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Note

Application of dimeric orthopalladated complex in Suzuki–Miyaura cross coupling reaction under microwave irradiation and conventional heating

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ABSTRACT

The Suzuki–Miyaura reaction of various aryl halides using [Pd{$C_6H_2(CH_2CH_2NH_2)$–$(OMe)_2$,3,4} (μ-Br)]$_2$ have been investigated. This orthopalladated complex is an efficient, stable and non-sensitive to air and moisture catalyst for the hetrocoupling reaction in DMF as the reaction solvent at 130 °C. The combination of dimeric complex as homogenous catalyst and microwave irradiation can be very useful and efficient methods in organic synthesis, so the application of microwave irradiation have been investigated using homogenous dimeric complex [Pd{$C_6H_2(CH_2CH_2NH_2)$–$(OMe)_2$,3,4} (μ-Br)]$_2$. Application of dimeric complex as catalyst caused to produce the desired coupling products and the using of microwave irradiation improving the yields of the reactions and shortening the reaction times.

1. Introduction

In modern synthetic chemistry the transition metals have been employed as efficient catalysts for C–C bond formation [1,2] and for this purpose the palladium catalysts are more efficient [3,4]. There are various cross coupling reactions and among them the Suzuki–Miyaura cross-coupling of aryl halides with aryl boronic acids is one of the most useful method for synthesis of biaryl and hetero biaryl derivatives [5–9]. Biaryls are basic intermediates in organic synthesis and as functional groups in many natural products compounds, bioactive products, and liquid crystal materials [10,11]. The special benefits of the Suzuki–Miyaura coupling are straightforward synthesize of the wide tolerance compounds with vast functional groups under normal conditions [12], commercial availability of organoboron reagents, easy handling of these materials [13]. In 1981, the application of $Pd(PPh_3)_4$ in Suzuki reaction has been reported for the first time [14] and recently, *N*-heterocyclic carbenes (NHC) have been applied as potentially effective ligands for Suzuki reactions [15–18], however they are usually either air/moisture sensitive or expensive [19]. The new palladacycles complexes as active and more air inert catalytic candidates have recently been employed in Suzuki reaction [20,21]. In many cases, these compounds are dimeric chloro-bridged ortho-palladated complexes [22–25].

One negative aspect of the Suzuki reaction is long reaction time, especially with satirically hindered coupling partners [26]. Modern techniques are focused on the design of new methodologies with ability to modify the known chemical transformations using simpler, faster, more inexpensive and in general, more efficient processes [27]. Microwave (MW) as a non-conventional energy source has become very popular and useful technology in organic chemistry [28], microwave irradiation has recently reported as a potential method for improving the reaction yields in shorter reaction times [28] under clean and green chemistry conditions [29]. The microwave-promoted Suzuki–Miyaura couplings were initially reported in 1996 [30]. The combination of immobilized homogenous catalysts and microwave irradiation can be very useful and is an efficient methods for modification of known procedure in organic synthesis [27].

In conjunction of our pervious works on the synthesis and application of palladacycle complexes [31–33], herein we report the application of homogeneous homoveratrylamine Pd(II) precatalyst **A** (Scheme 1) in Suzuki–Miyaura cross coupling reaction of various aryl halides under microwave irradiation and conventional heating conditions.

2. Results and discussion

Initially the affinity of catalyst **A** was tried for Suzuki–Miyaura coupling of various arylhalides with phenylboronic acid via conventional heating under air conditions (Scheme 1).

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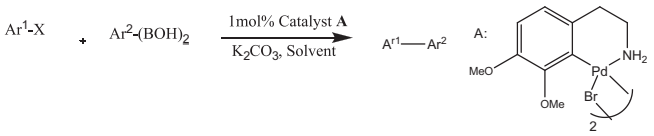


Scheme 1. The Suzuki cross-coupling reaction.

As demonstrated in Table 1, the corresponding coupled products were obtained using various amounts of catalyst **A** in the presence of K_2CO_3 as base [31,32] in different solvents.

