Available online at www.sciencedirect.com
SCIENCE DIRECT
Tetrahedron 61 (2005) 9767–9774
Tetrahedron

Ferrocenyl-palladium complexes in cross-coupling reactions: a comparative study

Tibor Zs. Nagy, Antal Csámpai* and András Kotschy*

Department of General and Inorganic Chemistry, Eötvös Loránd University, Pázmány P. s. 1/A, H-1117 Budapest, Hungary

Received 11 March 2005; revised 9 May 2005; accepted 17 June 2005

Available online 21 July 2005

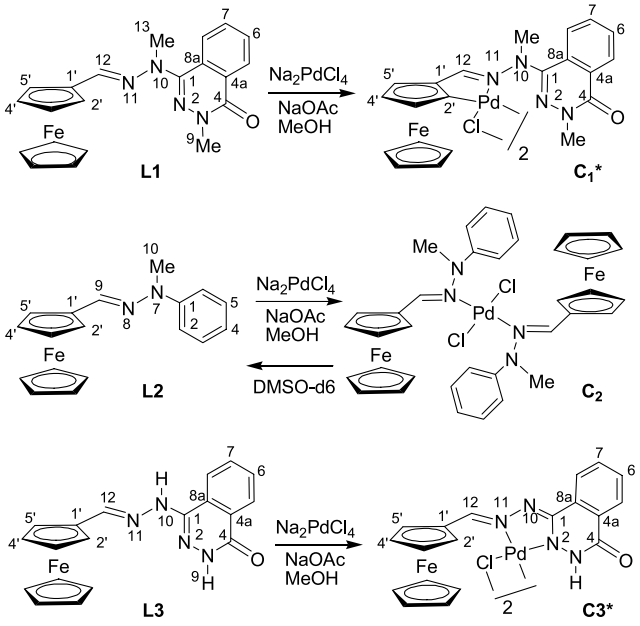
Dedicated to Professor András Lipták on the occasion of his 70th birthday.

Abstract—Ferrocenecarboxaldehyde hydrazones were converted into palladium complexes on treatment with sodium tetrachloropalladate. The substitution pattern of the ferrocenylhydrazones was found to have a marked influence on the mode the palladium was attached to the organic moiety. The catalytic activity of the new palladium complexes in cross-coupling reactions was examined in detail, and it was compared with conventional catalyst systems.

1. Introduction

The identification of cyclopalladated tri-*o*-tolylphosphine as a highly active catalyst in carbon–carbon bond forming reactions[1] has initiated the thorough study of the catalytic activity of palladacycles. These metallacycles, containing a carbon–palladium-heteroatom motif and in certain cases other ancillary ligands, are usually effective catalysts in cross-coupling reactions and a series of highly active systems were reported. The selection of ring heteroatoms includes phosphorous,[1–4] oxygen,[5] nitrogen,[6–9] or sulphur,[10,11] while additional ligands are mostly phosphanes.[12] On the evidence of the accumulated data[13,14] a debate commenced,[15] whether the high catalytic activity of such systems stems from the fact that palladacycles are robust catalysts, or they are merely a source of low-ligated palladium complexes.[16]

Our study was aimed at the synthesis of a series of ferrocene containing palladacycles, hopefully showing high activity, and the study of their catalytic behaviour in cross-coupling reactions. The catalysts were all based on the ferrocenylhydrazone framework, and the model reactions of our choice included the Heck, Suzuki and Sonogashira coupling. Detailed spectroscopic study of the prepared catalyst complexes revealed, that in spite of their similar ligand framework, each ferrocenylhydrazone gave a complex with a considerably different coordination mode. This unexpected finding provided us an additional opportunity to establish the influence of the coordination mode of palladium on its catalytic activity.



Scheme 1. The palladation of ferrocenylhydrazones **L1–L3** with sodium tetrachloropalladate.

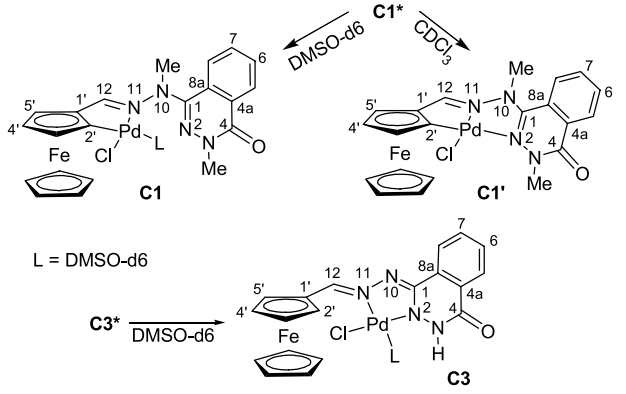
Keywords: Palladium complexes; Heck coupling; Tetrachloropalladate.
* Corresponding authors. Tel.: +36 1 372 2910; fax: +36 1 372 2909; e-mail: kotschy@chem.elte.hu

0040–4020/$ - see front matter © 2005 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tet.2005.06.072

2. Preparation of the ferrocene-based palladium complexes

The studied catalysts were obtained by the treatment of ferrocenylhydrazone type ligands **L1**–**L3** with Na_2PdCl_4 in methanol in the presence of NaOAc at rt (Scheme 1), a procedure widely applied in the synthesis of carbopalladated complexes.[17] Under this condition the chelating phthalazonyl derivatives **L1** and **L3**[18] underwent carbopalladation and azapalladation, respectively, affording chloro-brideged dimers **C1*** and **C3***, while the phenylhydrazone **L2**[19] simply coordinated to $PdCl_2$ to give **C2**. The dimeric structure of **C1*** is stated on the basis of its amide-I IR band (1652 cm^{-1}), which is very similar to that (1659 cm^{-1}) measured for ligand **L1**,[18] suggesting that the proximal nitrogen atom (N2) of the phthalazine ring is not coordinated to the palladium centre. As a consequence of this, we must assume the stabilization of the palladium by the formation of a μ-chloro-bridged dimmer (**C1***). The presence of the Pd–N2 bond in **C3*** in the solid state is clearly reflected in its amide-I frequency (1721 cm^{-1}), which is significantly higher than that of the free ligand **L3** (1652 cm^{-1}).[18] In **C3*** the coordinative saturation of the palladium centre also requires the formation of the μ-chloro-bridged dimer form. The proposed structures for **C1*** and **C3*** are also supported by other physical measurements (see later). The solid structure of **C2** is regarded to be analogous to that reported for the closely related $PdCl_2$ complex of *N*,*N*-dimethyl-ferrocenylhydrazone.[20]

The prepared ferrocenylhydrazone-palladium complexes were also characterized by ^1H, ^{13}C and ^{15}N NMR spectroscopy (Scheme 2). Dissolved in $CDCl_3$ **C1*** was transformed into the pentacyclic chelate **C1′** through the connection of the phthalazine moiety (N2) and the palladium centre, as followed by ^1H-^{15}N-HMBC spectroscopy. The ^{15}N signal of N2 shifts considerably upfield (245 ppm), relative to that measured for the non-coordinated N2 atom in the free ligand **L1** (284 ppm). In DMSO-d_6, representing the more polar conditions of the catalytic reactions, the weak Pd–N2 bond is cleaved by a coordinating solvent molecule as reflected by the downfield shift of the N2 signal to 304 ppm in complex **C1**. Since we were unable to grow crystals that were suitable for X-ray analysis, the relative configuration of the dimeric **C1*** structure (meso or racemic) could not be determined so far.



