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Complexation of 3-(2-pyridyl)substituted *N*-methyl isoxazolidine with Pd(II), Zn(II) and Cu(II): stereochemistry of co-ordination compounds in solution and solid-state

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Abstract

2-Methyl-3-(2-pyridyl)isoxazolidine (**L**) and its Pd(II), Zn(II) and Cu(II) complexes have been prepared and characterized by IR, ^{1}H, ^{13}C 1D and HMBC, NOESY 2D NMR spectroscopies. The stereochemistry of the 'free' and co-ordinated ligand has been assigned by nuclear Overhauser effect (NOE). The molecular structures of [Zn(*cis*-**L**)Cl_2]·0.5$CHCl_3$ (**2a**), [Zn(*cis*-/*trans*-**L**)Cl_2] (**2a**–**b**) and [Cu(*cis*-/*trans*-**L**)Cl_2]$_2$ (**4a**–**b**) have been established by means of X-ray crystallography. The crystal structure of **2a** consists of a racemic mixture of *cis*-**L** (3*SR*,5*RS*), while the crystal structure of **2b** comprises a racemate of *cis*- and *trans*-isomeric forms. For both complexes the zinc atoms adopt nearly tetrahedral co-ordination with two chlorine atoms and *N*,*N*-bidentate co-ordinated **L**. The crystal structure of **4a**–**b** consists of dinuclear [Cu(*cis*-/*trans*-**L**)Cl_2]$_2$ moieties with *N*,*N*-bidentate co-ordinated ligands. The square pyramidal co-ordination spheres of copper ions are completed by a bridging chloride ligand at the apex (Cu–Cl 2.79, 2.82 Å).

Keywords: Isoxazolidines; Pd-, Zn-, Cu-complexes; Syntheses; X-ray; NMR

1. Introduction

Isoxazolidine systems are important in bioscience as intermediates for organic synthesis of a number of natural compounds: 1,3-aminoalcohols, alkaloids and amino sugars [1–4]. Their pharmacological properties [5–9] have stimulated interest on the control of diastereo- and enantioselectivity in 1,3-nitrone-olefine dipolar cycloaddition as the isoxazolidine preparation method. The last decade has revealed a great deal of research on improving methods for stereoselective synthesis of isoxazolidines [10–18]. Thus, nitrone-tricarbonyl(η^6-arene)chromium(0) adducts undergo cycloaddition reactions in a highly stereoselective manner yielding *cis*-3,5-disubstituted isoxazolidines [19,20]. Very recently, Cu(II)- and Zn(II)-bisoxazoline [21] as well as (BINOL)–AlMe complexes (BINOL = 2,2′-dihidroxy-1,1′-binaphthyl) [22] have been utilized as catalysts in the enantioselective synthesis of isoxazolidines through 1,3-dipolar cycloadditions of nitrones to electron-rich olefins. The stereochemistry of the products has been explained by assuming the formation of a complex between the nitrone and the catalysts.

Our interest is focused on co-ordination chemistry of the isoxazolidine systems concerning possible application of the metal complexes for the asymmetric 1,3-dipolar cycloaddition reactions between alkenes and acyclic nitrones [23,24]. Elaboration of this approach is closely related with investigation of isoxazolidine co-ordination compounds themselves because it may give significant information for understanding the importance of inherent structure of the co-ordination compounds for 1,3-dipolar cycloaddition and processes of purification and separation of isomeric isoxazolidines.

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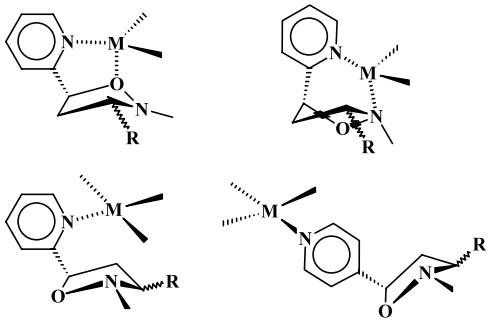
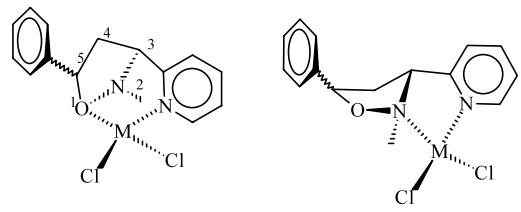
Recently, we have shown that the pyridyl substituted *N*-methyl isoxazolidines readily give co-ordination compounds with d-metal ions [23,25]. The 5-(2-pyridyl)substituted isoxazolidine core may act either as monodentate ligand through the nitrogen atom of the pyridyl substituent or as bidentate ligand (*N*,*N* for Pd, Pt; *N*,*O* for Zn). In each case, the metal co-ordinates the pyridyl nitrogen atom and one of the heteroatoms of the isoxazolidine ring (Scheme 1).

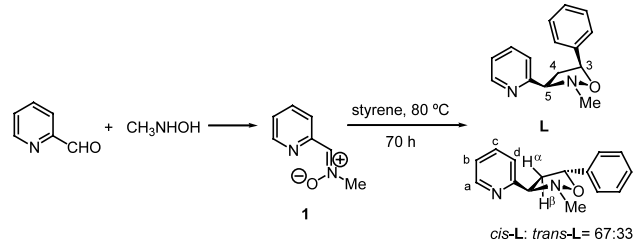
Herein we present our results on the synthesis of isomeric *cis*-/*trans*-2-methyl-3-(2-pyridyl)-5-phenylisoxazolidine (**L**) and the study of its co-ordination behavior with Pd, Zn and Cu metal ions. The presence of one co-ordinatively active substituent on the isoxazolidine ring may give rise to different co-ordination modes to the metals (Scheme 2).



Scheme 1. Co-ordination features of 5-pyridyl substituted isoxazolidines.



Scheme 2. The possible modes of chelate complexation for 2-methyl-3-(2-pyridyl)-5-phenylisoxazolidine.



Scheme 3. NOE correlations of **L**.

2. Results and discussion

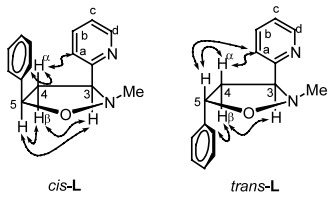
2.1. Synthesis and structural identification of *L*

The organic ligand **L** was obtained through the [3+2] dipolar cycloaddition of *N*-methyl-*C*-(2-pyridyl)nitrone (**1**) to freshly distilled styrene in refluxing toluene–benzene (1:1, v/v) (Scheme 3). Analysis of the crude reaction showed the presence of two products in an approximate ratio 67:33 which were identified, respectively, as the *cis*- and *trans*-stereoisomers of 2-methyl-3-(2-pyridyl)-5-phenylisoxazolidine, i.e. a single regioisomer was observed. Column chromatography on silicagel (acetone–hexane 1:1) of the crude product afforded pure *cis*-/*trans*-**L** without altering the relative ratio of isomers.