According to the obtained results, DMF as solvent and K_2CO_3 as base gave the best results. As is demonstrated in Tables 2 and 3, the catalysts can be used for cross-coupling reaction of aryl iodides, bromides and even less reactive aryl chlorides under both conventional heating and microwave irradiation conditions. However, aryl chlorides were reacted more slowly in comparison to the iodides and bromides derivatives. Longer reaction times were required under conventional heating (Table 2) and assistance of microwave irradiation did improve the yields of the reactions and shortening the reaction times from hours to minutes (Tables 2 and 3). As is exhibited in Tables 2 and 3 a wide range of aryl halides were transformed to the corresponding coupled products in good to excellent yields and short reaction times. The palladacycle complex **A** was entirely stable and thus the reactions could be carried out without using inert atmosphere.

In palladium catalyzed carbon–carbon bond formation reactions, it is commonly believed that better conversions are achieved for aryl halides with electron-withdrawing rather than electron donating substituent [34]. The electron deficient aryl bromides were transformed efficiently to the coupling products with 100% conversion in short reaction times (Table 3, entries 7–9, 11). 2-Bromoacetophenone produced corresponding coupling compound with 60% conversion (Table 3, entry 10) which may be attributed to the electronic and steric nature. Aryl iodide was examined in this reaction and the desired coupling product was obtained in excellent yield (Table 3, entries 1). The aryl iodide with electron donating substituent was examined and 90% conversion was

Table 1
Optimization of reaction condition on Suzuki reaction of different arylhalides with phenylboronic acid under reflux condition in oil bath.

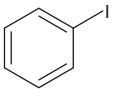
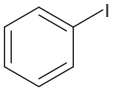
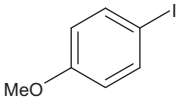
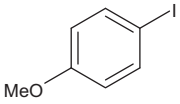
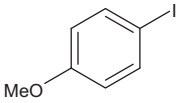
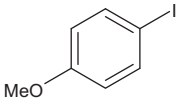
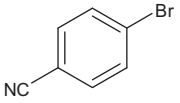
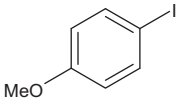
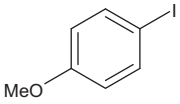
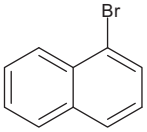
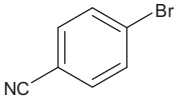
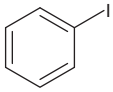
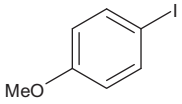
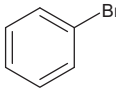
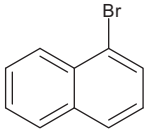
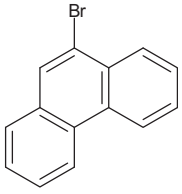
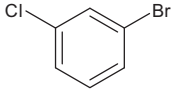
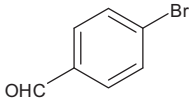
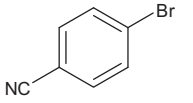
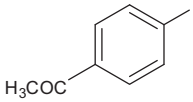
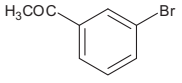
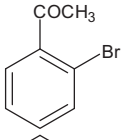
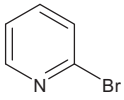
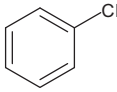
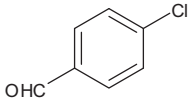
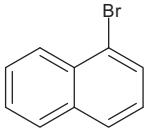
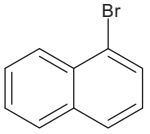
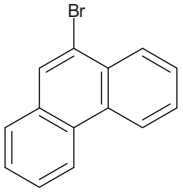
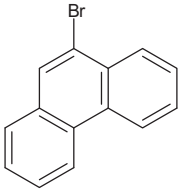
Entry	Ar–X	Base	Catalyst (mol%)	Solvent	Temperature (°C)	Time (h)	Conversion (%)
1		K_2CO_3	1	NMP	150	24	90
2		K_2CO_3	1	THF	80	1	95
3		K_2CO_3	0.5	THF	80	24	20
4		K_2CO_3	0.5	DMF	130	4	60
5		K_2CO_3	1	DMF	130	1.5	100
6		K_2CO_3	2	DMF	130	1	100
7		K_2CO_3	1	DMF	130	6	20
8		K_2CO_3	1	1,4-dioxane	80	1	10
9		K_2CO_3	1	methanol	80	3	100
10		K_2CO_3	1	methanol	80	5	0
11		K_2CO_3	1	methanol	80	5	40

Table 2
Suzuki reaction of aryl halides with phenylboronic acid using catalyst **A** under conventional heating conditions using an oil bath.[a]