Scheme 2. The different coordination modes of complexes **C1** and **C3**.

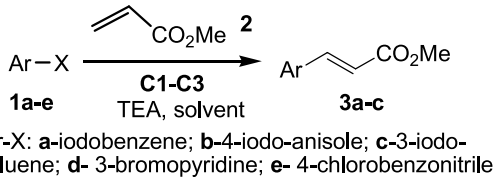
In DMSO-d_6 **C2** gives the ^1H and ^{13}C NMR spectra of **L2** referring to dissociation of both Pd–N bonds. In $CDCl_3$ two isomeric species (in ca. 70 and 30%) were detected, which may differ in the relative orientation of the two ferrocenyl groups (*N.B.* two analogous isomers were identified for the closely related $PdCl_2$ complex of *N*,*N*-dimethyl-ferrocenylhydrazone).[20] The presence of Pd–N bonds in both isomers of **C2** was supported by ^1H ^{15}N HMBC spectroscopy. The ^{15}N signals of N8 shift considerably upfield [234 and 226 ppm for the asymmetric major (**A**) and 229 ppm for the symmetric minor (**B**) component], relative to that measured for the non-coordinated N8 atom in the free ligand **L2** (325 ppm).

Under the same conditions (dissolved in DMSO-d_6) **C3*** presumably undergoes dissociation to **C3** whose strongly coordinated N2 atom has a significant sp^3 character, which is also reflected by its NMR shift of 154 ppm.[21–23] The strong coordination of the sp^2 nitrogen atom (N11) in **C1** and **C3** is evidenced by its signal (274 and 254 ppm, respectively), shifted substantially upfield relative to the free ligands **L1** (330 ppm) and **L3** (316 ppm). In **C3** the H-2′/5′ ^1H NMR signal (5.13 ppm) as well as the C1- and C12 ^{13}C NMR signals (158.2 and 149.2 ppm) are downfield shifted from those of **L3** (4.56 ppm for H-2′/5′, 143.0 ppm for C1 and 143.9 ppm for C12)[18] providing further evidence of the presence of the Pd–N2, and Pd–N11 bonds.

In summary, the formed ferrocenylhydrazone complexes under the conditions, where their catalytic activity is to be tested, contain the palladium centre in a NPdC attachment mode in a palladacycle (**C1**), in a NPdN attachment mode in a palladacycle (**C3**), or as part of a loosely coordinated NPdN complex (**C2**).

3. Catalysis studies

The first model reaction selected was the Heck coupling of different aryl halides and methyl acrylate in the presence of triethylamine as base (Scheme 3). The opening experiments were aimed at establishing the dependence of the catalytic activity of **C1**–**C3** on the reaction media. Iodobenzene was coupled in solvents of different polarity ranging from DCM to water, to find that polar coordinating solvents such as DMF or DMA gave the best results under the applied conditions (Table 1).



Scheme 3. The reactions used to test the catalytic activity of complexes **C1**–**C3** in Heck couplings.

All conversion measurements presented are an average of at least three parallel reactions and the determined values are based on internal standards. The first set of data obtained after running the reaction for 18 h at 50 °C (Table 1) revealed that in DMF and DMA both **C1** and **C2** gave near

Table 1. The catalytic activity of **C1–C3** in the model Heck coupling in various solvents[a,b]

	DCM	THF	MeCN	DMF	H_2O	DMA
C1	11.6	16.9	35.5	99.9	2.8	99.9
	16	*27.3*	*43.8*	*99.9*	*5.1*	*99.9*
C2	7.8	8.8	35.6	98.6	2.1	100
	11.6	*17.9*	*55.2*	*99.5*	*13.2*	*100*
C3	26.6	40.9	65.8	77.6	0.7	94.9
	43.8	*52.3*	*86.6*	*85.1*	*18.9*	*96.5*

[a] Iodobenzene (1 equiv), 1.2 equiv methyl acrylate, 1.4 equiv TEA, 1 ml/mmol solvent, 0.1% **C1**, 0.1% **C2**, or 0.2% **C3**, respectively.
[b] Normal numbers refer to the conversion values determined by GC analysis of the reaction mixtures after 18 h at 50 °C. Italics refer to the conversion values obtained after a further 2 h heating at 70 °C.

complete conversion. **C3** also gave good results, although, it was significantly less reactive. Of the other solvents tested in DCM, THF and MeCN the catalysts showed only mediocre activity, interestingly **C3** being more active than the other complexes (probably **C1*** and **C2***). Increase of the temperature to 70 °C for 2 h led to a considerable improvement of the catalytic activity in all possible cases.

In the first coupling experiments iodobenzene was reacted with methyl acrylate in the presence of the different palladium complexes **C1–C3** (Fig. 1). For the kinetic study of the Heck coupling catalyst loadings of 10^{-2}–$2*10^{-2}$% were found optimal. For comparison the reaction was also run in the presence of 10^{-2}% $Pd(OAc)_2$ with and without $2*10^{-2}$% PPh_3.

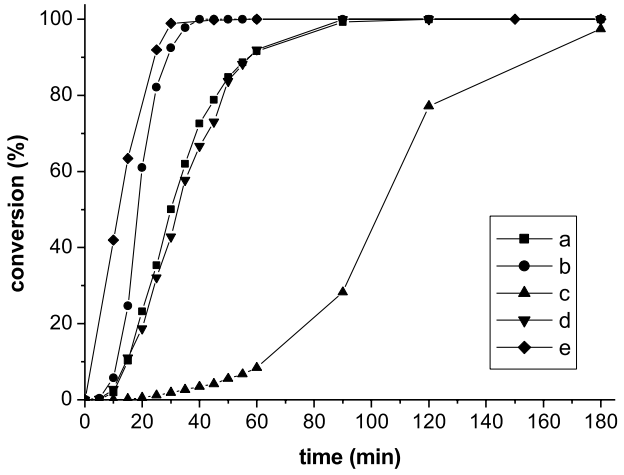


Figure 1. Kinetic study of the catalytic activity of **C1–C3** in the model Heck coupling. (a) 10^{-2}% **C1**; (b) 10^{-2}% **C2**; (c) $2*10^{-2}$% **C3**; (d) 10^{-2}% $Pd(OAc)_2$ and $2*10^{-2}$% PPh_3; (e) 10^{-2}% $Pd(OAc)_2$ at 100 °C.

