Synthesis of palladacycles employing iminoisoindolines as monoanionic bidentate ligands†

Jackson M. Chitanda,[a] Demyan E. Prokopchuk,[a] J. Wilson Quail[b] and Stephen R. Foley*[a]

Received 2nd May 2008, Accepted 29th July 2008
First published as an Advance Article on the web 22nd September 2008
DOI: 10.1039/b806544f

A series of air- and moisture-stable iminoisoindoline-based palladacycles have been prepared in two operationally simple steps from commercially available reagents. *para*-Substituted *N*,*N*′-diphenyliminoisoindoline ligands are easily synthesized from phthalaldehyde and *para*-substituted anilines and further reaction of the iminoisoindoline ligands with $Pd(OAc)_2$ in dichloromethane at room temperature results in formation of six-membered [C,N] dinuclear cyclopalladated complexes with the general formula $[(iminoisoindoline)Pd(\mu\text{-}OAc)]_2$. The resulting palladacyclic complexes were tested as precatalysts in Heck and Suzuki coupling reactions.

Introduction

Palladacycles represent an increasingly important class of organometallic compounds, where their influence is especially dominant in the field of coupling reactions for organic transformations.[1,2] This is reflected in the diversity of the palladacycles that have been reported in literature, the most common of which are palladacycles incorporating [C,P] and [C,N] metallacycle formations.[3] Many palladium-mediated coupling reactions are thought to involve palladacyclic intermediates[4] and several palladacycles are also reported to be biologically active compounds for cancer therapy.[5] The majority of palladacycles contain one $\sigma(M\text{–}C_{sp^2})$ or $\sigma(M\text{–}C_{sp^3})$ bond in a chelating bidentate monoanionic ligand environment, with five- or six-membered N- or P-containing ring systems.[3]

We previously reported the synthesis of a γ-diimine ligand in which intramolecular cyclization could be induced to form the corresponding iminoisoindoline.[6] Upon reaction of the γ-diimine with $Pd(OAc)_2$, a five-membered palladacycle was synthesized. With this in mind, we thought that iminoisoindoline ligands could represent a convenient and facile route into the formation of rare [C,N] imine-based six-membered palladacycles. Iminoisoindolines could coordinate to palladium through the imine functionality, followed by C–H activation of the N-bound aryl group and subsequent *ortho*-palladation. There are several examples of tridentate [N,N,N] and [C,N,N] iminoisoindolines as ligands in pincer-type complexes,[7] however we describe here the first synthesis and characterization of a palladacyclic species derived from monoanionic bidentate [C,N] iminoisoindoline ligands.

A wide variety of *para*-substituted iminoisoindoline ligands can be prepared in a one pot procedure from commercially available starting materials involving simple condensation reactions of phthalaldehyde and *para*-substituted anilines (Fig. 1). The ligands precipitate from the reaction mixture as analytically pure solids. Palladacyclic complex formation is also facile, simply involving reaction of the iminoisoindoline ligand with $Pd(OAc)_2$ resulting in precipitation of the desired palladacyclic species as air- and moisture-stable orange or green solids. Here we present a simple two step procedure for the synthesis of four iminoisoindoline-based palladacycles from commercially available starting materials. The catalytic activities of this new family of palladacycles were tested in standard Heck and Suzuki coupling reactions.

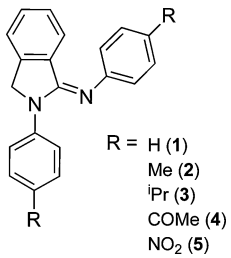


Fig. 1 Iminoisoindoline ligands.

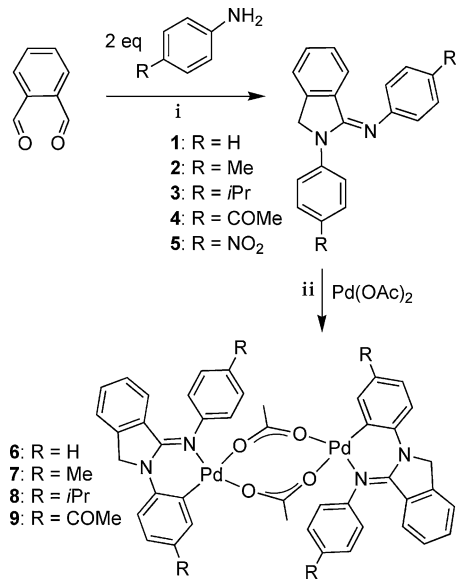
Results and discussion

Iminoisoindoline ligands **1–5** were prepared by the reaction of phthalaldehyde with 2 equiv. of the corresponding arylamine under dinitrogen in high yield according to Scheme 1. The particular ligands were chosen in order to investigate electronic and steric effects in the *para* positions of the N-aryl substituents (R = H (**1**), Me (**2**), ^{i}Pr (**3**), COMe (**4**), NO_2 (**5**) (Scheme 1)). The iminoisoindoline ligands precipitate from solution as analytically-pure white or yellow solids. Except for **3**, the iminoisoindolines have all been previously reported, however their potential as ligands has never before been investigated.[8]

It has been previously proposed that *in situ* formation of a γ-diimine followed by rapid intramolecular cyclization results in formation of the corresponding iminoisoindoline.[8,9] We have recently reported that a γ-diimine can be isolated, provided sufficient steric bulk is introduced in the *ortho* positions of the aryl-N

[a]*University of Saskatchewan, Department of Chemistry, 110 Science Place, S7N 5C9, Saskatoon, Saskatchewan, Canada. E-mail: stephen.foley@usask.ca*
[b]*Saskatchewan Structural Sciences Centre, 110 Science Place, S7N 5C9, Saskatoon, Saskatchewan, Canada*

† CCDC reference numbers 687003–687006 (**6**·CH_2Cl_2, **7**·$CHCl_3$, **8**·$CO(CH_3)_2$ and **9**·CH_2Cl_2). For crystallographic data in CIF or other electronic format see DOI: 10.1039/b806544f



Scheme 1 Preparation of iminoisoindoline ligands and their corresponding palladacycles. (i) Diethyl ether, 12 h, rt; (ii) dichloromethane, 12 h, rt.

substituent to retard cyclization. Even then, the γ-diimine was observed to undergo slow cyclization in the presence of catalytic amounts of H^+.[6]

Synthesis of [(iminoisoindoline)Pd(μ-OAc)]$_2$ palladacycles

Reaction of $Pd(OAc)_2$ with one equiv. of the respective iminoisoindoline **1–4** in dichloromethane at ambient temperature yielded the desired palladacycles **6–9** of the general formula [(iminoisoindoline)Pd(μ-OAc)]$_2$, as analytically pure precipitates (Scheme 1). Interestingly, no reaction was observed with NO_2-substituted iminoisoindoline **5** and $Pd(OAc)_2$. This is likely due to the electron-withdrawing/deactivating effects of the nitro substituent inhibiting both imine coordination and *ortho*-palladation. Complexes **6–9** are air- and moisture-stable complexes that decompose above 200 °C. No coordination complexes were observed prior to cyclopalladation. Palladacycles **6–9** were characterized by IR and NMR spectroscopy, mass spectrometry and elemental analysis. Crystal structures were obtained for complexes **6–9**.

