (the same amounts as for the first run; 5 mmol scale) were added to the flask thus repeating the reaction for 2 h. In this manner,

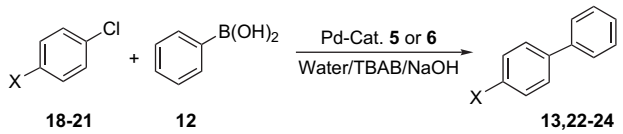
Table 3. The longevity effect of the Pd-precatalysts **5** and **6** in Suzuki–Miyaura cross-coupling of *p*-bromoacetophenone



Run	Number of mmol of **11**	GC yield, %	
		Pd-cat **5**	Pd-cat **6**
1	5	100	100
2	10	80	100
3	15	68	100
4	20	n.t.	86

Conditions: Bromide/boronic acid/K_2CO_3/TBAB/water (mL): 1:1.2:2:0.6:2; n.t.: not tested.

Table 4. Suzuki–Miyaura reactions of aryl chlorides under thermal and microwave heating



Run	X	Pd-cat/ mol %	Product	Thermal heating[a]		Microwave heating[a]	
				Time (h)	Yield,[b] %	Time (min)	Yield,[b] %
1	MeCO	**5**/1	**13**	7	100 (90)	10	100 (83)
2	MeCO	**5**/0.2	**13**	7	100	10	100
3	MeCO	**5**/0.02	**13**	7	73	10	85
4	MeCO	**6**/1	**13**	7	100 (94)	10	100 (86)
5	MeCO	**6**/0.2	**13**	7	92	10	98
6	NO_2	**5**/1	**22**	4	100 (89)	7	100 (84)
7	NO_2	**5**/0.2	**22**	4	100	7	100
8	NO_2	**5**/0.02	**22**	4	85	7	100 (90)
9	NO_2	**6**/1	**22**	4	100 (94)	7	100
10	NO_2	**6**/0.2	**22**	4	100	7	100 (95)
11	CN	**5**/1	**23**	4	100 (93)	7	100
12	CN	**6**/1	**23**	4	100	7	100 (92)
13	Me	**5**/1	**24**	20	15	30	7
14	Me	**6**/1	**24**	20	13	30	3

[a] Conditions: 1 mmol of aryl chloride, 1.2 mmol of phenylboronic acid, 2 mmol of NaOH, 0.6 mmol TBAB, water (2 mL), thermal heating at 100 °C, microwave heating at 160 °C (250 W).
[b] GC-yields; values in parentheses refer to isolated yields of pure products.

extra three successive runs were carried out with the same portion of Pd-precatalysts **5** and **6**. Full conversion was achieved till the third run when the Pd-precatalyst **6** that anchored to solid support was used and 86% conversion was obtained in the fourth run. The Pd-precatalyst **5** resulted in 80% conversion in the second run and lost its activity, after that where only 68% was observed in the third run. These findings demonstrate the high thermo stability of the solid-phase precatalyst **6** over its soluble analog **5**.

2.3. Precatalysts 5 and 6 in Suzuki–Miyaura cross-coupling reactions of activated and deactivated aryl chlorides

We next turned our attention on the cross-coupling reaction of phenylboronic acid with variety of aryl chlorides, which are of particular importance for highly active catalysts.[25] The results of their cross-couplings under thermal as well as microwave heating conditions are summarized in Table 4. At first, *p*-choloroacetophenone **18** (1 mmol) was coupled with phenylboronic acid (1.2 mmol) in water (2 mL) in the presence of tetrabutylammonium bromide (0.6 mmol) using NaOH (2 mmol) as base. Under this condition, full conversions were obtained after 7 h of thermal heating or 10 min of microwave irradiation when the palladium precatalyst **5** was used in either 1 or 0.2 mol %. As an evidence of its high activity, 0.02 mol % of the precatalyst **5** was enough for 73% conversion after 7 h of thermal heating and 85% conversion after 10 min of microwave irradiation of the above coupling reaction with turnover numbers (TON) 3650 and 4250, and turnover frequencies (TOF) 521 and 25,500 h^{-1}, respectively. The use of Pd-precatalyst **6** for similar coupling reaction in 1 and 0.2 mol % resulted in 100% and 92% conversions, respectively, after 7 h of thermal heating. It is noteworthy also to mention here that the activated *p*-nitrochlorobenzene **19** could be completely

coupled with phenylboronic acid under microwave (7 min) or thermal heating (7 h) with 100% conversion using Pd-precatalyst **5** in 1 or 0.2 mol %. Interestingly, at 0.02 mol % of Pd-precatalyst **5** the conversion was 100% under microwave (7 min) [TON=5000 and TOF=42,850 h^{-1}] and 85% under thermal heating (7 h) [TON=4250 and TOF=607 h^{-1}]. Similarly, Pd-precatalyst **6** when used in 1 or 0.2 mol % it resulted, in both cases, in 100% conversions after 7 h of thermal heating or 7 min of microwave irradiation. *p*-Chlorobenzonitrile **20** was also successfully coupled with phenylboronic acid under similar conditions with full conversion using either Pd-precatalyst **5** or **6** in 1 mol %. However, *p*-chlorotoluene **21** did not give reasonable coupling product even at 2 mol % of catalyst under thermal or microwave heating for long time (runs 13 and 14, Table 4).

2.4. Precatalysts 5 and 6 in Suzuki–Miyaura cross-coupling reactions of heterocyclic bromides

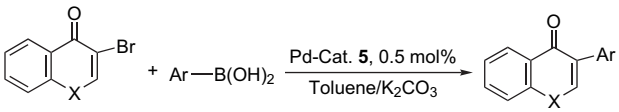
Isoflavones represent a very important class of natural products and exhibit remarkably diverse biological properties.[26,27] Therefore, we explored the synthesis of some isoflavones via the Suzuki–Miyaura cross-coupling reaction between arylboronic acids and 3-bromo-4-chromone. Thus, treatment of phenylboronic acid **12** (1.2 equiv) and 3-bromo-4-chromone **25** (1 equiv) in the presence of precatalyst **5** (0.5 mol %) in toluene (3 mL) and potassium carbonate (2 equiv) under thermal heating for 4 h afforded 100% GC-conversion (89% isolated yield) of the known isoflavone **28** (run 1, Table 5). Full conversion (93% isolated yield) was also achieved within 8 min when the same coupling in toluene was repeated under microwave irradiation. In contrast to phenylboronic acid, 3,4-methylenedioxyphenylboronic acid **27** did not give a satisfied coupling results with 3-bromo-4-chromone **25** neither thermal (15 h) nor under microwave irradiation (8 min), especially when toluene was used as reaction solvent (run 2, Table 5).

However, when water was used as the reaction solvent, full conversion into 3-(3,4-methylenedioxy-phenyl)-4-chromone **29** was achieved after 3 h of thermal heating or 8 min of microwave irradiation (run 3, Table 5). Coupling of 2-bromo-1,4-naphthoquinone **26** with phenylboronic acid **12** in refluxing toluene using 0.5 mol % of precatalyst **5** resulted in full conversion into 2-phenyl-1,4-naphthoquinone **30** (85% isolated yield) (run 4, Table 5). However, its coupling with 3,4-methylenedioxyphenylboronic acid **27** under similar reaction conditions gave much lower yield (30% GC-conversion) after longer time (15 h) (run 5, Table 5). Moreover, 2-bromo-1,4-naphthoquinone **26** was smoothly coupled with phenylboronic acid **12** and with 3,4-methylenedioxyphenylboronic acid **27** in toluene under microwave irradiation (8 min) with complete conversion into the corresponding 2-aryl-1,4-naphthoquinones **30** and **31** in high yields (runs 4 and 5, Table 5).