The IR spectrum of **L** is similar to the related 5-(2-pyridyl)isoxazolidine [23] and shows characteristic strong absorptions at 2990–3090 (ν(C–H) ph, py), 1490–1590 (ν(C=C) ph, py), 2780–2960, 1335–1475 cm^{-1} (ν(C–H) and δ(C–H) of the aliphatic groups).

The ^{1}H NMR spectrum of **L** suggests the presence of two diastereomers. The analysis of the coupling constants in combination with nuclear Overhauser effects (NOEs) (Scheme 3) allows facile determination of both the configurations for 3,5-disubstituted isoxazolidine systems.

The ^{1}H NMR spectrum measured in DMSO-d_6 showed separate signals for the most significant protons of both stereoisomers (overlap occurred for the phenyl protons and H(c) of the 2-pyridyl group). The HMQC and HMBC correlation spectra allowed the straightforward assignment of the ^{1}H and ^{13}C NMR spectra. The use of $CDCl_3$ as solvent produced only minor changes in the chemical shifts of the signals (see Section 4). In principle, the relative stereochemistry of the stereogenic centers of **L** could be established from the observed coupling constants for the proton at C(5) as it has been shown for several 3,5-disubstituted isoxazolidines [26] (H(5) proton appeared as a double doublet ($^3J_{HH}$ 3–6 Hz) for the *cis* isomer, and a doublet for the *trans* derivative ($^3J_{HH}$ $\sim$5 Hz). Unfortunately, in our case both isomers produced the same multiplicity pattern for H(5), a triplet, with the same vicinal couplings ($^3J_{HH}$ 7.7 Hz), precluding to draw any stereochemical conclusion of the configuration of the isoxazolidine moiety. The 2D NOESY spectrum of the *cis*-, *trans*-**L** mixture allowed to solve the ambiguity. The major isomer is assigned the *cis* stereochemistry based on the intense correlation observed between H(3) (δ 4.19) and H(5) (δ 5.32). Additionally, the methylene proton at δ 2.46 (H(4α), dt, $^2J_{HH}$ 12.3, $^3J_{H4\alpha H3} = {}^3J_{H4\alpha H5}$ 6.9 Hz) shows the expected cross peaks with both the 2-pyridyl (δ(H^d) 7.58, see Scheme 2 for labeling) and the phenyl (δ(H^o) 7.3) substituents corresponding to their *syn* orientation. Consequently, the double triplet at δ 3.23 ($^2J_{HH}$ 12.3, $^3J_{H4\beta H3} = {}^3J_{H4\beta H5}$ 7.7 Hz) is assigned to the other methylene proton H(4β) (Scheme 4).



Scheme 4. H(α) defines the proton *syn* to the 2-pyridyl ring.

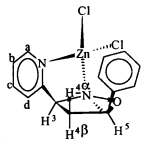
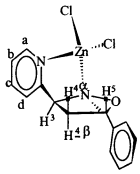
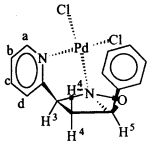
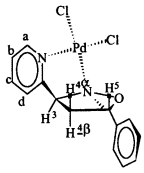
Therefore, the minor component of the mixture is the *trans* isomer. This assignment is supported by the NOE correlation between H(3) (δ 4.04, dd, $^3J_{H4\alpha H3}$ 6.5, $^3J_{H4\beta H3}$ 7.7 Hz) and the *ortho* protons (δ 7.42, m) of the phenyl ring linked to C(5) (δ 5.07, t, $^3J_{HH}$ 7.7 Hz). Again, the methylene protons are assigned from the respective correlations with H(3) and H(5) (see Section 4).

2.2. Synthesis and structural identification of complexes 2–4

Complexation of the isomeric mixture of isoxazolidines **L** with Pd(II), Zn(II) and Cu(II) metal ions was carried out by heating an alcoholic solution of the ligand with the corresponding zinc and copper chloride, or with the $Na_2[PdCl_4]$ complex for palladium. Cooling the reaction mixture to room temperature afforded a precipitate which was separated, washed with alcohol (methanol or 2-propanol) and dried, yielding the metal complexes [Zn(*cis*-/*trans*-**L**)Cl_2] (**2a**–**b**), [Pd(*cis*-/*trans*-**L**)Cl_2] (**3a**–**b**), and compound [Cu(*cis*-/*trans*-**L**)$Cl_2]_2$ (**4a**–**b**). All the compounds are air stable both as solids and in solution. They are readily soluble in acetonitrile, *N*,*N*-dimethylformamide, dimethyl sulfoxide and almost insoluble in hexane.

The ^{1}H and ^{13}C NMR data of compounds **2**–**4** acquired in DMSO-d_6 are given in Table 1. The assignment of the proton and carbon atom signals was easily made based on the analysis of the 1D (^{1}H, APT) and 2D (HMQC, HMBC) spectra. The NMR spectra of the complexes showed two sets of signals derived from the co-ordinated isomeric *cis*- and *trans*-isoxazolidines. The ratio of isomers was similar to that of the free ligand **L** (average *cis*–*trans* ratio of 65:35). As for the free ligand, the relative stereochemistry of the two carbon stereogenic centers was unambiguously deduced from the NOE correlations observed in the corresponding NOESY spectra. In all cases H(3) and H(5) exhibited a strong dipolar correlation for the *cis* isomers, while for the *trans* derivatives a correlation of low intensity was