Table 2. The catalytic efficiency of complexes **C1–C3** in the Heck coupling of different aryl halides (**1a–e**) at 0.05% catalyst loading[a,b]

ArX	C1	C2	C3
1a	100 (82)	100 (51)	100 (73)
1b	100 (93)	100 (99)	100 (98)
1c	100 (97)	100 (95)	100 (96)
1d	0	0	0
1e	0	0	0

[a] Numbers refer to conversion values determined by GC, numbers in parenthesis refer to isolated yields.
[b] Aryl halide (1 equiv), 1.2 equiv methyl acrylate, 1.4 equiv TEA, 1 ml/mmol DMF, 0.05% **C1**, 0.05% **C2** or 0.1% **C3** were heated at 100 °C for 1 h, or until full conversion.

The catalytic activity of **C1**, **C2** and the palladium–triphenylphosphine system were very similar, showing only a brief induction period, with $Pd(OAc)_2$ and **C2** being the most active under the applied conditions. The time-conversion curve of **C3** is significantly different from the other catalyst systems, exhibiting a prolonged induction phase and showing only decreased activity. In the light of the kinetic studies of Pfaltz and Blackmond on the Heck coupling reactions using palladacycles[24] it is probable, that the difference in the activity of the examined catalyst systems originates from the differences in the ease of formation of the catalytically active species.

The scope of the use of catalysts **C1–C3** in Heck couplings on a preparative scale is limited to aryl iodides (Table 2). Using 0.05–0.1% of the catalysts gave appreciable conversion only with iodobenzene (**1a**), 4-iodoanisole (**1b**) and iodotoluene (**1c**). The expected cynnamate derivatives were isolated in good to excellent yields, while less reactive aryl halides, such as 3-brompyridine (**1d**) or 4-chlorobenzonitrile (**1e**) gave no conversion. These results point out, that our catalysts fall into the same category with a series of other complexes, which show acceptable catalytic activity with highly reactive iodoarenes, but are inefficient when the coupling of bromo-, and chloroaromatics are concerned.[16]

The addition of external ligands, such as triphenylphosphine or tri(*tert*-butyl)phosphine has a profound effect on the activity of the catalysts. The coupling of bromobenzene and methyl acrylate catalysed by **C1**, not running in the absence of external ligands, was also tested in the

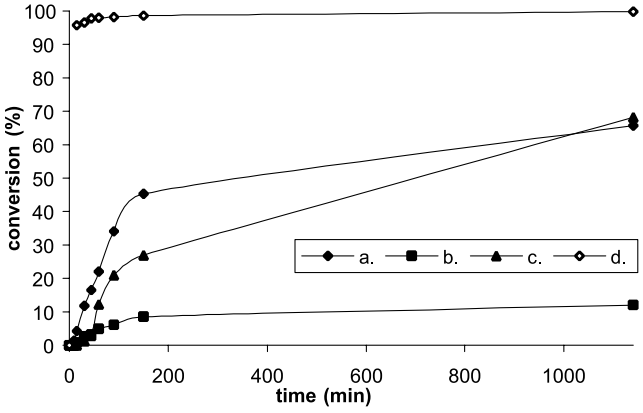


Figure 2. Kinetic study of the catalytic activity of **C1–C3** in the model Heck coupling, when the starting material is bromobenzene (a) 0.5% $Pd(OAc)_2$ and 1% PPh_3; (b) 0.5% **C1** and 0.5% PPh_3; (c) 0.5% **C1** and 1% PPh_3; (d) 0.5% **C1** and 2% P^tBu_3.

presence of added phosphins. For reference the reaction was also run in the presence of $Pd(OAc)_2$–2 PPh_3. The studied reactions revealed (Fig. 2) that the addition of PPh_3 has a marked influence on the catalytic activity of **C1**. Already the addition of 1 equiv PPh_3 to **C1** led to some product formation, and increase of the phosphine–palladium ratio to 2 resulted in a catalytic activity comparable to the $Pd(OAc)_2$–PPh_3 system. The addition of tri(*tert*-butyl)phosphine, as expected, led to the formation of a highly active catalyst species, giving nearly full conversion in 5 min. Tricyclohexylphosphine, although formed an active catalyst, initiated other transformations. The addition of tetrabutylammonium salts to the reaction mixture, or the change of base to *N*-methyl-dicyclohexylamine or sodium acetate had no significant effect on the catalytic activity of **C1**, even when the temperature was raised to 150 °C.

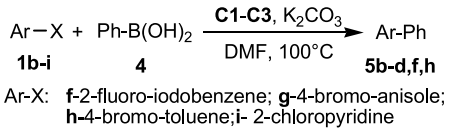
We also determined the longevity parameter (TON) for complexes **C1**–**C3** in the reaction of iodobenzene and methyl acrylate at 10^{-3} and 10^{-4}% catalyst loadings. The determined values, shown in Table 3., correspond to partial conversions, except for 10^{-3}% **C2**, where a near complete conversion was achieved before the catalyst was deactivated. Although, the TON values fall into the same range, a tendency might be observed, with the loosest bonded palladium complex (**C2**) giving the highest number and the complex where palladium is bound the strongest giving the lowest TON.

Table 3. The turnover numbers determined for complexes **C1**–**C3** in the model Heck coupling at 10^{-3} and 10^{-4}% catalyst loadings[a,b]

	C1	C2	C3
TON	62,000 *(48,000)*	92,500 *(96,000)*	23,000 *(35,000)*

[a] Regular numbers refer to values determined at 10^{-3}, and italic numbers to values determined at 10^{-4}% catalyst loading.
[b] Iodobenzene (1 mmol), 1.2 mmol methyl acrylate, 1.4 mmol TEA, 1 ml DMF, and 10^{-3} or 10^{-4}% of the appropriate catalyst (**C1**–**C3**) were heated at 100 °C for a period of time (maximum 72 h), after which no significant conversion was observed.

