PERGAMON

Polyhedron 20 (2001) 957–967

POLYHEDRON

www.elsevier.nl/locate/poly

Synthesis, solution and solid-state structure of Pd(II), Pt(II), Ir(III) and Zn(II) complexes with 5-pyridyl substituted *N*-methyl isoxazolidines

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Received 2 November 2000; accepted 29 January 2001

Abstract

Pd(II), Pt(II), Zn(II) and Ir(III) complexes with 5-pyridine substituted *N*-methyl isoxazolidines (4-(2-methyl-3-phenylisoxazolidin-5-yl)-pyridine (**L^1**), 2-(2-methyl-3-phenylisoxazolidin-5-yl)-pyridine (**L^2**), 2-(2-methyl-3-ferrocenylisoxazolidin-5-yl)-pyridine (**L^3**)) have been prepared and characterized by ^{1}H, ^{13}C, and ^{31}P NMR. The configurations of coordinated isoxazolidines have been assigned by the analysis of NMR coupling constants and by nuclear Overhauser measurements through 2D-ROESY experiments. The molecular structures of [Cp*Ir(**L^2**)Cl][BPh_4] (**6**) (Cp*-pentamethylcyclopentadienyl) and *trans*-[$PdCl_2$(**L^3**)PEt_3] (**8**) have been established by means of X-ray crystallography. The crystal structure of **6** consists of piano stool geometry with respect to the Ir(III) center with *N*,*N*-bidentate coordinated ligands. The six-membered chelate ring formed by Ir(1), N(1), C(5), C(6), O(1), N(2) possesses a 'twist-tub' conformation. The crystal structure of **8** consists of neutral square planar Pd(II) complexes. **L^3** is coordinated in a monodentate manner via the pyridine nitrogen atom. The isoxazolidine fragment of both compounds has an envelope conformation. NMR data are consistent with an *O*,*N*-bidentate coordination of **L^2** for [Zn(**L^2**)Cl_2] (**5**), while **L^1** act as a monodentate ligand through the nitrogen atom of the pyridine in [Zn(**L^1**)$_2Cl_2$] (**4**).

Keywords: Isoxazolidines; Complexes; X-ray data; NMR data

1. Introduction

Isoxazolidines have attracted a great deal of attention over recent years due to their applications in organic synthesis [1,2], the industrial uses they have [3] and the role they play as biologically active substances [4]. In contrast, the coordination chemistry of these five-membered heterocycles remains practically unexplored. A literature search revealed that previous to our work the molecular structure of only three complexes **1**–**3** of transition metals with isoxazolidine-containing ligands had been described [5–7]. Furthermore, in these compounds the heterocycle is not directly coordinated to the metal, except for the tungsten carbene **3** where the metal is bonded to the carbon adjacent to the nitrogen of the isoxazolidine ring. Recently, it has been shown that isoxazolidine derivatives can be used as mechanism-based inactivators of carboxypeptidase A, a zinc-containing protease [8].

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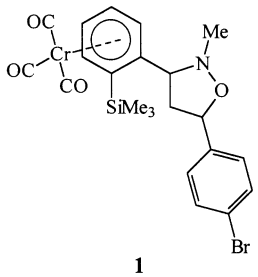
PII: S0277-5387(01)00711-2



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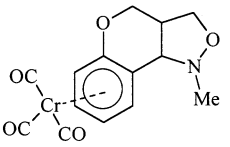

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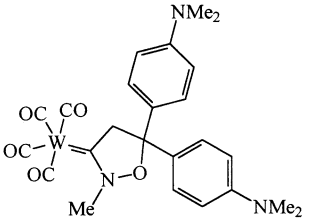

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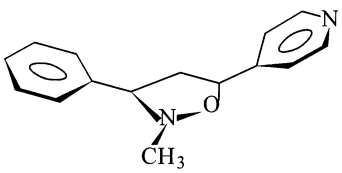
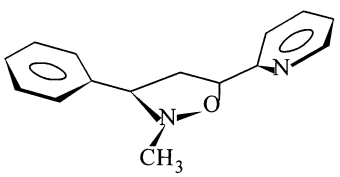
The highly flexible isoxazolidine ring [9] is an interesting ligand whose coordination properties may be tuned by introducing suitable substituents in the heterocycle. The substitution on the carbon skeleton renders the ligand chiral and the complexation to a metal could contribute to fix the conformation of the ring and therefore to define specific stereoelectronic interactions of relevance in asymmetric synthesis reactions [10].

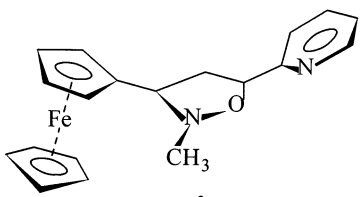
In order to enhance the coordination ability of the isoxazolidine heterocycle we decided to introduce a pyridine substituent on carbon 5. The isoxazolidine contains two neighboring σ-donor heteroatoms (*N*,*O*) and depending on the way of linking the pyridine moiety to the five-membered ring we have different coordination possibilities. We selected the 5-pyridine substituted *N*-methylisoxazolidines **L¹**–**L³** as ligands for complexation with d^8 and d^{10} transition metals.



L¹



L²



L³

The presence in **L¹** of a 4′-pyridine group implies that the compound may act as a monodentate ligand through any one of the three heteroatoms of the molecule. On the other hand, the 2′-pyridine substituent of **L²** and **L³** would allow the use of these reagents either as monodentate or as *N*,*O* versus *N*,*N* bidentate donor ligands affording five- or six-membered chelate rings through coordination to a metal.

We have recently described the syntheses of the above-mentioned organic ligands including a preliminary study of their coordinating behavior [11]. A series of palladium complexes were characterized based on their elemental analysis, UV–VIS and ^{1}H NMR spectroscopic data. The molecular structure of [Pd**L²**Cl_2] was determined by X-ray diffraction showing for the first time the link of an isoxazolidine ring to a metal [12]. In this particular case, **L²** was coordinated to palladium through the two nitrogen atoms.

Here we report the full details of the synthesis and characterization of a new complex of Pd(II), Pt(II), Zn(II) and Ir(III) with 5-pyridine substituted *N*-methylisoxazolidines **L¹**, **L²**, **L³**. The coordination pattern observed for these ligands was dependent of the metal used. According to the NMR spectra, the nitrogen atom of the pyridine is the preferred coordination site for **L¹** in the zinc complex [Zn(**L¹**)$_2$$Cl_2$] (**4**). **L²** showed in all cases a bidentate complexing behavior. Thus, **L²** is acting as an *N*,*N*-bidentate ligand in [Cp*Ir(**L²**)Cl][BPh_4] (**6**) and [Pt(**L²**)Cl_2] (**7**). For the iridium complex the assignment has been confirmed through its X-ray structure. However, the NMR spectra of [Zn(**L²**)Cl_2] (**5**) allows us to conclude that in this case **L²** is chelating the metal by *N*,*O* coordination. Interestingly, the crystal structure of *trans*-[$PdCl_2$(**L³**)PEt_3] (**8**) shows a coordination for **L³** exclusively through the nitrogen of the pyridine.