Entry	Ar^1–X	Ar^2	Time (h)	Conversion (%)	Yield[a] (%)
1		Ph	4	100	88
2		Ph	12	95	86
3		Ph	3	98	92
4		Ph	10	70	60
5		Ph	10	65	53
6		Ph	5	100	92
7		Ph	9	100	80
8		Ph	10	100	87
9			10	100	80
10		Ph	13	100	90
11		Ph	13	60	50
12		Ph	15	0	1
13		Ph	15	0	0
14		Ph	10	95	90
15		4-$MeOC_6H_4$	12	80	75
16		3,4-MeO C_6H_3	10	85	82
17		1-Naph	10	80	75
18		3,4-MeO C_6H_3	10	85	75

[a] Reaction condition: aryl bromide; 1 mmol, phenylboronic acid; 1.2 mmol, K_2CO_3; 1 mmol, catalyst; **3** 0.01 mmol, temperature; 130 °C.

observed (Table 3, entry 2). These results prompt us to extend the optional process to less reactive and non-expensive aryl chlorides. Chlorobenzene did not transform to the coupling product (Table 3, entry 13), however 4-chlorobenzaldehyde changed to desired product with 100% conversion (Table 2, entry 14). 1-Bromo-3-chlorobenzene led to the formation of only one product which is due to the chemo-selectivity of this method (Table 2, entry 6). Trying to apply 2-bromopyridine as an efficient substrate was not successful (Table 2, entry 12). We also tried the coupling reaction for more steric hindrance arylhalides and arylboranes with high yield and in short reaction time Tables 2 and 3, entries 15–18).

A mechanistic description of the Suzuki reaction has been presented in Scheme 2. Initially, Pd(II) converts to Pd(0) [35], followed by the oxidative addition of aryl halide to Pd(0) to form aryl palladium (II) intermediate **1**. Phenylboronic acid which is activated by K_2CO_3 reacts with intermediate **1**. After transmetallation reaction, the intermediate **2** obtains. Finally, reductive elimination of intermediate **2** produces the desired coupling products. Several study in palladacycle catalyst cross-coupling indicated that the catalyst role in these chemistry is probably involve the palladium nanoparticles and palladacycles behave as a mere resource for producing nanoparticles Pd(0) [36–38]. To evaluate the suggested mechanism, the mercury drop test was employed, since mercury leads to the amalgamation of the surface of a heterogeneous catalyst. In contrast, Hg(0) is not expected to have a poisoning effect on homogeneous palladium complexes, where the Pd(II) metal center is tightly bound to the ligand [36,37]. When a drop of Hg(0) was added to the reaction mixtures of bromobenzene under mentioned optimized conditions at $t = 0$ min and heated the reaction mixture using microwave irradiation, no catalytic activity was observed for the catalyst.

3. Experimental

3.1. General

^{1}H NMR spectra were recorded using 500 and 400 MHz in $CDCl_3$ solutions at room temperature (TMS was used as an internal

Table 3
Suzuki reaction of aryl halides with phenylboronic acid using catalyst **A** under microwave irradiation.[a]