The IR data confirmed the presence of the Pd–N bond in the cyclopalladated complexes. In the spectra of complexes **6–9**, the signals for the C=N bond vibrations were shifted to a lower wavenumber compared to those of the free iminoisoindoline ($\Delta\lambda \sim 35$ cm^{-1}).

Dinuclear palladacycles in which the two palladium centers are linked by two bridging acetato groups can exist as *anti*- or *syn*-isomers (Fig. 2).[10] In this case, NMR data allows for easy differentiation between the *anti*- and *syn*-conformations where the *anti*-isomer exhibits overall C_2 symmetry and the *syn*-isomer is C_s symmetric. A characteristic indication of cyclopalladation in complexes **6–9** is the observed ^{1}H NMR resonance for the CH_2 protons of the iminoisoindoline ring. The ligands (**1–5**) show a singlet corresponding to the two methylene protons at ~5 ppm. Upon cyclopalladation, these methylene protons become diastereotopic in the *anti*-isomer resulting in formation of two doublets at ~4.6 and ~3.5 ppm, each corresponding to one proton per ligand. As

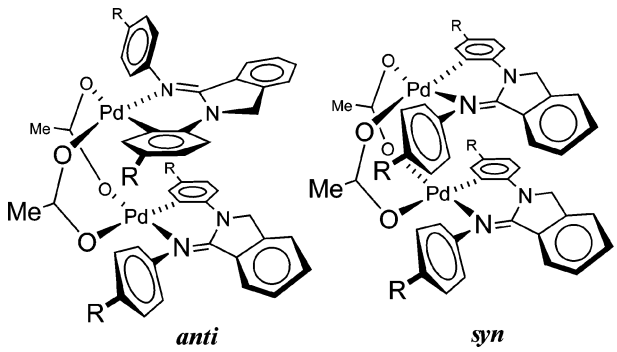


Fig. 2 Isomers of [(iminoisoindoline)Pd(μ-OAc)]$_2$ (**6–9**).

each pair of methylene protons constitute an AX system for both isomers, two doublets would be expected for the *syn*-isomer as well, however the methylene protons of the *syn*-isomer are coincident, appearing as a singlet shifted slightly downfield (~0.1 ppm) relative to that of the free ligand. Upon cooling to –40 °C in $CDCl_3$, only a slight broadening of the methylene resonances in the *syn*-isomer is observed. Due to steric effects, the *anti*-isomer is favored over the *syn*-isomer with *anti*/*syn* ratios increasing as the steric bulk in the *ortho* position of the iminoisoindoline ring increases. Thus, *anti*/*syn* isomers were observed in ratios from 8 : 1 for **9** (R = COMe) to 3 : 1 for **6** (R = H). The mass spectra of complexes **6–9** all showed a distinct signal which was assigned to their respective molecular cation $[M - OAc]^+$.

The crystal structures of palladacycles **6–9** were determined. All four structures co-crystallized with one molecule of the solvent they were grown from. Complexes **6** and **9** co-crystallized with one molecule of dichloromethane, while **7** co-crystallized with one molecule of chloroform and **8** co-crystallized with one molecule of acetone. All four complexes crystallized exclusively as the *anti*-isomer, unambiguously confirming the presence of a six-membered [C,N] palladacycle. The *anti*-configuration is also observed in the crystal structures of previously reported acetato-bridged dinuclear palladacycles,[10] with the exception of one report showing the exclusive crystallization of a *syn*-isomer.[11] The two palladium atoms in **6–9** are bridged by two acetate ligands and each palladium center has a chelating [C,N]-bound iminoisoindoline ligand forming the palladacycle. The dinuclear acetato-bridged complexes adopt a characteristic closed-book conformation where the two [C,N]-bound iminoisoindoline ligands stack on top of one another. As expected, the coordination geometry about the palladium atoms in all four structures is approximately square planar with the sum of the angles around the palladium atoms for all three complexes being 360 ± 1°. The Pd–Pd distance was found to be 2.9975(4) Å for **6**, 3.0049(3) Å for **7**, 3.1130(3) for **8** and 2.9685(6) Å for **9** which is consistent with previously reported acetato-bridged dinuclear palladacycles.[10] The Pd–C and Pd–N bond lengths of complexes **6–9** were all essentially identical (within esd) at 1.97(1) Å and 2.01(1) Å respectively. The Pd–O distances of the two acetate ligands differ by about 0.10 Å for **6–9** (for example, in **6**, Pd(1)–O(1) is 2.157 Å while Pd(1)–O(3) is 2.053 Å), indicative of the stronger *trans*-influence of the aryl carbon compared to that of the imine nitrogen.

ORTEP plots for **6–9** shown in Fig. 3 through 6. Crystallographic data is summarized in Table 1. Selected bond distances and angles are provided in Table 2.

Table 1 Crystal data and refinement parameters for complexes **6–9**

	6·CH_2Cl_2	**7**·$CHCl_3$	**8**·$CO(CH_3)_2$	**9**·CH_2Cl_2
Formula	$C_{45}H_{38}Cl_2N_4O_4Pd_2$	$C_{49}H_{45}Cl_3N_4O_4Pd_2$	$C_{59}H_{66}N_4O_5Pd_2$	$C_{53}H_{46}Cl_2N_4O_8Pd_2$
Formula wt	982.49	1073.04	1123.96	1150.64
Color	Green	Orange	Yellow	Orange
Crystal system	Monoclinic	Monoclinic	Monoclinic	Monoclinic
Space group	$P2_1/c$	$P2_1/c$	$P2_1/c$	$P2_1/c$
a/Å	12.5421(2)	23.1864(3)	13.7107(2)	18.6888(8)
b/Å	16.7665(3)	9.6437(1)	19.1758(3)	13.9845(11)
c/Å	18.9026(4)	20.2415(2)	21.3745(3)	21.6903(11)
β/°	91.3617(13)	105.026(1)	106.8883(1)	124.159(3)
Z	4	4	4	4
ρ_{calc}/Mg m^{-3}	1.642	1.630	1.388	1.629
Temp./K	173(2)	173(2)	173(2)	173(2)
F(000)	1976	2168	2320	2328
Reflns collected/unique	57 938/8109	77 979/11 273	77 135/12 313	55 029/8577
R_{int}	0.0866	0.0734	0.1066	0.0984
θ range/°	2.47 to 26.37	2.35 to 28.71	2.26 to 27.47	2.63 to 25.35
final $R_1(I > 2\sigma I)$	$R1 = 0.0384$, w$R2 = 0.0830$	$R1 = 0.0403$, w$R2 = 0.0809$	$R1 = 0.0426$, w$R2 = 0.0878$	$R1 = 0.506$, w$R2 = 0.1144$
R_1(all data)	$R1 = 0.0556$, w$R2 = 0.0924$	$R1 = 0.0615$, w$R2 = 0.0889$	$R1 = 0.0696$, w$R2 = 0.1004$	$R1 = 0.695$, w$R2 = 0.1247$