In the next set of experiments we studied the efficiency of our catalysts **C1**–**C3** in the Suzuki coupling of different aryl halides (**1b**–**i**) and phenylboronic acid (**4**) (Scheme 4). The reaction of 2-fluoro–bromobenzene (**1f**) and **4**, in the presence of potassium carbonate in DMF, was used to establish the kinetic profile of the transformations (Fig. 3).



Scheme 4. The reactions used to test the catalytic activity of complexes **C1**–**C3** in Suzuki couplings.

The ligands **C1** and **C2**, when added in 0.1 mol%, both showed a similar activity, giving acceptable conversions in about 3 h. **C2** was again slightly superior to **C1** (cf. Fig. 1), suggesting that the ease of palladium's release from the starting complex might have a major influence on the catalyst's activity. **C3**, alike in the Heck coupling, showed a prolonged induction period and decreased catalytic activity compared to the other complexes. For comparison the

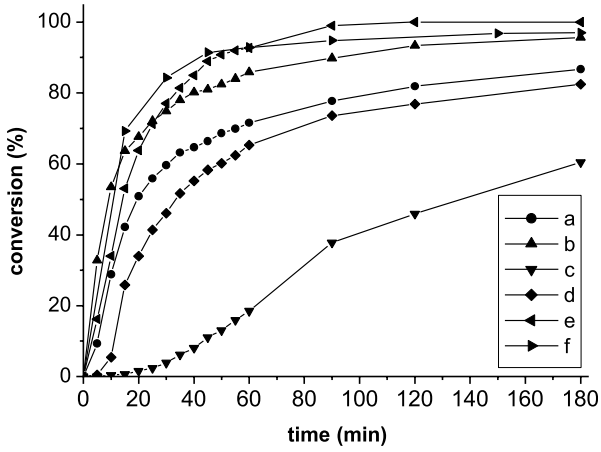


Figure 3. Kinetic study of the catalytic activity of **C1**–**C3** in the model Suzuki coupling. (a) 0.1% **C1**; (b) 0.1% **C2**; (c) 0.2% **C3**; (d) 0.1% **C2** and 0.2% PPh_3; (e) 0.1% $Pd(OAc)_2$ and 0.2% PPh_3; (f) 0.1% $Pd(OAc)_2$.

$Pd(OAc)_2$–PPh_3 and $Pd(OAc)_2$ catalyst systems were also examined under the same conditions (0.1% $Pd(OAc)_2$, 0.2% PPh_3) to reveal these catalysts as the most active of the studied systems. Surprisingly, the addition of triphenylphosphine to the active ferrocene based catalyst, **C2**, unlike in the **C1** catalysed Heck coupling of bromobenzene (Fig. 2), led to a marked decrease in the catalytic activity of the system.

The catalysts **C1**–**C3** were also tested in the Suzuki coupling of other substrates (Table 4). Comparison of the conversion data observed after running the reactions for 4 h are in good agreement with the kinetic measurements.

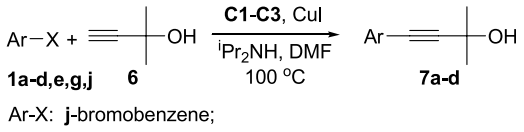
Table 4. The catalytic efficiency of complexes **C1**–**C3** in the Suzuki coupling of different aryl halides (**1b**–**i**) at 0.5% catalyst loading[a,b]

ArX	C1	C2	C3
1b	75 (97)	96	80
1c	89 (71)	99	90
1d	96 (95)	98	71
1e	0	0	0
1f	92 (67)	99	90
1g	21	33	15
1h	14	40	12
1i	0	0	0

[a] Numbers refer to conversion values determined by GC after 4 h, numbers in parenthesis refer to isolated yields after full conversion.
[b] Aryl halide (1 equiv), 1.5 equiv phenylboronic acid, 2 equiv K_2CO_3, 8 ml/mmol DMF, 0.5% **C1**, 0.5% **C2**, or 1% **C3**, respectively, were heated at 100 °C.

In each case, where appreciable conversion was observed (**1b**–**d**,**f**–**h**) **C2** gave the best results and **C3** the lowest conversion values. In case of **C1** the processes were repeated on a preparative scale too, and the products of the couplings were isolated where the conversion values were satisfactory giving the expected biaryls in good to excellent yield. Unlike in the Heck coupling, in these reactions we observed some conversion for bromoaromatics too, although, our catalysts are of limited synthetic value in this respect.

Finally, we also tested the activity of our catalysts in the Sonogashira coupling of different aryl halides (**1a**–**d**,**e**,**g**,**j**) and 2-methyl-3-butyn-2-ol (**6**) (Scheme 5). As it is well



Scheme 5. The reaction used to test the catalytic activity of complexes **C1**–**C3** in Sonogashira coupling.

known, the Sonogashira coupling is more sensitive to the nature and amount of the catalyst used, and we had to increase the loading of **C1**–**C3** a further order of magnitude to obtain reasonable conversions.

Iodobenzene (**1a**) and **6** were reacted in the presence of copper iodide and diisopropylamine in DMF. Addition of the catalysts **C1**–**C3** and $Pd(OAc)_2$ in 2 mol% to the reaction mixture led to no appreciable conversion and it was only after the addition of 4 mol% triphenylphosphine to the mixture that the Sonogashira coupling commenced. Comparison of the activity of **C1**–**C3** and $Pd(OAc)_2$ in the presence of 2 equiv of trihenylphosphine (relative to palladium), shows a picture that is analogous to the previous cases (Fig. 4).

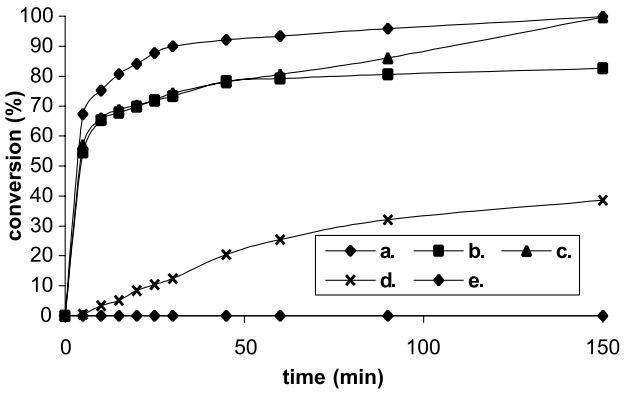


Figure 4. Kinetic study of the catalytic activity of **C1**–**C3** and $Pd(OAc)_2$ in the model Sonogashira coupling. (a) 2% $Pd(OAc)_2$ and 4% PPh_3; (b) 2% **C1** and 4% PPh_3; (c) 2% **C2** and 4% PPh_3; (d) 2% **C3** and 4% PPh_3 (e) 2% $Pd(OAc)_2$.

