

Oxazoline chemistry — Part IV: Synthesis and characterization of oxazoline complexes of the zinc halides¹

Tosha M. Barclay, Ignacio del Río, Robert A. Gossage, and Sarah M. Jackson

Abstract: The synthesis and characterization of 11 zinc halide derivatives that contain monodentate oxazoline ligands is described. The treatment of ether solutions of $[\text{ZnX}_2]$ ($X = \text{Cl}, \text{Br}, \text{I}$) with 2-aryl- or 2-methyl-2-oxazolines results in the formation of mildly hygroscopic complexes of the general formulae $[\text{ZnX}_2(\text{ox})_2]$ ($\text{ox} = 2\text{-methyl-2-oxazoline (1)}, 2,4,4\text{-trimethyl-2-oxazoline (2)}, 2\text{-phenyl-2-oxazoline (3)}, \text{ or } 4,4\text{-dimethyl-2-phenyl-2-oxazoline (4)}$), except in the case of ZnI_2 , which does not form an isolable complex — likely for steric reasons — with oxazoline **4**. Treatment of $[\text{ZnBr}_2(\mathbf{4})_2]$ with **1** reveals (¹H NMR) that **1** only sluggishly displaces coordinated **4** at temperatures below 50 °C. The structural characterization, via single crystal X-ray diffraction, of six of the complexes, viz. $[\text{ZnI}_2(\mathbf{1})_2]$, $[\text{ZnI}_2(\mathbf{2})_2]$, $[\text{ZnX}_2(\mathbf{3})_2]$ ($X = \text{Cl}, \text{Br}, \text{ or } \text{I}$), and $[\text{ZnBr}_2(\mathbf{4})_2]$, is also reported. All of these structurally characterized complexes are mononuclear zinc compounds with an overall distorted tetrahedral arrangement of the two halide and two oxazoline ligands around the zinc metal centre. The oxazoline series of complexes reported herein show little structural diversity, a facet which is in contrast to their substituted pyridine analogues.

Key words: oxazoline, zinc, X-ray crystal structure, coordination complex, NMR spectroscopy, Zn(II).

Résumé : On décrit la synthèse et la caractérisation d'onze dérivés d'halogénures de zinc contenant des ligands oxazolines monodentates. Le traitement de solutions étherées de $[\text{ZnX}_2]$ ($X = \text{Cl}, \text{Br}, \text{I}$) avec des 2-aryl- ou 2-méthyl-2-oxazolines conduit à la formation de complexes faiblement hygroscopiques de formule générale $[\text{ZnX}_2(\text{ox})_2]$ ($\text{ox} = 2\text{-méthyl-2-oxazoline [1]}, 2,4,4\text{-triméthyl-2-oxazoline [2]}, 2\text{-phényl-2-oxazoline [3]} \text{ ou } 4,4\text{-diméthyl-2-phényl-2-oxazoline [4]}$); exceptionnellement, la réaction ZnI_2 avec l'oxazoline **4** ne conduit pas à la formation d'un complexe isolable, probablement en raison d'un encombrement stérique. La RMN du ¹H montre que le traitement du $[\text{ZnBr}_2(\mathbf{4})_2]$ avec **1**, à des températures inférieures à 50 °C, montre que le déplacement de **4** ne se fait que très difficilement. On rapporte aussi la caractérisation par diffraction des rayons X de six de ces complexes, soit $[\text{ZnI}_2(\mathbf{1})_2]$, $[\text{ZnI}_2(\mathbf{2})_2]$, $[\text{ZnX}_2(\mathbf{3})_2]$ ($X = \text{Cl}, \text{Br}$ ou I) et $[\text{ZnBr}_2(\mathbf{4})_2]$. Tous les complexes dont la structure a été caractérisée sont des composés mononucléaires du zinc comportant un arrangement global tétraédrique déformé de deux halogènes et de deux ligands oxazoline autour du zinc central. La série de complexes avec des oxazolines qui est rapportée ici ne présente que de faibles variations structurales; cette caractéristique est en opposition avec ce qui a été observé avec leurs analogues comportant des pyridines substituées.

Mots clés : oxazoline, zinc, structure cristalline par diffraction des rayons X, complexe de coordination, spectroscopie RMN, Zn(II).

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Introduction

The chemistry of zinc is one of the cornerstones of inorganic biochemistry (1). The element is characterized by the high stability of the +2 oxidation state and by the numerous examples of robust four-, five-, and six-coordinate zinc com-

plexes (2, 3). The high Lewis acid character of the d^{10} Zn^{2+} ion leads to the formation of many stable compounds with *N*-donor ligands, including heterocycles such as pyridines (py), imidazoles, pyrazines, oxazoles, and others (3–8).