Table 1
^{1}H and ^{13}C NMR data of complexes **2**–**3**

Compound		^{1}H NMR (δ, ppm; *J* Hz)		Assignment	^{13}C NMR (δ, ppm)		Assignment
2a	**2b**	**2a**	**2b**		**2a**	**2b**	
		2.79 (s, 3H)	2.71 (s, 3H)	CH_3	44.63	44.38	C-4
		2.45 (m, 1H)	2.61 (m, 1H)	$H^{4\alpha}$	44.71	44.94	CH_3
		3.29 (m, 1H)	2.89 (m, 1H)	$H^{4\beta}$	72.70	73.11	C-3
		4.33 (m, 1H)	4.16 (m, 1H)	H^3	78.25	79.28	C-5
		5.36 (t, ^3J 7.6, 1H)	5.03 (dd, ^3J 7.2, 1H)	H^5	122.19	122.59	C^d
		7.1-7.3 (m, 3H)	7.1-7.3 (m, 3H)	*m,p*-Ph,	123.22	123.48	C^b
		7.24 (m, 2H)	7.48 (m, 2H)	*o*-Ph	126.95	127.09	*o*-Ph
		7.38 (m, 1H)	7.4 (m, 1H)	H^b	127.98	128.22	*p*-Ph
		7.6 (m, 1H)	7.6 (m, 1H)	H^d	128.67	128.82	*m*-Ph
		7.85 (m, 1H)	7.87 (m, 1H)	H^c	137.92	137.92	C^c
		8.54 (m, 1H)	8.57 (m, 1H)	H^a	141.35	140.85	*Ipso*-Ph
					149.00	149.23	C^a
					160.01	159.0	*Ipso*-Py
3a	**3b**	**3a**	**3b**		**3a**	**3b**	
		3.42 (s, 3H)	3.37 (s, 3H)	CH_3	45.16	43.82	C-4
		2.77 (dt, ^3J 8.4, ^2J 12.7, 1H)	3.07 (ddd, ^3J 6.8, 7.8, ^2J 12.7 1H)	$H^{4\alpha}$	53.35	52.09	CH_3
		3.42 (m, 1H)	2.96 (ddd, ^3J 7.8, 10.0, ^2J 12.7, 1H)	$H^{4\beta}$	81.60	81.37	C-3
		5.32 (dd, ^3J 7.4, 8.4, 1H)	5.12 (dd, ^3J 7.1, 10.0, 1H)	H^3	81.73	82.12	C-5
		5.58 (dd, ^3J 6.3, 8.4, 1H)	5.92 (t, ^3J 7.8, 1H)	H^5	123.74	123.34	C^d
		7.35 (m, 2H)	7.35 (m, 2H)	*m*-Ph	125.23	125.49	C^b
		7.42 (m, 1H)	7.42 (m, 1H)	*p*-Ph	127.21	127.75	*o*-Ph
		7.53 (m, 1H)	7.52 (m, 2H)	*o*-Ph	128.97	129.09	*m*-Ph
		7.61 (ddd, ^4J 1.4, ^3J 6.0, 7.9, 1H)	7.67 (ddd, ^4J 1.2, ^3J 6.0, 7.8, 1H)	H^b	129.03	129.38	*p*-Ph
		7.71 (dd, ^4J 1.4, ^3J 7.9, 1H)	7.77 (dd, ^4J 1.2, ^3J 7.8, 1H)	H^d	137.48	137.01	*Ipso*-Ph
		8.15 (dt, ^4J 1.8, ^3J 7.9, 1H)	8.21 (dt, ^4J 1.4, ^3J 7.8, 1H)	H^c	141.10	141.31	C^c
		8.88 (dd, ^4J 1.8, ^3J 6.0, 1H)	8.89 (dd, ^4J 1.4, ^3J 6.0, 1H)	H^a	149.23	149.63	C^a
					162.16	161.42	*Ipso*-Py

detected between H(5) and the *ortho* protons of the phenyl substituent on C(3). The methylene protons H(4) were again assigned through their respective correlations with the vicinal protons H(3)/H(5).

The complexation of both ligands is evidenced by the variations of the proton chemical shifts compared with the free isoxazolidines. In compounds **2a**–**b**, the co-ordination of **L** to Zn(II) produce a broadening of all proton signals and a partial overlap of the aromatic protons corresponding to both stereoisomers. Clearly, for **2a**–**b** co-ordination occurred in the proximity of H(3). This is the only proton of the isoxazolidine moiety showing a significant deshielding effect due to the complexation ($\Delta\delta$H(3)^{cis} (**2a**–**L**) = 0.14 ppm; $\Delta\delta$H(3)^{trans} (**2b**–**L**) = 0.12 ppm). Variations on H(4) and H(5) are lower than 0.05 ppm. In principle, the effect on H(3) is compatible with **L** acting either as a *N*-monodentate or *N*,*N*-bidentate ligand. Co-ordination through the nitrogen of the pyridine is supported by the deshielding observed for the protons H(b) ($\Delta\delta$H(b)^{cis} (**2a**–**L**) = 0.07 ppm; $\Delta\delta$H(b)^{trans} (**2b**–**L**) = 0.05 ppm) and H(c) ($\Delta\delta$H(c)^{cis} (**2a**–**L**) = 0.16 ppm; $\Delta\delta$H(c)^{trans} (**2b**–**L**) = 0.17 ppm) of the heterocycle. On the other hand, co-ordination to the nitrogen of the isoxazolidine would prevent rapid inversion of the heteroatom, originating a new stereogenic center which relative configuration could be identified in the NOESY spectrum. Indeed, the methyl protons of *cis*-**L** in **2a**–**b** (δ 2.74) showed a dipolar correlation with H(3) and H(5), while for *trans*-**L** only the correlation of the methyl protons at δ 2.67 with H(3) was detected. These evidences indicate that in complex **2a**–**b** the ligand is bonded to the metal in a *N*,*N*-bidentate mode.

The same trends have been observed in the proton spectrum of the mixture of isomers **3a**–**b**. In this case, co-ordination of **L** to palladium produced a much stronger effect on the proton spectrum of isoxazolidine and all signals appeared deshielded compared to the free ligand. The low field shift ranged from $\Delta\delta$(**3a**–**b**–**L**) = 0.19–0.85 ppm for H(4), H(5) and the methyl protons. Even though, the shifts for H(3) exceeded 1 ppm ($\Delta\delta$H(3)^{cis} (**3**–**L**) = 1.13 ppm; $\Delta\delta$H(3)^{trans} (**3**–**L**) = 1.08 ppm). Again, the deshielding of the pyridine protons (see Table 1) and the NOEs measured for the methyl protons are consistent with **L** being doubly co-ordinated to the metal through the nitrogen atoms.

The differences in line-broadening and range of chemical shifts variations promoted by Zn versus Pd co-ordination to **L** suggest that in DMSO the solvent is competing with the ligand **L** for binding to the zinc ion and therefore, the proton spectrum of **2a**–**b** corresponds to the average situation derived from the exchange between free and complexed ligand which is rapid on the NMR time scale.

2.3. Crystal structures of [Zn(*cis*-**L**)Cl_2]·0.5$CHCl_3$ (**2a**), [Zn(*cis*-/*trans*-**L**)Cl_2] (**2a**–**b**) and [Cu(*cis*-/*trans*-**L**)Cl_2]$_2$ (**4**)

The NMR results described above indicated that compounds **2**–**4** are mixtures of stereoisomers. Recrystallization of the crude products obtained opens up different possibilities for these systems: resolution of racemic *cis*-/*trans*-isomers, self-resolution of enantiomers and co-crystallization of *cis*- and *trans*-isomers. In all cases, further insight into the structural characteristic of the co-ordination complexes could be gained through the analysis of the solid state structure (Fig. 1).