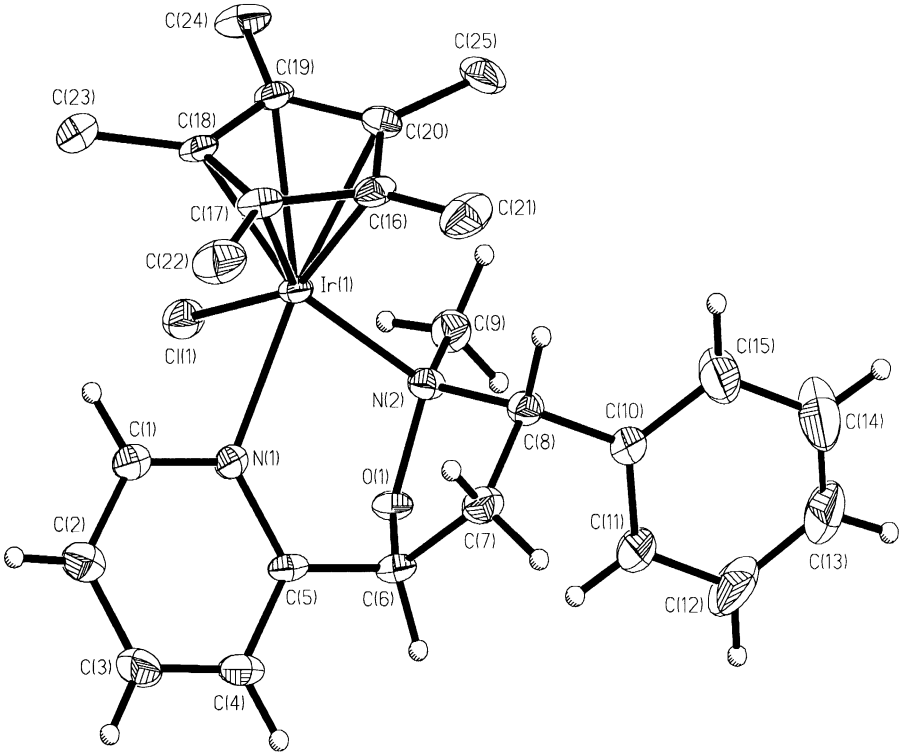


Fig. 1. View of the structure of the complex cation $[Cp^*Ir(L^2)Cl]^+$ with the numbering scheme adopted. Some hydrogen atoms are omitted for clarity and ellipsoids are drawn at 40% probability.

2. Results and discussion

2.1. Synthesis

The organic ligands $\mathbf{L^1}$–$\mathbf{L^3}$ were obtained as racemic mixtures of *cis*- and *trans*-isomers by [3 + 2] dipolar cycloaddition of *N*-methyl-*C*-phenylnitrone and *N*-methyl-*C*-ferrocenylnitrone with 2-vinylpyridine and 4-vinylpyridine [11,12]. For $\mathbf{L^1}$ and $\mathbf{L^2}$ the two stereisomers could not be separated and the crude mixtures (*trans*:*cis* ratio of 38:62 for $\mathbf{L^1}$and 75:25 for $\mathbf{L^2}$) were used directly in the complexation step. In the case of $\mathbf{L^3}$, the *trans*-isomer could be isolated through column chromatography [11]. The reaction of compounds $\mathbf{L^1}$–$\mathbf{L^3}$ with the selected metal halides was carried out by mixing hot solutions of both components in suitable solvents (see Section 4) in accordance with the scheme:

$$ZnCl_2 + n\mathbf{L}^m \rightarrow [Zn(\mathbf{L}^m)_nCl_2]$$

$$m = 1; n = 2; \mathbf{4}$$

$$m = 2; n = 1; \mathbf{5}$$

$$[Cp^*IrCl_2]_2 + 2\mathbf{L^2} + 2NaBPh_4 \xrightarrow[-2NaCl]{} 2Cp^*Ir(\mathbf{L^2})Cl]BPh_4:\mathbf{6}$$

$$K_2[PtCl_4] + \mathbf{L^2} \xrightarrow[-2KCl]{} \textit{cis}\text{-}[Pt(\mathbf{L^2})Cl_2]:\mathbf{7}$$

$$[PdPEt_3Cl_2]_2 + 2\mathbf{L^3} \rightarrow 2\ \textit{trans}\text{-}[Pd(\mathbf{L^3})PEt_3Cl_2]:\mathbf{8}$$

Compounds **4**–**8** were isolated in moderate to excellent yields through recrystallization of the reaction mixture. All the new complexes are air stable both as solids and in solution, except for compound **6** that decomposes in solution. They are readily soluble in chloroform, dichloromethane, acetonitrile, *N*,*N*-dimethylformamide, dimethyl sulfoxide and almost insoluble in hexane.

2.2. Crystal structures of $[Cp^*Ir(\mathbf{L^2})Cl][B(Ph)_4]$ (6) and $trans\text{-}[PdCl_2(trans\text{-}\mathbf{L^3})PEt_3]$ (8)

The yellow single crystals suitable for X-ray analysis were prepared by the slow liquid diffusion of a hexane–2-propanol solution into an acetone solution of **6**. The molecular structure of **6** is a salt formed by a cationic Ir(III) complex and a tetraphenylborate anion. The iridium ion adopts a nearly tetrahedral coordination with one chlorine atom, η^5-coordinated pentamethylcyclopentadienyl anion and the isoxazolidine ligand $\mathbf{L^2}$. The latter is bound to the metal center in a bidentate chelate manner via two nitrogen atoms. The six-membered chelate ring formed by Ir(1), N(1), C(5), C(6), O(1), N(2) has a twist-tub conformation. A view of the complex cation $[Cp^*Ir(\mathbf{L^2})Cl]^+$ is shown in Fig. 1. Selected bond distances and angles are given in Table 1. The crystal lattice consists of a racemate of {(3*R*,5*R*)-2-(2-methyl-3-phenyl-isoxazolidin-5-(yl)-pyridine} and

{(3*S*,5*S*) - 2 - (2 - methyl - 3 - phenylisoxazolidin - 5 - yl)-pyridine}. The crystal structure of **6** consists of the three-legged piano stool geometry polyhedrons of iridium ions. The plane of the pentamethylcyclopentadienyl fragment is slightly inclined to the Ir(1)–X vector (where X is a center of the pentamethylcyclopentadienyl cycle) with a corresponding angle of approximately 101.9° and a Ir(1)–X distance of 1.834 Å. Distances and angles of the iridium polyhedron of complex **6** are comparable with the corresponding related complexes with bidentate *N*,*N*-donors [13]. The distances O(1)–C(6), N(1)–C(5), N(2)–C(8), Ir(1)–Cl(1) (1.47(1), 1.39(1), 1.54(1), 2.433(2) Å) are elongated compared to their average values (1.43, 1.34, 1.47, 2.390 Å) [14] as a result of the coordination of the nitrogen atoms to the metal atom. The geometry parameters of the isoxazolidine ring in **6** are similar to those found for *cis*-[Pd(**L²**)Cl_2] [12] with deviations of O(1) and N(2) from the mean plane of others atoms of the isoxazolidine ring by 1.10 and 0.45 Å, respectively. The isoxazolidine heterocycle has an envelope conformation. The deviation of N(2) from the mean plane of atoms C(8)C(7)C(6)O(1) is 0.70 Å. The pyridine ring is located almost coplanar to C(6)–H(6) with a torsion angle for C(4)–C(5)–C(6)–H(6) equal to 14.2°. The methyl group has an equatorial orientation to the isoxazolidine ring (torsion angle C(6)–O(1)–N(2)–C(9) 165.2(6)°), while the phenyl group has an axial location (torsion angle C(6)–C(7)–C(8)–C(10) 95.7(8)°).