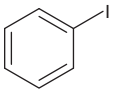
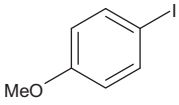
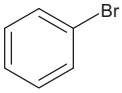
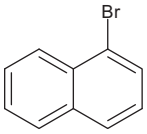
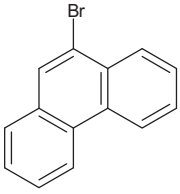
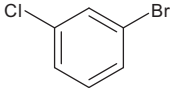
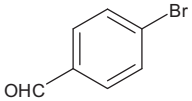
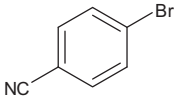
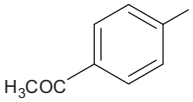
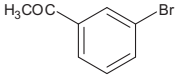
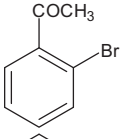
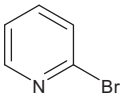
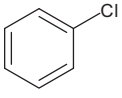
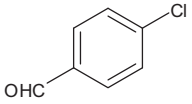
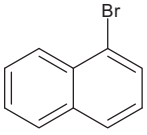
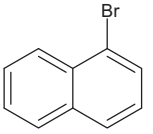
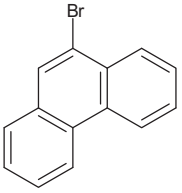
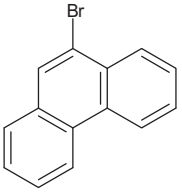
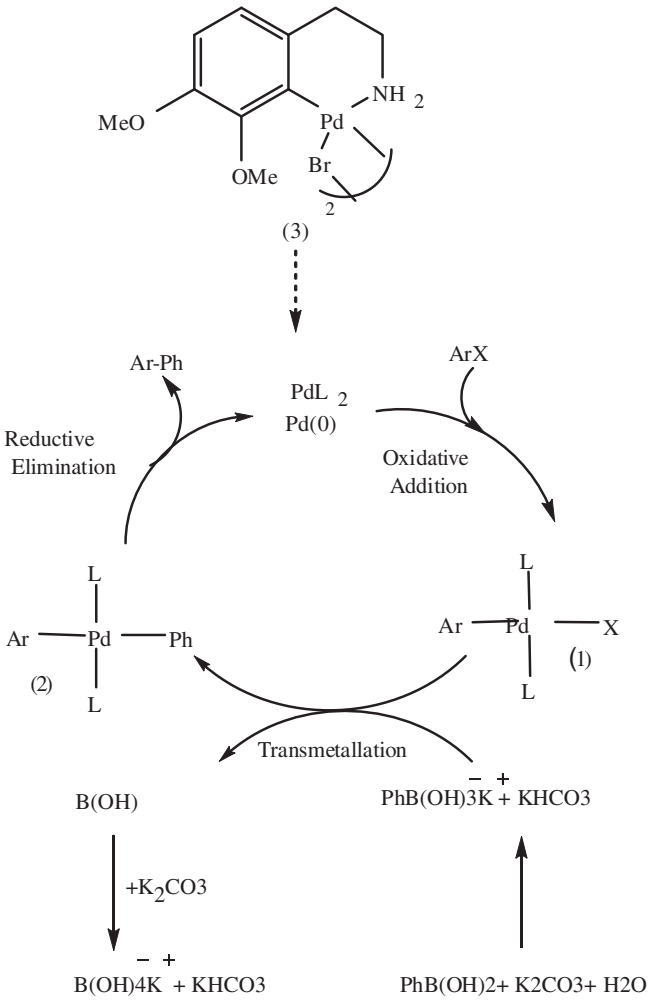
Entry	Ar^1–X	Ar^2	Time (min)	Conversion (%)	Yield[a] (%)
1		Ph	2	100	90
2		Ph	15	90	85
3		Ph	2	100	95
4		Ph	15	70	60
5		Ph	15	60	45
6		Ph	2	100	90
7		Ph	15	100	85
8		Ph	15	100	90
9			15	100	85
10		Ph	15	100	90
11		Ph	15	60	50
12		Ph	20	0	0
13		Ph	20	0	0
14		Ph	20	100	90
15		4-$MeOC_6H_4$	15	88	85

Table 3 (*continued*)

Entry	Ar^1–X	Ar^2	Time (min)	Conversion (%)	Yield[a] (%)
16		3,4-MeO C_6H_3	20	80	78
17		1-Naph	20	87	80
18		3,4-MeO C_6H_3	20	95	85

[a] Reaction condition: aryl bromide; 1 mmol, phenylboronic acid; 1.2 mmol, K_2CO_3; 1 mmol, catalyst; **3** 0.01 mmol, temperature; 130 °C.



Scheme 2. Proposed mechanism for Suzuki reaction.

standard) on a Bruker, Avance 500 instrument (Rheinstetten, Germany) and Varian 400 NMR. The FT-IR adsorption spectra were recorded on a Jasco-680 (Jasco, Japan) FT-IR spectrophotometer with KBr pellets. Vibration bands were reported as wave number (per centimeter). Homoveratrylamine, aryl halides, phenylboronic acid, solvents and palladium acetate were bought from Merck and Aldrich and used as received.

3.2. Synthesis of palladacycle complex (**A**)

[Pd{$C_6H_2(CH_2CH_2NH_2)$–$(OMe)_2$,3,4} (μ-Br)]$_2$ (**A**) was prepared using our reported method [31,32].