Table 2 Selected bond distances (Å) and angles (°) for complexes **6–9**

	6	**7**	**8**	**9**
Bond distances/Å				
Pd(1)–C(10)	1.972(3)	1.969(3)	1.960(3)	1.975(5)
Pd(1)–N(2)	2.004(3)	2.016(3)	2.004(3)	2.008(4)
Pd(1)–O(3)	2.053(3)	2.159(2)	2.139(2)	2.064(4)
Pd(1)–O(1)	2.157(2)	2.083(2)	2.055(2)	2.147(4)
Pd(1)–Pd(2)	2.9975(4)	3.0049(3)	3.1130(3)	2.9685(6)
Bond angles/°				
C(10)–Pd(1)–N(2)	90.40(13)	90.00(11)	88.62(12)	90.7(2)
C(10)–Pd(1)–O(1)	91.70(13)	91.77(11)	89.63(11)	92.70(19)
N(2)–Pd(1)–O(3)	95.31(10)	93.85(9)	93.95(10)	94.02(16)
O(3)–Pd(1)–O(1)	82.46(10)	84.22(9)	87.84(9)	82.65(15)

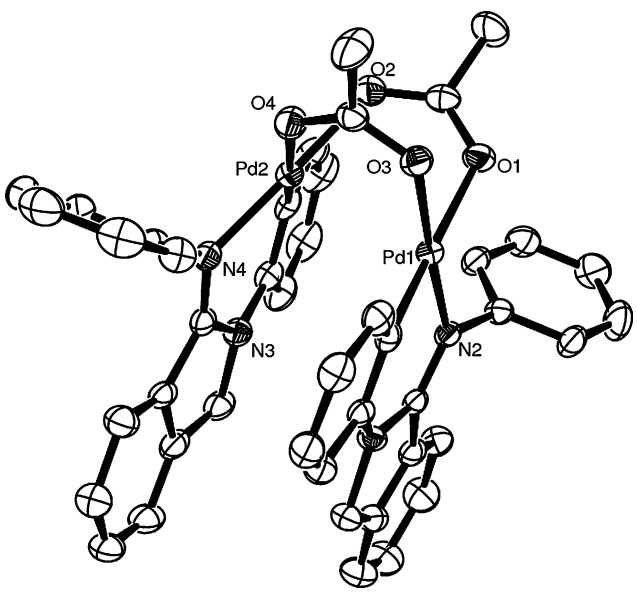


Fig. 3 ORTEP plot of **6** at the 50% probability level. The hydrogen atoms have been omitted for clarity.

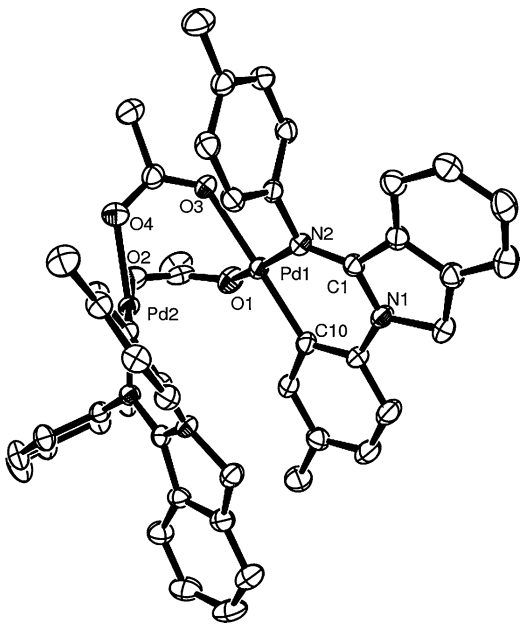


Fig. 4 ORTEP plot of **7** at the 50% probability level. The hydrogen atoms have been omitted for clarity.

Catalysis

While palladacycles have been around since 1965,[12] the first examples of palladacycles as precatalysts in the Heck and Suzuki reaction were not published until 1995.[13] Palladacyclic compounds currently rank among the best precatalysts for a variety of C–C coupling reactions.[1,3,13] Several palladacycles are now commercially available from chemical companies such as Aldrich and Strem and most notably include the imine-based Nájera catalyst[14], the amine-based Indolese catalyst[15] and Bedford's phosphite-based catalyst.[16]

The catalytic activity of palladacyclic complexes **6** and **9** was tested in the standard Suzuki coupling reaction of aryl halides with phenylboronic acid, using Cs_2CO_3 as a base, 1% precatalyst loading and dioxane as solvent at 80 °C. As shown in Table 3,

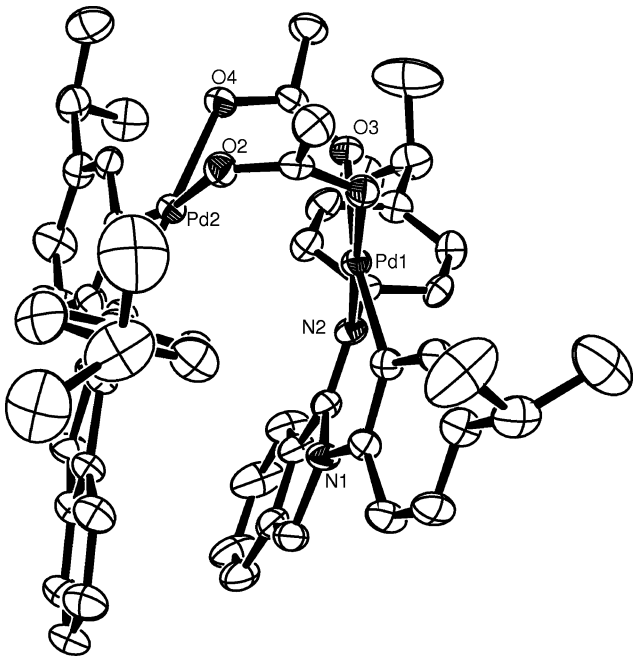


Fig. 5 ORTEP plot of **8** at the 30% probability level. The hydrogen atoms have been omitted for clarity.

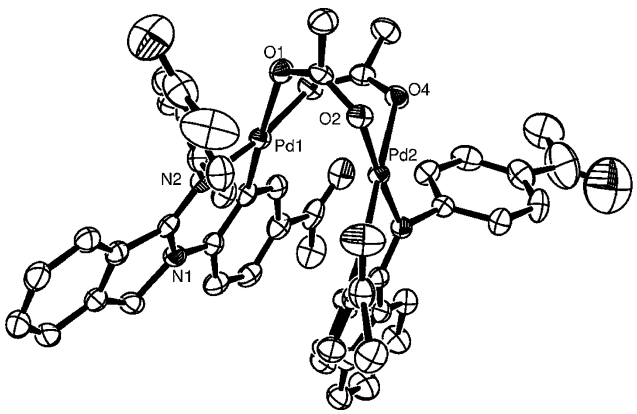
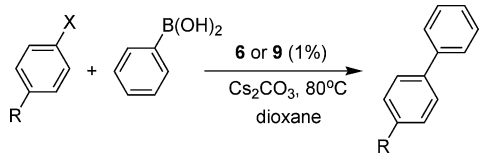


Fig. 6 ORTEP plot of **9** at the 50% probability level. The hydrogen atoms have been omitted for clarity.

good to excellent yields of biphenyls were obtained in the Suzuki coupling reaction for both activated and deactivated aryl bromides. Interestingly, for activated aryl chlorides, **6** gave only a 43% yield (entry 6), while **9** resulted in quantitative yields (entries 13 and 14). With deactivated chlorides however, low conversions were obtained.

