An intermolecular C–C coupling reaction of iridium complexes†

Kathrin Kutlescha,[a] Torsten Irrgang[ab] and Rhett Kempe*[a]

Received (in Victoria, Australia) 26th February 2010, Accepted 31st March 2010
DOI: 10.1039/c0nj00158a

Novel imidazo[1,5-*b*]pyridazine-substituted (pyridyl-methyl)amines were synthesized *via* the nucleophilic ring transformation of oxadiazolium halides and (aminomethyl)pyridines, followed by a cyclocondensation reaction with 1,3-diketones. After deprotonation, these monoanionic amido-pincer ligands are suitable for the stabilization of mononuclear iridium complexes. For 2-(pyridyl-methyl)-amine-derived complexes, we observed the formation of dimers *via* an intermolecular C–C coupling reaction, whilst the 3-(pyridyl-methyl)amine-derived complex did not react. We propose that enamine tautomerization plays an important role in the C–C coupling reaction.

Introduction

Recently, we described a novel ligand system for the stabilization of early and late transition metal complexes—imidazopyridazine-substituted bisamido ligands (Scheme 1).[1] Since salt metathesis reactions with group 9 metals (Ir, Rh) gave only dinuclear amido complexes with *trans* binding modes, we were interested in developing an amido-pincer type of ligand[2] that allows for the synthesis of mononuclear complexes (Scheme 1).

Our approach towards these novel amido-pincer ligands is based on classical bench-top chemistry, realizing a large variety of substitution patterns. Aryl amines are substantially synthesized *via* palladium-catalyzed aryl amination, which is highly efficient for the formation of C–N bonds but often employs rather expensive catalysts.[3]

Herein, we report the synthesis of imidazo-[1,5-*b*]pyridazine-substituted (pyridyl-methyl)amines **5** and their application as monoanionic ligands for the stabilization of iridium complexes **6**. For **6a** and **6b**, we observed an unusual intermolecular C–C coupling reaction, giving rise to dinuclear complexes **7**.

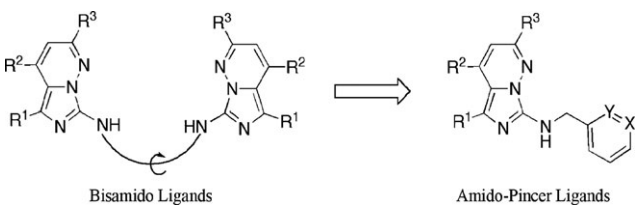
Results and discussion

2-Amino-5-methyl-1,3,4-oxadiazolium halides[4] **1a** and **1b** (Scheme 2) react with a large variety of *N*-nucleophiles, such as primary and secondary amines, to yield 2-amino-substituted 1-acetyl-amino-imidazoles *via* a nucleophilic ring transformation.[5,6] Thus, the reaction with (aminomethyl)-pyridines affords *N*-{4-alkyl/aryl-2-[(pyridin-2/3-ylmethyl)-amino]-imidazo-1-yl}-acetamides **2a–c**. Deacetylation by refluxing **2** in EtOH/HCl, followed by neutralization, gives rise to **4a–c** (Scheme 2). It is known that 1-amino-4-aryl-imidazoles[7] react with 1,3-diketones to yield imidazo-[1,5-*b*]pyridazines.[6] Analogously, **4** can be converted into imidazo[1,5-*b*]-pyridazine-substituted (pyridyl-methyl)amines **5a–c** (Scheme 2) *via* a cyclo-condensation with acetylacetone in moderate yields and high purity. The molecular structure of **5a** was confirmed by X-ray crystal structure analysis.[8]

The lithiation of **5a** at −78 °C using one equiv. of *n*-butyllithium and the addition of 0.5 equiv. of $[IrCl(cod)]_2$ (cod = 1,5-cyclooctadiene), afforded **6a** as a dark green crystalline material in moderate yield (Scheme 3).

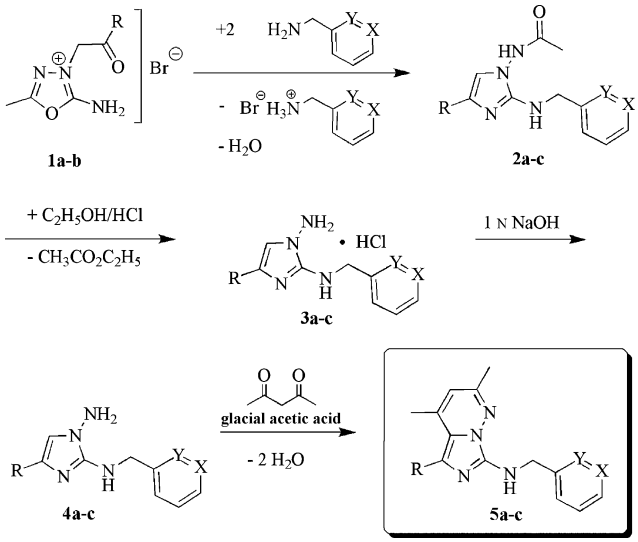
An X-ray crystal structure analysis[9] of **6a** was performed to determine the molecular structure (Scheme 3). The monoanionic tridentate ligand coordinates the iridium atom *via* the amido N atom (N4) and N1, forming a five-membered chelate. Since the Ir1–N4 bond (2.050 Å) is significantly shorter than the Ir1–N1 bond (2.143 Å), we propose that the anionic charge of the ligand is localized on the amido N atom. The standard deviation of the imidazopyridazine plane is 0.010 Å. The deviation of the N_{amido} atom out of this plane is 0.043 Å and for Ir it is 0.054 Å. The 2-pyridyl-methyl moiety is bent out of the imidazopyridazine plane (N4–C15–C16 116.6°) and coordination by the pyridine nitrogen does not occur. The NMR spectra of **6a** show a single signal set of deprotonated **5a** and a double-coordinated cyclooctadiene ligand.