Zinc complexes are also part of a burgeoning network of bio-active and (or) pharmaceutical inorganic compounds (9),

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and even simple solutions of Zn^{2+} ions or $[\text{Zn}(N\text{-donor})_x]^{2+}$ complexes have a number of noteworthy biological activities (10). For example, $[\text{ZnCl}_2(\text{H}_2\text{N}^i\text{Pr})_2]$ has recently been shown to prolong (i.e., stabilize) the potency of enzymes in aqueous media (11). The presence of zinc ions can also increase the potency of certain biologically active compounds, such as the enzyme inhibitory effect of bis(5-amidino-2-benzimidazolyl)methane (BABIM). This enhancement has been shown to be due to the binding of a $[\text{Zn}(\text{BABIM})]$ complex into the active site of a protease enzyme (12*a*). Recently, zinc complexes of neocuprine, a phenanthroline derivative, have been shown to be site-specific RNA cleavage agents (12*b*). Related simple Zn coordination complexes have also shown promise in the treatment of diabetes (12*c*, 12*d*).

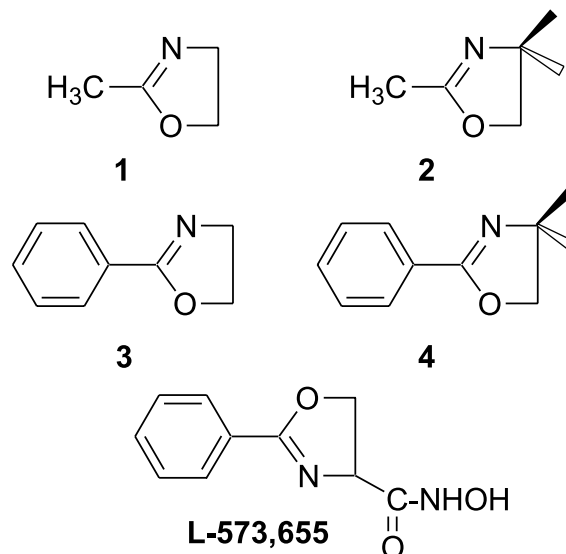
In direct relation to this study is the hypothesis that oxazoline-containing drug candidates (12*e*) such as 4-carbomethoxy-2-phenyl-2-oxazoline (viz., **L-573,655**; Fig. 1) inhibit lipid A biosynthesis by coordination with an enzyme-bound Zn atom (i.e., a Zn-oxazoline complex is formed with **L-573,655**; refs. 12*f*–12*i*). As part of a larger study concerning the coordination and medicinal chemistry of zinc (13) and oxazoline (i.e., 4,5-dihydro-2-oxazole) ligands in general (14),⁵ we have undertaken a study of simple monodentate oxazolines (**1**–**4**; Fig. 1) as ligands for binding to the zinc halides. In this report, we detail the synthesis and characterization (NMR and X-ray analyses, etc.) of a series of Zn halide complexes that incorporate monodentate 2-oxazoline (**15**) derivatives. A further reason for this investigation is the knowledge that zinc halides are commonly used as catalysts to form oxazolines via treatment of organic cyanides with amino-alcohols (14*c*). A possible by-product of this procedure is an oxazoline–Zn complex, and hence, we wanted to begin a general investigation of such species.

Results and discussion

Syntheses and spectroscopic characterization

The treatment of ether solutions (or suspensions) of the zinc halides (ZnX_2 ; X = Cl, Br, or I) with an excess of a 2-oxazoline (Fig. 1) leads to rapid formation of isolable white precipitates. A sole exception to this observation is the reaction of ZnI_2 with oxazoline **4**; this particular reaction invariably leads to the formation of oily inextractable mixtures, from which no pure compounds could be obtained. Metathesis reactions, involving exchange of Br or NO_3 anions with I^- sources, were likewise unsuccessful. The aforementioned isolated materials are moderately hygroscopic, a property that is more pronounced with the 2-methyl oxazoline complexes (i.e., **5**–**10**) when compared with the 2-phenyl derivatives **11**–**15**. All compounds decomposed on melting in air to form colourless oils. The initial isolated materials in all cases are white powders; crystalline samples, obtained as described in the Experimental section, are clear and colourless but darken over several weeks in air.

Fig. 1.