We further investigated the activity of palladacyclic complexes **6** and **9** in the standard Heck reaction of activated and deactivated aryl halides with butyl acrylate. The results are shown in Table 4. Quantitative yields were obtained when employing bromoanisole and bromobenzaldehyde in the presence of 0.01 and 0.1 mol% of **9** respectively (entries 5 and 6), even at lower temperature (100 °C, entry 7). A decrease in activity was observed when deactivated aryl bromides such as *p*-bromotoluene (61%) and *p*-bromoanisole (56%) were used. Among the activated aryl chlorides only chlorobenzaldehyde and bromobenzonitrile gave

Table 3 Suzuki cross-coupling of aryl halides with phenylboronic acid[a]



Entry	R	X	Time/h	Catalyst	Conversion[b] (%)
1	H	I	3	**6**	> 99
2	H	Br	3	**6**	94
3	Me	Br	3	**6**	92
4	COMe	Br	3	**6**	75
5	CN	Br	3	**6**	80
6	COMe	Cl	18	**6**	43
7	Me	Br	24	**9**	94
8	CN	Br	24	**9**	> 99
9	COMe	Br	24	**9**	> 99
10	OMe	Br	24	**9**	90
11	OMe	Cl	96	**9**	18
12	Me	Cl	24	**9**	27
13	COMe	Cl	24	**9**	> 99
14	CN	Cl	24	**9**	> 99

[a] Reaction conditions: 1 mmol of aryl halides, 1.5 mmol phenyl boronic acid, 2 mmol Cs_2CO_3, 1 mmol% Pd precatalyst, 3 mL of dioxane. [b] Determined by ^{1}H NMR in reference to the residue aryl-halide.[15,16]

a fairly good conversion of 60% and 53% respectively, while *p*-acetochlorobenzene resulted in only 16% conversion (entry 11). Under the same conditions, coupling of deactivated aryl chlorides was unsuccessful.

Conclusion

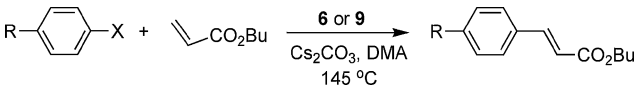
We have synthesized and studied a series of air- and moisture-stable iminoisoindoline-based palladacycles. These complexes are easily prepared in two operationally simple steps from commercially available reagents. Complexes **6** and **9** were found to be active precatalysts for the Suzuki and Heck C–C coupling reactions with precatalyst **9** (R = COMe) exhibiting significantly higher activity than **6** (R = H). If highly electron-withdrawing groups are employed on the diphenyliminoisoindoline ligands (*i.e.* iminoisoindoline **5**, R = NO_2), palladacyclic formation is completely inhibited. Further investigations on the reactivity and catalytic activity of this family of palladacycles are underway and this work will be reported at a later date.

Experimental

General Information

Unless otherwise stated, all reactions were performed under N_2 using standard Schlenk techniques or in a N_2-filled drybox. All reaction temperatures for catalytic reactions refer to the temperature of pre-equilibrated oil or sand baths. All melting points were recorded on a Gallenkamp melting point apparatus and are uncorrected. ^{1}H and ^{13}C{^{1}H} NMR spectra were recorded on a Bruker 500 MHz Avance spectrometer. Chemical shifts for ^{1}H and ^{13}C NMR are reported in ppm in reference to the residual ^{1}H and ^{13}C resonances of $CDCl_3$ (^{1}H: δ 7.24; ^{13}C: δ 77.23) and DMSO-d_6 (^{1}H: δ 2.50; ^{13}C: δ 39.51). Coupling constants are given in Hz. Elemental analyses were performed on a Perkin-Elmer

Table 4 Heck cross-coupling of aryl halides with butyl acrylate[a]



Entry	R	X	Time/h	Catalyst (mol%)	Conversion[b] (%)	TON[c]
1	H	I	3	**6** (0.001)	> 99	100 000
2	H	Br	3	**6** (1)	71	71
3[d]	H	Cl	12	**6** (3)	0	0
4	CN	Br	3	**9** (1)	96	96
5[d]	COMe	Br	3	**9** (0.01)	> 99	10 000
6	COH	Br	3	**9** (0.1)	> 99	1000
7[e]	COH	Br	24	**9** (1)	> 99	100
8	Me	Br	3	**9** (1)	61	61
9	OMe	Br	3	**9** (1)	56	56
10	COH	Cl	3	**9** (1)	60	60
11[d]	COMe	Cl	24	**9** (1)	16	16
12	CN	Cl	24	**9** (1)	53	53

[a] Reaction conditions: aryl halide (1.0 mmol), acrylate (2.0 mmol), base (2.0 mmol), Pd precatalyst, solvent (DMA, 3 ml), 145°C. [b] Determined by ^{1}H NMR based on residual aryl halide.[15,16] [c] TON = turnover number (mol product per mol catalyst). [d] CsOAc used as base. [e] Performed at 100 °C.

2400 CHN elemental analyzer. IR data was collected by Diffuse Reflectance Spectroscopy. $Pd(OAc)_2$ was purchased from PMO Pty Ltd, Australia. Aniline, *p*-methylaniline, *p*-isopropylaniline, *p*-acetoaniline, *p*-nitroaniline and phthalaldehyde were purchased from the Sigma-Aldrich Chemical Company and used as received. The syntheses of iminoisoindolines **1**, **2**, **4** and **5** have been reported in the literature, however spectral data for these compounds has not been communicated and is thus included here.[8]

General synthesis for iminoisoindolines 1–5

Phthalaldehyde (17.2 mmol), arylamine (36.1 mmol, 2.1 equiv.), formic acid (0.05 mL) and ether (30 mL) were combined in a 100 mL Schlenk flask equipped with a stir bar. The solution was stirred for 12 h at ambient temperature under dinitrogen. The resulting precipitate was filtered and washed with ether (3 × 20 mL), then dried under vacuum to obtain white or yellow solids.

1-Phenylimino-2-phenylisoindoline (1). (75.0% yield, white powder, mp = 127.8–129.5 °C.) ^{1}H NMR ($CDCl_3$, ppm): δ 8.01 (d, J = 6.0, 2H, Ar), 7.44 (d, J = 7.5, 1H, Ar), 7.38 (m, 3H, Ar), 7.31 (m, 2H, Ar), 7.04 (m, 3H, Ar), 6.99 (d, J = 6.7, 2H, Ar), 6.66 (d, J = 7.1, 1H, Ar), 4.94 (s, 2H, CH_2). ^{13}C NMR ($CDCl_3$, ppm): δ 153.52, 150.87, 141.81, 140.59, 130.48, 129.34, 129.12, 127.53, 126.70, 123.33, 122.92, 122.44, 121.44, 120.18, 53.18 (CH_2). Anal. calcd (%) for $C_{20}H_{16}N_2$: C 84.48, H 5.67, N 9.85; found: C 84.57, H 5.62, N 9.60. FT-IR (KBr, cm^{-1}): 1646 (C=N), 1590, 1498. ESI-MS m/z calcd for $C_{20}H_{16}N_2$: 284.1313; found: 285.1392 [M + H]$^+$.