While compound **6a** is stable as a solid, in solution we observed the formation of orange-red crystalline material **7a** (Scheme 4) after a few weeks at room temperature. We were able to synthesize **7a** in moderate yields by the reaction of **5a** with 0.5 equiv. of $[IrOCH_3(cod)]_2$.[10] The resulting green solution was heated at 50 °C for 2 weeks and the precipitated red crystalline material isolated (30%). An X-ray crystal structure analysis[11] of **7a** (Fig. 1) revealed that intermolecular C–C bond formation between the 2-pyridyl-methyl substituents of two amido ligands had occurred. The two imidazopyridazine

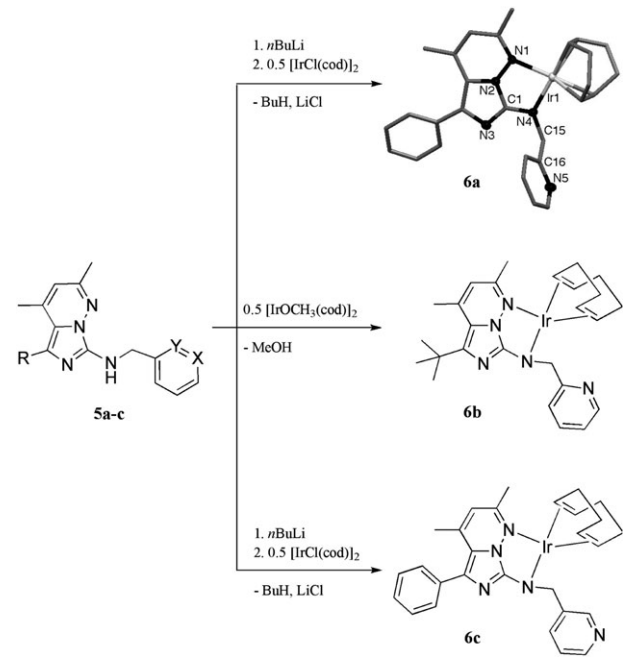


Scheme 1 Imidazo[1,5-*b*]pyridazine-substituted bisamido ligands and amido-pincer ligands (R^{1-3} = aryl or alkyl substituents; Y, X = C or N).

[a] *Lehrstuhl für Anorganische Chemie 2, Universität Bayreuth, Bayreuth, Germany. E-mail: kempe@uni.bayreuth.de; Fax: +49 (0) 921-55-2157; Tel: +49 (0) 921-55-2541*
[b] *AIKAA-Chemicals GmbH, Kämmereigasse 11, Bayreuth, Germany*
† CCDC reference numbers 729909–729912. For crystallographic data in CIF or other electronic format see DOI: 10.1039/c0nj00158a

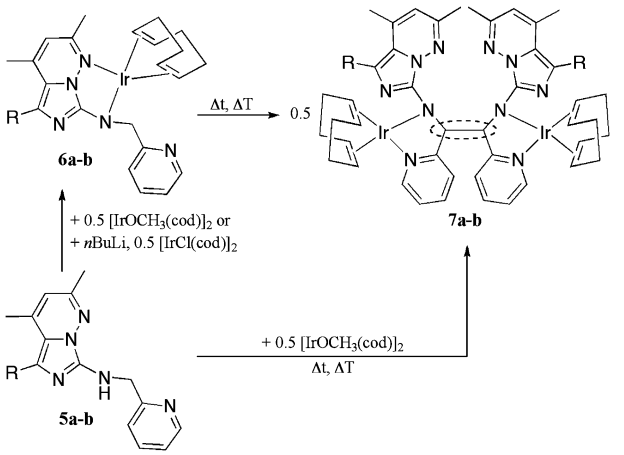


Scheme 2 Ring transformation with (aminomethyl)pyridines [R = C_6H_5, Y = N, X = C (**1a–5a**); R = *t*-butyl, Y = N, X = C (**1b–5b**); R = C_6H_5, Y = C, X = N (**1c–5c**)].



Scheme 3 Synthesis of iridium complexes **6a–c** [R = C_6H_5, Y = N, X = C (**5a–6a**); R = *t*-butyl, Y = N, X = C (**5b–6b**); R = C_6H_5, Y = C, X = N (**5c–6c**)] and molecular structure of **6a**. Selected bond lengths [Å] and angles [°]: Ir1–N1 2.143(3), Ir1–N4 2.05(3), C1–N2 1.360(4), C1–N3 1.341(5), C1–N4 1.351(5), N1–N2 1.393(4); N1–Ir1–N4 80.61(11), Ir1–N1–N2 106.87(19), C1–N2–N1 121.5(3).

planes are orientated nearly parallel (dihedral angle 2.24°) to each other. The deviation of the N_{amido} atom out of this plane (0.085 Å for N7 and 0.113 Å for N2) is larger than in **6a**, which is due to the altered coordination mode. In contrast to **6a**, the iridium in **7a** is coordinated by the N_{amido} atom and the $N_{pyridine}$ *via* a five-membered chelate, leading to smaller N–Ir–N angles than in **6a** of 78.7° (N7–Ir2–N6) and 79.5° (N2–Ir1–N1), respectively. The Ir–N bond lengths of 2.019

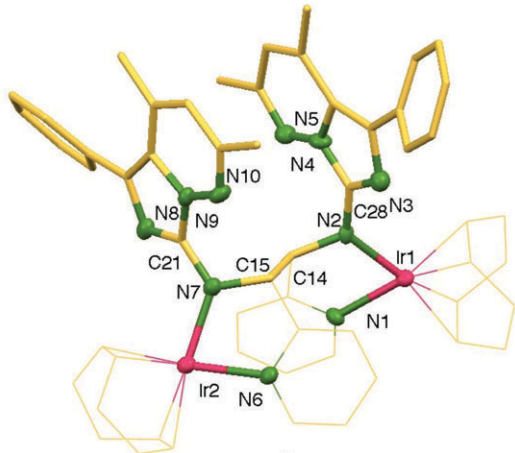


Scheme 4 Evolution of C–C coupled dimers **7a** and **7b**; the newly formed C–C bond is highlighted by a dashed line.

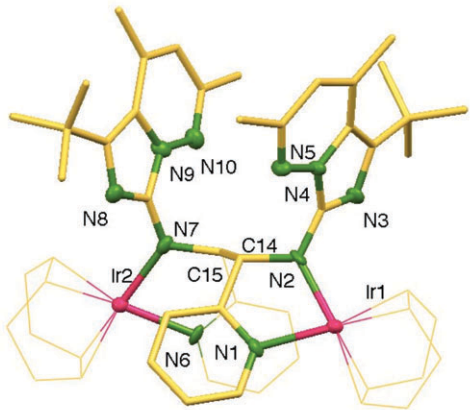
(Ir2–N7), 2.084 (Ir2–N6), 2.013 (Ir1–N2) and 2.088 (Ir1–N1) Å indicate a rather localized bonding mode. No solution NMR data could be obtained for **7a**, since it is insoluble in common solvents. MAS-NMR data are in accordance with the signals expected for the C–C-coupled deprotonated ligand and cod.