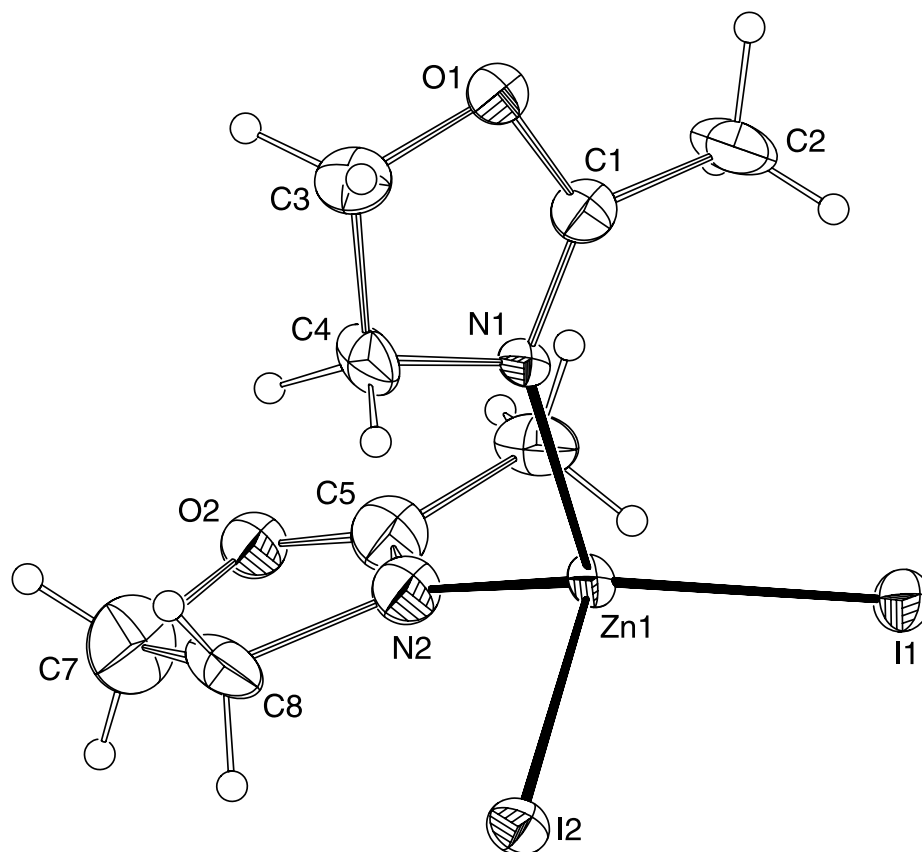
Examination of **5**–**15** by elemental analysis measurements are, in all cases, consistent with the formation of complexes of general formula $[\text{Zn}_n\text{X}_{2n}(\text{oxazoline})_{2n}]$ (i.e., 2:1 ligand:ZnX₂ species). Characterization of these complexes by ^1H NMR spectroscopy reveals the presence of a single oxazoline ligand environment. Further to this, the ^1H NMR resonances for the presumably coordinated oxazolines are shifted relative to that of the free ligands,⁶ a situation that is mimicked by observation of a decrease in the $\nu(\text{C}=\text{N})$ IR stretching frequencies of the oxazoline for the complexes, as expected. Specifically, all ^1H NMR chemical shifts of complexes incorporating **1** are notably deshielded relative to the free ligand form,⁶ an observation consistent with donation of electron density from the ligand to the Lewis acidic Zn centre. Complexes of **2** show a similar trend; however, the methyl resonances on C-2 of the oxazoline are notably shielded relative to free **2**. This suggests that this methyl group is forced to be in close proximity to the metal centre, likely because of steric effects of the methyl substituents on C-4 (vide infra). In the case of ligands **3** and **4**, shifts are less pronounced relative to the free ligands, although the methylene protons of **3** show a small shift (positive in the case of the Br and I derivatives and negative for the Cl) upon coordination.

Zinc halides are often employed as catalysts for the synthesis of 2-oxazolines via treatment of an alkyl or aryl cyanide with an appropriate amino-alcohol at elevated temperatures (14*c*, 15, 16). With this in mind, it seems feasible that Zn-oxazoline complexes may also be produced as by-products in these reactions. We have taken a cursory look at the stability of some of these species by a simple metathesis reaction. Treatment of complex **15** in an NMR tube with 2 equiv of **1** and maintenance at room temperature (RT) for a period of 1 day does not result in any loss of signal intensity of **15**, nor presence of any form of an intermediate, and

⁵R.A. Gossage, K.J. Haller, H. Jenkins, and S.M. Jackson. Unpublished results.