1-*p*-Methylphenylimino-2-*p*-methylphenylisoindoline (2). (51% yield, white powder.) ^{1}H NMR ($CDCl_3$, ppm): δ 7.83 (d, J = 7.8, 2H, Ar), 7.41 (d, J = 7.6, 1H, Ar), 7.35 (m, 1H, Ar), 7.18 (d, J = 7.8, 2H, Ar), 7.11 (d, J = 7.4, 2H, Ar), 7.05 (m, 1H, Ar), 6.87 (d, J = 7.4, 2H, Ar), 6.71 (d, J = 7.6, 1H, Ar), 4.89 (s, 2H, CH_2), 2.36 (s, 3H, CH_3), 2.32 (s, 3H, CH_3). ^{13}C NMR ($CDCl_3$, ppm): δ 153.67 (C=N), 148.37, 140.67, 139.29, 130.27, 129.89, 129.67, 129.38, 127.39, 126.70, 124.30, 122.87, 121.04, 121.44, 120.47, 53.27 (CH_2), 21.14 (Ar-CH_3), 21.03 (Ar-CH_3). Anal. calcd (%) for $C_{22}H_{20}N_2$: C 84.58, H 6.45, N 8.97; found: C 84.30, H 7.57, N 8.69. FT-IR (KBr, cm^{-1}): 1650 (C=N), 1633, 1615, 1615, 1609. ESI-MS m/z calcd for $C_{22}H_{20}N_2$: 312.16; found: 313.16 [M + H]$^+$.

1-*p*-Isopropylphenylimino-2-*p*-isopropylphenylisoindoline (3). (98% yield, white powder.) ^{1}H NMR ($CDCl_3$): δ 7.88 (d, J = 7.9, 2H, Ar), 7.42 (d, J = 7.3, 1H, Ar), 7.35 (m, 1H, Ar), 7.24 (d, J = 7.5, 2H, Ar), 7.17 (d, J = 7.5, 2H, Ar), 7.05 (m, 1H, Ar), 6.91 (d, J = 7.5, 2H, Ar), 6.70 (d, J = 7.5, 1H, Ar), 4.91 (s, 2H, CH_2), 2.89 (m, 2H, $CH(CH_3)_2$), 1.28 (d, J = 6.7, 6H, $CH(CH_3)_2$), 1.25. (d, J = 6.7, 6H, $CH(CH_3)_2$). ^{13}C NMR ($CDCl_3$, ppm): δ 153.56 (C=N), 148.58, 143.71, 143.00, 140.62, 139.56, 139.54, 131.81, 130.22, 127.38, 127.17, 126.96, 126.64, 122.85, 121.16, 120.20, 53.13 (CH_2), 33.74 ($CH(CH_3)_2$), 24.52 ($CH(CH_3)_2$), 24.25 ($CH(CH_3)_2$). Anal. calcd (%) for $C_{24}H_{20}N_2O_2$: C 78.24, H 5.47, N 7.60; found: C 78.45, H 5.17, N 7.38. FT-IR (KBr, cm^{-1}): 1648 (C=N), 1642, 1606. EI-MS m/z calcd for $C_{26}H_{28}N_2$: 368.22; found: 368.22.

1-*p*-Acetophenylimino-2-*p*-acetophenylisoindoline (4). Methanol was used in place of ether to obtain a higher yield (72% yield, yellow powder, mp: 170.5–171.8 °C.) ^{1}HNMR ($CDCl_3$, ppm): δ 8.10 (d, J = 8.4, 2H, Ar), 8.00 (d, J = 8.9, 2H, Ar), 7.99 (d, J = 8.4, 2H, Ar), 7.50 (d, J = 7.5, 1H, Ar), 7.43 (m, 1H, Ar), 7.09 (m, 1H, Ar), 7.04 (d, J = 8.4, 2H, Ar), 6.76 (d, J = 7.3, 1H, Ar), 5.00 (s, 2H, CH_2), 2.62 (s, 3H, $COCH_3$), 2.58 (s, 3H, $COCH_3$). ^{13}C NMR ($CDCl_3$, ppm): δ 197.3 ($COCH_3$), 196.9 ($COCH_3$), 154.8 (C=N), 152.7, 145.2, 140.0, 132.1, 131.9, 131.7, 131.2, 130.8, 130.2, 129.7, 126.3, 123.0, 120.8, 117.4, 99.9, 52.9 (CH_2), 25.5 ($COCH_3$). Anal. calcd (%) for $C_{24}H_{20}N_2O_2$: C 78.24, H 5.47, N 7.60; found: C 78.45, H 5.17, N 7.38. FT-IR (KBr, cm^{-1}): 1662 (C=N), 1589. ESI-MS m/z calcd for $C_{24}H_{20}N_2O_2$: 368.15; found: 369.16 [M + H]$^+$.

1-*p*-Nitrophenylimino-2-*p*-nitrophenylisoindoline (5). (80% yield, yellow powder.) ^{1}H NMR ($CDCl_3$): δ 8.27 (m, 4H, Ar), 8.17 (d, J = 9.3, 2H, Ar), 7.52 (m, 2H, Ar), 7.16 (m, 1H, Ar), 7.07 (d, J = 8.84, 2H, Ar), 6.78 (d, J = 7.90, 1H, Ar), 5.05 (s, 2H, CH_2). ^{13}C NMR ($CDCl_3$): δ 156.4 (C=N), 152.9, 146.6, 142.6, 142.0, 141.2, 132.1, 129.7, 128.0, 125.7, 125.5, 124.9, 124.0, 121.5, 119.4, 53.2 (CH_2). Anal. calcd. for $C_{20}H_{14}N_4O_4$: C 64.48, H 3.77, N 14.97; found: C 64.38, H 3.61, N 15.24.

General synthesis for palladacycles 6–9

Iminoisoindoline (1.765 mmol) and $Pd(OAc)_2$ (1.765 mmol, 1.0 equiv.) were dissolved in dichloromethane (30 mL) in an oven dried 100 mL Schlenk flask equipped with a stir bar. After 12 h of stirring at ambient temperature under dinitrogen, the reaction mixture was filtered to remove palladium black. The filtrate was then concentrated and ether (30 mL) added to precipitate the desired palladacycle. The resulting precipitate was filtered, washed with cold ether (3 × 10 mL) then dried under vacuum. Crystals suitable for X-ray diffraction studies were obtained by slow evaporation from a 50 : 50 dichloromethane–hexane solution for **6** and **9**. Crystals of **7** were obtained from $CHCl_3$ and crystals of **8** were grown from a 50 : 50 acetone–hexane solution all at ambient temperature.