C1, **C2** and $Pd(OAc)_2$ show a similar activity, with $Pd(OAc)_2$ being slightly more efficient than the ferrocene containing catalysts. The activity of **C3**, as in all other cases, is inferior to the other systems. Of **C1** and **C2** the latter has a longer lifetime, reaching near complete conversion (just as $Pd(OAc)_2$), while **C1** is deactivated at ca. 80% conversion.

The catalysts **C1**–**C3** were also tested in the Sonogashira coupling of other substrates (**1a**–**d**,**e**,**g**,**j**; Table 4). Comparison of the conversion data observed after running the reactions for 4 h are in good agreement with the kinetic measurements. All aryl iodides and the reactive bromopyridine gave near complete conversion with **C2**, while of the other complexes **C1** gave the higher conversion values. The catalysts were also active with bromobenzene (**1j**), while the less reactive bromoanisole (**1g**) was only partially converted and 4-chlorobenzonitrile (**1e**) remained intact. These results are comparable with our recent observations using the Pd/C–PPh_3 catalyst system[25] (Table 5).

Table 5. The catalytic efficiency of complexes **C1**–**C3** in the Sonogashira coupling of different aryl halides (**1a**–**d**,**e**,**g**,**j**) at 2% catalyst loading[a,b]

ArX	C1	C2	C3
1a	99 (56)	99	65
1b	44 (25)	99	26
1c	65 (46)	99	36
1d	100 (89)	99	99
1e	0	0	0
1g	20	30	30
1j	100 (51)	80	65

[a] Numbers refer to conversion values determined by GC after 4 h, numbers in parenthesis refer to isolated yields.
[b] Aryl halide (1 equiv), 1.2 equiv 2-methyl-3-butyn-2-ol, 2 equiv diisopropylamine, 5 ml/mmol DMF, 2% **C1**–**C3**, respectively, and 4% PPh_3 were heated at 100 °C.

The similarity of the catalytic behaviour of complexes **C1** and **C2** in cross-coupling reactions, as well as the resemblance of their activity to palladium acetate suggests, that the active species in these catalytic systems are probably of alike nature. The minor differences might arise from the difference in the way the catalytically active species is formed from the starting complex, and the presence of different loosely coordinating ferrocenylhydrazone moieties in the reaction mixture. In case of complex **C3** we observed a decreased activity in all cases, which might be attributed to the strong coordination of the phtalazolyl moiety to the palladium, hindering the formation of the catalytically active species and leading to an elongated induction period and different kinetic characteristics.

In summary, three palladium complexes were prepared containing similar ferrocenylhydrazone-based ligands in different coordination modes: one a palladacycle, the other a palladium-imine and the third a palladium-amide connection. The catalytic activity of the complexes was compared with the palladium acetate–triphenylphosphine system in cross-coupling reactions. On the basis of the accumulated data it is proposed, that the catalytically active species is of similar nature in most cases, and the differences in the behaviour of the examined complexes originate in the mode and kinetics of the formation of the active species. The weaker the attachment of the palladium to the ligand, the higher the observed activity of the catalyst system. The results suggest that the principal role of the organic backbone (ligand) is to make the palladium available for activation in the reaction media. Although, the described complexes are not highly active, the authors hope that the presented data contributes to the better understanding of catalytic processes and thereby helps in the future to design highly active catalyst systems.

4. Experimental

4.1. General

Melting points (uncorrected) were determined on a Boetius hotplate. The ^{1}H, ^{13}C and ^{15}N NMR spectra were recorded in 5 mm tubes at rt on a Bruker DRX-500 spectrometer at 500 MHz (^{1}H), 125 MHz (^{13}C) and 50 MHz (^{15}N) (for **C1**–**C3**) or on a Bruker DRX-250 spectrometer (**3a**–**c**, **5b**–**h**) at 250 MHz (^{1}H), 62.5 MHz (^{13}C) with the deuterium signal of

the solvent as the lock. In ^{1}H and ^{13}C measurements the residual peaks of the solvent were used as reference, while in the ^{15}N measurements the scale was adjusted to the reference signal of liquid NH_3 ($\delta=0$ ppm). The exact assignment of the ^{1}H, ^{13}C and ^{15}N signals for **C1–C3** were based on 2D-COSY, 2D-HSQC and 2D-HMBC measurements. The IR spectra were obtained on a Bruker IFS-55 FTIR spectrometer. Gas chromatography was carried out on a Hewlett-Packard 5790A instrument. Silica gel (0.04–0.063 mm) was used for flash column chromatography.

4.2. Preparation of complexes C1*, C2 and C3*

A mixture of the corresponding hydrazone (1 mmol), Na_2PdCl_4 (0.294 g, 1 mmol) and NaOAc*3H_2O (0.136 g, 1 mmol) was dissolved in dry methanol (20 mL). The deep red solution was stirred at rt for 1 day. The resulted precipitate was filtered off and the solution was evaporated to dryness. Complex **C2** was purified by washing the precipitate with cold methanol. For the isolation of **C1*** the precipitate was subjected to column chromatography on Silica using chloroform as eluent. The second deep orange band was collected and after the evaporation of the chloroform the oily residue was crystallized with cold methanol. The first orange band consists of the unchanged hydrazone **L1**. For the isolation of **C3*** the residue, obtained by the evaporation of the volatiles from the reaction mixture, was purified by chromatography on Silica using chloroform as eluent. The first deep red band was collected and after the evaporation of the chloroformic solution the oily residue was crystallized with cold methanol–diethylether (3–3 mL).