⁶ ^1H NMR data (300 MHz, CDCl_3) δ : **1**: 4.12 (t, 2H, $J = 9.5$, CH_2O), 3.73 (t, 2H, CH_2N), 1.86 (s, 3H, CH_3); **2**: 3.80 (s, 2H, CH_2O), 1.83 (s, 3H, $\text{N}=\text{C}-\text{CH}_3$), 1.14 (s, 6H, CH_3); **3**: 7.95 (m, 2H, ArH), 7.42 (m, 3H, ArH), 4.40 (t, 2H, CH_2O), 4.04 (t, 2H, CH_2N); **4**: 7.86 (m, 2H, ArH), 7.28 (m, 3H, ArH), 3.95 (s, 2H, CH_2), 1.25 (s, 6H, CH_3). IR data (thin film; KBr; $\nu(\text{C}=\text{N})$): **1**: 1670 (st); **2**: 1670 (st); **3**: 1645 (st); **4**: 1648 (st).

Fig. 2. ORTEP representation of complex 7.



no evidence for the formation of complex **5**. Heating this mixture for 12 h at about 50 °C results in only a small amount (<10%) of **5** being detected. These results indicate a robust nature of these materials, and it seems that only by treating with a large excess of water, as is typically done in the synthesis of ligands **1–4** employing Zn halides (14c, 15, 16), are the free oxazolines released. This is also suggested by the relatively hygroscopic nature of these complexes, a property that is a likely cause of our inability to obtain a reproducible elemental analysis in the case of complex **14**.