Due to the insolubility of **7a**, we were interested in synthesizing a more soluble derivative, namely *t*-butyl-substituted **7b**. When we tried to synthesize **6b** *via* salt metathesis from lithiated **5b** and $[IrCl(cod)]_2$ using the same protocol as for **6a**, we observed that C–C coupling took place more rapidly; thus, we chose an alcohol elimination reaction. The addition of 0.5 equiv. of $[IrOCH_3(cod)]_2$ to a solution of **5b** in THF gave rise to a dark green material **6b** in quantitative yield (Scheme 3). The NMR spectra show a single signal set of signals for deprotonated **5b** and the signals for a double-coordinated cyclooctadiene. The C–C coupling product, **7b**, was isolated in moderate yield (28%) using the same protocol as for **7a** (Scheme 4). An X-ray crystal structure analysis[12] of **7b** was performed to determine its molecular structure (Fig. 1). The bond length of the new C–C bond (C14–C15) is 1.597 Å. Due to the bulky *t*-butyl substituents, the dihedral angle between these planes is extended to 24.84° (2.24° in **7a**). This also has an effect on the deviation of the N_{amido} atom out of the imidazopyridazine plane (0.252 Å for N2 and 0.055 Å for N7). The iridium is coordinated by the N_{amido} and the $N_{pyridine}$ *via* a five-membered chelate, resulting in N–Ir–N angles of 78.99 (N7–Ir2–N6) and 79.09 (N2–Ir1–N1)°. Since the Ir–N_{amido} bond lengths of 1.984 Å (N7–Ir2) and 1.991 Å (N2–Ir1) are similar to the Ir–$N_{pyridine}$ bond lengths (2.090 Å (N6–Ir2); 2.085 Å (N1–Ir1)), the bonding mode is localized. The NMR spectra of **7b** show a single signal set of signals for the deprotonated ligand and the two double-coordinated cyclooctadiene molecules. The new CH group, which was formed due to the C–C coupling, is characterized as a doublet (^{1}H NMR) at 5.75 ppm with a coupling constant of 4.7 Hz.

Regarding C–C coupling reactions with pyridines, the reactivity of the carbon atom can arise from the enamine tautomer. This is reinforced by the fact that pyridines (or unsubstituted aromatics), which are unable to tautomerize into enamines, do not participate in the reactions.[13]



7a

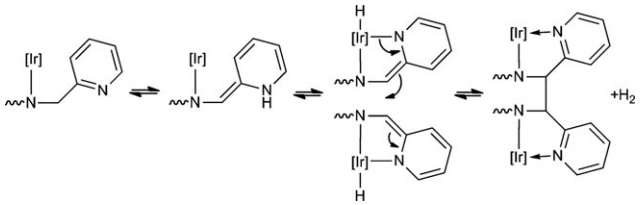


7b

Fig. 1 The molecular structures of **7a** and **7b**; selected bond lengths [Å] and angles [°]: **7a** (the asymmetric unit contained two independent molecules of **7a**, one molecule is omitted for clarity): Ir1–N1 2.088(8), Ir1–N2 2.013 (8), Ir2–N6 2.084(8), Ir2–N7 2.019(8), C14–C15 1.589(11), C14–N2 1.448(13), C15–N7 1.432(13); N2–Ir–1–N1 79.5(3), N7–Ir2–N6 78.7(3), N2–C14–C15 111.7(8), N7–C15–C14 112.2(7), C14–N2–Ir1 115.6(6), C15–N7–Ir2 117.2(6); **7b**: Ir1–N1 2.084(5), Ir2–N6 2.090(4), Ir1–N2 1.992(6), Ir2–N7 1.983(7), C15–N7 1.447(8), C14–N2 1.468(8), C14–C15 1.597(8); N2–Ir1–N1 79.1(2), N7–Ir2–N6 79.0(2), C14–N2–Ir2 117.4(3), C6–N2–Ir2 117.7(5), N2–C14–C15 112.4(5), N7–C15–C14 112.0(5).

Therefore, we additionally synthesized the 3-(aminomethyl)-pyridine derivative of ligand **5c**; herein, the formation of an enamine tautomer is not possible. Complex **6c** was obtained *via* salt metathesis upon deprotonation with *n*BuLi. Since the formation of a C–C coupling product could not be detected *via* NMR for **6c**, we propose a coupling mechanism based on the formation of the enamine tautomer, followed by an intermolecular attack of the carbon atom next to the pyridine moiety (Scheme 5). The altered coordination mode in **7** cannot be realized in ligand **5c**, which might additionally hinder the C–C coupling reaction.

The iridium is thought to mediate the reaction *via* activation of the enamine and hydride transfer, thereby generating molecular hydrogen. Hydrogen evolution could be detected *via* NMR studies; a small singlet appeared at 4.21 ppm ([d_8]THF).



Scheme 5 The proposed mechanism based on tautomerization into an enamine and iridium-mediated hydride transfer.

Regarding the mechanism, double C–H activation followed by an intermolecular dehydrogenative C–C coupling reaction of the two iridium complexes **6a** and **6b** cannot be ruled out completely. The addition of a radical scavenger doesn't inhibit the formation of dimer **7b** and doesn't decrease the rate of dimer formation significantly. Thus, radical-based C–C coupling reactions are not very likely.

The reaction does not proceed completely, yielding only 19% of **7b** in 24 h and about 35% in 8 d.

The closest reactivity pattern we could find is the coupling reaction of zinc complexes of *N*-substituted (2-pyridyl-methyl)-amines *via* oxidative pathways due to addition of white phosphorous or dimethylzinc by Westerhausen *et al*. Since no radicals were observed by ESR, they propose that the reaction is strongly based on the redox potential of the metal, and that the driving force of the reaction is the regeneration of aromaticity after metalation of the methylene group and charge migration to the pyridine nitrogen.[14]

Conclusions

In conclusion, imidazo[1,5-*b*]pyridazine-substituted (pyridyl-methyl)amines can be synthesized *via* the nucleophilic ring transformation of oxadiazolium halides **1** with 2- or 3-(aminomethyl)pyridine, followed by deacetylation and cyclo-condensation with 1,3-diketones, in moderate yields and high purity. The deprotonated amines can act as amido ligands, binding transition metals as five-membered chelates *via* the amido *N*-atom and N-1 of the imidazopyridazine.

An unusual intermolecular C–C coupling reaction for 2-(aminomethyl)pyridine derived complexes **6a** and **6b** takes place in solution, giving rise to dinuclear complexes **7**. We have proposed a mechanism based on enamine tautomerization, and intermolecular attack accompanied by iridium-mediated activation and hydride transfer, thereby evolving molecular hydrogen.

Experimental section

General procedures

Syntheses of the starting materials and ligands were performed under standard conditions. Complex syntheses were conducted in an oven (95 °C) and in vacuum dried glassware under an inert atmosphere of dry argon 5.0 *via* standard Schlenk or glove box techniques. NMR spectra were recorded on a Bruker ARX 250/300 (250 or 300 MHz) or a Varian Inova 300/400 (300/400 MHz) NMR spectrometer. Chemical shifts are reported in ppm from tetramethylsilane, with the solvent

resonance resulting from incomplete deuteration as the internal standard. Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, br = broad, m = multiplet or combinations thereof), integration and coupling constant. Mass spectra were recorded on a Finnigan MAT 8500 spectrometer *via* electron ionization (70 eV). Melting points were determined in sealed capillaries by using a Stuart SMP3 melting point apparatus. Elemental analysis was performed with a Vario Elementar EL III or Leco CHN-932 elemental analyser.