2.5. Precatalysts 5 and 6 in Heck–Mizoroki cross-coupling reactions of activated and deactivated aryl chlorides

Palladium-catalyzed Heck–Mizoroki cross-coupling reactions of aryl halides with alkenes have become one of the most powerful tools in organic synthesis for the construction

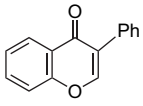
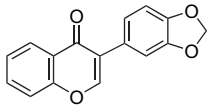
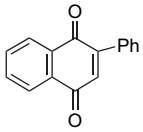
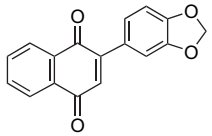
Table 5. Suzuki–Miyaura coupling of 3-bromo-4-chromone and 2-bromo-1,4-naphthoquinone



25: X = O
26: X = CO

12, 27

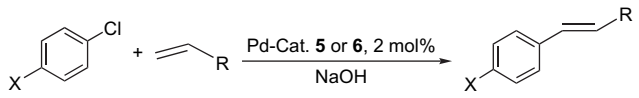
28-31

Run	Product		Thermal heating[a]		Microwave heating[a]	
			Time (h)	Yield,[b] %	Time (min)	Yield,[b] %
1		**28**	4	100 (89)	8	100 (93)
2		**29**	15	36	8	60
3			3	100 (79)[c]	8	100[c]
4		**30**	4	100 (85)[d]	8	100 (90)
5		**31**	15	30	8	100 (87)

[a] Conditions: 1 mmol of aryl bromide, 1.2 mmol of boronic acid, 2 mmol of K_2CO_3, toluene (3 mL), 110 °C for conventional heating; 150 °C for microwave irradiation (200 W).
[b] GC-yields; values in parentheses refer to isolated yields of pure products.
[c] Water/TBAB was used instead of toluene.
[d] When water was used, full conversion (100%) was obtained after 2 h heating.

of carbon–carbon bond. Generally, aryl bromides, iodides, and activated alkenes are typically employed as the cross-coupling partners.[28] Aryl chlorides are cheaper and more readily available than bromides and iodides, but less reactive. The catalyst systems, which show high catalytic activity in Heck–Mizoroki reactions of aryl chlorides are of great importance.[29] Our research work aims also at developing efficient catalyst systems for the cross-coupling of aryl chlorides with activated and deactivated alkenes. Thus, the catalytic activities of the benzothiazole-oxime Pd(II)-precatalysts **5** and **6** were tested in Heck–Mizoroki cross-coupling reaction of aryl chlorides with styrene and *tert*-butyl acrylate under various reaction conditions and the results are summarized in Table 6. In contrast to its suitability for Suzuki–Miyaura cross-couplings for aryl bromides, as shown above, water as a solvent was not suitable enough for Heck–Mizoroki cross-coupling of aryl chlorides (runs 1 and 12 Table 6). Tetrabutylammonium bromide is essential for the Heck–Mizoroki cross-coupling of aryl chlorides[30] as shown in Table 6 and its absence even with highly activated chlorides and olefins (run 10) resulted in sharp decrease of the coupling products regardless of the heating technique. Both Pd-precatalysts **5** and **6** showed high activity for the Heck–Mizoroki coupling of activated aryl chlorides **18** and **19**

Table 6. Heck–Mizoroki cross-coupling reaction of aryl chlorides



18-21 32-37

Run	X/R	Pd-cat	Product	Thermal heating[a]		Microwave heating[a]	
				Time (h)	Yield[b] %	Time (min)	Yield[b] %
1	MeCO/Ph	**5**[c]	**32**	30	61	30	21
2	MeCO/Ph	**5**[d]	**32**	10	87	30	52
3	MeCO/Ph	**6**[d]	**32**	10	89 (83)	30	100 (88)
4	NO_2/Ph	**5**[d]	**33**	8	100 (96)	10	100 (98)
5	NO_2/Ph	**6**[d]	**33**	8	100	10	100
6	Me/Ph	**5**[d]	**34**	30	0	30	5
7	MeCO/COO^{t}Bu	**5**[d]	**35**	12	100 (83)	20	100 (77)
8	MeCO/COO^{t}Bu	**6**[d]	**35**	12	100	20	100
9	NO_2/COO^{t}Bu	**5**[d]	**36**	4	100 (82)	10	100 (95)
10	NO_2/COO^{t}Bu	**5**[e]	**36**	15	13	15	30
11	NO_2/COO^{t}Bu	**6**[d]	**36**	4	100 (88)	10	100 (96)
12	NO_2/COO^{t}Bu	**6**[c]	**36**	15	0	30	0
13	Me/COO^{t}Bu	**5**[d]	**37**	10	3	30	5

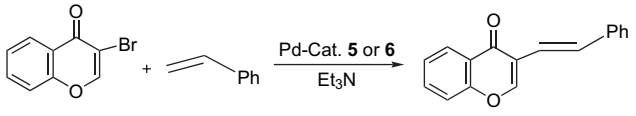
[a] Condition: chloride/olefin/NaOH/TBAB=1:1.5:3:0.6, DMF or water (3 mL), 100 °C for thermal heating in water and 130 °C in DMF; 150 °C (200 W) for microwave irradiation in water or DMF.
[b] GC-yields; isolated yields are in parentheses.
[c] Solvent: water with TBAB.
[d] Solvent: DMF with TBAB.
[e] Solvent: DMF without TBAB.

with both *tert*-butyl acrylate and styrene either thermal or under microwave heating. Using DMF/TBAB cross-coupling of 4-chloroacetophenone **18** with *tert*-butyl acrylate was slightly better than with styrene although in all cases high yields were obtained (runs 2, 3 and 7, 8, Table 6). Under similar reaction conditions, the cross-coupling of 4-chloronitrobenzene **19** with both *tert*-butyl acrylate and styrene resulted, in all cases, in full conversion to the corresponding disubstituted olefins in high yields (runs 4, 5 and 9, 11, Table 6). Heck–Mizoroki cross-coupling is, however, not effective for 4-chlorotoluene **21** (runs 6 and 13, Table 6). Interestingly, the cross-coupling reaction of aryl chlorides was highly regio- and stereoselective and provided only the thermodynamically more stable *E*-isomer of stilbene derivatives **32–33** and β-substituted *tert*-butyl acrylates **35–36** where GC, GC–MS, and ^{1}H NMR spectra of the crude reaction mixture did not reveal any evidence for the formation of *Z*-isomers.