Solid-state (crystal) structures

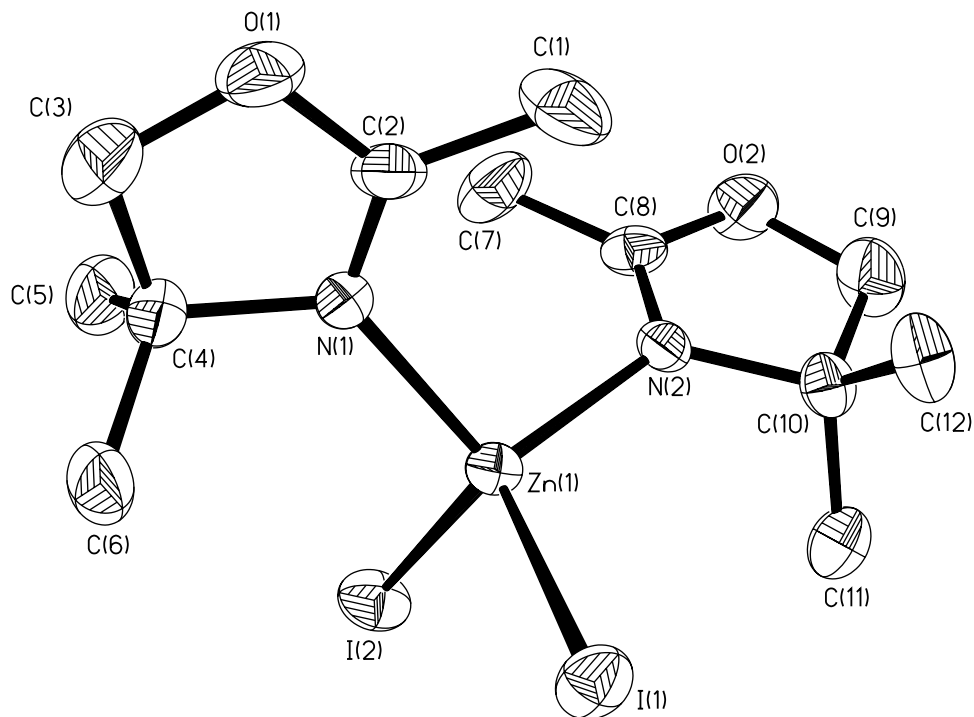
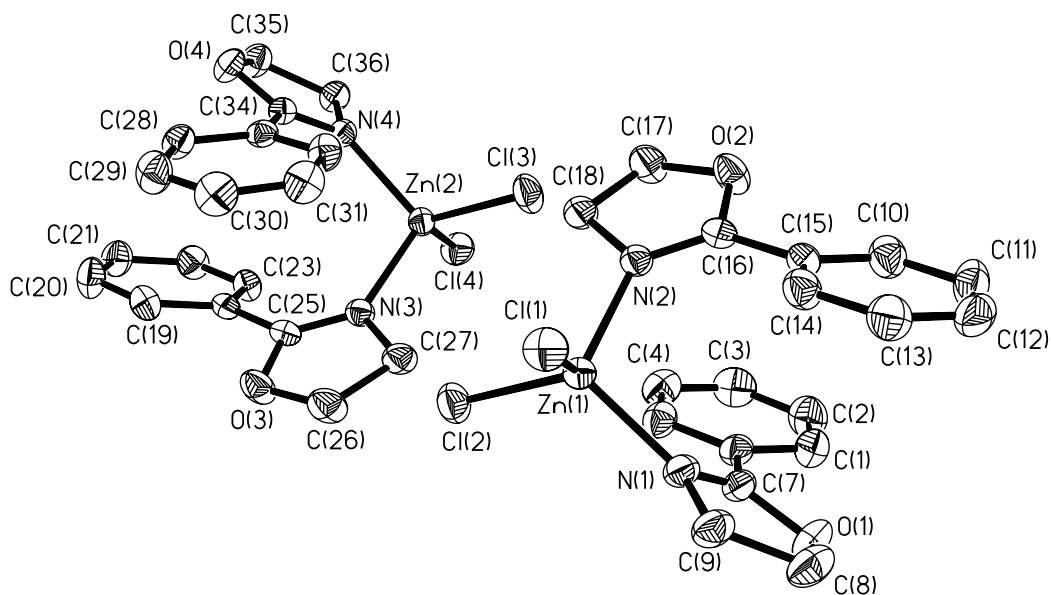
Zinc halides are well known to react with *N*-donor compounds to form mononuclear complexes with an overall distorted tetrahedral disposition of ligands around the Zn atom. For example, ZnCl₂ forms simple complexes of the general formulae [ZnCl₂(*N*)₂] with *N* = py, 4-(vinyl)py, 4-(NC)py, 4-(acetyl)py, 3,4,5-Cl₃py, 3-(F₃C)py, and 4-(Me)py (17). However, a number of interesting polymeric materials are formed (3, 6, 17a) with other pyridine derivatives. For example, both 3,5-Cl₂py and 3,5-Br₂py form polymeric complexes with ZnCl₂ (i.e., [Zn(μ-Cl)₂(3,5-Xpy)₂]_∞) in which the Zn atom is in an octahedral coordination geometry. Linear (and tetrahedral at Zn) bridged species are formed with 4,4'-bipy and ZnCl₂ (i.e., [ZnCl₂(4,4'-bipy)]_∞), but Magnus-type salts (i.e., [Zn([MeO]₂py)₄]²⁺ [Zn₂Br₆]²⁻) can be formed by treating ZnBr₂ with 2,6-(MeO)₂-py (17a).