Table 1
Selected bond lengths (Å) and angles (°) for structure of the complex cation [Cp*Ir(L¹)Cl]⁺

Bond lengths			
Ir(1)–C(18)	2.190(8)	Ir(1)–N(1)	2.191(6)
Ir(1)–C(16)	2.210(8)	Ir(1)–N(2)	2.218(7)
Ir(1)–C(19)	2.218(7)	Ir(1)–C(20)	2.224(8)
Ir(1)–C(17)	2.226(8)	Ir(1)–Cl(1)	2.433(2)
O(1)–C(6)	1.47(1)	O(1)–N(2)	1.477(8)
N(2)–C(9)	1.49(1)	N(2)–C(8)	1.54(1)
C(6)–C(7)	1.56(1)	C(7)–C(8)	1.55(1)
Bond angles			
C(18)–Ir(1)–N(1)	109.5(3)	C(18)–Ir(1)–C(16)	65.3(3)
N(1)–Ir(1)–C(16)	114.0(3)	C(18)–Ir(1)–N(2)	161.4(3)
N(1)–Ir(1)–N(2)	89.0(2)	C(16)–Ir(1)–N(2)	105.6(3)
C(18)–Ir(1)–C(19)	38.5(3)	N(1)–Ir(1)–C(19)	147.4(3)
C(16)–Ir(1)–C(19)	64.7(3)	N(2)–Ir(1)–C(19)	123.4(3)
C(18)–Ir(1)–C(20)	64.4(3)	N(1)–Ir(1)–C(20)	152.2(4)
C(16)–Ir(1)–C(20)	38.3(3)	N(2)–Ir(1)–C(20)	98.1(3)
C(19)–Ir(1)–C(20)	38.3(3)	C(18)–Ir(1)–C(17)	38.5(3)
N(1)–Ir(1)–C(17)	94.2(3)	C(16)–Ir(1)–C(17)	38.6(3)
N(2)–Ir(1)–C(17)	141.1(3)	C(19)–Ir(1)–C(17)	63.9(3)
C(20)–Ir(1)–C(17)	63.7(3)	C(18)–Ir(1)–Cl(1)	95.9(2)
N(1)–Ir(1)–Cl(1)	83.9(2)	C(16)–Ir(1)–Cl(1)	157.0(2)
N(2)–Ir(1)–Cl(1)	88.2(2)	C(19)–Ir(1)–Cl(1)	92.5(2)
C(20)–Ir(1)–Cl(1)	122.9(3)	C(17)–Ir(1)–Cl(1)	130.7(2)
C(6)–O(1)–N(2)	104.4(5)	C(1)–N(1)–Ir(1)	123.5(5)
O(1)–N(2)–C(9)	103.6(6)	O(1)–N(2)–C(8)	100.9(5)
C(9)–N(2)–C(8)	114.4(6)	O(1)–N(2)–Ir(1)	109.7(4)
C(9)–N(2)–Ir(1)	113.1(5)	C(8)–N(2)–Ir(1)	113.8(5)
O(1)–C(6)–C(5)	109.5(6)	O(1)–C(6)–C(7)	106.6(6)
C(5)–C(6)–C(7)	113.6(7)	C(8)–C(7)–C(6)	102.9(7)
N(2)–C(8)–C(10)	116.1(7)	N(2)–C(8)–C(7)	101.3(6)
C(10)–C(8)–C(7)	112.9(7)		

Yellow single crystals of compound **8** suitable for X-ray analysis were grown by the slow diffusion of hexane into a chloroform solution containing this complex. The structure of **8** (Fig. 2, Table 2) consists of neutral square planar complexes of Pd(II) in which two chlorine atoms and two neutral ligands (**L³** and PPh_3) are *trans*-coordinated. The crystal lattice consists of {(3*S*,5*S*) - 2 - (2 - methyl - 3 - ferrocenylisoxazolidin - 5 - yl)-pyridine}. The ligand **L³** is coordinated to the metal center in a monodentate manner via the pyridine nitrogen atom. The bond angles at the palladium atom are in the range of 88.1(1)–93.68(6) and their sum is close to 360°. The distances N(1)–C(5), N(1)–C(1) (1.362(7) and 1.376(8) Å; averaged values 1.337 Å) are elongated, while the bonds Pd(1)–N(1), Pd(1)–Cl(1), Pd(1)–P(1) (2.173(5), 2.346(2), 2.271(1) Å) are shorter than their average values (2.089, 2.326 and 2.315 Å) as a result of the coordination of the pyridine nitrogen atom and the phosphorus atom to the palladium ion. The isoxazolidine ring has an envelope conformation. The deviation of N(2) from the mean plane of atoms C(8)C(7)C(6)O(1) is 0.72 Å. The pyridine ring is coplanar to O(1)–C(6) (torsion angle N(1)–C(5)–C(6)–O(1) 179.0(5)°) and located *anticlinal* to C(7)–C(8) (torsion angle C(5)–C(6)–C(7)–C(8) 127.7(5)°). The methyl group has an equatorial orientation on the isoxazolidine ring (torsion angle C(19)–N(2)–O(1)–C(6) 169.9(5)°). The ferrocenyl fragment is also found in an *anticlinal* arrangement with the C(6)–C(7) bond (torsion angle C(6)–C(7)–C(8)–C(9) 143.6(5)°).

2.3. NMR studies

^1H and ^{13}C NMR data of the complexes **4**–**6** are collected in Table 3. We will focus on complexes **4** and **5** because both contain the same metal and therefore the electronic effects induced on the respective organic ligands will be similar and could be used as a tool of diagnostic value in the identification of the coordination mode of the same ligands to different metals.