3.3. General procedure for the Suzuki reaction of aryl halides with phenylboronic acid

A mixture of the appropriate aryl halide (1 mmol), phenylboronic acid (1.2 mmol), palladium pre-catalyst **A** (1 mmol%), K_2CO_3 (1 mmol) was added to DMF (2 mL) in round-bottom flask equipped with condenser and placed into the Milestone Microwave or an oil bath. Initially the microwave irradiation of was set at 500 W, the temperature was ramped from room temperature to the desired temperature of 130 °C. Once this was reached, the reaction mixture was held at this temperature until the reaction was completed. During this time, the power was modulated automatically to keep the reaction mixture at 130 °C. The mixture was stirred continuously during the reaction. After the reaction was completed (monitored by TLC), the mixture was cooled to room temperature and the reaction mixture was poured into a separating funnel and water (30 mL) and *n*-hexane (30 mL) were added. The organic phase was dried over $CaCl_2$, filtered, and the solvent was evaporated. The residue was purified by silica gel column chromatography (*n*-hexane:EtOAc, 90:10) or recrystallization.

3.3.1. 4-Cyanobiphenyl (entry 8, Table 2)

mp 89–90 °C (Ref. 27, mp 91–92 °C), ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ = 7.74 (d, 2H, J = 8.0 Hz), 7.70 (d, 2H, J = 8.4 Hz), 7.60 (d, 2H, J = 7.6 Hz), 7.50 (brs t, 2H), 7.44 (brs d, 1H). FT-IR (KBr, 8 cm^{-1}): ν 2215.

3.3.2. 9-Phenylphenantrene (entry 5, Table 2)

mp 58–60 °C, ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ = 8.80 (d, 1H, J = 8.4 Hz), 8.74 (d, 1H, J = 8.0 Hz), 8.10 (s, 1H), 7.92 (t, 2H, J = 8.8 Hz), 7.62–7.73 (m, 4H), 7.54–7.58 (m, 4H), 7.50 (brs d, 1H). ^{13}C NMR (400 MHz, ppm, $CDCl_3$) δ = 140.8, 138.8, 130.1, 128.7, 128.3, 128.1, 127.9, 127.6, 127.5, 127.4, 127.3, 127.1, 126.9, 126.8, 126.6, 126.5, 126.4, 122.9, 122.6. FT-IR (KBr, cm^{-1}): ν 1600.

3.3.3. 4-Methoxybiphenyl (entry 2, Table 2)

mp 85–87 °C (Ref. 27, mp 87–88 °C), ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ = 7.31–7.59 (m, 7H), 6.89–6.99 (m, 2H), 3.85 (s, 3H).

3.3.4. 2-Acetylbiphenyl (entry 11, Table 2)

^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ = 7.27–7.96 (m, 9H), 2.8 (s, 3H), ^{13}C NMR (400 MHz, ppm, $CDCl_3$) δ = 141.5, 140.5, 134.3, 131.8, 130.8, 130.3, 128.9, 128.7, 127.9, 127.5, 127.2, 30.3. FT-IR (KBr, cm^{-1}): ν 1705.

4. Conclusions

In this work, we used ortho-palladated complex of homoveratrylamine as an efficient catalyst for the Suzuki reaction of various aryl halides. This catalyst was stable under heating conditions without using inert atmosphere due to its inherent air and moisture resistances. A general protocol was applied for the palladium-catalyzed Suzuki reaction of electron-rich and electron-poor aryl halides using phenylboronic acid. The catalytic amounts of this catalyst converted various aryl bromides and iodides to the corresponding products in good yields. Moreover, the aryl chlorides with electron withdrawing group were converted to the corresponding products in excellent yields.