Reagents

Non-halogenated solvents were distilled from sodium benzophenone ketyl and halogenated solvents from P_2O_5. Deuterated solvents were obtained from Cambridge Isotope Laboratories and were de-gassed, dried and distilled prior to use. All chemicals were purchased from commercial vendors and used without further purification.

***N*-{4-Phenyl-2-[(pyridin-2-ylmethyl)-amino]imidazo-1-yl}-acetamide monohydrate (2a).** 2.00 g (6.71 mmol) 2-amino-5-methyl-3-phenacyl-1,3,4-oxadiazoliumbromide and 1.37 mL (1.45 g; 13.43 mmol) 2-(aminomethyl)pyridine were stirred for 1 min on a hot plate (250 °C). Then, the reaction mixture was allowed to cool to room temperature. Water (20 mL) was added and colourless crystals formed after several hours. After recrystallization from ethanol–water (1 : 1 ratio) *N*-{4-phenyl-2-[(pyridin-2-yl-methyl)amino]imidazo-1-yl}acetamide monohydrate (**2a**) (1.95 g, 89%) was obtained; mp 180 °C (decomposition). Found: C, 62.3; H, 5.7; N, 21.5. Calc. for $C_{17}H_7N_5O_2$: C, 62.8; H, 5.9; N, 21.5%. δ_H (400.13 MHz, [d_6]DMSO, 298 K, TMS) 10.94 (s, 1H, NH, acetylamino), 8.58–8.56 (m, 1H, pyridine), 7.80–7.15 (m, 8H, C_6H_5/pyridine), 7.23 (s, 1H, H-5, imidazole), 6.77–6.74 (t, 1H, N*H*–CH_2, J = 6.1), 4.66–4.65 (d, 2H, CH_2–NH, J = 6.1) and 2.08 (s, 3H, CH_3); δ_C (100.63 MHz, [d_6]DMSO, 298 K, TMS) 169.53 (C═O), 160.34 (C-2′′, pyridine), 149.43 (C-2, imidazole), 148.97 (C-6′′, pyridine), 136.82 (C-4′′, pyridine), 135.12 (C-1′, C_6H_5), 133.85 (C-4, imidazole), 128.57, 124.08 ($C_{o,m}$, C_6H_5), 125.99 (C_p, C_6H_5), 122.23 (C-3′′, pyridine), 121.28 (C-5′′, pyridine), 112.60 (C-5, imidazole), 47.87 (CH_2) and 21.16 (CH_3); m/z = 307 (M^+), 249, 118, 93 and 43.

4-Phenyl-N^2-pyridine-2-ylmethyl-imidazol-1,2-diamine dihydrochloride dihydrate (3a). To a suspension of 3.00 g (9.22 mmol) of **2a** in 20 mL ethanol was added 2 mL of concentrated HCl. The reaction mixture was refluxed for 1 h, during which a precipitate was formed after 30 min. After cooling to room temperature and evaporation of the solvent, the colourless product was recrystallized from water–ethanol (1 : 4 ratio) to yield **3a** (2.17 g, 63%). Found: C, 48.1; H, 5.8; N, 18.7. Calc. for $C_{15}H_{21}N_5O_2Cl_2$: C, 48.1; H, 5.7; N, 18.7%. δ_H (400.13 MHz, [d_6]DMSO, 298 K, TMS) 8.91–8.89 (m, 1H, H-6′′, pyridine), 8.71–8.68 (t, 1H, N*H*–CH_2, J = 5.9), 8.39–7.48 (m, 8H, C_6H_5/pyridine), 7.79 (s, 1H, H-5, imidazole) and 5.34–5.32 (d, 2H, CH_2–NH, J = 5.9); δ_C (100.63 MHz, [d_6]DMSO, 298 K, TMS) 154.85 (C-2′′, pyridine), 147.51 (C-2, imidazole), 144.64 (C-6′′, pyridine), 143.19 (C-4′′, pyridine), 135.63 (C-1′, C_6H_5), 129.16, 125.13 ($C_{o,m}$, C_6H_5), 128.47 (C_p, C_6H_5), 127.80 (C-4, imidazole), 124.97, 124.10 (C-3′′, C-5′′, pyridine), 115.97 (C-5, imidazole) and 45.54 (CH_2); m/z = 265 (M^+), 249, 118, 93, 77 and 36.

4-Phenyl-N^2-pyridine-2-ylmethyl-imidazol-1,2-diamine semihydrate (4a). 2.12 g (5.66 mmol) of **3a** was dissolved in water (10 mL) and 1 N NaOH was added until a weak basic reaction (pH 8) occurred. The white precipitate was washed with water and recrystallized from water–ethanol (1 : 4 ratio) yielding **4a** (1.55 g, 100%); mp 152 °C (decomposition). Found: C, 65.7; H, 5.9; N, 25.5. Calc. for $C_{15}H_{16}N_5O_{0.5}$: C, 65.6; H, 5.7; N, 25.2%. δ_H (400.13 MHz, $CDCl_3$, 298 K, TMS) 8.72–8.70 (m, 1H, H-6′′, pyridine), 7.94–7.23 (m, 8H, C_6H_5/pyridine), 7.32 (s, 1H, H-5, imidazole), 6.36–6.33 (t, 1H, N*H*–CH_2, J = 6.2), 5.83 (s, 2H, NH_2) and 4.77–4.76 (d, 2H, CH_2, J = 6.2); δ_C (100.63 MHz, $CDCl_3$, 298 K, TMS) 159.80 (C-2′′, pyridine), 150.01 (C-2, imidazole), 149.01 (C-6′′, pyridine), 136.86 (C-4′′, pyridine), 135.67 (C-1′, C_6H_5), 132.79 (C-4, imidazole), 128.2, 123.87 ($C_{o,m}$, C_6H_5), 125.52 (C_p, C_6H_5), 122.31, 121.67 (C-3′′, C-5′′, pyridine), 113.83 (C-5, imidazole) and 48.14 (CH_2).