The ^1H NMR spectrum of **4** shows the presence of two diastereomeric complexes formed by coordination of the zinc to the *trans*-(*trans*-**L¹**) and *cis*-isoxazolidines (*cis*-**L¹**) in an approximate ratio of 40:60, respectively. The complexation of both ligands is easily deduced from the variations of the proton chemical shifts compared with the free isoxazolidines. Thus, hydrogens *ortho* to the pyridine nitrogen appear as a multiplet centered at 8.8 and 8.77 ppm for the minor [Zn(*trans*-**L¹**)Cl_2] (**4a**) and major [Zn(*cis*-**L¹**)Cl_2] (**4b**) stereoisomers, respectively. These values represent a low field shift of 0.2–0.17 ppm relative to **L¹** [$\delta(H^0_{py})$ 8.60 ppm,

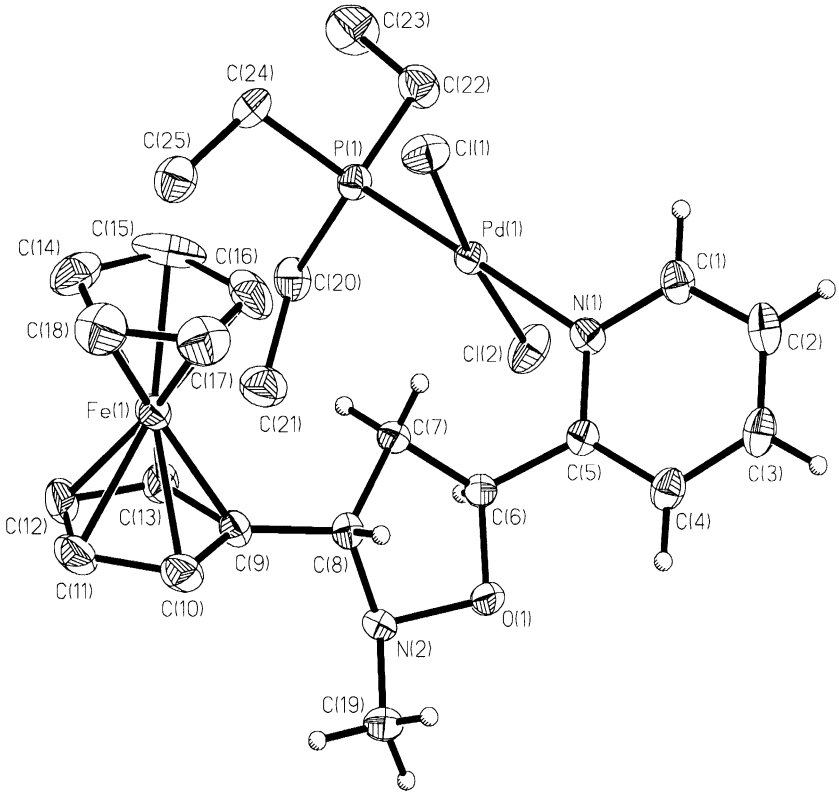


Fig. 2. View of the structure of complex **8** with the numbering scheme adopted. Some hydrogen atoms are omitted for clarity and ellipsoids are drawn at 40% probability.

overlapped for the two isomers at 300 MHz]. The *meta* protons of the pyridine are also significantly deshielded ($\Delta\delta$ 0.2 and 0.28 for the *trans* and *cis* isomer, respectively). In contrast, the aliphatic protons of the isoxazolidine ring and the methyl group are not affected by the complexation and are found practically at the same field as the corresponding non-coordinated **L[1]** isomers. Therefore, we can conclude that **L[1]** behaves as a monodentate ligand and is coordinated only via the pyridine nitrogen atom.

It has been shown in a series of 3,5-disubstituted isoxazolidines, that the relative stereochemistry of the stereogenic centers can be assigned based on the analysis of the coupling constants and NOEs observed for the proton at C-5 [15]. For the compounds referred to in that study this proton appeared systematically as a double doublet ($^3J_{HH}$ 3 ~ 6 Hz) for the *cis* isomer, and a doublet for the *trans* ($^3J_{HH}$ ~ 5 Hz) one. Unfortunately, both isomers **4a**,**b** produced the same multiplicity pattern for H-5, a double doublet, with vicinal couplings of the same magnitude ($^3J_{HH}$ 6 and 9 Hz) (see Table 3), precluding the assignment of the configuration of the isoxazolidine moiety. To our delight the 2D-NOESY spectrum of the mixture **4a** and **4b** allowed us to assign the stereochemistry of the two isomers. The *cis* arrangement of the substituents on C-3 and C-5 of the heterocycle in the major isomer **4b** is deduced from the intense cross peak observed between H-3 and H-5.[1] Consequently, compound **4a** is the *trans*-**L[1]** isomer. This assignment is corroborated by the small NOE correlation between H3 and the *meta* protons of the pyridine ring at δ 7.64. Additionally, in the *cis* isomer **4b** the methylene proton at δ 2.30 shows the expected

Table 2
Selected bond lengths (Å) and angles (°) for structure of complex **8**

Bond lengths			
Pd(1)–N(1)	2.173(5)	Pd(1)–P(1)	2.271(1)
Pd(1)–Cl(2)	2.331(2)	Pd(1)–Cl(1)	2.346(2)
N(2)–C(19)	1.469(8)	N(2)–O(1)	1.491(7)
N(2)–C(8)	1.513(8)	O(1)–C(6)	1.462(7)
C(6)–C(7)	1.57(1)	C(7)–C(8)	1.559(8)
Bond angles			
N(1)–Pd(1)–P(1)	175.3(1)	N(1)–Pd(1)–Cl(2)	88.1(1)
P(1)–Pd(1)–Cl(2)	87.24(6)	N(1)–Pd(1)–Cl(1)	90.9(1)
P(1)–Pd(1)–Cl(1)	93.68(6)	Cl(2)–Pd(1)–Cl(1)	174.13(7)
C(24)–P(1)–Pd(1)	117.1(2)	C(22)–P(1)–Pd(1)	108.4(2)
C(20)–P(1)–Pd(1)	113.0(2)	C(5)–N(1)–Pd(1)	124.3(3)
Cl(1)–N(1)–Pd(1)	116.6(4)	C(19)–N(2)–O(1)	104.5(5)
C(19)–N(2)–C(8)	113.2(5)	O(1)–N(2)–C(8)	100.9(4)
C(6)–O(1)–N(2)	102.5(4)	O(1)–C(6)–C(5)	109.0(4)
O(1)–C(6)–C(7)	104.8(4)	C(5)–C(6)–C(7)	115.0(5)
C(8)–C(7)–C(6)	103.6(5)	C(9)–C(8)–N(2)	111.2(4)

[1] The signal for H3 in both isomers is practically overlapped. Only H-3 of the *cis* isomer can give a NOE enhancement on H-5.