There is currently a dearth of structural information on *monodentate* oxazoline complexes (15), despite the fact that the coordination chemistry of bis-oxazolines and cyclo-

metallated (i.e., η²-*N,C*) 2-aryl-2-oxazolines has been the subject of numerous studies (15). To our knowledge, there is no structural data of any Zn halide complex with a monodentate oxazoline; hence, we felt a structural investigation of this class of materials was in order. Thus, we have carried out single crystal X-ray structure analysis of six of the complexes (**7**, **10–13**, and **15**) synthesized herein. In addition, there are very few structurally characterized [ZnI₂(*N*-donor)_{*n*}] complexes (18–20), and thus the characterization of three (**7**, **10**, and **13**) such derivatives will help to expand the structural database on this class of ZnI₂ coordination compounds.

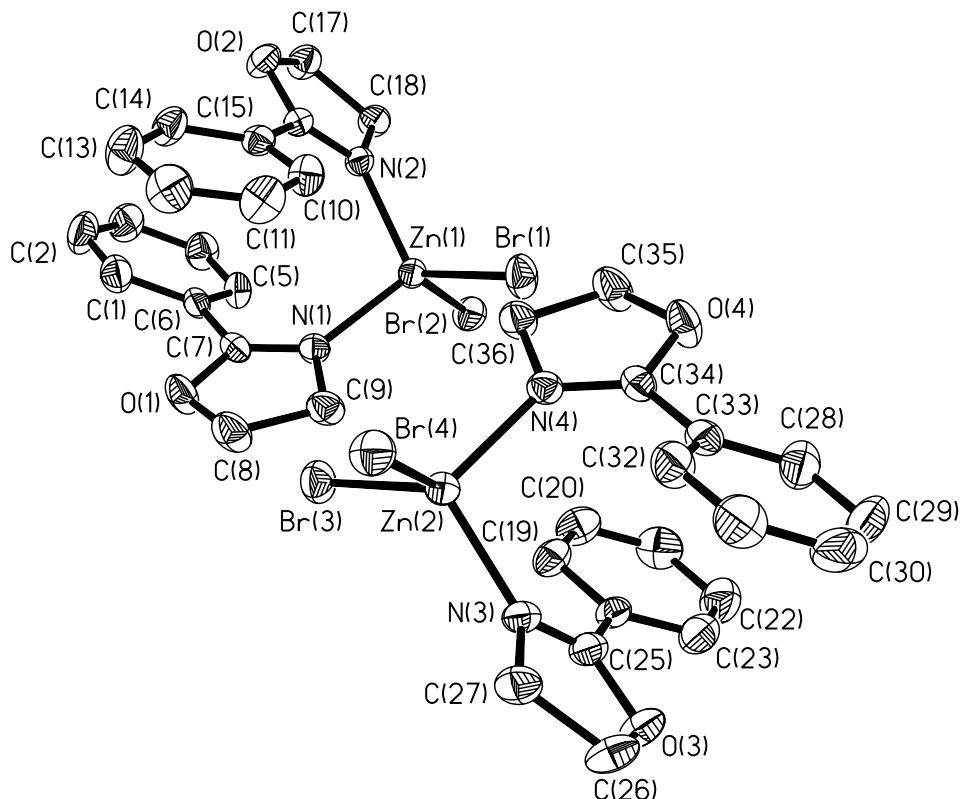
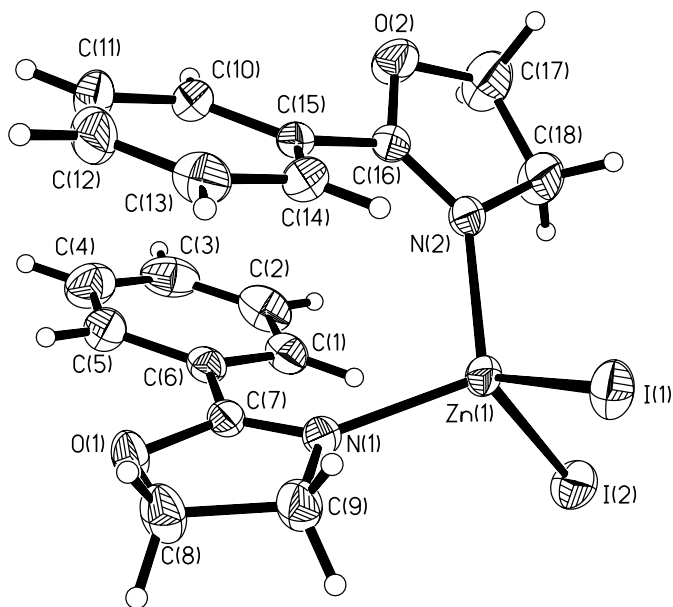
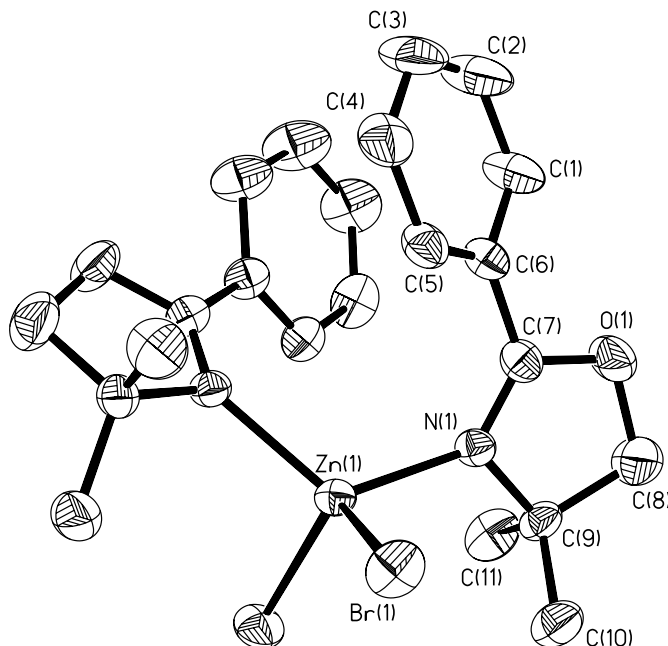
The molecular structures of complexes **7**, **10–13**, and **15** can be found in Figs. 2–7, respectively, and the general crystal data can be found in Tables 1 and 2.