(2,4-Dimethyl-5-phenyl-imidazo[1,5-*b*]pyridazin-7-yl)pyridin-2-ylmethyl-amine (5a). To a suspension of 1.10 g (4.01 mmol) of **4a** in 7 mL glacial acetic acid 0.40 g (0.41 mL; 4.01 mmol) acetylacetone was added. The reaction mixture was refluxed for 2 h; afterwards, the solvent was evaporated and 20 mL of water was added. After a few days, orange needles were obtained. Recrystallization from water–ethanol (1 : 2 ratio) yielded **5a** (0.55 g, 42%); mp 110 °C. Found: C, 73.2; H, 5.8; N, 21.4. Calc. for $C_{20}H_{19}N_5$: C, 72.9; H, 5.8; N, 21.3%. δ_H (400.13 MHz, $CDCl_3$, 298 K, TMS) 8.51–8.50 (d, 1H, H-6′′, pyridine), 7.57–7.06 (m, 8H, C_6H_5/pyridine), 5.82–5.81 (d, 1H, H-3, imidazopyridazine, ^4J = 1.2), 5.76–5.73 (t, 1H, N*H*–CH_2, J = 5.8), 4.84–4.82 (d, 2H, CH_2–NH, J = 5.8), 2.23 (s, 3H, C(2)–CH_3) and 2.08–2.07 (d, 3H, C(4)–CH_3, ^4J = 1.2); δ_C (100.61 MHz, $CDCl_3$, 298 K, TMS) 158.59 (C-2′′, pyridine), 152.00 (C-7, imidazopyridazine), 149.52 (C-6′′, pyridine), 143.68 (C-2, imidazopyridazine), 139.30 (C-4, imidazopyridazine), 136.94 (C-4′′, pyridine), 136.44 (C-1′, C_6H_5), 130.70, 128.24 ($C_{o,m}$, C_6H_5), 128.91 (C-4a, imidazopyridazine), 127.38 (C_p, C_6H_5), 122.55, 122.50 (C-3′′, C-5′′, pyridine), 118.18 (C-5, imidazopyridazine), 112.01 (C-3, imidazopyridazine), 48.14 (CH_2), 21.85 (C(2)–CH_3) and 19.86 (C(4)–CH_3).

The ligands' synthesis was simplified for **5b** and **5c** by sparing the characterization and purification of the intermediates.

(5-*tert*-Butyl-2,4-dimethyl-imidazo[1,5-*b*]pyridazin-7-yl)pyridin-2-ylmethyl-amine hydrate (5b). 4.00 g (14.38 mmol) 2-amino-3-(3,3-dimethyl-2-oxo-butyl)-5-methyl-1,3,4-oxadiazolium bromide and 3.23 mL (31.68 mmol; 3.42 g) 2-(aminomethyl)pyridine were stirred for 1 min on a hot plate (250 °C) and allowed to cool to room temperature. Next, the reaction mixture was extracted with $CHCl_3$ (20 mL) to separate the insoluble 2-(aminomethyl)pyridine hydrobromide by-product. After filtration, the solvent was evaporated, the residue dissolved in 20 mL of ethanol, and 1.49 mL (1.44 g; 14.38 mmol)

acetylacetone and 2 mL concentrated HCl were added. After refluxing the orange solution for 2 h, the solvent was evaporated, and the red-orange product dissolved in water (20 mL) and filtrated. Then, 1 N NaOH was added to the filtrate until a weak basic reaction was observed and no more product precipitated. Afterwards, red viscid product **5b** (1.1 g, 25%) was dried *in vacuo*. Found: C, 65.75; H, 7.2; N 21.85. Calc. for $C_{18}H_{25}N_5O$: C, 65.9; H, 7.7; N 21.4%. δ_H (250.13 MHz, $CDCl_3$, 298 K, TMS) 8.47–8.44 (d, 1H, H-6′′, pyridine, J = 4.9), 7.51–7.47 (t, 1H, H-5′′, pyridine, J = 7.7), 7.36–7.33 (d, 1H, H-3′′, pyridine, J = 7.8), 7.07–7.04 (m, 1H, H-4′′, pyridine), 5.71–5.70 (d, 1H, H-3, imidazopyridazine, ^4J = 1.1), 5.43–5.38 (t, 1H, N*H*–CH_2, J = 6.2), 4.75–4.72 (d, 2H, C*H*$_2$–NH, J = 6.2 Hz), 2.43–2.32 (d, 3H, C(4)–C*H*$_3$, ^4J = 1.1), 2.13 (s, 3H, C(2)–C*H*$_3$) and 1.32 (s, 9H, C(C*H*$_3$)$_3$); δ_C (62.89 MHz, $CDCl_3$, 298 K, TMS) 158.91 (C-2′′, pyridine), 150.45 (C-7, imidazopyridazine), 148.88 (C-6′′, pyridine), 140.63 (C-2, imidazopyridazine), 138.16 (C-4, imidazopyridazine), 137.81 (C-4a, imidazopyridazine), 110.34 (C-3, imidazopyridazine), 48.31 (CH_2), 33.00 (*C*H–(CH_3)$_3$), 32.24 (CH–(*C*H$_3$)$_3$), 23.09 (C(4)–*C*H$_3$) and 20.95 (C(2)–*C*H$_3$); m/z = 309 (M^+), 294, 218, 203, 93, 65 and 41.

(2,4-Dimethyl-5-phenyl-imidazo[1,5-*b*]pyridazin-7-yl)-pyridin-3-ylmethyl-amine (5c). 2.50 g (8.39 mmol) 2-amino-5-methyl-3-phenacyl-1,3,4-oxadiazolium bromide and 1.88 mL (2.0 g; 18.46 mmol) 3-(aminomethyl)pyridine were stirred for 1 min on a hot plate (250 °C) and allowed to cool to room temperature. Next, water was added and the white precipitate recrystallized from water–ethanol (1 : 2). 3.00 g (9.76 mmol) *N*-{4-phenyl-2-[(pyridin-3-ylmethyl)amino]imidazo-1-yl}acetamide was dissolved in 10 mL of ethanol and 2–3 mL concentrated HCl was added. The solution was refluxed for 1 h and afterwards the solvent evaporated. The residue was dissolved in water and 1 N NaOH was added until a weak basic reaction occurred and no more product precipitated. The white product was filtered and dried. To a suspension of 1.48 g (5.58 mmol) 4-phenyl-N^2-pyridine-3-ylmethyl-imidazol-1,2-diamine in 7 mL glacial acetic acid was added 578 μL (5.58 mmol) acetylacetone and the reaction mixture refluxed for 2 h. Afterwards, the solvent was evaporated and 20 mL of water was added. After a few days, orange needles of **5c** (0.66 g, 24%) were obtained. Found; C, 72.7; H, 6.05; N, 21.7. Calc. for $C_{20}H_{19}N_5$: C, 72.9; H, 5.8; N, 21.3%. δ_H (250.13 MHz, $CDCl_3$ 298 K) 8.65 (s, 1H, C-2′′, pyridine), 8.46–8.45 (d, 1H, C-6′′, pyridine, J = 3.8), 7.75–7.62 (d, 1H, C-4′′, pyridine, J = 7.8), 7.52–7.40 (d, 2H, C$_o$ C_6H_5, J = 7.0), 7.36–7.30 (m, 4 H, C-5′′, pyridine/C_6H_5), 5.86 (s, 1H, H_3, imidazopyridazine), 4.98–4.94 (t, 1H, NH, J = 5.8), 5.21–5.16 (d, 2H, CH_2, J = 5.8), 2.23 (s, 3H, c(2)–C*H*$_3$) and 2.12 (s, 3H, C(4)–C*H*$_3$); δ_C (75.39 MHz, $CDCl_3$, 298 K) 151.22 (C-7, imidazopyridazine), 148.87 (C-2′′, pyridine), 148.11 (C-6′′, pyridine), 142.34 (C-2, imidazopyridazine), 138.53 (C-4, imidazopyridazine), 135.33 (C-3′′, pyridine), 135.20 (C-5′′, pyridine), 134.70 (C-1′, C_6H_5), 129.72, 127.36 (C$_{o,m}$, C_6H_5), 128.04 (C-4a, imidazopyridazine), 126.55 (C$_p$, C_6H_5), 122.92 (C-4′′, pyridine), 117.27 (C-5, imidazopyridazine), 111.15 (C-3, imidazopyridazine), 44.20 (CH_2), 20.86 (C(2)–*C*H$_3$) and 18.94 (C(4)–*C*H$_3$).