2.6. Precatalysts 5 and 6 in synthesis of 3-styryl-4-chromone via Heck–Mizoroki cross-coupling reactions

Synthesis of 3-styryl-4-chromone could be easily conducted through Heck–Mizoroki cross-coupling of 3-bromo-4-chromone **25** (1 equiv) with styrene (1.5 equiv) using the precatalyst **5** or **6** (0.5 mol %) in either toluene or DMF in the presence triethylamine under thermal and microwave heating as shown in Table 7. Full conversion (86% isolated yield) was obtained when DMF was used as solvent especially under microwave irradiation in the presence of precatalyst **5** (run 2, Table 7), the precatalyst **6** was, however, not convenient and resulted in about 40% conversion under both thermal as well as microwave heating (run 3, Table 7). Toluene was not appropriate for similar cross-coupling reaction neither thermal nor under microwave heating (run 1, Table 7).

Table 7. Synthesis of 3-(β-styryl)-4-chromone via Heck–Mizoroki cross-coupling



25 38

Run	Pd-cat	Solvent	Thermal heating[a]		Microwave heating[a]	
			Time (h)	Yield,[b] %	Time (min)	Yield,[b] %
1	**5**	Toluene	15	12	15	23
2	**5**	DMF	12	79	15	100 (86)[c]
3	**6**	DMF	12	37	15	40

[a] Conditions: 1 mmol of 3-bromochromone **25**, 2 mmol of styrene, 3 mmol of Et_3N, 3 mL solvent, 0.5 mol % Pd-precatalyst **5** or **6** at 110 °C for conventional heating in toluene and 130 °C in DMF; 150 °C (200 W) for microwave irradiation in toluene or DMF.
[b] Isolated yields are given in parentheses.
[c] The product was associated with the formation of 2-(α-styryl)-4-chromone in 9%.

In conclusion, the benzothiazole-oxime-based palladium(II) precatalysts **5** and **6** were found to be efficient and highly active precatalysts for Suzuki–Miyaura and Heck–Mizoroki cross-coupling reactions of activated aryl bromides and chlorides and heterocyclic bromides, with very high TON, under thermal heating as well as microwave irradiation conditions. Deactivated aryl bromides were more effective for both C–C cross-coupling reactions than their chloride analogs. The immobilized catalyst **6** was found to have high longevity compared with its mobilized one **5**. The high turnover number associated with the catalytic activity of the aforementioned precatalysts is highly important for mass production in industrial scales.

3. Experimental

3.1. Materials and methods

NMR spectra were recorded with a Bruker DPX-400 spectrometer at 400 MHz (^{1}H NMR) and at 100 MHz (^{13}C NMR) using $CDCl_3$ as solvent and internal standard (δ=7.26 and 77.36 ppm, for ^{1}H NMR and ^{13}C NMR, respectively). Mass spectra (EI) were obtained at 70 eV with a type VG autospec apparatus (Micromass). GC analyses were conducted using an HPGC series 6890 Series Hewlett Packard equipped with an SE-54 capillar column (25 m, Macherey–Nagel) and an FID detector 19231 D/E. Melting points were determined in open glass capillaries with a Gallenkamp apparatus and are uncorrected. Microwave experiments were carried out using a CEM Discover Labmate™ microwave apparatus (300 W with ChemDriver™ Software). Commercially available reagents and dry solvents were used as received. 2-Acetylbenzothiazole **7**[31] and its oxime derivative **8**[32] were prepared as reported in the literature.

3.2. Preparation of Pd-precatalyst 5

A solution of sodium tetrachloropalladate (294 mg, 1 mmol) in MeOH (2 mL) was added dropwise to a stirred solution of 1-(benzothiazol-2-yl)ethanone oxime (**8**) (192 mg, 1 mmol) in dioxane/methanol (4 mL, 1:1 v/v). After stirring for 2 h, the yellow precipitate was filtered off, washed with methanol then with water, and dried in vacuum over P_2O_5. The precatalyst **5** (Scheme 1) was obtained as a yellow powder (339 mg, 90%) after recrystallization from DMSO. The ^{1}H NMR spectrum revealed the presence of two isomers in a ratio of about 13:1. Mp>300 °C; ^{1}H NMR (DMSO-d_6) δ 2.34 (s, 3H, CH_3), 7.46–7.55 (m, 2H, ArH), 8.03–8.08 (m, 2H, ArH), 12.26 (s, 1H, OH); ^{13}C NMR δ 11.9, 123.1, 123.9, 127.1, 127.2, 134.9, 152.3, 153.6, 167.0. Anal. Calcd for $C_9H_8Cl_2N_2OPdS$: C, 29.25; H, 2.18; N, 7.58. Found: C, 29.14; H, 2.40; N, 7.59.

3.3. Preparation of Pd-precatalyst 6

To a mixture of glass/polymer composite shaped Raschig rings **9** (10 g, 5 mmol) containing 10% chloromethylpolystyrene–divinylbenzene polymer (0.53 mmol polymer/g Raschig rings) and 1-(benzothiazol-2-yl)ethanone oxime **8** (1.92 g, 10 mmol) in dimethylformamide (DMF) (50 mL), sodium hydride (0.72 g, 60% in oil, 30 mmol) was added portionwise over a period of 20 min. The mixture was shaken at 80 °C for 3 days then cooled to room temperature and quenched with water (100 mL). The Raschig rings were filtered and washed successively with DMF, water, ethanol, dichloromethane, and again with ethanol (20 mL, each time), and finally well-dried under vacuum These well-dried Raschig rings **10** (10.934 g) were added to a solution of sodium tetrachloropalladate (1.8 g, 6 mmol) in methanol (80 mL) and the mixture was left to be shaken at room temperature for additional 3 days. The resulting Raschig rings were dried in vacuo and the loading of catalyst **6** was estimated to be ca. 0.07 mmol/g Raschig rings according to weight increase (the weight increase of each single Raschig ring was determined; each ring was loaded with about 2 mol % palladium with reference to 1 mmol scaled reactions).[20]

3.4. Effect of concentration of the palladium precatalyst 5 on the Suzuki–Miyaura cross-coupling in water under thermal heating

A mixture of *p*-bromoacetophenone (1 mmol), phenylboronic acid (1.2 mmol), TBAB (0.6 mmol), palladium catalyst **5** (1 mol %), KOH (2 mmol), and water (3 mL) was shaken at 100 °C under air for 2 h (monitored by GC). The same experiment was repeated using 0.5 mol % of palladium precatalyst. The amount (mol %) of the palladium precatalyst **5** was changed with respect to *p*-bromoacetophenone (0.1, 0.05, 0.01, 0.005, and 0.001 mol % Pd-catalyst with scales of 1, 5, 10, 20 and 40 mmol of *p*-bromoacetophenone with reaction times 2, 2, 2, 2.5 and 2.5 h, respectively). Finally, the same reaction was repeated using 60 mmol of *p*-bromoacetophenone and only 0.0007 mol % palladium complex **5** and the reaction mixture was heated for 2.5 h at 100 °C under air. The molar ratio of the reaction components was in all cases as follows; *p*-bromoacetophenone/phenylboronic acid/tetrabutylammonium bromide (TBAB)/KOH/water: 1:1.2:0.6:2:2 mL. The conversion (in %) versus concentration of palladium catalyst **5** is outlined in Table 1.