4.2.1. Description of C1*. Deep red powder; 0.189 g (35%); mp: 213–216 °C (decomp.); IR ν_{max} 1652, 1578, 1540 cm^{-1}; the NMR spectra for **C1′**: δ_H ($CDCl_3$) 8.42 (1H, d, $J=7.8$ Hz, H5), 7.96 (1H, s, H12) 7.97 (1H, d, $J=7.8$ Hz, H8), 7.88 (1H, t, $J=7.8$ Hz, H7), 7.84 (1H, t, $J=7.8$ Hz, H6), 5.30 (1H, br s, H3′), 4.38 (2H, br s, H4′ and H5′), 4.34 (5H, s, Cp ring), 4.03 (3H, s, H9), 3.57 (3H, s, H13); δ_C ($CDCl_3$) 168.4 (C12), 157.8 (C4), 150.2 (C1), 133.6 (C7), 129.0 (C4a), 129.7 (C6), 128.3 (C5), 126.6, (C8a) 126.4 (C8), 100.5 (C2′), 86.5 (C1′), 74.3 (C3′), 71.8 (Cp ring), 69.0 (C4′), 67.0 (C5′), 46.5 (C9), 41.0 (C13); δ_N ($CDCl_3$) 254 (N11), 245 (N2), 178 (N3), 126 (N10); the NMR spectra for **C1**: δ_H (DMSO-d_6) 8.38 (1H, s, H12), 8.27 (1H, d, $J=7.8$ Hz, H5), 8.12 (1H, d, $J=7.8$ Hz, H8), 7.98 (1H, t, $J=7.8$ Hz, H7), 7.85 (1H, t, $J=7.8$ Hz, H6), 5.13 (1H, br s, H3′), 4.43 (1H, br s, H4′), 4.41 (1H, br s, H5′), 4.18 (5H, s, Cp ring), 3.69 (3H, s, H9), 3.20 (3H, s, H13); δ_C (DMSO-d_6) 172.8 (C12), 159.0 (C4), 145.5 (C1), 133.8 (C7), 132.5 (C6), 129.2 (C4a), 127.3 (C5), 127.0, (C8a) 126.5 (C8), 108.5 (C2′), 83.6 (C1′), 75.6 (C3′), 70.9 (Cp ring), 70.0 (C4′), 68.6 (C5′), 40.5 (C13), 39.6 (C9); δ_N (DMSO-d_6) 304 (N2), 274 (N11), 182 (N3), 127 (N10). Anal. Calcd for $C_{21}H_{19}ClFeN_4PdO$ (541.40) C 46.59, H 3.54, N 10.35; Found C 46.50, H 3.60, N 10.38%.

4.2.2. Description of C2. Deep red powder; 0.338 g (83%); mp: 178–184 °C (decomp.); IR ν_{max} 1597, 1495, 1107 and 476 cm^{-1}; (for comparision the IR for **L2**: 1590, 1500, 1112 and 488 cm^{-1}); δ_H (DMSO-d_6) 7.44 (1H, s, H9), 7.29 (2H, d, $J=8.1$ Hz, H2/6), 7.24 (2H, t, $J=8.1$ Hz, H3/5), 6.81 (1H, t, $J=8.1$ Hz, H4), 4.61 (2H, br s, H2′/5′), 4.31 (2H, br s, H3′/4′), 4.15 (5H, s, Cp ring), 3.16 (3H, s, H10); δ_C (DMSO-d_6) 148.5 (C1), 133.4 (C9), 129.8 (C3/5), 120.1 (C4), 115.4 (C2/6), 83.6 (C1′), 69.8 (Cp ring), 69.6 (C3′/4′), 67.2 (C2′/5′), 33.6 (C10) (the spectra are identical with those measured for ligand **L2**): δ_H ($CDCl_3$) 8.26, 7.59 (2×s, H9, **A**), 8.16 (s, H9, **B**), 7.5–7.0 (overlapping m's, H2-6 **A** and **B**), 4.6–4.5 (overlapping m's, H2′-5′, **A**), 4.46 (t, $J=$ 1.8 Hz, H2′/5′, **B**), 4.23 (t, $J=1.8$ Hz, H3′/4′, **B**), 4.31 and 4.20 (2×s, Cp rings, **A**), 4.23 (s, Cp ring, **B**), 3.57 and 3.19 (2×s, H10, **A**), 3.13 (s, H10, **B**); δ_N ($CDCl_3$) 234 and 226 (N8, **A**), 229 (N8, **B**), 130 and 127 (N7, **A**), 125 (N7, **B**). For comparison the ^{15}N NMR data of **L2**: δ_N ($CDCl_3$) 325 (N8), 129 (N7). Anal. Calcd for $C_{36}H_{36}Cl_2Fe_2N_4Pd$ (814.00) C 53.12, H 4.46, N 6.88; Found C 53.05, H 4.55, N 6.81%.

4.2.3. Description of C3*. Deep red powder; 0.140 g (27%); mp: 190–194 °C (decomp.); ν_{max} 1721, 1642, 1571, 1506 cm^{-1}; δ_H (DMSO-d_6) 9.42 (1H, s, H3), 8.18 (1H, d, $J=7.8$ Hz, H5), 8.15 (1H, d, $J=7.8$ Hz, H8), 7.87 (1H, t, $J=7.8$ Hz, H7), 7.80 (1H, t, $J=7.8$ Hz, H6), 7.62 (1H, s, H12), 5.13 (2H, br s, H2′/H5′), 4.55 (2H, br s, H3′/H4′), 4.20 (5H, s, Cp ring); δ_C (DMSO-d_6) 158.2 (C11), 157.1 (C4), 149.2 (C12), 134.5 (C7), 132.2 (C6), 128.0 (C5), 127.6 (C8),125.7 (C8a), 125.5, (C4a), 75.8 (C1′), 72.9 (C3′/C4′), 72.2 (C2′/C5′), 70.2 (Cp ring); δ_N (DMSO-d_6) 254 (N11), 243 (N10), 154 (N2), 134 (N3) (the spectra for **C3**); for comparison the ^{15}N NMR data of **L3**: δ_N (DMSO-d_6) 316 (N11), 261 (N2), 175 (N3), 138 (N10). Anal. Calcd for $C_{19}H_{15}ClFeN_4PdO$ (515.37) C 44.28, H 2.93, N 10.87; Found C 44.35, H 3.00, N 10.82%.

4.3. General conditions for cross-coupling reactions

A mixture of the aryl halide, coupling partner, catalyst, base, internal standard and co-catalyst (where applicable) were taken up in the appropriate solvent in a vial. After flushing with argon and sealing, the vial was placed in a temperated oil bath and the contents were stirred. Samples were taken by a Hamilton syringe and were diluted by DCM before analysis. The work-up of the reactions included the addition of aqueous ammonium chloride, separation, extraction with DCM, drying of the combined organic phases and purification by column chromatography after evaporation of the solvent under reduced pressure.

4.3.1. Component ratios for the coupling reactions and the characterization of isolated products.

4.3.1.1. Heck coupling. Aryl halide (**1a–e**) (1 equiv), 1.2 equiv methyl acrylate (**2**) and 1.4 equiv triethylamine were stirred under argon in 1 mL solvent/1 mmol aryl halide at 70–100 °C.

4.3.1.2. Suzuki coupling. Aryl halide(**1b–i**) (1 equiv), 1.5 equiv phenylboronic acid (**4**), and 2 equiv of K_2CO_3, in 8 mL DMF/1 mmol aryl halide were stirred under argon at 100 °C.