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References

[1] B.C.G. Soederberg, Coord. Chem. Rev. 241 (2003) 147.
[2] (a) I.J.S. Fairlamb, Tetrahedron 61 (2005) 9661;
(b) A. John, M.M. Shaich, P. Ghosh, Inorg. Chim. Acta 363 (2010) 3113.
[3] S. Vuoti, J. Autio, M. Haukka, J. Pursiainen, Inorg. Chim. Acta 362 (2009) 4685.
[4] J. Tsuji, Palladium Reagents and Catalysts: Innovations in Organic Synthesis, Wiley, Chichester, 1995.
[5] N. Miyaura, A. Suzuki, Chem. Rev. 95 (1995) 2457.
[6] A. Suzuki, J. Organomet. Chem. 576 (1999) 147.
[7] N.E. Leadbeater, M. Marco, J. Org. Chem. 68 (2003) 888.
[8] Y. Gong, Org. Lett. 4 (2002) 3803.
[9] B. Basu, P. Das, M.M.H. Bhuiyan, S. Jha, Tetrahedron Lett. 44 (2003) 3817.
[10] G. Bringmann, C. Gunther, M. Ochse, O. Schupp, S. Tasler, in: W. Herz, H. Falk, G.W. Kirby, R.E. Moore (Eds.), Progress in the Chemistry of Organic Natural Products, vol. 82, Springer, New York, NY, 2001. p. 1.
[11] L.S. Hegedus, in: M. Schlosser (Ed.), Organometallics in Synthesis, John Wiley and Sons, Chichester, UK, 2002. p. 1123.
[12] P. Wawrzyniak, J. Heinicke, Tetrahedron Lett. 47 (2006) 8921.
[13] S. Kotha, K. Lahiri, D. Kashinath, Tetrahedron 58 (2002) 9633.
[14] N. Miyaura, T. Yanagi, A. Suzuki, Synth. Commun. 11 (1981) 513.
[15] O. Navarro, R.A. Kelly, S.P. Nolan, J. Am. Chem. Soc. 125 (2003) 16194.
[16] M.S. Viciu, R.A. Kelly, E.D. Stevens, F. Naud, M. Studer, S.P. Nolan, Org. Lett. 5 (2003) 1479.
[17] J. Yin, M.P. Rainka, X.X. Zhang, S.L. Buchwald, J. Am. Chem. Soc. 124 (2002) 1162.
[18] J.P. Stambuli, R. Kuwano, J.F. Hartwig, Angew. Chem., Int. Ed. 41 (2002) 4746.
[19] Y.C. Lai, H.Y. Chen, W.C. Hung, C.C. Lin, F.E. Hong, Tetrahedron 61 (2005) 9484.
[20] V. Farina, Adv. Synth. Catal. 346 (2004) 1553.
[21] J. Dupont, C.S. Consorti, J. Chem. Rev. 105 (2005) 2527.
[22] L. Botella, C. Nájera, Tetrahedron Lett. 45 (2004) 1833.
[23] L. Botella, C. Nájera, Tetrahedron 60 (2004) 5563.
[24] L. Botella, C. Nájera, Angew. Chem., Int. Ed. 41 (2002) 179.
[25] L. Botella, C. Nájera, J. Org. Chem. 70 (2005) 4360.
[26] M. Genov, A. Almorín, P. Espinet, Tetrahedron: Asymmetry 18 (2007) 625.
[27] K.M. Dawood, Tetrahedron 63 (2007) 9642.
[28] C.O. Kappe, Angew. Chem., Int. Ed. 43 (2004) 6250.
[29] C.A. Leach, T.H. Brown, R.J. Ife, D.J. Keeling, S.M. Laing, M.E. Parsons, C.A. Price, K.J. Wiggall, J. Med. Chem. 35 (1992) 1845.
[30] M. Larhed, A. Hallberg, J. Org. Chem. 61 (1996) 9582.
[31] A.R. Hajipour, K. Karami, A. Pirisedigh, A.E. Ruoho, J. Organomet. Chem. 694 (2009) 2548.
[32] A.R. Hajipour, K. Karami, A. Pirisedigh, Appl. Organometal. Chem. (2009) 504.
[33] A.R. Hajipour, K. Karami, A. Pirisedigh, A.E. Ruoho, Amino Acids 37 (2009) 537.
[34] N. Kataoka, Q. Shelby, J.P. Stambuli, J.F. Hartwig, J. Org. Chem. 67 (2002) 5553.
[35] T. Rosner, J.L. Bars, A. Pfaltz, D.G. Blackmond, J. Am. Chem. Soc. 123 (2001) 1848.
[36] M.R. Eberhard, Org. Lett. 6 (2004) 2125.
[37] D.E. Bergbreiter, P.L. Osburn, J.D. Frels, Adv. Synth. Catal. X 347 (2004) 172.
[38] L. Djakovitch, K. Kçhler, J.G. de Vries, in: D. Astruc (Ed.), Nanoparticles and Catalysis, Wiley-VCH, Weinheim, 2008. p. 303.