3.5. Effect of concentration of the palladium precatalysts 5 and 6 for the Suzuki–Miyaura coupling of deactivated aryl bromides in water with thermal heating

A mixture of *p*-bromoanisole (1 mmol), phenylboronic acid (1.2 mmol), tetrabutylammonium bromide (TBAB) (0.6 mmol), palladium precatalyst **5** (0.5 mol %), K_2CO_3 (2 mmol), and distilled water (2 mL) was shaken at 100 °C under air for 4 h. The same experiment was repeated and the amount (mol %) of the palladium precatalyst **5** was changed with respect to *p*-bromoanisole (0.05, 0.005 and 0.001 mol % Pd-catalyst with scales of 5, 10 and 20 mmol of *p*-bromoanisole with reaction time, in all cases, 4 h). The molar ratio of the reaction components was in all cases as follows; *p*-bromoanisole/phenylboronic acid/tetrabutylammonium bromide (TBAB)/K_2CO_3/water: 1:1.2:0.6:2:2 mL. The conversion (in %) versus concentration of palladium catalyst **5** is outlined in Table 2. The reaction product was extracted with EtOAc (3×30 mL). The combined organic extracts were dried over anhydrous $MgSO_4$, filtered, and the solvent was evaporated under reduced pressure. The product was purified by flash column chromatography on silica gel using EtOAc/petroleum ether (1:20) as an eluant.

Similarly, a mixture of *p*-bromotoluene (1 mmol), phenylboronic acid (1.2 mmol), tetrabutylammonium bromide (TBAB) (0.6 mmol), palladium precatalyst **5** or **6** (0.5 or 0.05 mol %), K_2CO_3 (2 mmol), and distilled water (2 mL) was shaken at 100 °C under air for 6 h. The conversion (in %) versus palladium catalysts is outlined in Table 2. The product was purified as above.

3.6. Longevity of the palladium precatalysts 5 and 6 with thermal heating in water

A mixture of *p*-bromoacetophenone (5 mmol), phenylboronic acid (6 mmol), TBAB (3 mmol), palladium catalyst **5** or **6** (0.5 mol %), K_2CO_3 (10 mmol), and water (10 mL) was shaken at 100 °C under air for 2 h, where all *p*-bromoacetophenone was completely consumed (GC-monitored).

At this point, fresh portions of the coupling partners and the base (the same amounts as for the first run) were added to the flask thus repeating the reaction. In this manner, four successive runs were carried out with the same portion of precatalyst **5** or **6** as shown in Table 3. Finally the product was purified by flash column chromatography on silica gel using EtOAc/petroleum ether (1:10) as an eluant.

3.7. Effect of mol % of precatalysts 5 and 6 for the Suzuki–Miyaura coupling of deactivated aryl bromides in water with thermal heating

A mixture of *p*-bromoanisole (1 mmol), phenylboronic acid (1.2 mmol), tetrabutylammonium bromide (TBAB) (0.6 mmol), palladium precatalyst **5** (0.5 mol %), K_2CO_3 (2 mmol), and distilled water (2 mL) was shaken at 100 °C under air for 4 h. The same experiment was repeated and the amount (mol %) of the palladium precatalyst **5** was changed with respect to *p*-bromoanisole (0.05, 0.005 and 0.001 mol % Pd-catalyst with scales of 5, 10 and 20 mmol of *p*-bromoanisole with reaction time, in all cases, 4 h). The molar ratio of the reaction components were in all cases as follows; *p*-bromoanisole/phenylboronic acid/tetrabutylammonium bromide (TBAB)/K_2CO_3/water: 1:1.2:0.6:2:2 mL. The conversion (in %) versus concentration of palladium catalyst **5** is outlined in Table 2. The reaction product was extracted with EtOAc (3×30 mL). The combined organic extracts were dried over anhydrous $MgSO_4$, filtered, and the solvent was evaporated under reduced pressure. The product was purified by flash column chromatography on silica gel using EtOAc/petroleum ether (1:20) as an eluant.

3.8. General procedure for the Suzuki–Miyaura coupling of aryl chlorides in water with thermal heating

A mixture of the appropriate aryl chlorides **18**–**21** (1 mmol), phenylboronic acid **12** (1.2 mmol), tetrabutylammonium bromide (TBAB) (0.6 mmol), palladium precatalyst **5** or **6** (1, 0.2 or 0.02 mol %), NaOH (2 mmol), and distilled water (2 mL) was shaken at 100 °C under air for 4–20 h (GC-monitored) as outlined in Table 4. The product was extracted with EtOAc (3×20 mL). The combined organic extracts were dried over anhydrous $MgSO_4$, filtered, and the solvent was evaporated under reduced pressure. The product was purified with flash column chromatography as described above.

3.9. General procedure for the Suzuki–Miyaura coupling of aryl chlorides in water with microwave heating

A mixture of the appropriate aryl chlorides **18**–**21** (1 mmol), phenylboronic acid (1.2 mmol), tetrabutylammonium bromide (TBAB) (0.6 mmol), palladium precatalyst **5** or **6** (1, 0.2 or 0.02 mol %), NaOH (2 mmol), and distilled water (2 mL) was mixed in a process vial. The vial was capped properly, and thereafter the mixture was heated under microwave irradiation conditions at 160 °C and 250 W for the appropriate reaction time 7–30 min as listed in Table 4. After the reaction was almost complete (monitored by GC), the reaction mixture was extracted with EtOAc (3×20 mL). The combined organic extracts were dried over anhydrous $MgSO_4$, filtered, and the solvent was evaporated under reduced pressure. The product was purified with flash column chromatography as described above.

3.10. Suzuki–Miyaura coupling in the synthesis of 3-aryl-4-chromone and 1,4-naphthoquinone derivatives with thermal heating

To a mixture of 3-bromo-4-chromone **25** or 2-bromo-1,4-naphthoquinone **26** (1 mmol) and the appropriate arylboronic acid **12** or **17** (1.2 mmol) dissolved in toluene (3 mL) in the presence of K_2CO_3 (0.28 g, 2 mmol), palladium precatalyst **5** (0.5 mol %) was added. The reaction mixture was then heated to reflux temperature with stirring for a period of 4–15 h, and the reaction flask was then allowed to cool to room temperature. The reaction mixture was extracted three times with EtOAc (60 mL total) and then the organic fractions were combined together, dried over Na_2SO_4, filtered, and then the solvent was removed under vacuum. The residue was then subjected to separation via flash column chromatography with petroleum ether/EtOAc (10:1) as an eluant to give the pure products **28**–**31**.

3.11. Suzuki–Miyaura coupling in the synthesis of 3-aryl-4-chromone and 1,4-naphthoquinone derivatives with microwave heating

To a mixture of 3-bromo-4-chromone **25** or 2-bromo-1,4-naphthoquinone **26** (1 mmol) and the appropriate arylboronic acid **12** or **17** (1.2 mmol), K_2CO_3 (2 mmol) and palladium precatalyst **5** (0.5 mol %) in toluene (3 mL) were thoroughly mixed in a process vial. The vial was capped properly, and thereafter the mixture was heated under microwave irradiation conditions at 150 °C and 200 W for 8 min, and then the process vial was allowed to cool to room temperature. The reaction mixture was extracted three times with EtOAc (60 mL total) and then the organic fractions were combined together, dried over Na_2SO_4, filtered, and then the solvent was removed under vacuum. The pure products were obtained as described above.