4.3.1.3. Sonogashira coupling. Iodobenzene (**1a**) (1 equiv), 1.2 equiv 2-methylbut-3-yn-2-ol (**6**) and 2 equiv of diisopropylamine were stirred under argon in 5 mL DMF/1 mmol iodobenzene at 100 °C.

4.3.1.4. Methyl cinnamate (3a).[26] Starting from **1a** (302 mg, 1.48 mmol) we obtained 197 mg (82%) **3a**. δ_H ($CDCl_3$) 7.43 (1H, d, $J=16.1$ Hz), 7.20–7.15 (2H, m), 7.07–7.01 (3H, m), 6.17 (1H, d, $J=16.1$ Hz), 3.48 (3H, s); δ_C ($CDCl_3$) 166.4, 144.0, 133.7, 129.6, 128.2, 127.4, 117.2, 50.8 ppm.

4.3.1.5. Methyl 4′-methoxy-cinnamate (3b).[27] Starting from **1b** (346 mg, 1.48 mmol) we obtained 263 mg (93%) **3b**. δ_H ($CDCl_3$) 7.56 (1H, d, $J=16.0$ Hz), 7.40 (2H, d, $J=8.8$ Hz), 6.83 (2H, d, $J=8.8$ Hz) 6.21 (1H, d, $J=16.0$ Hz), 3.76 (3H, s) ppm.

4.3.1.6. Methyl 3′-methyl-cinnamate (3c).[28] Starting from **1c** (323 mg, 1.48 mmol) we obtained 252 mg (97%) **3c**. δ_H ($CDCl_3$) 7.54 (1H, d, $J=16.1$ Hz), 7.42–7. 00 (4H, overlapping m's), 6.30 (1H, d, $J=16.1$ Hz), 3.67 (3H, s), 2.22 (3H, s) ppm.

4.3.1.7. 4-Methoxybiphenyl (5b).[29] Starting from **1b** (61 mg, 0.26 mmol) we obtained 46 mg (97%) **5b**. δ_H ($CDCl_3$) 7.44 (2H, d, $J=7.7$ Hz), 7.41 (2H, d, $J=8.6$ Hz), 7.30 (1H, t, $J=7.7$ Hz), 7.18 (1H, t, $J=7.7$ Hz), 6.86 (2H, d, $J=8.2$ Hz), 3.71 (3H, s); δ_C ($CDCl_3$) 159.1, 140.7, 133.7, 128.7, 128.1, 126.7, 126.6, 114.2, 55.2 ppm.

4.3.1.8. 3-Methylbiphenyl (5c).[30] Starting from **1c** (57 mg, 0.26 mmol) we obtained 31 mg (71%) **3c**. δ_H ($CDCl_3$) 7.56 (2H, d, $J=7.5$ Hz), 7.44–7.26 (6H, overlapping m's), 7.12 (1H, d, $J=7.0$ Hz), 2.38 (3H, s); δ_C ($CDCl_3$) 141.3, 141.2, 138.2, 128.71, 128.65, 127.95, 127.92, 127.20, 127.13, 124.2, 21.5 ppm.

4.3.1.9. 3-Phenylpyridine (5d).[31] Starting from **1d** (41 mg, 0.26 mmol) we obtained 38 mg (95%) **3d**. δ_H ($CDCl_3$) 8.85 (1H, dd, $J=1.6$ Hz), 8.59 (1H, dd, $J=4.7$, 1.2 Hz), 7.86 (1H, d, $J=6.3$ Hz), 7.58 (2H, d, $J=7.6$ Hz), 7.48 (2H, t, $J=7.6$ Hz), 7.42 (1H, t, $J=7.6$ Hz), 7.35 (1H, dd, $J=6.3$, 4.7 Hz), 3.71 (3H, s); δ_C ($CDCl_3$) 148.4, 148.3, 137.7, 126.5, 134.3, 129.0, 128.0, 127.1, 123.5 ppm.

4.3.1.10. 2-Fluorobiphenyl (5f).[32] Starting from **1f** (58 mg, 0.26 mmol) we obtained 30 mg (67%) **3f**. δ_H ($CDCl_3$) 7.54 (2H, d, $J=7.8$ Hz), 7.45–7.40 (3H, overlapping m's), 7.36 (1H, t, $J=7.8$ Hz), 7.29–7.13 (3H, overlapping m's); δ_C ($CDCl_3$) 158.7 (d, $J=227.7$ Hz), 134.8, 129.7 (d, $J=3.3$ Hz), 128.1, 128.0, 127.9, 127.4, 126.6, 123.3 (d, $J=3.7$ Hz) 115.0 (d, $J=22.5$ Hz) ppm.

4.3.1.11. 4-Methylbiphenil (5h).[33] Starting from **1h** (44 mg, 0.26 mmol) we obtained 35 mg (81%) **5h**. δ_H ($CDCl_3$) 7.49 (2H, d, $J=7.7$ Hz), 7.41 (2H, d, $J=8.2$ Hz), 7.36 (1H, t, $J=7.7$ Hz), 7.23 (1H, t, $J=7.7$ Hz), 7.16 (2H, d, $J=8.2$ Hz) 2.31 (3H, s); δ_C ($CDCl_3$) 141.1, 138.3, 137.0, 129.5, 128.73, 128.68, 126.97, 126.95, 21.5 ppm.

4.3.1.12. 2-Methyl-4-phenylbut-3-yn-2-ol (7a).[34] Starting from **1a** (94 mg, 0.462 mmol) we obtained 41 mg (56%) **11**. δ_H ($CDCl_3$) 7.44–7.40 (2H, m), 7.31–7.27 (3H, m), 2.15 (1H, d), 1.62 (6H, s); δ_C ($CDCl_3$) 131.6, 128.2 (two coalesced lines), 122.6, 93.7, 82.1, 65.6, 31.5 ppm.

4.3.1.13. 4-(4′-Methoxyphenyl)-2-methylbut-3-yn-2-ol (7b).[35] Starting from **1b** (108 mg, 0.46 mmol) we obtained 23 mg (25%) **7b**. δ_H ($CDCl_3$) 7.29–7.24 (2H, m), 6.77–6.71 (2H, m), 3.71 (3H, s), 2.19 (1H, s), 1.52 (6H, s); δ_C ($CDCl_3$) 159.47, 133.01, 114.79, 113.82, 92.4, 81.93, 65.57, 55.21, 31.53 ppm.