Recrystallization of **2** by slow diffusion of 2-propanol into a chloroform solution of the metal complex afforded two products suitable for X-ray analysis. One of them, [Zn(*cis*-**L**)Cl_2]·0.5$CHCl_3$ (**2a**) consists of racemic mixture of *cis*-**L** (3*SR*,5*RS*), while another one [Zn(*cis*-/*trans*-**L**)Cl_2] (**2a**–**b**) is a racemate including both *cis*- and *trans*-forms. These structures are built up from molecular [Zn(**L**)Cl_2] species, but are dramatically different in the spatial arrangement of the molecules (Figs. 2 and 3). There is a lack of strong intermolecular interactions such as co-ordination or hydrogen bonding. However, the packing pattern for the compounds is determined by stacking interactions between two aromatic functions of the ligand. Complex **2a** consists of dimers sustained by π–π, or face-to-face, stacking between pyridine groups. These weak but commonly encountered interactions contribute to crystal structures of aromatic species [27] and may be loosely regarded as a kind of 'supramolecular synthon' [28]. Two pyridine rings are parallel and the distance between their planes is approximately 3.28 Å. Two molecular complexes being paired in such a way (Py–Py) evidently generates a center of inversion in the triclinic crystal, and the lattice comprises a racemic mixture.

Stacking interactions are also present in the packing pattern of complex **2a**–**b** but between different functions, the pyridyl and phenyl groups. They also appear to be parallel with interplanar separation at approximately 3.45 Å. From this point of view, structures **2a** and **2a**–**b** may be regarded as supramolecular isomers (see Fig. 3). For complex **2a**–**b**, face-to-face stacking interactions connect the molecules into 1D chain and unsymmetric pairing results in the absence of a center of inversion. Nevertheless, the crystal also comprises both enantiomers that are related by a glide plane.

Another important feature of the structure **2a**–**b** is disordering of the C(3)–Ph fragment. This disorder has a clear chemical significance as two components correspond to *cis*- and *trans*-isomeric forms of the ligand. Refinement of partial occupancies suggested contributions of *cis*- (72%) and *trans*- (28%) isomers similar to that found in the crude product mixture (67 and 33%). Both isomers have actually the same size, shape and

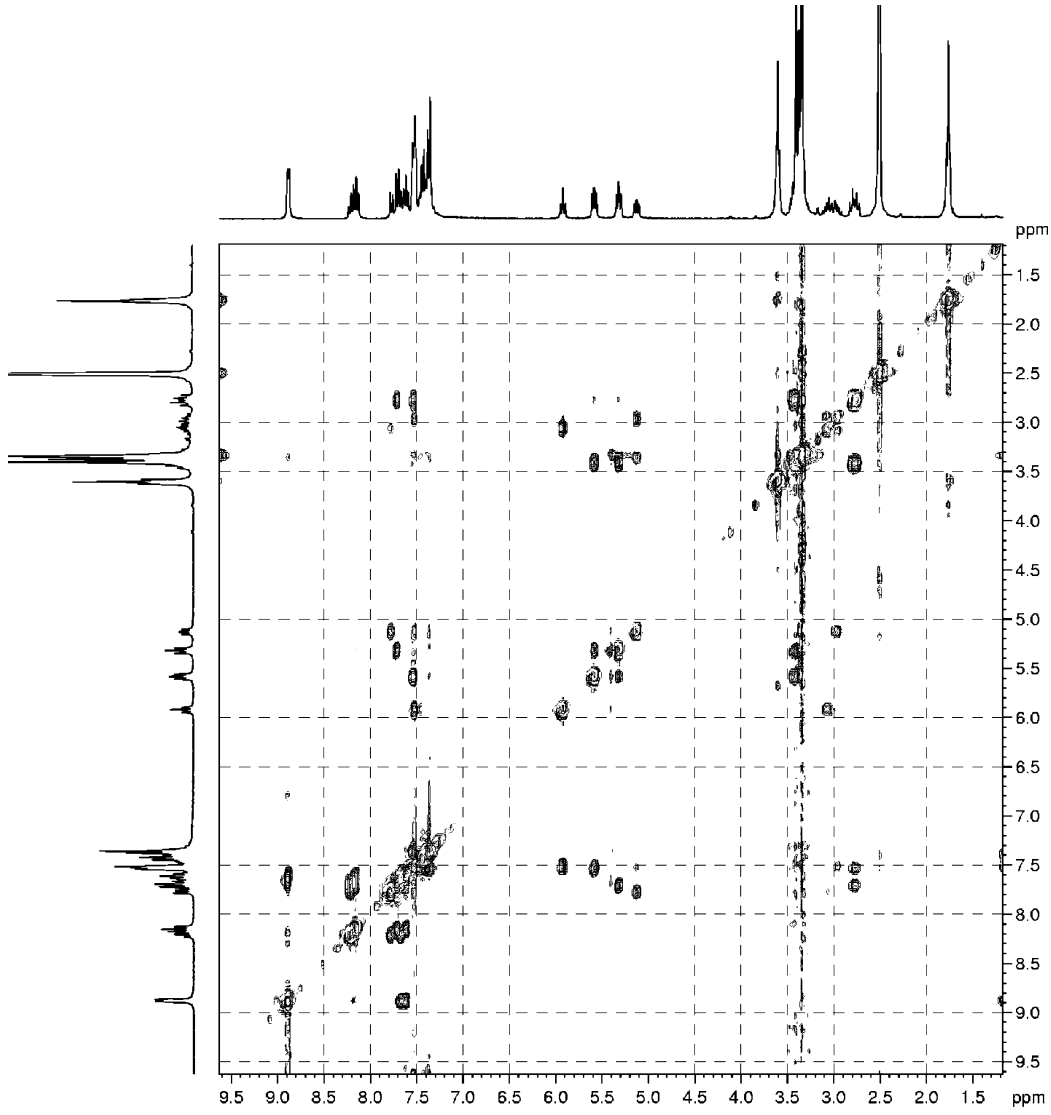


Fig. 1. The 2D NOESY spectrum of [Pd(*cis*-/*trans*-**L**)Cl_2] (300 MHz, DMSO-d_6/THF-d_8).

orientation of functional groups and (Fig. 2) therefore statistically occupy positions in the crystal. The resulting structure may be described as a solid-state solution of isomeric complexes. The existence of such phases may preclude the possibility of separation of isomeric isoxazolidines and their metal complexes by crystallization.