3.12. General procedure for the Heck–Mizoroki coupling of aryl chlorides with thermal heating

A mixture of the appropriate aryl chloride (1 mmol), the appropriate olefin (1.5 mmol), TBAB (0.6 mmol), precatalyst **5** or **6** (2 mol %), and sodium hydroxide (3 mmol) in water or DMF (3 mL) was shaken at 100 °C (for water as solvent) or at 130 °C (for DMF as solvent) under air for the given reaction time listed in Table 6. After the reaction was almost completed (monitored by GC), the reaction mixture was cooled to room temperature The reaction mixture was extracted three times with EtOAc (60 mL total) and then the organic fractions were combined together, dried over Na_2SO_4, filtered, and then the solvent was removed under vacuum. The residue was then subjected to purification via flash column chromatography with petroleum ether/EtOAc (10:1) as an eluant to give the pure products **32**–**36**.

3.13. General procedure for the Heck–Mizoroki coupling of aryl chlorides under microwave irradiation

To a mixture of the appropriate aryl chloride (1 mmol) and the appropriate olefin (1.5 mmol), TBAB (0.6 mmol), precatalyst **5** or **6** (2 mol %), and sodium hydroxide (3 mmol) in water or DMF (3 mL) were mixed in a process vial. The vial was capped properly, and thereafter the mixture was

heated under microwave irradiation conditions at 150 °C and 200 W in either solvents for the appropriate reaction time as listed in Table 6. The products were purified as described above.

3.14. General procedure for the Heck–Mizoroki synthesis of 3-styryl-4-chromone under thermal and microwave heating

A mixture of 3-bromo-4-chromone **25** (1 mmol), styrene (1.5 mmol), precatalyst **5** or **6** (0.5 mol %), and triethylamine (3 mmol) in toluene or DMF (3 mL) was shaken at 110 °C (for toluene as solvent) or at 130 °C (for DMF as solvent) under air for 12 or 15 h as listed in Table 7. Similar components were also mixed in the same ratio in a process vial. The vial was capped properly, and thereafter the mixture was heated under microwave irradiation conditions at 150 °C and 200 W in either solvents for 15 min. The reaction mixture, in both case, was cooled to room temperature then extracted three times with EtOAc (60 mL total) and the organic fractions were combined together, dried over Na_2SO_4, filtered, and then the solvent was removed under vacuum. The residue was then subjected to purification via flash column chromatography with petroleum ether/EtOAc (10:1) as an eluant to give the pure product **38**.

3.14.1. 4-Acetyl-1,1′-biphenyl (13). Colorless crystals, mp 119–120 °C (Ref. 33, mp 118–120 °C); ^{1}H NMR ($CDCl_3$) δ 2.64 (s, 3H, CH_3CO), 7.36–7.42 (m, 1H), 7.46–7.49 (m, 2H), 7.62–7.65 (m, 2H), 7.69 (d, 2H, J=8.52 Hz), 8.03 (d, 2H, J=8.52 Hz); ^{13}C NMR δ 27.0, 127.5, 127.6, 128.6, 129.2, 129.3, 136.2, 140.2, 146.1, 198.1; MS (*m/e*) 196 (M^+), 181, 152, 127, 102, 91, 76.

3.14.2. 4-Methoxy-1,1′-biphenyl (16). Pale yellow powder, mp 87–88 °C (Ref. 34, mp 86–87 °C); ^{1}H NMR ($CDCl_3$) δ 3.87 (s, 3H, –OCH_3), 6.99–7.02 (m, 2H), 7.31–7.59 (m, 7H); ^{13}C NMR δ 55.7, 114.5, 126.9, 127.1, 128.5, 129.1, 134.1, 141.2, 159.5; MS (*m/e*) 184 (M^+), 169, 141, 115, 89, 76, 63.

3.14.3. 4-Methyl-1,1′-biphenyl (17). White crystals, mp 44–45 °C (Ref. 35, mp 43.5–44.5 °C); ^{1}H NMR ($CDCl_3$) δ 2.41 (s, 3H, –CH_3), 7.25–7.60 (m, 9H); ^{13}C NMR δ 21.4, 127.31, 127.32, 127.34, 129.1, 137.4, 138.7, 141.5; MS (*m/e*) 168 (M^+), 152, 139, 115, 91, 82, 63.

3.14.4. 4-Nitro-1,1′-biphenyl (22). Pale yellow powder, mp 107–108 °C (Ref. 36, mp 107.5–108.5 °C); ^{1}H NMR ($CDCl_3$) δ 7.41–7.55 (m, 3H), 7.61–7.75 (m, 4H), 8.29 (d, 2H, J=8.78 Hz); MS (*m/e*) 199 (M^+), 169, 141, 127, 115, 101, 76, 63.

3.14.5. 4-Phenylbenzonitrile (23). White solid, mp 91–92 °C (Ref. 37, mp is not mentioned); ^{1}H NMR ($CDCl_3$) δ 7.41–7.51 (m, 3H), 7.58–7.61 (m, 2H), 7.67–7.74 (m, 4H); ^{13}C NMR δ 111.2, 119.3, 127.5, 128, 128.9, 129.4, 132.9, 139.5, 145.9; MS (*m/e*) 179 (M^+), 164, 151, 126, 100, 76, 63.

3.14.6. 3-Phenyl-4-chromone (isoflavone) (28). White powder, mp 132–133 °C (Ref. 38, mp 131.5–132 °C); ^{1}H NMR ($CDCl_3$) δ 7.39–7.49 (m, 5H), 7.56–7.58 (m, 2H), 7.59–7.70 (m, 1H), 8.03 (s, 1H), 8.35–8.36 (m, 1H); ^{13}C NMR δ 118.4, 124.9, 125.6, 125.7, 126.8, 128.5, 128.8, 129.3, 132.2, 133.9, 153.4, 156.5, 176.5; MS (*m/e*) 222 (M^+), 194, 165, 120, 111, 92, 82, 76.

3.14.7. 3-(3,4-Methylenedioxyphenyl)-4-chromone (29). Pale yellow powder, mp 156–158 °C; ^{1}H NMR ($CDCl_3$) δ 5.99 (s, 2H, –OCH_2O–), 6.86 (d, 1H, J=8.04 Hz), 6.98 (dd, 1H, J=8.04, 1.76 Hz), 7.1 (d, 1H, J=1.76 Hz), 7.39–7.48 (m, 2H), 7.65–7.69 (m, 1H), 7.98 (s, 1H), 8.28 (m, 1H); ^{13}C NMR δ 101.5, 106.9, 108.7, 110, 118.3, 122.7, 124.7, 125.4, 125.5, 125.9, 126.7, 133.9, 148, 148.1, 153, 156.5, 176.6; MS (*m/e*) 266 (M^+), 209, 180, 146, 118, 104, 88, 76. Anal. Calcd for $C_{16}H_{10}O_4$: C, 72.18; H, 3.79. Found: C, 71.74; H, 3.93.

3.14.8. 2-Phenyl-1,4-naphthoquinone (30). Yellow crystals, mp 106–108 °C (Ref. 39, mp is not mentioned); ^{1}H NMR ($CDCl_3$) δ 7.08 (s, 1H), 7.46–7.57 (m, 3H), 7.58–7.59 (m, 2H), 7.75–7.80 (m, 2H), 8.11–8.15 (m, 2H); ^{13}C NMR δ 126.3, 127.4, 128.8, 129.8, 130.4, 132.4, 132.8, 133.7, 134.1, 134.2, 135.6, 148.5, 184.7, 185.5; MS (*m/e*) 234 (M^+), 206, 178, 151, 129, 105, 89, 76.