4.3.1.14. 2-Methyl-4-(3′-methylphenyl)-3-butyn-2-ol (7c).[25] Starting from **1c** (100 mg, 0.46 mmol) we obtained 37 mg (46%) **7c**. δ_H ($CDCl_3$) 7.18–7 (4H, m), 2.42 (1H, br s), 2.31 (3H, s), 1.6 (6H, s) ppm.

4.3.1.15. 2-Methyl-4-(3′-pyridyl)-3-butyn-2-ol (7d).[25] Starting from **1d** (73 mg, 0.46 mmol) we obtained 66 mg (89%) **7d**. δ_H ($CDCl_3$) 8.74 (1H, br s), 8.47 (1H, br s), 7.65 (1H, d, $J=7.9$ Hz), 7.26–7.12 (1H, m), 5.14 (1H, br s), 2.29 (6H, s); δ_C ($CDCl_3$) 151.64, 147.66, 138.75, 123.23, 120.5, 98.53, 78.02, 64.68, 31.23 ppm.

Acknowledgements

Financial support of the Hungarian Research Fund (OTKA F047125) is gratefully acknowledged.

References and notes

1. Herrmann, W. A.; Brossmer, C.; Ofele, K.; Reisinger, C. P.; Priermeier, T.; Beller, M.; Fischer, H. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 1844.
2. Shaw, B. L.; Perera, S. D.; Staley, E. A. *Chem. Commun.* **1998**, 1361.
3. Bedford, R. B.; Hazlewood, S. L.; Limmert, M. E.; Albisson, D. A.; Draper, S. M.; Scully, P. N.; Coles, S. J.; Hursthouse, M. B. *Chem. Eur. J.* **2003**, *9*, 3216.
4. Miyazaki, F.; Yamaguchi, K.; Shibasaki, M. *Tetrahedron Lett.* **1999**, *40*, 7379.
5. Beletskaya, I. P.; Kashin, A. N.; Karlstedt, N. B.; Mitin, A. V.; Cheprakov, A. V.; Kazankov, G. M. *J. Organomet. Chem.* **2001**, *622*, 89.
6. Schnyder, A.; Indolese, A. F.; Studer, M.; Blaser, H. U. *Angew. Chem., Int. Ed.* **2002**, *41*, 3668.
7. Bedford, R. B.; Cazin, C. S. J.; Coles, S. J.; Gelbrich, T.; Hursthouse, M. B.; Scordia, V. J. M. *J. Chem. Soc., Dalton Trans.* **2003**, 3350.
8. Alonso, D. A.; Najera, C.; Pacheco, M. C. *J. Org. Chem.* **2002**, *67*, 5588.
9. Iyer, S.; Jayanthi, A. *Tetrahedron Lett.* **2001**, *42*, 7877.
10. Dupont, J.; Gruber, A. S.; Fonseca, G. S.; Monteiro, A. L.; Ebeling, G.; Burrow, R. A. *Organometallics* **2001**, *20*, 171.
11. Bergbreiter, D. E.; Li, J. *Chem. Commun.* **2004**, *42* and references therein.
12. For an example of a palladacycle containing a carbene ligand see: Viciu, M. S.; Kelly, R. A., III; Stevens, E. D.; Naud, F.; Studer, M.; Nolan, S. P. *Org. Lett.* **2003**, *5*, 1479.
13. Herrmann, W. A.; Ofele, K.; von Preysing, D.; Schneider, S. K. *J. Organomet. Chem.* **2003**, *687*, 229.
14. Bedford, R. B. *Chem. Commun.* **2003**, 1787.
15. Beletskaya, I. P.; Cherpakov, A. V. *Chem. Rev.* **2000**, *100*, 3009.

16. For a critical survey of the application of palladacycles see: Beletskaya, I. P.; Cherpakov, A. V. *J. Organomet. Chem.* **2004**, *689*, 4055.
17. Albert, J.; Ceder, R.; Gómez, M.; Granell, M.; Sales, J. *Organometallics* **1992**, *11*, 1536 and references therein.
18. Abrán, Á.; Csámpai, A.; Harmath, V.; Sohár, P. *Models in Chemistry, Acta Chim. Hung.* **1998**, *135*, 439.
19. Kobayashi, T.; Macusima, Y.; Hagiwara, T. *Jpn. Kokai Tokkyo Koho* **1991**. *Chem. Abstr.* **1992**, *116*, 204493.
20. López, C.; Bosque, R.; Solans, X.; Font-Bardia, M. *J. Organomet. Chem.* **1997**, *535*, 99.
21. Martin, G. J.; Gouesnard, J. P.; Dorie, J.; Rabiller, C.; Martin, M. L. *J. Am. Chem. Soc.* **1977**, *99*, 1381.
22. Burgar, M. I.; St Amour, T. E.; Fiat, D. *J. Phys. Chem.* **1981**, *85*, 502.
23. Nagy, P.; Csámpai, A.; Szabó, D.; Varga, J.; Harmat, V.; Ruff, F.; Kucsman, Á. *J. Chem. Soc., Perkin Trans.* **2001**, *2*, 339.
24. Rosner, T.; Le Bars, J.; Pfaltz, A.; Blackmond, D. G. *J. Am. Chem. Soc.* **2001**, *123*, 1848.
25. Novak, Z.; Szabo, A.; Repasi, J.; Kotschy, A. *J. Org. Chem.* **2003**, *68*, 3327.
26. Nakamura, S.; Hayakawa, T.; Nishi, T.; Watanabe, Y.; Toru, T. *Tetrahedron* **2001**, *57*, 6703.
27. Moiseev, D. V.; Gushchin, A. V.; Shavirin, A. S.; Kursky, Y. A.; Dodonov, V. A. *J. Organomet. Chem.* **2003**, *667*, 176.
28. Dai, M.; Liang, B.; Wang, C.; Chen, J.; Yang, Z. *Org. Lett.* **2004**, *6*, 221.
29. Moore, L. R.; Shaughnessy, K. H. *Org. Lett.* **2004**, *6*, 225.
30. Mowery, M. E.; DeShong, P. *J. Org. Chem.* **1999**, *64*, 3266.
31. Feuerstein, M.; Doucet, H.; Santelli, M. *J. Organomet. Chem.* **2003**, *687*, 327.
32. Kelm, J.; Strauss, K. *Spectrochim. Acta A* **1981**, *37*, 689.
33. Phil, H. L.; Sung, W. L.; Dong, S. *Org. Lett.* **2003**, *5*, 4963.
34. Pal, M.; Subramanian, V.; Parasuraman, K.; Yeleswarapu, K. R. *Tetrahedron* **2003**, *59*, 9563.
35. Markert, C.; Bannwarth, W. *Helv. Chim. Acta* **2002**, *85*, 1877.