The zinc atoms in **2a**–**b** adopt a nearly tetrahedral co-ordination polyhedron with two chloride ligands and one *N*,*N*-bidentate co-ordinated **L**. In contrast to the X-ray data for a related structure of the palladium complex with *trans*-2-methyl-5-(2-pyridyl)-3-phenylisoxazolidine, the structure of **2a** possesses a Zn–N(1) bond (2.134(4) Å) longer than Zn–N(2) 2.049(4) Å) [23]. The five-membered chelate ring in both structures of zinc complex is almost planar. The atoms Zn(1) and N(1) deviate by −0.12 and 0.18 Å, respectively, from the mean plane of the other atoms this cycle. The isoxazolidine ring in the structures possesses an envelope conformation. In structure **2a**, the methyl group has an axial orientation to the isoxazolidine ring, while the phenyl and pyridine substituents are situated in an equatorial manner (C(6)–C(7)–C(8)–C(9) 159.5(4)°) (Table 2). In structure **2a**–**b**, the phenyl group and pyridyl ring are situated in an equatorial manner at the isoxazolidine cycle (C(10)–C(3)–C(2)–C(1) 153.7°) while the methyl group is located in an axial position (C(4)–N(1)–O(1)–C(3) −93.4°) (Table 3). The structure of copper complex **4a**–**b** (Fig. 4) consists of a neutral dimers [Cu(*cis*-/*trans*-**L**)Cl_2]$_2$. The copper atoms are co-ordinated in a distorted square pyramid comprising two nitrogen and two chlorine atoms in an equatorial plane (Cu–Cl 2.244(2)–2.262(2) Å) and an additional chloride ligand is situated in the apex (Cu–Cl 2.795(2), 2.818(2) Å). Thus two bridging chlorine atoms

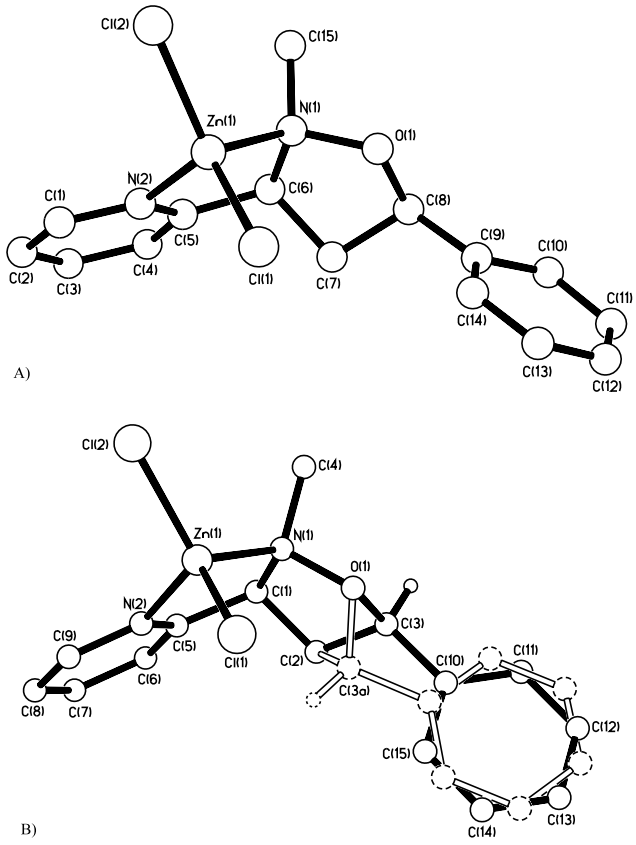


Fig. 2. Molecular structure of [Zn(**L**)Cl_2]: (A) *cis*-isomeric form of the ligand in structure **1a**. Selected bond length, Å: Zn(1)–N(2) 2.049(4); Zn(1)–N(1) 2.134(4); Zn(1)–Cl(2) 2.208(1); Zn(1)–Cl(1) 2.209(1); (B) disordering scheme for C–C_6H_5 fragment in structure **1b** suggests presence of *cis*- and *trans*-isomeric forms that possess the same shape and form mixed crystal. Selected bond length, Å: Zn(1)–N(2) 2.038(3); Zn(1)–N(1) 2.109(4); Zn(1)–Cl(1) 2.202(1); Zn(1)–Cl(2) 2.211(1).

connects molecular units [Cu(**L**)Cl_2] into the dimer (Table 4). The latter one is actually centrosymmetric, and all three pairs of isoxazolidine asymmetric atoms within the dimer frame possess opposite chirality. N-co-ordination of the isoxazolidine to the metal atom also makes impossible pyramidal inversion at the nitrogen atom, and the co-ordinated isoxazolidine core possesses three chiral centers simultaneously. Nevertheless, systematic absences suggest the chiral space group $P2_12_12_1$. The structure also shows high parameters for thermal motion of the isoxazolidine C–Ph fragment (U_{iso} 0.1–0.2 $Å^2$) that may be ascribed to co-crystallization of *cis*- and *trans*-isomeric forms, by analogy with **2a**–**b**. Both five-membered chelate rings formed are almost planar. The isoxazolidine ring has an envelope conformation and the methyl group possesses the axial position in the isoxazolidine ring (C(1A)–N(1A)–C(4A)–C(3A) 115.0°), whereas the pyridyl substituted is located in an *anticlinal* arrangement with the C(2)–C(3) bond.

3. Conclusions

2-Methyl-3-(2-pyridyl)-5-phenylisoxazolidine has been regioselectively synthetized as a 67:33 *cis*–*trans* mixture by reaction of *N*-methyl-*C*-(2-pyridyl)nitrone with styrene. The new ligand readily forms co-ordination compounds with Zn(II), Cu(II) and Pd(II) chlorides which solution structure has been assigned through 1D and 2D NMR spectroscopy. The organic ligand in the complexes is co-ordinated in a *N*,*N*-bidentate chelating mode, in contrast to isomeric 5-(2-pyridyl)substituted *N*-methyl isoxazolidine. The configuration and conformation of the isoxazolidine ring have been determined by NOE NMR experiments and confirmed by means of the X-ray diffraction data for zinc and copper chloride complexes. The crystal structure of [Zn(*cis*-/*trans*-**L**)Cl_2] (**2a**–**b**) and [Cu(*cis*-/*trans*-**L**)Cl_2] (**4a**–**b**) revealed the co-crystallization of *cis*- and *trans*-isomers of the ligand. For the zinc complex it has been also possible to isolate and characterize the co-ordination compound derived from the *cis*-isoxazolidine [Zn(*cis*-**L**)Cl_2]·0.5$CHCl_3$ (**2a**).

4. Experimental

4.1. Synthesis

All solvents were used as supplied or distilled using standard methods. The starting materials for the synthesis of organic ligands and complexes were commercial products of reagent grade (Fluka, Aldrich). The *N*-methyl-*C*-(2-pyridyl)nitrone (**1**) was prepared as previously described [24].