All six complexes are mononuclear species in the solid state with an approximate tetrahedral array of the two halide and two oxazoline ligands around the metal centre. As expected, the binding of the oxazoline fragment is, in all cases, via coordination of the imine *N*-atom of the heterocyclic ring (15). Comparative examples of related structurally characterized Zn oxazolines are few (21–24) but include complexes such as [η²-*N,N'*-(1,2-bis{4*S*-4-isopropyl-2-oxazolin-2-yl}benzene) zinc(II) chloride] (21). The bond lengths between Zn and the donor ligands for complexes **7**, **11–13**, and **15** are in the range typical (3–8, 15–25) for Zn—N and Zn—X bonds (Table 2). These data can be compared with, for example, the halide complexes (4c, 17a, 18b) [ZnCl₂(4-Me-py)₂] (Zn—N_{av} = 2.044 Å; Zn—Cl_{av} = 2.208 Å), [ZnBr₂(3-CF₃-py)₂] (Zn—N = 2.084 Å; Zn—Br = 2.375 Å),

Fig. 3. ORTEP representation of complex **10**.**Fig. 4.** ORTEP representation depicting both molecules of complex **11** found in the unit cell.

and $[\text{ZnI}_2(2\text{-amino-2-thiazole})_2]$ (**17**: $\text{Zn}-\text{N}_{\text{av}} = 2.023 \text{ \AA}$; $\text{Zn}-\text{I}_{\text{av}} = 2.384 \text{ \AA}$). Complex **10** is perhaps the most unusual of the set, as it displays $\text{Zn}-\text{I}$ bonds that are at the upper range of known $\text{Zn}-\text{I}$ bond lengths (cf. **17**). Similar long $\text{Zn}-\text{I}$ bonds are found (*18a*) in the complex $[\text{ZnI}_2(\eta^2\text{-}N,N'\text{-}\{\text{C}_5\text{H}_4\text{N}\}_3\text{N})]$ (**18**). The reason for the long bonds found here may be because of steric effects imposed on the large I atoms relative to tightly bound oxazoline **2** (**26**). Note that this particular fragment contains two sterically bulky methyl substituents on carbons (labelled) C4 and C10 (Fig. 3) of the oxazoline ring. This structure sheds some light on the observed solution properties that involve the shielding of the

proton resonances (vide supra) of the methyl group (C1). The $\text{Zn1}-\text{C1}$ and C7 distances are 3.43 and 3.38 \AA , respectively. The $\text{I}-\text{Zn}-\text{I}$ angles (Table 2) of **10** and **13** are considerably narrower than that of **18** ($117.48(3)^\circ$) but similar to that found in the complexes $[\text{ZnI}_2(\text{Bps}^{\text{Me}2})]$ ($113.48(5)^\circ$; $\text{Bps}^{\text{Me}2} = [\text{bis}(3,5\text{-dimethylpyrazolyl})\text{dimethylsilane}]$), $[\text{ZnI}_2(\text{C}_6\text{H}_{12}\text{N}_4)_2]$ ($111.5(1)^\circ$), and $[\text{ZnI}_2(3,5\text{-[Buph]}_2\text{pzH})_2]$ ($112.2(1)^\circ$), all of which have sterically demanding N -donor ligands (**19**, **20a**, **20b**). Complexes **11** and **12** both contain two unique molecules of the complex in the unit cell. The main differences between these molecules is the torsion angles between the phenyl group formally on C-2 and the

Fig. 5. ORTEP representation depicting both molecules of complex **12** found in the unit cell.**Fig. 6.** ORTEP representation of complex **13**.**Fig. 7.** ORTEP representation of complex **15**.

oxazoline unit. These two materials are virtually isomorphous. Further structural details for all six complexes reported here can be found in the supporting data.⁷

⁷Supplementary data may be purchased from the Depository of Unpublished Data, Document Delivery, CISTI, National Research Council Canada, Ottawa, ON K1A 0S2, Canada (http://www.nrc.ca/cisti/irm/unpub_e.shtml for information on ordering electronically). CCDC 213243–213248 contain the supplementary data for complexes **7**, **10–12**, and **15** respectively. These data can be obtained, free of charge, via www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, U.K.; fax +44 1223 336033; or deposit@ccdc.cam.ac.uk).

Table 1. General crystal data for complexes 7, 10–13, and 15.