Table 3
^{1}H and ^{13}C NMR data of complexes **4–8**

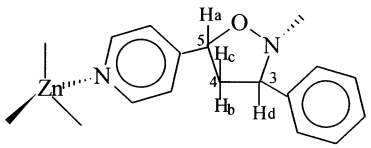
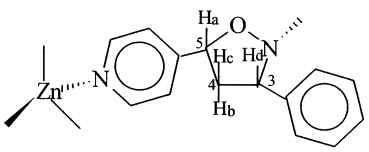
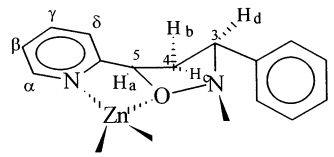
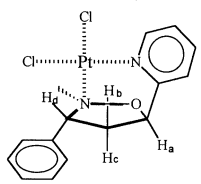
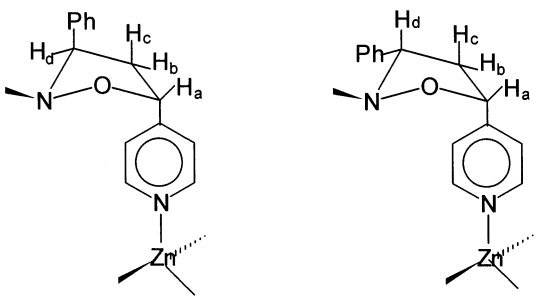
Compound	^{1}H NMR (δ)	Assignment	^{13}C NMR (δ)	Assignment
[Zn(*trans*-**L^1**)$_2$Cl$_2$] **4a**, minor isomer, ($CDCl_3$, 20°C) 	2.52 (ddd, 12.3, 8.3, 6.3 Hz, 1H)	H_b	43.03	NCH_3
	2.74 (s, 3H)	NCH_3	47.79	C^4
	2.96 (bm [a], 1H)	H_c	72.80	C^3
	3.72 (bm [a], 1H)	H_d	76.49	C^5
	5.37 (dd, 9.2, 6.3 Hz, 1H)	H_a	122.71	C^β
	7.20–7.50 (m, 5H)	Ph	127.61	*p*-Ph
	7.64 (m, 2H)	β-py	128.84	*m*-Ph
	8.8 (m, 2H)	α-py		
			137.46	*ipso*-Ph
			148.66	C^α
			158.69	*ipso*-Py
[Zn(*cis*-**L^1**)$_2$Cl$_2$] **4b**, major isomer, ($CDCl_3$, 20°C) 	2.30 (ddd, 12.3, 9.5, 6.0 Hz, 1H)	H_b	43.03	NCH_3
	2.68 (s, 3H)	NCH_3	47.79	C^4
	3.29 (ddd, 12.3, 9.0, 7.3 Hz, 1H)	H_c	73.85	C^3
	3.72 (bm [a], 1H)	H_d	75.67	C^5
	5.30 (dd, 9.0, 6.0 Hz, 1H)	H_a	122.45	C^β
	7.20–7.50 (m, 5H)	Ph	127.61	*p*-Ph
	7.69 (m, 2H)	β-py	128.29	*o*-Ph
	8.77 (m, 2H)	α-py	128.80	
			137.41	*ipso*-Ph
			148.57	C^α
			155.50	*ipso*-Py
[Zn(*trans*-**L^2**)Cl$_2$] **5a**, major isomer ($CDCl_3$, 20°C) 	2.70 (s, 3H)	NCH_3	41.76	NCH_3
	3.13 (dd, 13.6, 9.5 Hz, 1H)	H_c	43.86	C^4
	3.34 (ddd, 13.6, 7.9, 5.8 Hz, 1H)	H_b	69.38	C^3
	5.18 (d, 7.9 Hz, 1H)	H_d	77.95	C^5
	5.58 (dd, 9.5, 5.8 Hz, 1H)	H_a	123.15	Cδ
	7.30–7.5 (m, 5H)	Ph	125.51	C^β
	7.5 (m, overlapped, 1H)	δ-Py	129.11	*m*-Ph
	7.63 (m, overlapped, 2H)	β-Py	129.32	*o*-Ph
	8.03 (m, 1H)	γ-Py	129.42	*p*-Ph
	8.78 (m, 1H)	α-Py	134.66	*ipso*-Ph
			140.84	C^γ
			150.80	C^α
			159.84	*ipso*-Py
[Pt(*trans*-**L^2**)Cl$_2$] **7a**, ($CDCl_3$, 20°C) 	3.13 (s, 3H)	NCH_3	48.22	NCH_3
	3.15 (m, 1H)	H_c	41.04	C^4
	4.31 (ddd, 13.6, 9.7, 4.5, 1H)	H_b	78.80	C^3
	5.45 (dd, 9.7, 4.5, 1H)	H_a	80.0	C^5
	6.05 (d, 8.0, 1H)	H_d	124.76–138.86	$C^{\beta,\gamma,\delta}$ + Ph
	7.2–7.6 (m, 8H)	Ph + 3HPy	154.28	C^α
	9.78 (d, 5.2 Hz, 1H)	α-Py	155.72	*ipso*-Py

Table 3 (*Continued*)

Compound	^{1}H NMR (δ)	Assignment	^{13}C NMR (δ)	Assignment
[Pt(*cis*-**L²**)Cl$_2$] **7b**, (CDCl$_3$, 20°C)	3.57 (s, 3H)	NCH_3	51.15	NCH_3
	3.11 (m, 1H)	H_c	38.46	C^4
	3.73 (ddd, 13.6, 9.7, 4.5, 1H)	H_b	78.65	C^5
	4.0 (dd, 9.7, 4.5, 1H)	H_d	83.43	C^3
	5.29 (dd, 9.7, 4.5, 1H)	H_a	124.76–138.86	$C^{\beta,\gamma,\delta}$ + Ph
	7.2–8.1 (m, 8H)	Ph + 3HPy	154.49	C^α
	10.13 (d, 5.2 Hz, 1H)	α-Py	155.11	*ipso*-Py
Trans-[PdCl$_2$(*trans*-**L³**)PEt$_3$] **8**, (CDCl$_3$, 20°C)	1.34 (m, 9H)	–CH$_3$, (PEt$_3$)	8.35	–CH$_3$, (PEt$_3$)
	1.99 (m, 6H)	–CH$_2$–, (PEt$_3$)	16.26	–CH$_2$–, (PEt$_3$)
	2.69 (s, 3H)	NCH_3	43.23	NCH_3
	3.05 (m [a], 1H)	H_c	46.02	C-4
	3.53 (m [a], 1H)	H_b	66.33	*ipso*-Cp
	4.33 (m [a], 1H)	H_a	68.04	α-Cp
	4.13 (s, 9H)	Fc	68.83	unsubstituted-Cp
	6.30 (m [a], 1H)	H_d	69.53	β-Cp
	7.28 (q, 4.5 Hz, 1H)	γ-Py	77.92	C-3
	7.78 (d, 3.8 Hz, 2H)	β-Py	83.49	C-5
	8.80 (m [a], 1H)	α-Py	122.59	C^δ
			123.33	C^β
			138.30	C^γ
			150.10	C^α

[a] Broad multiplet.

cross peaks with both the pyridine and the phenyl substituents corresponding to their *syn* orientation (δ H4^{anti} 3.29). For the *trans* isomer **4a** the highest shielded methylene proton is the one *syn* to the pyridine ring (cf. δ H4$^{syn(py)}$ 2.52 vs H4$^{anti(py)}$ 2.96).