3.14.9. 2-(3,4-Methylenedioxyphenyl)-1,4-naphthoquinone (31). Orange-red crystals, mp 184–186 °C; ^{1}H NMR ($CDCl_3$) δ 6.04 (s, 2H, –OCH_2O–), 6.90 (d, 1H, J=8 Hz), 7.02 (s, 1H), 7.09–7.13 (m, 2H), 7.75–7.78 (m, 2H), 8.09–8.16 (m, 2H); ^{13}C NMR δ 101.9, 108.9, 110.1, 124.4, 126.2, 127.4, 127.5, 132.4, 132.8, 134.1, 134.2, 134.5, 147.8, 148.2, 149.8, 184.9, 185.4; MS (*m/e*) 278 (M^+), 248, 220, 192, 163, 124, 104, 76. Anal. Calcd for $C_{17}H_{10}O_4$: C, 73.38; H, 3.62. Found: C, 73.03; H, 3.48.

3.14.10. (*E*)-4-Acetylstilbene (32). Colorless crystals, mp 143–144 °C (Ref. 40, mp 141–142 °C); ^{1}H NMR ($CDCl_3$) δ 2.58 (s, 3H, CH_3CO), 7.10 (d, 1H, J=16.4 Hz), 7.20 (d, 1H, J=16.4 Hz), 7.27–7.31 (m, 1H), 7.36 (m, 2H), 7.51–7.53 (m, 2H), 7.56 (d, 1H, J=8.4 Hz), 7.93 (d, 1H, J=8.4 Hz); ^{13}C NMR δ 26.9, 126.8, 127.1, 127.7, 128.6, 129.1, 129.2, 131.7, 136.2, 136.9, 142.3, 197.7; MS (*m/e*) 222 (M^+), 207, 178, 152, 103, 89, 76, 63, 51.

3.14.11. (*E*)-4-Nitrostilbene (33). Yellow powder, mp 146–148 °C (Ref. 41, mp 140 °C); ^{1}H NMR ($CDCl_3$) δ 7.13 (d, 1H, J=16.4 Hz), 7.26 (d, 1H, J=16.4 Hz), 7.32–7.36 (m, 1H), 7.39–7.42 (m, 2H), 7.54–7.56 (m, 2H), 7.61 (d, 2H, J=8.52 Hz), 8.21 (d, 2H, J=8.52 Hz); ^{13}C NMR δ 124.4, 126.5, 127.1, 127.3, 129.1, 129.2, 133.6, 136.4, 144.1, 147; MS (*m/e*) 225 (M^+), 195, 178, 165, 152, 102, 89, 76, 63, 51.

3.14.12. (*E*)-*tert*-Butyl 3-(4-acetylphenyl)prop-2-enoate (35). Yellowish-white crystals, mp 99–100 °C (Refs. 24, 42, mp is not mentioned); ^{1}H NMR ($CDCl_3$) δ 1.54 (s, 9H, $C(CH_3)_4$), 2.61 (s, 3H, CH_3CO), 6.46 (d, 1H, J=16.04 Hz), 7.58 (d, 1H, J=16.04 Hz), 7.60 (d, 2H, J=8.52 Hz), 7.95 (d, 2H, J=8.52 Hz); ^{13}C NMR δ 26.9, 28.3, 81.2, 123.1, 128.3, 129.1, 138.1, 139.4, 142.3, 166.1, 197.6; MS (*m/e*) 246 (M^+), 190, 175, 147, 131, 102, 91, 79, 57.

3.14.13. (*E*)-*tert*-Butyl 3-(4-nitrophenyl)prop-2-enoate (36). White crystals, mp 144–146 °C (Ref. 43, mp is not mentioned); ^{1}H NMR ($CDCl_3$) δ 1.54 (s, 9H, $C(CH_3)_4$), 6.48 (d, 1H, J=16.04 Hz), 7.60 (d, 1H, J=16.04 Hz), 7.64

(d, 2H, J=8.84 Hz), 8.23 (d, 2H, J=8.84 Hz); ^{13}C NMR δ 28.4, 81.7, 124.5, 124.9, 128.8, 140.9, 141.2, 148.7, 165.6; MS (*m*/*e*) 249 (M^+), 234, 194, 176, 146, 130, 102, 90, 76, 57.

3.14.14. (*E*)-3-(β-Styryl)-4-chromone (38). Yellowish-white powder, mp 169–170 °C (Ref. 44, mp 170–171 °C); ^{1}H NMR ($CDCl_3$) δ 6.98 (d, 1H, J=16.32 Hz), 7.25–7.29 (m, 1H), 7.34–7.38 (m, 2H), 7.41–7.54 (m, 4H), 7.63 (d, 1H, J=16.32 Hz), 7.65–7.69 (m, 1H), 8.1 (s, 1H), 8.31–8.36 (m, 1H); ^{13}C NMR δ 118.4, 119.4, 122.2, 124.4, 125.6, 126.6, 126.9, 128.2, 128.9, 132, 133.9, 137.7, 153.4, 156.2, 176.9; MS (*m*/*e*) 248 (M^+), 231, 189, 171, 155, 128, 115, 92, 77, 63.

Acknowledgements

The author is very thankful to Prof. Dr. A. Kirschning, Institute of Organic Chemistry, University of Hanover, for providing polymer glass composite material, arylboronic acids, and sod tetrachloropalladate. He is also deeply indebted to the Alexander-von-Humboldt (AvH) Foundation for donating him a CEM Discover Labmate™ microwave apparatus.