4.1.1. 2-Methyl-3-(2-pyridyl)-5-phenylisoxazolidine (**L**)

Freshly distilled styrene (20.2 ml, 18.36 g, 176.54 mmol) was added to a $C_6H_5CH_3$–C_6H_6 solution (1:1 v/v, 30 ml) of *N*-methyl-*C*-(2-pyridyl)nitrone (3.00 g, 22.06 mmol). The reaction mixture was stirred at reflux for 70 h and then concentrated in vacuo. Undesired side products were removed by means of column chromatography on silica gel with C_3H_6O–C_6H_{14} (1:1) as an eluent. The yield of **L** (yellow oil, mixture of *cis*–*trans* isomers in a ratio 67:33) was 3.18 g ($\sim$60%).

IR (film between KBr discs, cm^{-1}): 3085, 3065, 3035, 3010, 2990, 2960, 2960, 2915, 2875, 2850, 2780, 1670, 1590, 1570, 1495, 1475, 1450, 1440, 1400.

cis-**L**, ^1H NMR spectrum ($CDCl_3$): δ 2.54 (dt, 1H, ^3J 7.9, ^2J 12.7, H(4α)), 2.84 (s, 3H, NCH_3), 3.24 (dt, 1H, ^3J 7.9, ^2J 12.7, H(4β)), 4.17 (t, 1H, ^3J 7.9, H(3)), 5.33 (t, 1H, ^3J 7.9, H(5)), 7.15 (m, 1H, H^b), 7.25 (m, 1H, H^p–Ph), 7.31 (m, 2H, H^m–Ph), 7.36 (m, 2H, H^o–Ph), 7.58 (dt, 1H, ^4J 1.0, ^3J 7.9, H^d), 7.66 (dt, 1H, ^4J 1.9, ^3J 7.7, H^c), 8.51 (ddd, 1H, ^4J 1.0, 1.9, ^3J 5, H^a). ^{13}C NMR ($CDCl_3$): δ 44.61 (Me), 45.61 (C(4), 74.28 (C(3)), 78.49 (C(5)), 121.35 (C(d)), 122.46 (C(b)), 126.41 (C^o–Ph),

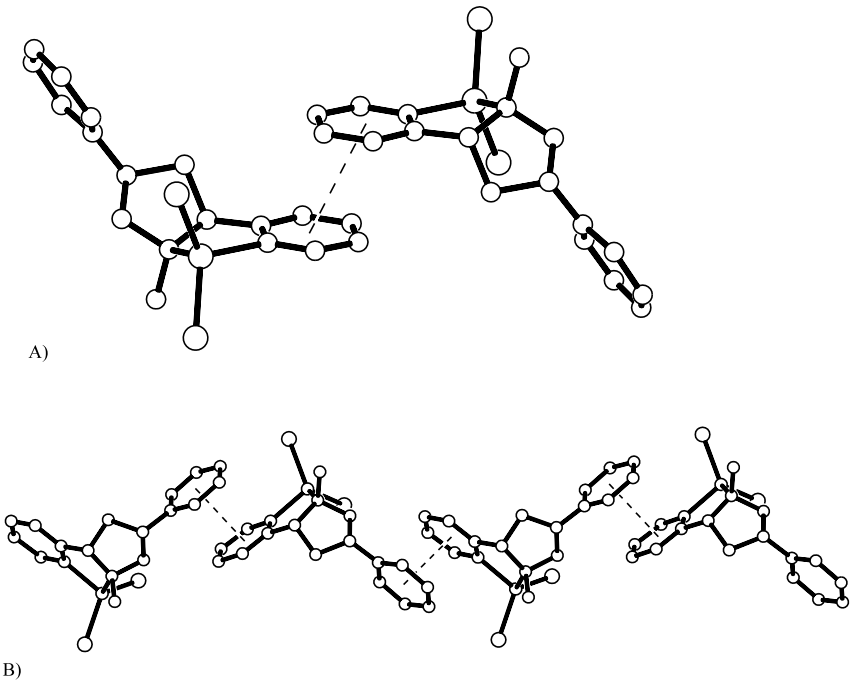


Fig. 3. Intermolecular interactions in the structures of $[Zn(\mathbf{L})Cl_2]$ complex and nature of its supramolecular isomerism: (A) dimeric centrosymmetric ensemble sustained by $\pi\cdots\pi$ stacking interaction between pyridine functions in **1a**; (B) polar chain formed by $\pi\cdots\pi$ stacking between pyridine and phenyl groups in structure **1b**.

Table 2
Selected angles (°) for structure of **2a** ($[Zn(cis\text{-}\mathbf{L})Cl_2]\cdot 0.5CHCl_3$)

Bond angles			
N(2)–Zn(1)–N(1)	81.43(16)	N(1)–C(6)–C(5)	110.8(4)
Cl(2)–Zn(1)–Cl(1)	119.97(5)	N(1)–C(6)–C(7)	102.3(4)
C(8)–O(1)–N(1)	109.5(3)	N(2)–Zn(1)–N(1)–C(6)	−21.5(3)
O(1)–N(1)–C(15)	106.9(4)	N(1)–Zn(1)–N(2)–C(1)	−164.7(4)
O(1)–N(1)–C(6)	106.3(3)	N(1)–Zn(1)–N(2)–C(5)	12.9(3)
C(15)–N(1)–C(6)	111.2(4)	O(1)–N(1)–C(6)–C(5)	145.1(4)
C(8)–C(7)–C(6)	101.9(4)	Zn(1)–N(1)–C(6)–C(5)	26.4(4)
O(1)–C(8)–C(7)	101.4(4)	O(1)–N(1)–C(6)–C(7)	20.5(5)
C(6)–N(1)–Zn(1)	108.1(3)	C(15)–N(1)–C(6)–C(7)	136.5(4)
C(5)–N(2)–Zn(1)	114.8(3)	C(8)–O(1)–N(1)–C(15)	−112.5(4)
N(2)–C(5)–C(6)	118.4(4)	C(6)–C(7)–C(8)–C(9)	159.5(4)

Table 3
Selected angles (°) for structure of **2a**–**b**

Bond angles			
N(2)–Zn(1)–N(1)	81.98(16)	C(4)–N(1)–C(1)	112.0(4)
Cl(1)–Zn(1)–Cl(2)	115.82(7)	N(1)–C(1)–C(2)	105.1(3)
C(3)–O(1)–N(1)	106.8(4)	O(1)–C(3)–C(2)	102.0(5)
O(1)–N(1)–C(4)	106.8(3)	C(1)–N(1)–Zn(1)	111.2(3)
O(1)–N(1)–C(1)	106.6(3)	C(5)–N(2)–Zn(1)	116.7(3)
C(3A)–O(1)–N(1)	106.3(5)	O(1)–C(3A)–C(2)	101.6(9)

127.6 (C^p–Ph), 128.44 (C^m–Ph), 136.95 (C(c)), 141.4 (C^{ipso}–Ph), 149.08 (C(a)), 160.29 (C^{ipso}–Py).