Preparation of 6a. To an orange solution of 0.55 g (1.66 mmol) (2,4-dimethyl-5-phenyl-imidazo[1,5-*b*]pyridazin-7-yl)pyridine-2-ylmethyl-amine (**5a**) in THF (20 mL) were added carefully (at −78 °C) 1.0 mL (1.66 mmol) *n*-butyllithium (1.6 M in *n*-hexane). The purple reaction mixture was stirred at −78 °C for another 30 min and was then allowed to warm to room temperature. At room temperature, an orange solution of 0.56 g (0.83 mmol) chloro-1,5-cyclooctadiene iridium(I) dimer in THF (10 mL) was added. The green solution was stirred for 16 h. Next, the solvent was evaporated and the residue dissolved in toluene, filtrated and washed with ether. At −30 °C, a dark green crystalline product **6a** (0.45 g, 44%) was obtained from the combined filtrates. Found: C, 53.2; H, 5.1; N, 10.7. Calc. for $C_{28}H_{30}IrN_5$: C, 53.5; H, 4.8, N, 11.1%. δ_H (300.13 MHz, CD_2Cl_2, 298 K, TMS) 8.03–8.02 (d, 2H, H-6′′, pyridine, J = 5.5), 7.72–7.67 (t, 1H, pyridine, J = 7.7), 7.50–7.45 (t, 2H, C_6H_5, J = 8.0), 7.35–7.21 (m, 3H, C_6H_5/pyridine), 7.12–7.10 (m, 2H, C_6H_5), 5.93, 5.90 (2 s, 1H, H-3, imidazopyridazine), 5.24, 5.22 (2s, 2H, C*H*$_2$–NH), 3.97 (br s, 2H, CH cod), 3.17 (br s, 2H, CH cod), 2.26 (s, 3H, C(2/4)–C*H*$_3$), 2.13 (s, 3H, C(4/2)–C*H*$_3$), 2.25–2.09 (br m, 4H, CH_2 cod) and 1.60–1.57 (br d, 4H, CH_2 cod); δ_C (75.48 MHz, CD_2Cl_2, 298 K, TMS) 146.60, 139.35, 137.22, 136.91, 134.38, 130.57, 130.42, 128.75 (C$_{o,m}$, C_6H_5), 128.04, 127.06, 122.22, 121.07, 118.64 (C-5, imidazopyridazine), 112.20, 111.93 (C-3, imidazopyridazine), 66.83 (4 × CH, cod), 55.14 (CH_2–N), 31.77 (4 × CH_2 cod), 21.70, 21.31 (C(2/4)–*C*H$_3$) and 19.84 (C(4/2)–*C*H$_3$).

Preparation of 6b. To an orange solution of 0.20 g (0.65 mmol) (5-*tert*-butyl-2,4-dimethyl-imidazo[1,5-*b*]pyridazin-7-yl)pyridin-2-ylmethyl-amine (**5b**) in THF (5 mL) was added a yellow solution of 0.21 g (0.32 mmol) 1,5-cyclooctadiene-methoxy iridium(I) dimer in THF (10 mL). The dark green solution was immediately concentrated to dryness *in vacuo*, yielding **6b** (0.39 g, 100%). Found: C, 51.5; H, 6.1; N, 11.2. Calc. for $C_{26}H_{34}IrN_5$: C, 51.3; H, 5.6; N, 11.5%. δ_H (250.13 MHz, [d_8]THF, 298 K, TMS) 8.15–8.13 (d, 1H, H-6′′, pyridine, J = 4.7), 7.59–7.53 (t, 1H, H-5′′, pyridine, J = 7.4), 7.39–7.36 (d, 1H, H-3′′, pyridine, J = 7.8), 7.07–7.02 (t, 1H, H-4′′, pyridine, J = 8.3), 5.76 (s, 1H, H-3, imidazopyridazine), 5.08 (s, 2H, C*H*$_2$–N), 4.12 (br s, 2H, CH cod), 3.55–3.49 (m, 2H, CH cod), 2.49 (d, 3H, C(2)–C*H*$_3$), 2.22 (s, 3H C(4)–C*H*$_3$), 2.03 (b s, 4H, CH_2 cod), 1.59 (b s, 4H, CH_2 cod) and 1.24 (s, 9H, $(CH_3)_3$); δ_C (75.39 MHz, C_6D_6, 298 K, TMS) 147.42, 139.91, 139.00, 136.33, 121.71, 121.18, 118.53 (C-5, imidazopyridazine), 110.04 (C-3, imidazopyridazine), 68.15 (CH_2–N), 57.04, 53.35, 52.33 (CH cod), 32.46, 31.95, 26.17 (CH_2 cod), 23.22 (C(2)–*C*H$_3$) and 21.00 (C(4)–*C*H$_3$). Although different solvents, such as C_6D_6, [d_8]THF and CD_2Cl_2, were tested and up to 10 000 scans performed, not all of the quaternary C atoms could be detected.