References and notes

1. (a) *Handbook of Organopalladium Chemistry for Organic Synthesis*; Negishi, E., Ed.; Wiley-Interscience: Hoboken, NJ, 2002; (b) Soederberg, B. C. G. *Coord. Chem. Rev.* **2003**, *241*, 147–247; (c) Fairlamb, I. J. S. *Tetrahedron* **2005**, *61*, 9661–9662.
2. Corey, E. J.; Cheng, X. M. *The Logic of Chemical Synthesis*; John Wiley and Sons: New York, NY, 1989.
3. Bringmann, G.; Gunther, C.; Ochse, M.; Schupp, O.; Tasler, S. *Progress in the Chemistry of Organic Natural Products*; Herz, W., Falk, H., Kirby, G. W., Moore, R. E., Eds.; Springer: New York, NY, 2001; Vol. 82, pp 1–293.
4. Hegedus, L. S. *Organometallics in Synthesis*; Schlosser, M., Ed.; John Wiley and Sons: Chichester, UK, 2002; p 1123.
5. Diederich, F.; Stang, P. J. *Metal-Catalyzed Cross-Coupling Reactions*; Wiley-VCH: Weinheim, 1998.
6. (a) Miyaura, N.; Suzuki, A. *Chem. Rev.* **1995**, *95*, 2457–2483; (b) Miyaura, N. *Cross-Coupling Reactions;* Springer: Berlin, 2002.
7. (a) *Homogeneous Catalysis with Metal Phosphine Complexes*; Pignolet, L. H., Ed.; Plenum: New York, NY, 1983; (b) Parshall, G. W.; Ittel, S. *Homogeneous Catalysis*; John Wiley and Sons: New York, NY, 1992.
8. Bellina, F.; Carpita, A.; Rossi, R. *Synthesis* **2004**, *15*, 2419–2440.
9. (a) Dai, M.; Liang, B.; Wang, C.; Chen, J.; Yang, Z. *Org. Lett.* **2004**, *6*, 221–224; (b) Yang, D.; Chen, Y. C.; Zhu, N. Y. *Org. Lett.* **2004**, *6*, 1577–1580; (c) Li, J. H.; Liu, W. J. *Org. Lett.* **2004**, *6*, 2809–2811; (d) Colacot, T. J.; Shea, H. A. *Org. Lett.* **2004**, *6*, 3731–3734.
10. (a) Old, D. W.; Wolfe, J. P.; Buchwald, S. L. *J. Am. Chem. Soc.* **1998**, *120*, 9722–9723; (b) Wolfe, J. P.; Singer, R. A.; Yang, B. H.; Buchwald, S. L. *J. Am. Chem. Soc.* **1999**, *121*, 9550–9561; (c) Littke, A. F.; Dai, C.; Fu, G. C. *J. Am. Chem. Soc.* **2000**, *122*, 4020–4028; (d) Mori, K.; Yamaguchi, K.; Hara, T.; Mizugaki, T.; Ebitani, K.; Kaneda, K. *J. Am. Chem. Soc.* **2002**, *124*, 11572–11573; (e) Yin, J.; Rainka, M. P.; Zhang, X. X.; Buchwald, S. L. *J. Am. Chem. Soc.* **2002**, *124*, 1162–1163.
11. (a) Bedford, R. B.; Cazin, C. S. J.; Hazelwood, S. L. *Angew. Chem., Int. Ed.* **2002**, *41*, 4120–4122; (b) Littke, A. F.; Fu, G. C. *Angew. Chem., Int. Ed.* **2002**, *41*, 4176–4211; (c) Zhang, W.; Shi, M. *Tetrahedron Lett.* **2004**, *45*, 8921–8924.
12. Alonso, F.; Beletskaya, I. P.; Pages, M. Y. *Tetrahedron* **2005**, *61*, 11771–11835.
13. (a) Blaser, H.-U. *Chem. Commun.* **2003**, 293–296; (b) Blaser, H.-U.; Siegrist, U.; Steiner, H. M. *Fine Chemicals Through Heterogeneous Catalysis*; Wiley-VCH: 2001; p 389; (c) Schöning, K. U.; End, N. Kirschning, A., Ed.; *Top. Curr. Chem.* **2004**, *242*, 241–271 and 273–317; (d) Blaser, H.-U.; Indolese, A.; Naud, F.; Nettekoven, U.; Schnyder, A. *Adv. Synth. Catal.* **2004**, *346*, 1583–1599.
14. (a) Desai, B.; Kappe, C. O. Kirschning, A., Ed.; *Top. Curr. Chem.* **2004**, *242*, 177–208; (b) Kappe, C. O. *Angew. Chem., Int. Ed.* **2004**, *43*, 6250–6284; (c) Hoz, A.; Ortiz, A. D.; Moreno, A. *Chem. Soc. Rev.* **2005**, *34*, 164–178.
15. (a) Li, C. J.; Chan, T. H. *Organic Reactions in Aqueous Media*; Wiley: New York, NY, 1997; (b) *Organic Synthesis in Water*; Grieco, P. A., Ed.; Thomson Science: Glasgow, Scotland, 1998; (c) Li, C. J. *Chem. Rev.* **1993**, *93*, 2023–2035.
16. (a) Farina, V. *Adv. Synth. Catal.* **2004**, *346*, 1553–1582; (b) Dupont, J.; Consorti, C. S.; Spencer, J. *Chem. Rev.* **2005**, *105*, 2527–2572.
17. (a) Botella, L.; Nájera, C. *Tetrahedron Lett.* **2004**, *45*, 1833–1836; (b) Botella, L.; Nájera, C. *Tetrahedron* **2004**, *60*, 5563–5570; (c) Botella, L.; Nájera, C. *Angew. Chem., Int. Ed.* **2002**, *41*, 179–181; (d) Botella, L.; Nájera, C. *J. Org. Chem.* **2005**, *70*, 4360–4369.
18. Solodenko, W.; Schön, U.; Messinger, J.; Glinscher, A.; Kirschning, A. *Synlett* **2004**, 1699–1702.
19. (a) Baleizao, C.; Corma, A.; Garcia, H.; Leyva, A. *Chem. Commun.* **2003**, 606–607; (b) Baleizao, C.; Corma, A.; Garcia, H.; Leyva, A. *J. Org. Chem.* **2004**, *69*, 439–446.
20. (a) Solodenko, W.; Brochwitz, C.; Wartchow, R.; Hashem Md., A.; Vaultier, M.; Dawood, K. M.; Kirschning, A. *Mol. Div.* **2005**, *9*, 333–339; (b) Dawood, K. M.; Kirschning, A. *Tetrahedron* **2005**, *61*, 12121–12130; (c) Dawood, K. M.; Solodenko, W.; Kirschning, A. *ARKIVOC* **2007**, 104–124.
21. Gai, X.; Grigg, R.; Ramzan, M. I.; Sridharan, V.; Collard, S.; Muir, J. E. *Chem. Commun.* **2000**, 2053–2054.
22. Dupont, J.; Pfeffer, M.; Spencer, J. *Eur. J. Inorg. Chem.* **2001**, 1917–1927.
23. (a) Bedford, R. B.; Hazelwood, S. L.; Horton, P. N.; Hursthouse, M. B. *Dalton Trans.* **2003**, 4164–4174; (b) Yamada, Y. M. A.; Takeda, K.; Takahashi, H.; Ikegami, S. *J. Org. Chem.* **2003**, *68*, 7733–7741; (c) Alonso, D. A.; Najera, C.; Pacheco, M. C. *J. Org. Chem.* **2002**, *67*, 5588–5594; (d) Feuerstein, M.; Doucet, H.; Santelli, M. *Tetrahedron Lett.* **2001**, *42*, 6667–6670; (e) Shaughnessy, K. H.; Booth, R. S. *Org. Lett.* **2001**, *3*, 2757–2759; (f) Zapf, A.; Beller, M. *Chem.—Eur. J.* **2000**, *6*, 1830–1833; (g) Sava, X.; Ricard, L.; Mathey, F.; Le Floch, P. *Organometallics* **2000**, *19*, 4899–4903; (h) Weissman, H.; Milstein, D. *Chem. Commun.* **1999**, 1901–1902.
24. Herrmann, W. A.; Brossmer, C.; Reisinger, C.-P.; Riermeier, T. H.; Oefele, K.; Beller, M. *Chem.—Eur. J.* **1997**, *3*, 1357–1364.
25. Herrmann, W. A.; Böhm, V. P. W.; Reisinger, C.-P. *J. Organomet. Chem.* **1999**, *576*, 23–41.
26. (a) Kinghorn, A. D.; Su, B.-N.; Jang, D. S.; Chang, L. C.; Lee, D.; Gu, J.-Q.; Carache-Blanco, E. J.; Pawlus, A. D.; Lee, S. K.; Park, E. J.; Cuendet, M.; Gills, J. J.; Bhat, K.; Park, H.-S.;

Mata-Greenwood, E.; Song, L. L.; Jang, M.; Pezzuto, J. M. *Planta Med.* **2004**, *70*, 691–705; (b) Galati, G.; O'Brien, P. J. *Free Radical Biol. Med.* **2004**, *37*, 287–303; (c) *Phytochemicals: A New Paradigm*; Bidlack, W. R., Omaye, S. T., Meskin, M. S., Jahmer, D., Eds.; Technomic: Lancaster, 1998; (d) Shahidi, F.; Naczk, M. *Phenolics in Food and Nutraceuticals*; CRC: New York, NY, 2004; (e) Johnson, I.; Williamson, G. *Phytochemical Functional Foods*; CRC: Cambridge, 2003.