Bis(μ-acetato)bis(1-phenylimino-2-phenylisoindoline)dipalladium(II) (6). (42% yield, green powder, mp = 222.5–224.8 °C (decomp.).) ^{1}H NMR ($CDCl_3$, ppm): anti : syn = *ca.* 3 : 1; *anti*-isomer δ 7.67 (d, J = 7.6, 2H, Ar), 7.44–6.88 (m, 20H, Ar), 6.24 (d, J = 7.6, 2H, Ar), 5.68 (d, J = 8.1, 2H, Ar), 4.62 (d, J = 16.8, 2H, CH_2), 3.61 (d, J = 16.8, 2H, CH_2), 1.62 (s, 6H, CH_3COO); *syn*-isomer δ 7.44–6.88 (m, 20H, Ar), 5.94 (m, 6H, Ar), 5.09 (s, 4H, CH_2), 1.96 (s, 6H, CH_3COO). ^{13}C NMR ($CDCl_3$, ppm): *anti*-isomer δ 179.33 (CH$_3$*C*OO), 151.63 (*C*=N), 146.37, 140.72, 136.67, 136.04, 131.01, 130.91, 129.01, 128.09, 127.67, 127.44, 127.21, 125.98, 125.90, 124.85, 124.56, 122.04, 121.97, 111.83, 52.93 (CH_2), 24.45 (CH$_3$*C*OO). Anal. calcd (%) for $C_{44}H_{36}N_4O_4Pd_2$: C 58.87, H 4.04, N 6.24; found: C 59.70, H 4.23, N 6.10. FT-IR (KBr, cm^{-1}): 1614 (C=N), 1603, 1585. EI-MS m/z calcd for $C_{44}H_{36}N_4O_4Pd_2$: 896.08 [M], 897.08 [M + H]$^+$; found 897.0878 [M + H]$^+$.

Bis(μ-acetato)bis(1-*p*-methylphenylimino-2-*p*-methylphenylisoindoline)dipalladium(II) (7). (46% yield, orange powder.) ^{1}H NMR ($CDCl_3$): *anti* : *syn* = *ca.* 3 : 1); *anti*-isomer δ 7.47–6.96 (m, 12H, Ar), 6.85 (m, 4H, Ar) 6.57 (d, J = 7.9, 2H, Ar), 6.17 (d, J = 8.0, 2H, Ar), 5.74 (d, J = 8.0, 2H, Ar), 4.60 (d, J = 16.8, 2H, CH_2), 3.77 (d, J = 16.8, 2H, CH_2), 2.30 (s, 6H, Ar–CH_3), 2.20 (s, 6H, Ar–CH_3), 1.64 (s, 6H, CH_3COO); *syn*-isomer δ 7.47–6.96 (m, 16H, Ar), (d, J = 7.9, 2H, Ar), 6.00 (d, J = 7.9, 4H, Ar), 5.04 (s, 4H, CH_2), 2.42 (s, 6H, Ar–CH_3), 2.22 (s, 6H, Ar–CH_3), 1.98 (s, 6H, CH_3COO). ^{13}C NMR ($CDCl_3$): *anti*-isomer δ 179.3 (CH$_3$*C*OO), 151.1 (*C*=N), 144.0, 140.7, 137.0, 135.4, 133.8, 131.1, 130.9, 130.7, 129.7, 127.9, 127.8, 127.4, 127.0, 125.9, 125.4, 124.1, 121.9, 111.4, 53.1 (*C*H$_2$), 24.6 (CH$_3$*C*OO), 21.3 (Ar–*C*H$_3$), 20.9 (Ar–*C*H$_3$). Anal. calcd (%) for $C_{48}H_{44}N_4O_4Pd_2$: C 60.38, H 4.75, N 5.87; found: C 60.43, H 4.64, N 6.95. FT-IR (KBr, cm^{-1}): 1619 (C=N), 1615, 1508. ESI-MS m/z calcd for $C_{48}H_{44}N_4O_4Pd_2$: 952.14 [M], 893.13 [M – OAc]$^+$; found 893.1554 [M – OAc]$^+$.

Bis(μ-acetato)bis(1-*p*-isopropylphenylimino-2-*p*-isopropylphenylisoindoline)dipalladium(II) (8). (30% yield, yellow powder.) ^{1}H NMR ($CDCl_3$): *anti* : = *ca.* 5 : 1; *anti*-isomer δ 7.54 (s, 2H, Ar), 7.41 (m, 2H, Ar), 7.24 (d, J = 7.9, 2H, Ar), 7.00 (m, 4H, Ar), 6.83 (d, J = 7.9, 2H, Ar), 6.80 (d, J = 8.2, 2H, Ar), 6.65 (d, J = 8.2, 2H, Ar), 6.16 (d, J = 8.2, 2H, Ar), 5.83 (d, J = 8.2, 2H, Ar), 5.74 (d, J = 8.2, 2H, Ar), 4.53 (d, J = 16.9, 2H, CH_2), 3.30 (d, J = 16.9, 2H, CH_2), 2.91 (sept, J = 6.9, 2H, CH(CH$_3$)$_2$), 2.81 (sept, J = 6.9, 2H, CH(CH$_3$)$_2$), 1.64 (s, 6H, CH_3COO), 1.32 (d, J = 6.9, 6H, CH(CH_3)$_2$), 1.28 (d, J = 6.9, 6H, CH(CH_3)$_2$), 1.18 (d, J = 6.9, 12H, CH(CH_3)$_2$); *syn*-isomer δ 7.51 (d, J = 8.0, 2H, Ar), 7.34 (m, 4H, Ar), 7.31 (d, J = 7.9, 2H, Ar), 7.24 (m, 4H, Ar), 7.20 (d, J = 7.9, 2H, Ar), 7.00 (m, 2H, Ar), 7.10 (d, J = 7.9, 2H, Ar), 6.90 (d, J = 7.9, 2H, Ar), 5.83 (m, 2H, Ar), 5.05 (s, 4H, CH_2), 2.98 (m, 4H, CH(CH$_3$)$_2$)), 1.98 (s, 6H, CH_3COO), 1.30 (d, J = 6.9, 6H, CH(CH_3)$_2$), 1.25 (d, J = 6.9, 6H, CH(CH_3)$_2$), 1.20 (d, J = 6.9, 12H, CH(CH_3)$_2$). ^{13}C NMR ($CDCl_3$): *anti*-isomer δ 179.0 (CH$_3$*C*OO), 151.5 (*C*=N), 146.5, 144.2, 142.3, 140.9, 134.4, 134.3, 131.1, 130.7, 128.0, 127.5, 127.3, 126.8, 125.7, 125.2, 124.9, 122.9, 122.0, 111.6, 52.8 (*C*H$_2$), 34.0 (*C*H(CH$_3$)$_2$), 33.8 (*C*H(CH$_3$)$_2$), 24.59 (*C*H$_3$COO), 24.57 (CH(*C*H$_3$)$_2$), 24.5 (CH(*C*H$_3$)$_2$), 24.3 (CH(*C*H$_3$)$_2$), 24.1 (CH(*C*H$_3$)$_2$). Anal. calcd (%) for $C_{56}H_{62}N_4O_4Pd_2$: C 63.10, H 5.67, N 5.26; found: C 62.96, H 5.68, N 5.32. FT-IR (KBr, cm^{-1}): 1615.4 (C=N), 1578.9, 1552.1, 1504.2, 1415.1. ESI-MS m/z calcd for $C_{56}H_{60}N_4O_4Pd_2$: 1067.2841 [M], 1005.26 [M – OAc]$^+$; found: 1005.26 [M – OAc]$^+$.