Preparation of 6c. To an orange solution of 0.56 g (1.70 mmol) (2,4-dimethyl-5-phenyl-imidazo[1,5-*b*]pyridazin-7-yl)pyridin-3-ylmethyl-amine (**5c**) in THF (15 mL) was added carefully (at −78 °C) 1.06 mL (1.70 mmol) *n*-butyllithium (1.6 M in *n*-hexane). The purple reaction mixture was stirred at −78 °C for another 30 min and then allowed to warm to room

temperature. At room temperature, an orange solution of 0.57 g (0.85 mmol) chloro-1,5-cyclooctadiene iridium(I) dimer in THF (10 mL) was added. The green solution was stirred for 16 h, the solvent evaporated, and the residue dissolved in toluene, filtrated and washed with ether. At −30 °C, from the combined filtrates in toluene, the dark green crystalline product **6c** (0.33 g, 32%) was obtained. Found: C, 53.25; H, 5.3; N, 10.7. Calc. for $C_{28}H_{30}IrN_5$: C, 53.5; H, 4.8; N 11.1%. δ_H (250.13 MHz, $CDCl_3$, 298 K, TMS) 8.61 (s, 1H, pyridine), 8.41–8.39 (d, 1H, pyridine, J = 4.3), 7.69–7.66 (d, 1H, pyridine, J = 5.5), 7.51–7.12 (m, 6H, pyridine/phenyl), 5.75 (s, 1H, H-3, imidazopyridazine), 4.95 (s, 2H, CH_2), 4.41 (br s, 2H, CH cod), 4.08 (br s, 2H, CH cod), 2.48 (s, 3H, C(2)–CH_3), 2.28 (s, 3H, C(4)–CH_3), 2.33–2.16 (m, 4H, CH_2 cod) and 1.82–1.61 (m, 4 H, CH_2 cod); δ_C (62.89 MHz, $CDCl_3$, 298 K, TMS) 160.41 (C-7, imidazopyridazine), 156.86 (C-3′′, pyridine), 148.78, 147.52 (C-2′′, C-6′′, pyridine), 141.90 (C-2, imidazopyridazine), 138.11 (C-4′′, pyridine), 136.15 (C-1′, C_6H_5), 134.54 (C-5′′, pyridine), 130.02, 127.94 ($C_{o,m}$, C_6H_5), 128.98 (C-4a, imidazopyridazine), 127.52 (C_p, C_6H_5), 119.20 (C-5, imidazopyridazine), 110.17 (C-3, imidazopyridazine), 62.86, 53.12 (CH cod), 46.03 (CH_2), 31.65, 30.40 (CH_2 cod), 20.29 (C(2)–CH_3) and 19.03 (C(4)–CH_3).

Preparation of 7a. Into a pressure tube containing an orange solution of 0.21 g (0.65 mmol) (2,4-dimethyl-5-phenyl-imidazo-[1,5-*b*]pyridazin-7-yl)pyridin-2-ylmethyl-amine (**5a**) in THF (10 mL) was added 0.21 g (0.32 mmol) 1,5-cyclooctadiene-methoxy iridium(I) dimer. The solution immediately changed its colour to dark green. The solution was heated at 50 °C for several days, while its colour changed to brown and red crystals formed. The crystalline material, **7a** (0.12 g, 30%), was filtered and washed three times with THF. Found: C, 53.2; H, 4.8; N, 10.8. Calc. for $C_{56}H_{58}Ir_2N_{10}$: C, 53.6; H, 4.7; N, 11.2%). **7a** is insoluble in all common solvents, such as methanol, isopropanol, CH_2Cl_2, THF, toluene, benzene and DMSO; due to this, no solution NMR data is available.) MAS solid state ^{13}C NMR: δ_C 166.31, 149.78, 148.29, 143.20, 137.02, 128.51, 122.91 (imidazopyridazine, pyridine, C_6H_5), 118.08 (C-5, imidazopyridazine), 110.73 (C-3, imidazopyridazine), 75.37 (CH), 67.64, 63.00, 54.69 (CH cod), 32.85, 26.28 (CH_2 cod) and 21.84 (C(2/4)–CH_3).

Preparation of 7b. Into a pressure tube containing an orange solution of 0.20 g (0.65 mmol) (5-*tert*-butyl-2,4-dimethyl-imidazo[1,5-*b*]pyridazin-7-yl)pyridin-2-ylmethyl-amine (**5b**) in hexane (10 mL) was added 0.21 g (0.32 mmol) 1,5-cyclo-octadiene-methoxy iridium(I) dimer. The solution immediately changed its colour to dark green. After several weeks, a red crystalline material, **7b** (0.11 g, 28%), was obtained. Found: C, 51.2; H, 5.7; N, 11.2. Calc. for $C_{52}H_{66}Ir_2N_{10}$: C, 51.3; H, 5.5; N, 11.5%. δ_H (250.13 MHz, [d_8]THF, 298 K, TMS) 9.38–9.35 (d, 1H, pyridine, J = 7.8), 8.14–8.11 (t, 1H, pyridine, J = 8.3), 7.59–7.57 (d, 1H, pyridine, J = 5.6), 7.19–7.14 (t, 1H, pyridine, J = 7.1), 5.75–5.74 (m, 2H, C*H*–N, H-3, imidazo-pyridazine), 2.69 (m, 2H, CH cod), 2.37–2.33 (m, 2H, CH cod), 2.59 (s, 3H, C(2/4)–CH_3), 1.79 (s, 3H, C(4/2)–CH_3), 1.99–1.86 (m, 4H, CH_2 cod), 1.49–1.28 (m, 4H, CH_2 cod) and 1.53 (s, 9H, $C(CH_3)_3$); δ_C (62.89 MHz, [d_8]THF, 298 K, TMS) 166.67, 148.12, 144.90, 136.04, 127.78 (C-7, C-2, C-4, C-4a, imidazopyridazine; C-1′′, pyridine), 143.56, 134.74, 126.71, 121.46 (CH, pyridine), 116.59 (C-5, imidazopyridazine), 109.85 (C-3, imidazopyridazine), 74.88 (CH), 65.56, 67.96, 54.03, 52.08 (CH cod), 33.42, 33.11, 30.17, 28.82 (CH_2 cod), 32.71 ($C(CH)_3$), 31.98 (C($CH)_3$), 22.40 and 20.55 (C(2/4)–CH_3).

Acknowledgements

We thank Wolfgang Saak, Germund Glatz and Tobias Bauer for their support in the X-ray laboratories.