27. (a) Dastidar, S. G.; Manna, A.; Kumar, K. A.; Mazumdar, K.; Dutta, N. K.; Chakrabarty, A. N.; Motohashi, N.; Shirataki, Y. *Int. J. Antimicrob. Agents* **2004**, *23*, 99–102; (b) Young, D. Y.; Khalil, D. A.; Arquitt, A. B.; Smith, B. J.; Hammond, L. J.; Droke, E. A.; Lewis, E. A.; Devareddy, L.; Arjmandi, B. H. *Phytomedicine* **2004**, *11*, 303–308; (c) Kim, Y.-W.; Hackett, J. C.; Brueggemier, R. W. *J. Med. Chem.* **2004**, *47*, 4032–4040; (d) Clifford, M. N. *Planta Med.* **2004**, *70*, 1103–1114; (e) Harborne, J. B.; Mabry, T. J. *The Flavanoids: Advances in Research*; Chapman and Hall: New York, NY, 1982; Chapter 10; (f) Le'vai, A. *J. Heterocycl. Chem.* **2004**, *41*, 449–460.
28. For reviews, see: (a) Heck, R. F. *Acc. Chem. Res.* **1979**, *12*, 146–151; (b) Cabri, W.; Candiani, I. *Acc. Chem. Res.* **1995**, *28*, 2–7; (c) Negishi, E.; Coperet, C.; Ma, S.; Liou, S.; Liu, F. *Chem. Rev.* **1996**, *96*, 365–394; (d) Crisp, G. T. *Chem. Soc. Rev.* **1998**, *27*, 427–436; (e) Beletskaya, J. P.; Cheprakov, A. V. *Chem. Rev.* **2000**, *100*, 3009–3066; (f) Biffis, A.; Zecca, M.; Basato, M. *J. Mol. Catal. A* **2001**, *173*, 249–274; (g) Whitcombe, N. J.; Hii, K. K.; Gibson, S. E. *Tetrahedron* **2001**, *57*, 7449–7476; (h) Dounay, A. B.; Overman, L. E. *Chem. Rev.* **2003**, *103*, 2945–2964.
29. (a) Reetz, M. T.; Lohmer, G.; Schwickardi, R. *Angew. Chem., Int. Ed.* **1998**, *37*, 481–483; (b) Gruber, A. S.; Pozebon, D.; Monteiro, A. L.; Dupont, J. *Tetrahedron Lett.* **2001**, *42*, 7345–7348; (c) Loch, J. A.; Albrecht, M.; Peris, E.; Mata, J.; Faller, J. W.; Grabtree, R. H. *Organometallics* **2002**, *21*, 700–706; (d) Alonso, D. A.; Najera, C.; Pacheco, M. C. *Adv. Synth. Catal.* **2002**, *344*, 172–183; (e) Selvakumar, K.; Zapf, A.; Beller, M. *Org. Lett.* **2002**, *4*, 3031–3033; (f) Schnyder, A.; Aemmer, J.; Indolese, A. F.; Pittelkow, U.; Studer, M. *Adv. Synth. Catal.* **2002**, *344*, 495–498; (g) Diez-Barra, E.; Guerra, J.; Hornillos, V.; Merino, S.; Tejeda, J. *Organometallics* **2003**, *22*, 4610–4612; (h) Consorti, C. S.; Zanini, M. L.; Leal, S.; Ebeling, G.; Dupont, J. *Org. Lett.* **2003**, *5*, 983–986; (i) Consirti, C. S.; Ebeling, G.; Flores, F. R.; Rominger, F.; Dupont, J. *Adv. Synth. Catal.* **2004**, *346*, 617–624; (j) Prockl, S. S.; Kleist, W.; Gruber, M. A.; Kohler, K. *Angew. Chem., Int. Ed.* **2004**, *43*, 1881–1882; (k) Frey, G. D.; Schutz, J.; Herdtweck, E.; Herrmann, W. A. *Organometallics* **2005**, *24*, 4416–4426; (l) Prockl, S.; Kleist, W.; Kohler, K. *Tetrahedron* **2005**, *61*, 9855–9859.
30. Zapf, A.; Beller, M. *Chem.—Eur. J.* **2001**, *7*, 2908–2915.
31. (a) Sawhney, S. N.; Singh, J. *Indian J. Chem.* **1970**, *8*, 882–884; (b) Farag, A. M.; Dawood, K. M.; Abdelhamid, A. O. *Tetrahedron* **1997**, *53*, 17461–17468; (c) Farag, A. M.; Dawood, K. M. *Heteroat. Chem.* **1997**, *8*, 45–50.
32. Bushey, D. F.; Johnson, B. F.; Haung, J. *J. Org. Chem.* **1985**, *50*, 2091–2095.
33. Robinson, G. E.; Vernon, J. M. *J. Chem. Soc. C* **1971**, 3363–3367.
34. Shneider, S.; Bannwarth, W. *Helv. Chim. Acta* **2001**, *84*, 735–742.
35. Mowery, M. E.; Deshong, P. *J. Org. Chem.* **1999**, *64*, 3266–3270.
36. Wallow, T. L.; Novak, B. M. *J. Org. Chem.* **1994**, *59*, 5034–5037.
37. Liu, L.; Zhang, Y.; Wang, Y. *J. Org. Chem.* **2005**, *70*, 6122–6125.
38. Hoshino, Y.; Miyaura, N.; Suzuki, A. *Bull. Chem. Soc. Jpn.* **1988**, *61*, 3008–3010.
39. Hagelin, H.; Oslob, J. D.; Akermark, B. *Chem.—Eur. J.* **1999**, 2413–2416.
40. (a) Denmark, S. E.; Wang, Z. *Org. Lett.* **2001**, *3*, 1073–1076; (b) Bezou, P.; Hilberer, A.; Hadziioannou, G. *Synthesis* **1996**, 449–451.
41. Eisnor, C. R.; Gossage, R. A.; Yadav, P. N. *Tetrahedron* **2006**, *62*, 3395–3401.
42. Li, G. Y.; Zheng, G.; Noonan, A. F. *J. Org. Chem.* **2001**, *66*, 8677–8681.
43. Haung, Z.-Z.; Ye, S.; Xia, W.; Yu, Y.-H.; Tang, Y. *J. Org. Chem.* **2002**, *67*, 3096–3103.
44. Davies, S. G.; Mobbs, B. E.; Goodwin, C. J. *J. Chem. Soc., Perkin Trans. 1* **1987**, 2597–2604.