trans-**L**, ^{1}H NMR ($CDCl_3$): δ 2.71 (ddd, 1H, ^3J 7.2, 7.9, ^2J 12.7, H(4α)), 2.80 (s, 3H, NCH_3), 2.88 (dt, 1H, ^3J 7.9, ^2J 12.7, H(4β)), 4.03 (dt, 1H, ^3J 7.2, 7.9 H(3)), 5.22 (t, 1H, ^3J 7.9, H(5)), 7.21 (m, 1H, H^b), 7.25 (m, 1H, H^p–Ph), 7.35 (m, 2H, H^m–Ph), 7.43 (m, 2H, H^o–Ph), 7.56 (dt, 1H, ^4J 1.0, ^3J 7.9, H^d), 7.69 (dt, 1H, ^4J 1.9, ^3J 7.7, H^c), 8.57 (ddd, 1H, ^4J 1.0, 1.9, ^3J 5, H^a). ^{13}C NMR ($CDCl_3$): δ 44.25 (C(4)), 46.26 (Me), 74.28 (C(3)), 79.31 (C(5)), 121.94 (C(d)), 122.73 (C(b)), 126.68 (C^o–Ph), 127.93 (C^p–Ph), 128.52 (C^m–Ph), 136.95 (C(c)), 140.49 (C^{ipso}–Ph), 149.40 (C(a)), 159.47 (C^{ipso}–Py).

cis-**L**, ^{1}H NMR (DMSO-d_6): δ 2.46 (dt, 1H, ^3J 6.9, ^2J 12.3, H(4α)), 2.74 (s, 3H, NCH_3), 3.23 (dt, 1H, ^3J 7.7, ^2J 12.3, H(4β)), 4.19 (t, 1H, ^3J 6.9, H(3)), 5.32 (t, 1H, ^3J 7.7, H(5)), 7.19–7.36 (m, 3H, H^m–, H^p–Ph), 7.22 (m, 1H, H^b), 7.3 (m, 2H, H^o–Ph), 7.58 (dt, 1H, ^4J 1.0, ^3J 7.9, H^d), 7.78 (dt, 1H, ^4J 1.9, ^3J 7.7, H^c), 8.51 (ddd, 1H, ^4J 1.0, 1.9, ^3J 5, H^a). ^{13}C NMR (DMSO-d_6): δ 45.0 (C(4)), 44.57 (Me), 73.37 (C(3)), 77.95 (C(5)), 121.69 (C(d)), 122.83 (C(b)), 126.90 (C^o–Ph), 127.81 (C^p–Ph), 128.62 (C^m–Ph), 137.23 (C(c)), 142.02 (C^{ipso}–Ph), 149.27 (C(a)), 160.78 (C^{ipso}–Py).

trans-**L**, ^{1}H NMR (DMSO-d_6): δ 2.56 (ddd, 1H, ^3J 7.7, 8.5, ^2J 12.3, H(4β)), 2.67 (s, 3H, NCH_3), 2.88 (ddd, 1H, ^3J 6.5, 7.7, ^2J 12.3, H(4α)), 4.04 (dd, 1H, ^3J 6.5, 8.5, H(3)), 5.07 (t, 1H, ^3J 7.7, H(5)), 7.19–7.36 (m, 3H, H^m–, H^p–Ph), 7.33 (m, 1H, H^b), 7.42 (m, 2H, H^o–Ph), 7.58 (dt, 1H, ^4J 1.0, ^3J 7.9, H^d), 7.82 (dt, 1H, ^4J 1.9, ^3J 7.7, H^c), 8.55 (ddd, 1H, ^4J 1.0, 1.9, ^3J 5, H^a). ^{13}C NMR (DMSO-d_6): δ 44.71 (C(4)), 44.57 (Me), 73.65 (C(3)), 78.99 (C(5)), 122.37 (C(d)), 123.19 (C(b)), 127.07 (C^o–Ph), 128.13 (C^p–Ph), 128.77 (C^m–Ph), 137.34 (C(c)), 141.15 (C^{ipso}–Ph), 149.40 (C(a)), 159.59 (C^{ipso}–Py).

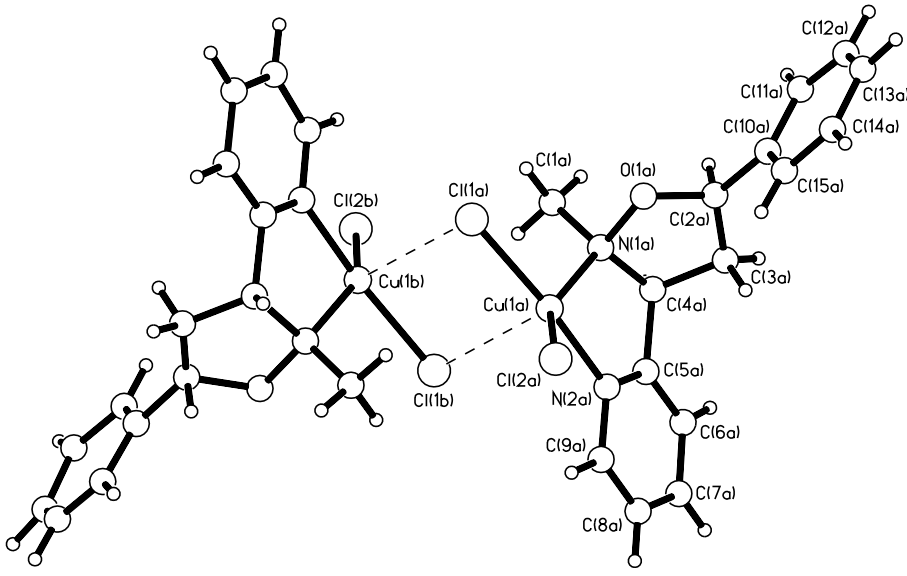


Fig. 4. Structure of the dimeric $[Cu(\mathbf{L})Cl_2]_2$ complex. Selected bond lengths, Å: Cu(1A)–N(2A) 1.996(7); Cu(1A)–N(1A) 2.077(7); Cu(1A)–Cl(2A) 2.245(3); Cu(1A)–Cl(1B) 2.795(2).