References

1 T. Irrgang and R. Kempe, *Eur. J. Inorg. Chem.*, 2005, 4382–4392.
2 O. Vechorkin, Z. Csok, R. Scopelliti and X. Hu, *Chem.–Eur. J.*, 2009, **15**, 3889–3899; T. A. Betley, B. A. Quian and J. C. Peters, *Inorg. Chem.*, 2008, **47**, 11570–11582; Z. Csok, O. Vechorkin, S. B. Harkins, R. Scopelliti and X. Hu, *J. Am. Chem. Soc.*, 2008, **130**, 8156–8157; Z.-X. Wang and Li Wang, *Chem. Commun.*, 2007, 2423–2425; O. V. Ozerov, L. A. Watson, M. Pink and K. G. Caulton, *J. Am. Chem. Soc.*, 2007, **129**, 6003–6016; S. B. Harkins and J. C. Peters, *Inorg. Chem.*, 2006, **45**, 4316–4318; L. Fan, B. M. Foxman and O. V. Ozerov, *Organo-metallics*, 2004, **23**, 326–328.
3 D. S. Surry and S. L. Buchwald, *Angew. Chem., Int. Ed.*, 2008, **47**, 6338–6361; D. S. Surry and S. L. Buchwald, *Angew. Chem.*, 2008, **120**, 6438–6461; M. R. Buchmeiser, T. Schareina, R. Kempe and K. Wurst, *J. Organomet. Chem.*, 2001, **634**, 39–46; T. Schareina, G. Hillebrand, H. Fuhrmann and R. Kempe, *Eur. J. Inorg. Chem.*, 2001, 2421–2426; J. Silberg, T. Schareina, R. Kempe, K. Wurst and M. R. Buchmeiser, *J. Organomet. Chem.*, 2001, **622**, 6–18; J. F. Hartwig, *Synlett*, 1997, 329–340; S. Wagaw and S. L. Buchwald, *J. Org. Chem.*, 1996, **61**, 7240–7241.
4 H. Beyer and A. Hetzheim, *Chem. Ber.*, 1964, **97**, 1031–1036; A. Hetzheim and G. Müller, *Ger. Pat.* DD200023, 1983/1981; A. Hetzheim and G. Müller, *Chem. Abs.*, 1983, **99**, 88205; K. Peters, E.-M. Peters, A. Hetzheim and T. Irrgang, *Z. Kristallogr.-New Cryst. Struct.*, 2000, **215**, 381–382.
5 A. Hetzheim, O. Peters and H. Beyer, *Chem. Ber.*, 1967, **100**, 3418–3426; A. Hetzheim and G. Manthey, *Chem. Ber.*, 1970, **103**, 2845–2852; T. Irrgang, Dissertation, EMAU Greifswald, 2000.
6 G. M. Golubushina, G. N. Poshtaruk and V. A. Chuiguk, *Chem. Heterocycl. Compd.*, 1974, **10**, 735–739; G. M. Golubushina, G. N. Poshtaruk and V. A. Chuiguk, *Khim. Geterosikl. Soedin.*, 1974, **6**, 846–850; R. Brückner, J. P. Lavergne and P. Viallefont, *Liebigs Ann. Chem.*, 1979, 639–649; V. P. Kruglenko, A. A. Timoshin, V. A. Idzikovskii, N. A. Klyuev and M. V. Povstyanoi, *Ukr. Khim. Zh.*, 1988, **54**, 612–615.
7 H. Beyer, A. Hetzheim, H. Honek, D. Ling and T. Pyl, *Chem. Ber.*, 1968, **101**, 3151–3162.
8 X-Ray crystal structure analysis of **5a**. STOE-IDPS II equipped with an Oxford Cryostream low-temperature unit, graphite monochromatized Mo-K_α radiation, λ = 0.71069 Å. Structure solution and refinements were accomplished using SHELXL-97 (G. M. Sheldrick, *SHELXL-97, Program for Crystal Structure Analysis Release 97-2*, University of Göttingen, Germany, 1997), WinGX (L. J. Farrugia, *J. Appl. Crystallogr.*, 1999, **32**, 837–838) and SIR97 (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). Crystal size 0.40 × 0.19 × 0.07 mm, symmetry space group $P2_1/c$, monoclinic, a = 7.2845(5), b = 13.4530(8), c = 17.5656(14) Å, β = 92.241(9)°, V = 1720.1(2) Å^3, Z = 4, ρ_{calc} = 1.272 g cm^{-3}, 3256 reflections, 1989 independent reflections, R = 0.0391 [$I > 2\sigma(I)$], wR_2 (all data) = 0.0879, 226 parameters. CCDC 729909†.
9 X-Ray crystal structure analysis of **6a**. Crystal size 0.38 × 0.10 × 0.05 mm, symmetry space group $P\bar{1}$, triclinic, a = 7.9017(4), b = 8.9335(6), c = 16.8930(10) Å, β = 80.191(6)°, V = 1174.39(12) Å^3,

$Z = 2$, $\rho_{calc} = 1.778$ g cm^{-3}, 14134 reflections, 4192 independent reflections, $R = 0.0200$ [$I > 2\sigma(I)$], wR_2 (all data) = 0.0487, 620 parameters. CCDC 729910†.

10 R. Uson, L. A. Oro and J. A. Cabeza, *Inorg. Synth.*, 1985, **23**, 126–130.

11 X-Ray crystal structure analysis of **7a**. Crystal size 0.26 × 0.20 × 0.20 mm, symmetry space group $P2_1/n$, monoclinic, a = 15.5840(7), b = 22.6799(8), c = 26.5520(12) Å, β = 98.245(3)°, V = 9287.6(7) Å^3, $Z = 8$, $\rho_{calc} = 1.796$ g cm^{-3}, 17540 reflections, 9598 independent reflections, $R = 0.0501$ [$I > 2\sigma(I)$], wR_2 (all data) = 0.0924, 1233 parameters. CCDC 729911†.

12 X-Ray crystal structure analysis of **7b**. Crystal size 0.64 × 0.53 × 0.19 mm, symmetry space group $P2_1/n$, monoclinic, a = 14.2110(6), b = 23.5720(10), c = 14.6060(6) Å, β = 103.436(3)°, V = 4758.8(3) Å^3, $Z = 4$, $\rho_{calc} = 1.697$ g cm^{-3}, 8987 reflections, 6493 independent reflections, $R = 0.0361$ [$I > 2\sigma(I)$], wR_2 (all data) = 0.0764, 587 parameters. CCDC 729912†.

13 B. Blank and R. Kempe, *J. Am. Chem. Soc.*, 2010, **132**, 924–925; J. J. Klappa, A. E. Rich and K. McNeill, *Org. Lett.*, 2002, **4**, 435–437.

14 C. Koch, M. Kahnes, M. Schulz, H. Görls and M. Westerhausen, *Eur. J. Inorg. Chem.*, 2008, 1067–1077; M. Westerhausen, A. N. Kneifel and P. Mayer, *Z. Anorg. Allg. Chem.*, 2006, **632**, 634–638; M. Westerhausen, T. Bollwein, P. Mayer and H. Piotrowski, *Z. Anorg. Allg. Chem.*, 2002, **628**, 1425–1432; M. Westerhausen, T. Bollwein, K. Karaghiosoff, S. Schneiderbauer, M. Vogt and H. Nöth, *Organometallics*, 2002, **21**, 906–911; M. Westerhausen, T. Bollwein, N. Makropoulos, S. Schneiderbauer, M. Suter, H. Nöth, P. Mayer, H. Piotrowski, K. Polborn and A. Pfitzner, *Eur. J. Inorg. Chem.*, 2002, 389–404; M. Westerhausen, T. Bollwein, N. Makropoulos, T. M. Rotter, T. Habereder, M. Suter and H. Nöth, *Eur. J. Inorg. Chem.*, 2001, 851–857.