Bis(μ-acetato)bis(1-*p*-acetophenylimino-2-*p*-acetophenylisoindoline)dipalladium(II) (9). (40% yield, orange powder, mp = 242.5–244.5 °C (decomp.).) ^{1}H NMR ($CDCl_3$, ppm): *anti* : *syn* = *ca.* 8 : 1; *anti*-isomer δ 8.26 (s, 2H, Ar), 7.85 (d, J = 8.0, 2H, Ar), 7.53 (m, 4H, Ar), 7.38 (m, 4H, Ar), 7.10 (d, J = 8.2, 2H, Ar), 7.04 (m, 2H, Ar), 6.36 (d, J = 8.5, 2H, Ar), 5.95 (d, J = 8.0, 2H, Ar), 5.77 (d, J = 8.1, 2H, Ar), 4.76 (d, J = 16.8, 2H, CH_2), 3.82 (d, J = 16.8, 2H, CH_2), 2.58 (s, 6H, COCH_3), 2.56 (s, 6H, COCH_3), 1.66 (s, 6H, CH_3COO); *syn*-isomer 8.10 (d, J = 7.9, 4H, Ar), 7.90 (m, 6H, Ar), 7.56–7.02 (m, 8H, Ar), 5.95 (d, J = 7.9, 4H, Ar), 5.17 (s, 4H, CH_2), 2.67 (s, 6H, COCH_3), 2.65 (s, 6H, COCH_3), 1.96 (s, 6H, CH_3COO). ^{13}C NMR (DMSO, ppm): *anti*-isomer δ 197.07 (*C*OCH$_3$), 196.64 (*C*OCH$_3$), 178.60 (CH$_3$*C*OO), 151.37 (*C*=N), 150.01, 141.42, 138.73, 135.66, 134.47, 131.92, 130.13, 129.90, 128.97, 127.76, 126.94, 126.59, 126.11, 125.26, 123.18, 122.71, 112.79, 53.49 (*C*H$_2$), 26.68 (CO*C*H$_3$), 26.23 (CO*C*H$_3$), 24.41 (*C*H$_3$COO). Anal. calcd (%) for $C_{52}H_{44}N_4O_4Pd_2$: C 58.60, H 4.16, N 5.26; found: C 58.38, H 4.01, N 5.13. FT-IR (KBr, cm^{-1}): 1667 (C=N), 1623, 1484. ESI-MS m/z calcd for $C_{52}H_{44}N_4O_8Pd_2$: 1064.1 [M], 1005.1 [M – OAc]$^+$; found 1005.2 [M – OAc]$^+$.

General procedure for Heck coupling reactions

In a typical run, an oven-dried 25 mL two-necked flask equipped with a stir bar was charged with a known mol% catalyst and base (2.0 mmol). Under nitrogen, *N*,*N*-dimethylacetamide (DMA) (3 mL), arylhalide (1.0 mmol) and *n*-butylacrylate (2.0 mmol) were added *via* syringe. The flask was then placed in a pre-heated sand bath at 145 °C. After the specified time the flask was removed from the sand bath and water (20 mL) was added followed by extraction with dichloromethane (4 × 10 mL). The combined organic layers were washed with water (3 × 10 mL), dried over anhydrous $MgSO_4$, and filtered. Solvent was removed under vacuum. The residue was dissolved in $CDCl_3$ and analyzed by ^{1}H NMR. Percent conversions were determined against the remaining aryl halide.[16,17]

General procedure for Suzuki coupling reactions

In a typical run, an oven dried 25 mL two-necked flask equipped with a stir bar was charged with a known mol% catalyst, base (2.0 mmol) and phenylboronic acid (1.5 mmol). Under nitrogen, DMA (3 mL) and aryl halide (1.0 mmol) were added *via* syringe. The flask was placed in pre-heated sand bath at 80 °C. After the

specified time the flask was removed from the sand bath and water (20 mL) was added followed by extraction with dichloromethane (3 × 10 mL). The combined organic layers were washed with water (3 × 10 mL), dried over anhydrous $MgSO_4$, and filtered. Solvent was removed under vacuum. The residue was dissolved in $CDCl_3$ and analyzed by ^1H NMR. Percent conversions were determined against the remaining aryl halide.[16,17]

X-Ray structure determinations

Data was collected at −100 °C on a Nonius Kappa CCD diffractometer, using the COLLECT program.[18] Cell refinement and data reductions used the programs DENZO and SCALEPACK.[19] SIR97[20] was used to solve the structures and SHELXL97[21] was used to refine the structures. ORTEP-3 for Windows[22] was used for molecular graphics and PLATON[23] was used to prepare material for publication. H atoms were placed in calculated positions with U_{iso} constrained to be 1.5 times U_{eq} of the carrier atom for methyl protons and 1.2 times U_{eq} of the carrier atom for all other hydrogen atoms. For complex **9** there are four acetyl groups in the molecule, attached on atoms C12, C18, C42 and C48. The acetyl group on C48 is badly disordered and would not refine to reasonable bond angles and bond lengths. To avoid putting meaningless values into the CSD, the average of the bond lengths and bond angles of the other three acetyl groups was used to form a rigid acetyl group on C48. The thermal ellipsoids on C52 and O51 were restrained using the ISOR command in SHELXL. The resulting displacements for these atoms were much larger than for the equivalent groups. Consequently, C52 (and the attached H atoms) and O51 had very large U_{eq}.

Acknowledgements

We gratefully thank NSERC for financial support and the Canadian Government through the Commonwealth Scholarship fund for J.M.C.'s doctoral fellowship.