4a **4b**

The proton spectrum of complex **5** also shows a mixture of two compounds in a ratio 88:12. Due to the low concentration of the minor component and the overlap of some signals with those of the major one, we could achieve the structural assignment of only the major species labeled as **5a**. We have followed a similar analysis to that carried out with complex **4**. First, we have identified the coordination mode of the ligand **L²** by comparing the ^{1}H chemical shifts of the complex and the free ligand. The complexation produces a low field shift of the pyridine protons ($\Delta\delta \sim 0.1$–0.3 ppm) and the proton at C-5 ($\Delta\delta$ 0.2 ppm). On the contrary, the methyl protons remain practically unaffected ($\Delta\delta$ 0.03 ppm). These shift effects are consistent with a coordination of **L²** in a bidentate manner via the nitrogen of the pyridine and the oxygen of the isoxazolidine. It is worth noting the large downfield shift of the proton at C-3 (δ 5.19 for **5a** vs 3.72 for **L²**) which suggests the proximity of this proton to the positively charged metal ion. This type of interaction would be possible assuming a *trans* arrangement of the substituents on the isoxazolidine ring, as is proved to be the case (see below).

The stereochemistry of the stereogenic carbons C-3 and C-5 could not be determined from the multiplicity pattern or the magnitude of the coupling constants of the respective protons. H-5 appeared at δ 5.58 again as a double doublet with vicinal couplings of 6.2 and 9.2 Hz. Interestingly, zinc coordination of **L¹** in **4** and of **L²** in **5** produce similar effects on the couplings of H-5 with its neighbor protons. The proton H-3 exhibit only one vicinal coupling $^3J_{H3H4} = 7.5$ Hz (Table 3). This is a common property of isoxazolidine systems, where the dihedral angle between H-3 and Hβ-4 is close to 90° and therefore the corresponding coupling vanishes [15].

The 2D-NOESY spectra of **5ba** do not allow us to identify the stereochemistry. All signals show negative cross peaks with all other protons, which is a typical spin diffusion problem [16]. The relative *trans* arrangement of the substituents at C-3/C-5 of the isoxazolidine

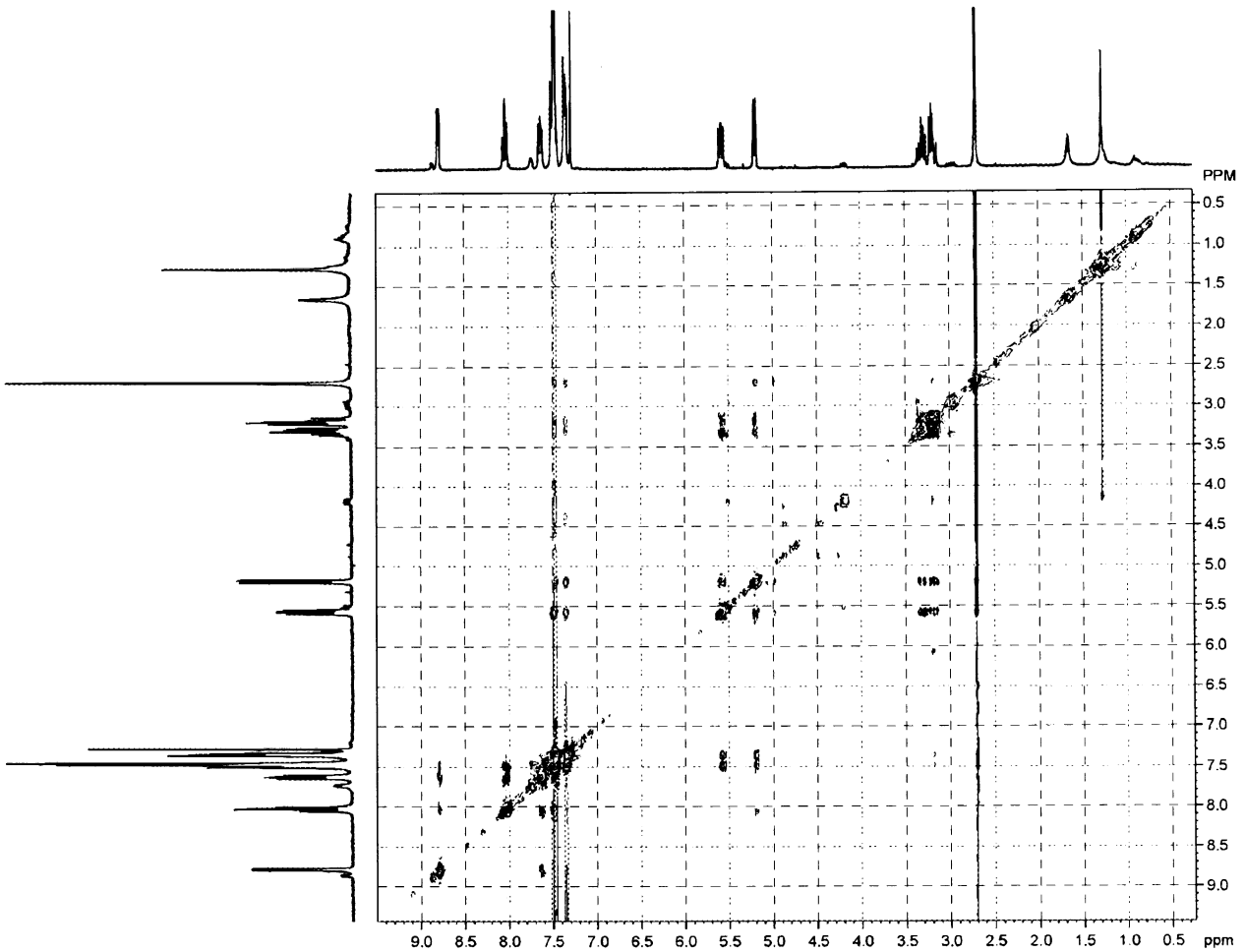
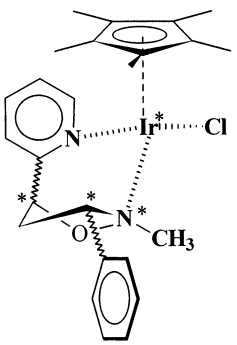
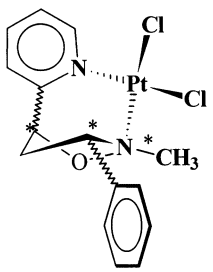


Fig. 3. The 2D-ROESY spectrum of [Zn($\mathbf{L^2}$) Cl_2] complex (300 MHz, $CDCl_3$).

ring could be established by acquiring the 2D-ROESY [17] spectrum (Fig. 3). Thus, H-3 shows a cross peak with pyridine protons at δ 8.03 (H-4′) and 7.5 (H-3′), while H-5 exhibits a ROE cross peak with the *ortho* protons of the phenyl ring on carbon C-3. Moreover, the cross peaks of H-3 and H-5 with the methylene protons of C-4 allow us to assign $H4^{syn(py)}$ and $H4^{anti(py)}$ as the multiplets centered, respectively at δ 3.19 and 3.30 ppm.