Table 4
Selected angles (°) for structure of **4a**–**b**

Bond angles			
N(2A)–Cu(1A)–N(1A)	80.6(3)	C(2A)–O(1A)–N(1A)	105.5(7)
Cl(2A)–Cu(1A)–Cl(1A)	94.33(10)	C(4A)–N(1A)–O(1A)	106.3(6)
N(2A)–Cu(1A)–Cl(2A)	94.4(2)	O(1A)–N(1A)–C(1A)	105.5(7)
N(1A)–Cu(1A)–Cl(2A)	148.1(2)	C(4A)–N(1A)–C(1A)	111.8(8)
N(2A)–Cu(1A)–Cl(1A)	168.9(2)	C(3A)–C(2A)–O(1A)	107.7(12)
N(1A)–Cu(1A)–Cl(1A)	95.4(2)	O(1A)–N(1A)–Cu(1A)	102.1(4)
C(2A)–C(3A)–C(4A)	107.6(10)	C(1A)–N(1A)–Cu(1A)	116.3(6)
N(1A)–C(4A)–C(3A)	105.1(8)		

4.1.2. *[Zn(cis-/trans-**L**)Cl$_2$] (**2a**–**b**)*

A warm mixture 2-propanol–C_3H_6O solution (8/4 ml) of **L** (0.090 g, 0.375 mmol) was added to 2-propanol (5 ml) containing $ZnCl_2$ (0.051 g, 0.375 mmol). The red precipitate was formed immediately. After cooling to room temperature (r.t.), the precipitate of **1** was separated, washed with cold 2-propanol and dried in vacuum. Yield: 0.086 g (61%). *Anal*. Found: C, 48.4; H, 4.3; N, 7.4. Calc. for $C_{15}H_{16}Cl_2N_2OZn$: C, 47.84; H, 4.28; N, 7.44%. Recrystallization from 2-propanol–$CHCl_3$ afforded single crystals of **1a** (orange) and **1b** (white).

4.1.3. *[Pd(cis-/trans-**L**)Cl$_2$] (**3a**–**b**)*

A warm methanolic solution (5 ml) of **L** (0.156 g, 0.65 mmol) was added to a warm MeOH (5 ml) containing $Na_2[PdCl_4]$ (0.191 g, 0.65 mmol). A yellow precipitate was formed at once. The reaction mixture was cooled to r.t., the precipitate of **3a**–**b** was filtered, washed with cold MeOH and dried. Yield: 0.185 g (65%). *Anal*. Found: C, 43.2; H, 3.8; N, 6.6. Calc. for $C_{15}H_{16}Cl_2N_2OPt$: C, 43.62; H, 3.93; N, 6.60%.

4.1.4. *[Cu(cis-/trans-**L**)Cl$_2$]$_2$ (**4a**–**b**)*

A sample of **L** (0.065 g, 0.27 mmol) in warm 2-propanol (5 ml) was added to a $C_5H_{11}O$ solution (10 ml) of $CuCl_2 \cdot 2H_2O$ (0.046 g, 0.27 mmol). A light-green precipitate was formed at once. After cooling to r.t., the precipitate was separated, washed with cold 2-propanol and dried in vacuo to afford a solid 0.062 g (74%). *Anal*. Found: C, 48.0; H, 4.1; N, 7.4. Calc. for $C_{15}H_{16}Cl_2CuN_2O$: C, 47.94; H, 4.29; N, 7.46%. Crystals of the complex, green platelets, were grown by the slow liquid diffusion in next mixtures $CHCl_3$–2-propanol–C_6H_{14} and 2-propanol–DMF as well as an isothermal evaporation of $CHCl_3$ solution.

Table 5
Crystal data and structure refinement for compounds **2a**, **2a**–**b** and **4a**–**b**

Compound	**2a**	**2a**–**b**	**4a**–**b**
Temperature (K)	100(2)	223(2)	293(2)
Crystal system	triclinic	orthorhombic	orthorhombic
Space group	$P\bar{1}$	$Pna2_1$	$P2_12_12_1$
a (Å)	8.5986(4)	16.9776(11)	8.9215(11)
b (Å)	9.9688(4)	7.3273(5)	14.9093(18)
c (Å)	23.1035(12)	13.1536(9)	25.089(3)
α (°)	80.410(3)	90.00	90.00
β (°)	80.170(3)	90.00	90.00
γ (°)	65.075(3)	90.00	90.00
U (Å^3)	1759.61(14)	1636.3(2)	3337.1(7)
Z	4	4	8
D_{calc} (Mg m^{-3})	1.647	1.529	1.492
μ (mm^{-1})	1.931	1.826	1.628
Reflections collected	10 601	8322	15 181
Reflections unique	6840	2667	4761
R_{int}	0.0807	0.0622	0.1013
R_1	0.0582	0.0371	0.0569
wR_2	0.1757	0.0885	0.1325

4.2. Measurements

The IR spectrum of liquid **L** was recorded on a UR-10 (Carl Zeiss, Jena) spectrometer (film between KBr discs; 400–4000 cm^{-1}).

^{1}H (300 MHz), ^{13}C (75.5 MHz) NMR spectra were recorded at r.t. on a Bruker Avance DPX300 spectrometer equipped with a 5 mm QNP-Z probe (^{1}H, ^{13}C, ^{15}N, ^{31}P). The solvents were $CDCl_3$, C_3H_6O-d_6 and DMSO-d_6–THF-d_8 mixture (internal standard—TMS). Standard Bruker software and microprograms were applied for all NMR experiments. The sweep width covered was 3000 Hz for ^{1}H, digitalized in 16 K, and 15 000 Hz for ^{13}C, digitalized in 64 K.

Crystallographic measurements were made using a Siemens SMART CCD area-detector three-circle diffractometer (KappaCCD for **2a**). Graphite monochromated Mo Kα radiation ($\lambda = 0.71073$ Å) was employed. The data frames were integrated using SAINT [29] and empirical absorption corrections (SADABS) [29] were employed. The essential experimental conditions and resulting crystal data are given in Table 5. All structures were solved by direct methods using the SHELXTL-PLUS set of programs [30], and refined by full-matrix least-squares methods. Positions of the hydrogen atoms were idealized.

The $CHCl_3$ of crystallization in structure **2a** have no close contacts with other atoms and fill up emptiness of the crystal. These solvate molecules are disordered over two closely situated positions with partial site occupancy factors at 0.7 and 0.3.

In structure **2a**–**b** high anisotropy of thermal motion for C(3)–C_6H_5 carbon atoms suggested that this fragment of the molecule is disordered. The disorder was resolved under constraining the standard geometry of the phenyl rings and refinement of partial occupancies led to values of 0.72 and 0.28. Refinement of the disorder proceeded smoothly and therefore it was possible to refine all atoms of the major component anisotropically, while atoms of the minor component were left isotropic and the hydrogen atoms of phenyl cycle were not included. Actually the same problem was observed for copper complex **4**. In this case, all attempts to divide the oscillatory movement of C–C_6H_5 between two positions with different partial occupancies were not successful.

5. Supplementary material

Crystallographic data for the structural analysis have been deposited with the Cambridge Crystallographic Data Centre, CCDC No. 164044–164046 for compounds **2a**, **2a**–**b** and **4**. 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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