References

1 J. Dupont, C. S. Consorti and J. Spencer, *Chem. Rev.*, 2005, **105**, 2527–2572.
2 (*a*) J. Tsuji, *Palladium Reagents and Catalysts*, Wiley, New York, 2004; (*b*) *Metal-catalyzed Cross-coupling Reactions*, ed. A. de Meijere and P. J. Diederich, Wiley-VCH, Weinheim, 2004; (*c*) E. Negishi and A. de Mejere, *Handbook of Organopalladium Chemistry for Organic Synthesis*, Wiley-VCH, Weinheim, 2002.
3 For reviews on palladacycles, see: (*a*) R. B. Bedford, C. S. J. Cazin and D. Holder, *Coord. Chem. Rev.*, 2004, **248**, 2283–2321; (*b*) V. Farina, *Adv. Synth. Catal.*, 2004, **346**, 1553–1582; (*c*) I. P. Beletskaya and A. V. Cheprakov, *J. Organomet. Chem.*, 2004, **689**, 4055–4082; (*d*) W. A. Herrmann, K. Ofele, S. K. v. Preysing and D. Schneider, *J. Organomet. Chem.*, 2003, **687**, 229–248; (*e*) E. Alacid, D. A. Alonso, L. Botella, C. Nájera and M. C. Pacheco, *Chem. Rec.*, 2006, **6**, 117–132; (*f*) J. Vicente and I. Saura-Llamas, *Comments Inorg. Chem.*, 2007, **28**, 39–72; (*g*) D. A. Albison, R. B. Bedford and P. N. Scully, *Tetrahedron Lett.*, 1998, **39**, 9793–9796.
4 *Handbook of C–H Transformations*, ed. G. Dyker, Wiley-VCH, Weinheim, 2005.
5 (*a*) A. C. F. Caires, *Anticancer Agents Med. Chem.*, 2007, **7**, 484–491; (*b*) C. M. V. Barbosa, C. R. Oliveira, F. D. Nascimento, M. C. M. Smith, D. M. Fausto, M. A. Soufen, E. Sena, R. C. Araújo, I. L. S. Tersariol, C. Bincoletto and A. C. F. Caires, *Eur. J. Pharmacol.*, 2006, **542**, 37–47.
6 J. M. Chitanda, D. E. Prokopchuk, J. W. Quail and S. R. Foley, *Organometallics*, 2008, **27**, 2337–2345.
7 (*a*) M. Broering and C. Kleeberg, *Inorg. Chim. Acta*, 2007, **360**, 3281–3286; (*b*) M. Broering, C. Kleeberg and E. C. Tejero, *Eur. J. Inorg. Chem.*, 2007, 3208–3216; (*c*) M. Wicholas, A. D. Garret, M. Gleaves, A. M. Morris, M. Rehm, O. P. Anderson and A. la Cour, *Inorg. Chem.*, 2006, **45**, 5804–5811; (*d*) É. Balogh-Hergovich, G. Speier, M. Réglier, M. Giorgi, E. Kuzmann and A. Vértes, *Inorg. Chem. Commun.*, 2005, **8**, 457–459; (*e*) M. B. Meder and L. H. Gade, *Eur. J. Inorg. Chem.*, 2004, **13**, 2716–2722; (*f*) É. Balogh-Hergovich, G. Speier, M. Réglier, M. Giorgi, E. Kuzmann and A. Vértes, *Eur. J. Inorg. Chem.*, 2003, 1735–1740; (*g*) O. P. Anderson, A. la Cour, A. Dodd, A. D. Garret and M. Wicholas, *Inorg. Chem.*, 2003, **42**, 4513–4515; (*h*) F. A. Chavez and P. K. Mascharak, *Acc. Chem. Res.*, 2000, **33**, 539–545.
8 (*a*) I. Takahashi, R. Miyamoto, K. Nishiuchi, M. Hatanaka, A. Yamano, A. Sakushima and S. Hosoi, *Heterocycles*, 2004, **63**, 1267–1271; (*b*) I. Takahashi, K. Nishiuchi, R. Miyamoto, M. Hatanaka, H. Uchida, K. Isa, A. Sakushima and S. Hosoi, *Lett. Org. Chem.*, 2005, **2**, 40–43.
9 (*a*) I. Takahashi, M. Tsuzuki, H. Yokota, H. Kitajima and K. Isa, *Heterocycles*, 1994, **37**, 933–942; (*b*) I. Takahashi and M. Hatanaka, *Heterocycles*, 1997, **12**, 2475–2499; (*c*) T. DoMinh, A. L. Johnson, J. E. Jones and P. P. Senise, *J. Org. Chem.*, 1977, **42**, 4217–4221; (*d*) R. Grigg, H. Q. N. Gunaratne and V. Sridharan, *J. Chem. Soc., Chem. Commun.*, 1985, 1183–1184.
10 (*a*) A. D. Tanase, G. D. Frey, E. Herdtweck, S. D. Hoffmann and W. A. Herrmann, *J. Organomet. Chem.*, 2007, **692**, 3316–3327; (*b*) F. Tjosaas and A. Fiksdahl, *J. Organomet. Chem.*, 2007, **692**, 5429–5439; (*c*) S. F. Kirsch and L. E. Overman, *J. Org. Chem.*, 2005, **70**, 2859–2861; (*d*) J. Vicente, I. Saura-Llamas, J. Cuadrado and M. C. Ramirez de Arellano, *Organometallics*, 2003, **22**, 5513–5517; (*e*) B. Teijido, A. Fernández, M. López-Torres, S. Castro-Juiz, A. Suárez, J. M. Ortigueira, J. M. Vila and J. J. Fernández, *J. Organomet. Chem.*, 2000, **598**, 71–79; (*f*) M. Ohff, A. Ohff and D. Milstein, *Chem. Commun.*, 1999, 357–358.
11 A. Fernández, D. Vázquez-García, J. J. Fernández, M. López-Torres, A. Suárez, S. Castro-Juiz and J. M. Vila, *Eur. J. Inorg. Chem.*, 2002, 2389–2401.
12 A. C. Cope and R. W. Siekman, *J. Am. Chem. Soc.*, 1965, **87**, 3272–3273.
13 (*a*) W. A. Herrmann, C. Brossmer, K. Ofele, C.-P. Reisinger, T. Priermeier, M. Beller and H. Fischer, *Angew. Chem., Int. Ed. Engl.*, 1995, **34**, 1844–1848; (*b*) M. Beller, H. Fischer, W. A. Herrmann, K. Olefe and C. Brossmer, *Angew. Chem., Int. Ed. Engl.*, 1995, **34**, 1848–1849.
14 (*a*) D. A. Alonso, L. Botella, C. Nájera and C. Pacheco, *Synthesis*, 2004, 1713–1718; (*b*) E. Alacida and C. Nájera, *Adv. Synth. Catal.*, 2006, **348**, 2085–2091.
15 A. Schnyder, A. F. Indolese, M. Studer and H.-U. Blaser, *Angew. Chem., Int. Ed.*, 2002, **41**, 3668–3671.
16 D. A. Albisson, R. B Bedford, S. E. Lawrence and P. N. Scully, *Chem. Commun.*, 1998, 2095–2096.
17 (*a*) E. Peris, J. Mata, J. A. Loch and R. H. Crabtree, *Chem. Commun.*, 2001, 201–202; (*b*) C. L. Chen, Y. H. Liu, S. H. Peng and S. T. Liu, *Organometallics*, 2005, **24**, 1075–1081; (*c*) P. Evans, P. Hogg, R. Grigg, M. Nurnabi, J. Hinsley, V. Sridharan, S. Suganthan, S. Korn, S. Collard and J. E. Muir, *Tetrahedron*, 2005, **61**, 9696–9704.
18 *Nonius COLLECT*. Nonius BV, Delft, The Netherlands, 1998.
19 Z. Otwinowski and W. Minor, *Methods Enzymol.*, 1997, **276**, 307–326.
20 A. Altomare, M. C. Burla, M. Camalli, G. L. Cascarano, C. Giacovazzo, A. Guagliardi, A. G. G. Moliterni, G. Polidori and R. Spagna, *J. Appl. Crystallogr.*, 1999, **32**, 115–119.
21 G. M. Sheldrick, *SHELXL-97*. University of Göttingen. Germany, 1997.
22 L. J. Farrugia, *J. Appl. Crystallogr.*, 1997, **30**, 565.
23 A. L. Spek, *PLATON*. University of Utrecht, The Netherlands, 2001.