6



7

The ^1H NMR spectra of complexes **6** and **7** show a low-field shift of almost all resonances of $\mathbf{L^2}$ compared to those of the 'free' ligand. Relatively large shifts are observed for the protons of the *N*-methyl group, the pyridine substituent and the proton at C-5. The deshielding observed for the protons close to the nitrogen atoms of the isoxazolidine allows us to conclude that in these complexes the organic ligand is coordinated to the metal in a bidentate manner via the two nitrogen atoms. Analogous shift effects have been previously observed for complex [Pd$\mathbf{L^2}Cl_2$], whose molecular structure, determined by X-ray diffraction, showed that the ligand acts as a *N*,*N*-bidentate donor.

Complex **6** has four stereocenters (C*-3, C*-5, Ir* and N*) and the ^1H NMR spectrum indicates that a complex mixture of compounds is present. A group of peaks in the range δ 1.25–2.05 can be assigned to the methyl protons of Cp* and the tetraphenylboron anion shows several multiplets in the aromatic region δ 6.8–7.1. Unfortunately, the signals of the isoxazolidine ring are broadened and partially overlapped. Furthermore, the relative intensity of *ortho* protons of the pyridine

Table 4
Crystal data and structure refinement for compounds **6** and **8**

Compound	**6**	**8**
Chemical formula	$C_{47}H_{50}ClN_2OBIr$	$C_{25}H_{35}Cl_2N_2OFePPd$
M	897.35	643.67
T (K)	293(2)	293(2)
λ (Å)	0.71073	0.71073
Crystal system	triclinic	monoclinic
Space group	$P\bar{1}$	$P2_1$
Unit cell dimensions		
a (Å)	12.697(5)	8.405(2)
b (Å)	13.632(5)	16.394(4)
c (Å)	14.564(6)	10.433(3)
α (°)	96.36(1)	
β (°)	113.84(0)	96.94(2)
γ (°)	89.73(1)	
U (Å^3)	2289.3(16)	1427.0(6)
Z	2	2
D_{calc} (Mg m^{-3})	1.302	1.498
μ (mm^{-1})	3.008	1.401
Reflections collected, unique	8262, 7878	3780, 3563
R_{int}	0.0788	0.0494
R_1	0.0707	0.0418
wR_2	0.1757	0.1077

rings is very low, indicating that in solution the sample decomposes to a large extent.

The ^{1}H NMR spectrum of **7** consists of a mixture of four compounds in a relative ratio 14:18:50:18 determined through the integrals of the *ortho* pyridine protons appearing at δ 10.1, 9.74, 9.39, 9.18 ppm, respectively. On standing in the $CDCl_3$ solution, the two signals at δ 9.39, 9.18 ppm disappear and the intensity of the lowest field multiplet increases to afford a new mixture of two components in a ratio 1:1. The chemical shifts and multiplicity patterns of the signals are very similar to the corresponding signals of complex [Pd**L**^{2}Cl$_2$] previously characterized. The strong low field shift of the *ortho* protons of the pyridine ring ($\Delta\delta$ H°_{cis} 1.6, $\Delta\delta$ H°_{trans} 1.2 ppm) and the *N*-methyl protons ($\Delta\delta$ Me_{cis} 0.88, $\Delta\delta$ Me_{trans} 0.41 ppm) compared to the free ligands are strong indications that in both cases the two nitrogen atoms are involved in the coordination to the platinum. The NOESY spectrum showed that the two compounds correspond to the expected *cis–trans* isomers derived from the orientation of the substituents in the isoxazolidine ring (see assignment in Table 3). In order to understand the evolution of the original four components in solution to a new mixture of two species we can assume that no epimerization occurs by allowing the sample to stand in chloroform. A reasonable explanation would be to consider that the compounds with the H°_{py} protons absorbing at δ 9.39, 9.18 ppm are complexes where the metal is coordinated to *cis*-**L**^{2} either through only one nitrogen atom of the ligand and/or in a bidentate manner involving the pyridine nitrogen and the oxygen atom of the isoxazolidine ring. On standing in solution the thermodynamically favored *N*,*N*-complex is formed.

Complex [$PdCl_2$(*trans*-**L**^{3})PEt_3] **8** is isolated as a single species as deduced from the only signal observed in the ^{31}P spectrum at δ 36.5 corresponding to the coordinated PEt_3. The ^{1}H NMR spectrum differs significantly from that of the ligand. Upon complexation the protons of the pyridine substituent of isoxazolidine *trans*-**L**^{3} shift to low field (δ: α-Py 8.55, 7.67 β-Py, 7.15 γ-Py for *trans*-**L**^{3}; α-Py 8.80, 7.78 β-Py, 7.28 γ-Py for **8**). This shift is a clear indication of the coordination of palladium to the nitrogen atom of the pyridine group. The signal of the methyl group in complex and in 'free' ligand appears at the same shift at δ 2.69 ppm. These results suggests that *trans*-**L**^{3} is acting as a monodentate ligand through the nitrogen of the pyridine, in agreement with the X-ray structure discussed above. Interestingly, the signals of all the protons of the isoxazolidine ring are also found at lower field (cf. Table 3, δ 3.52 (H-3), 5.28 (H-5), 3.27 and 2.75 (H-4) for *trans*-**L**^{3}). The η^1 coordination of the ligand and the deshielding effects observed can be explained by considering that the large size of the ferrocenyl substituents sterically hinders the approach of palladium to the nitrogen of the isoxazolidine, though its proximity to the five-membered heterocycle promotes a deshielding of the protons of the ring.

3. Conclusions

We have demonstrated that pyridyl-substituted *N*-methyl isoxazolidines are suitable ligands to form complexes with halides of metals of the Groups IIB and VIIIB. In the case of 5-(4-pyridyl)-substituted *N*-methyl isoxazolidines the coordination takes place exclusively through the nitrogen of the pyridine. On the other hand, 5-(2-pyridyl)-substituted *N*-methyl isoxazolidines are more versatile ligands and all heteroatoms may be used for coordination to a metal. We have shown they may act either as monodentate ligands through the nitrogen of the pyridine or bidentate ligands (*N*,*N*; *N*,*O*), where the metal coordinates to the pyridine and one of the heteroatoms of the isoxazolidine ring. The different coordination modes observed may be explained in terms of the hardness of the metal and the constraints derived by the steric hindrance in its surroundings. Current work is aimed to validate this hypothesis by studying a larger set of complexes of the same metals with a large variety of isoxazolidine ligands. The configuration and conformation of the isoxazolidine ring have been determined by NOE NMR experiments and confirmed by means of the corresponding X-ray structure for complexes **6** and **8**.

4. Experimental

All solvents were used as supplied or distilled using standard methods. The compounds $ZnCl_2$, $K_2[PtCl_4]$, $[Cp^*IrCl_2]_2$, *trans*-$[PdCl_2PEt_3]_2$ were obtained from Fluka Chemical Company and Aldrich Chemical Company Ltd. The organic ligands **L¹**, **L²** **L³** have been prepared according to previously described procedures [11,12].

^1H (300 MHz), ^{13}C (75.5 MHz), ^{31}P (121.49 MHz) NMR spectra were recorded at room temperature on a Bruker Avance DPX300 spectrometer equipped with a 5 mm QNP-Z probe (^1H, ^{13}C, ^{15}N, ^{31}P). Deuterochloroform was used as the solvent. Chemical shifts are given relative to internal tetramethylsilane for ^1H and ^{13}C spectra, and to external 85% phosphoric acid for ^{31}P spectra. Standard Bruker software and microprograms were applied for all NMR experiments. The sweep width covered was 3000 Hz for ^1H, digitalized in 16 K, and 15,000 Hz for ^{13}C, digitalized in 64 K.

Phase sensitive 2D ROESY spectra were recorded with a spin-lock field of 2.5 kHz, a mixing time of 200 ms and 256 increments. The 2048×1024 final matrix was apodized by a sine squared of factor 2 in both dimensions prior to Fourier transformation.

5. Crystal structure determination

For compounds **6** and **8** a four circle Siemens P3/PC automated diffractometer with graphite monochromatized Mo Kα radiation ($\lambda = 0.7173$ Å) was employed. Crystallographic data are presented in Table 4. The structures for **6** and **8** were solved by direct methods using the SHELXTL PLUS set of programs [18], and refined by full-matrix least-squares methods. For both structures all H atoms were placed in geometrically calculated positions and included in the refinement using the riding model with $U_{iso}(H) = 1.2U_{eq}(C)$ with the exception of H atoms of methyl groups ($U_{iso}(H) = 1.5U_{eq}(C)$). For **6** the final $wR(F^2)$ was 0.176 (on F^2 for 7978 reflections), with conventional $R_1 = 0.071$ (on F for 6980 reflections with $I > 2\sigma(I)$), for 503 parameters, goodness of fit = 1.045. For **8** the final $wR(F^2)$ was 0.108 (on F^2 for 3563 reflections), with conventional $R_1 = 0.042$ (on F for 3144 reflections with $I > 2\sigma(I)$), for 303 parameters, goodness of fit = 1.017.

*[Zn(L¹)₂Cl₂] (**4**).* $ZnCl_2$ (0.034 g, 0.25 mmol) dissolved in a mixture of warm 2-propanol (5 ml) and acetone (2 ml) was added to a warm 2-propanol solution (5 ml) of **L¹** (0.12 g, 0.50 mmol) The reaction mixture was stirred at room temperature for 12 h. Solvent evaporation under vacuum afforded a white solid residue, that was recrystallized from chloroform to yield **4** 0.142 g (0.23 mmol, 92%) (*Anal.* Found: C, 58.12; H, 5.02; N, 8.92. Calc. for $C_{30}H_{32}Cl_2N_4O_2Zn$: C, 58.41; H, 5.23; N, 9.08%).

*[Zn(L²)Cl₂] (**5**).* A warm 2-propanol solution (5 ml) of **L²** (0.129 g, 0.54 mmol) was added to a warm mixture of 2-propanol (5 ml) and acetone (2 ml) containing $ZnCl_2$ (0.074 g, 0.54 mmol). The reaction mixture was stirred at ~50°C for 0.5 h. After cooling to room temperature, the white precipitate of **5** was filtered off, washed with cold 2-propanol and recrystallized from chloroform to afford a white solid **5** 0.119 g (0.32 mmol, 59%) (*Anal.* Found: C, 48.00; H, 4.53; N, 7.34. Calc. for $C_{15}H_{16}Cl_2N_2OZn$: C, 47.84; H, 4.28; N, 7.44%).

*[Cp*Ir(L²)Cl][BPh₄] (**6**).* A chloroform–acetonitrile solution (1:1 v/v, 5 ml) of $NaBPh_4$ (0.078 g, 0.23 mmol) was added to a mixture of chloroform (5 ml) and acetonitrile (5 ml) containing **L²** (0.055 g, 0.23 mmol) and $[Cp^*IrCl_2]_2$ (0.091 g, 0.114 mmol). The color changed immediately from orange to yellow. The solution was stirred at room temperature for 1 h. The white precipitate of NaCl was filtered off and the filtrate was evaporated under reduced pressure. The yellow solid residue was recrystallized from chloroform to afford crystalline **6** 0.177 g (0.20 mmol, 87%) (*Anal.* Found: C, 63.14; H, 5.93; N, 2.99. Calc. for $C_{47}H_{50}ClN_2OBIr$: C, 62.91; H, 5.62; N, 3.12%).

*cis-[Pt(L²)Cl₂] (**7**).* A warm aqueous methanolic solution (1:1 v/v, 10 ml) of **L²** (0.095 g, 0.40 mmol) was added to a mixture of warm methanol (5 ml) and water (5 ml) containing $K_2[PtCl_4]$ (0.164 g, 0.40 mmol). The reaction mixture was stirred at ~50°C for 0.5 h. After evaporating of the methanol, the solution was cooled to room temperature. The brown precipitate of **7** was filtered, washed with cold aqueous methanol and recrystallized from dichloromethane to afford a yellow solid. Yield: 0.127 g (0.25 mmol, 63%) (*Anal.* Found: C, 35.80; H, 3.33; N, 5.50. Calc. for $C_{15}H_{16}Cl_2N_2OPt$: C, 35.59; H, 3.19; N, 5.53%).

*trans-[PdCl₂(L³)PEt₃] (**8**).* *trans*-Bis(triethylphosphine)palladium(II) chloride (0.044 g, 0.80 mmol) in dichloromethane (5 ml) was added to a dichloromethane solution (2 ml) of **L³** (0.052 g, 0.40 mmol); the yellow mixture was stirred at room temperature for 12 h. Addition of 15 ml hexane to the reaction mixture produced the precipitation of **8**, that was filtered and dried in vacuo to afford a yellow solid 0.085 g (0.32 mmol, 88%) (*Anal.* Found: C, 46.65; H, 5.48; N, 4.35. Calc. for $C_{25}H_{35}Cl_2N_2OFePPd$: C, 46.10; H, 5.59; N, 4.35%).

6. Supplementary material

Crystallographic data for the structural analysis have been deposited with the Cambridge Crystallographic Data Centre, CCDC No. 139277 (for complex **6**) and

CCDC No. 139278 (for complex **8**). Copies of this information may be obtained free of charge from The Director, CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: 44-1223-336033; e-mail: deposit@ccdc.cam.ac.uk or www: http://www.ccdc.cam.ac.uk).

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