Complex	7	10	11	12	13	15
Formula	C ₈ H ₁₄ N ₂ O ₂ ZnI ₂	C ₁₂ H ₂₂ N ₂ O ₂ ZnI ₂	C ₁₈ H ₁₈ N ₂ O ₂ ZnCl ₂	C ₁₈ H ₁₈ N ₂ O ₂ ZnBr ₂	C ₁₈ H ₁₈ N ₂ O ₂ ZnI ₂	C ₂₂ H ₂₆ N ₂ O ₂ ZnBr ₂
fw	489.38	545.49	430.61	519.53	613.51	575.64
Crystal size (mm)	0.35 × 0.13 × 0.10	0.22 × 0.29 × 0.37	0.39 × 0.41 × 0.57	0.35 × 0.38 × 0.43	0.47 × 0.51 × 0.61	0.31 × 0.34 × 0.38
<i>a</i> (Å)	6.5379(7)	8.8696(18)	22.644(4)	23.242(4)	9.248(2)	0.205(5)
<i>b</i> (Å)	8.1537(9)	12.562(3)	8.5488(17)	8.6299(14)	26.251(6)	7.9088(13)
<i>c</i> (Å)	14.2453(14)	15.602(3)	19.544(4)	19.618(3)	8.999(2)	19.808(3)
α (°)	83.439(7)		92.229(4)	91.710(3)		
β (°)	77.100(7)				110.618(4)	
γ (°)	69.879(7)					
<i>V</i> (Å ³)	694.46(13)	1876.8(7)	3778.7(13)	3933.0(11)	2044.7(8)	4731.8(14)
Cell detn, refls	756	343	793	552	779	514
<i>D</i> _{calcd} (g·cm ⁻³)	2.340	1.93	1.51	1.76	1.99	1.62
Space group	<i>P</i> $\bar{1}$	<i>P</i> ₂ ₁ ₂ ₁	<i>P</i> ₂ ₁ ₁ ₁	<i>P</i> ₂ ₁ ₁ ₁	<i>P</i> ₂ ₁ ₁ ₁	<i>Fdd</i> ₂
<i>Z</i>	2	4	8	8	4	8
<i>F</i> (000)	456	1040	1760	2048	1168	2304
<i>T</i> (K)	120(2)	293	293	293	293	293
Absorption coefficient (mm ⁻¹)	37.258	4.60	1.60	5.33	4.23	4.44
2 θ range (°)	5.78–68.61	4–50	4–50	4–50	4–50	4–50
Limiting indices	0 ≤ <i>h</i> ≤ 7 –8 ≤ <i>k</i> ≤ 9 –16 ≤ <i>l</i> ≤ 17	–10 ≤ <i>h</i> ≤ 10 –15 ≤ <i>k</i> ≤ 16 –18 ≤ <i>l</i> ≤ 11	–26 ≤ <i>h</i> ≤ 26 –10 ≤ <i>k</i> ≤ 6 –23 ≤ <i>l</i> ≤ 23	–27 ≤ <i>h</i> ≤ 22 –8 ≤ <i>k</i> ≤ 10 –21 ≤ <i>l</i> ≤ 23	–10 ≤ <i>h</i> ≤ 7 –31 ≤ <i>k</i> ≤ 30 –9 ≤ <i>l</i> ≤ 10	–27 ≤ <i>h</i> ≤ 35 –9 ≤ <i>k</i> ≤ 8 –23 ≤ <i>l</i> ≤ 23
Reflections collected	10 983	9894	19 030	19 962	10 551	5902
Reflections unique	2550	3318	6664	6939	3589	2095
Reflections <i>I</i> > 2 σ (<i>I</i>)	2376	2991	5095	4611	3030	1985
Parameters	120	172	451	451	226	132
GOF on <i>F</i> ²	1.05	1.07	1.07	0.99	1.06	0.98
Final <i>R</i> indices <i>I</i> > 2 σ (<i>I</i>)	<i>R</i> ₁ = 0.0838 <i>wR</i> ₂ = 0.2323	<i>R</i> ₁ = 0.026 <i>wR</i> ₂ = 0.059	<i>R</i> ₁ = 0.025 <i>wR</i> ₂ = 0.067	<i>R</i> ₁ = 0.031 <i>wR</i> ₂ = 0.074	<i>R</i> ₁ = 0.031 <i>wR</i> ₂ = 0.074	<i>R</i> ₁ = 0.023 <i>wR</i> ₂ = 0.054
<i>R</i> indices (all data)	<i>R</i> ₁ = 0.0870	<i>R</i> ₁ = 0.030	<i>R</i> ₁ = 0.039	<i>R</i> ₁ = 0.057	<i>R</i> ₁ = 0.038	<i>R</i> ₁ = 0.027
$\rho_{\text{min,max}}$ (e·Å ⁻³)	–2.920, 2.720	–0.72, 0.33	–0.23, 0.26	–0.33, 0.79	–1.15, 0.63	–0.21, 0.41

Table 2. Selected bond lengths (Å) and angles (°) for complexes **7**, **10–13**, and **15**.

Complex	Bond	Bond lengths (Å)	Bonds	Bond angles (°)
7	Zn1—I1	2.567(2)	I1-Zn1-I2	111.67(6)
	Zn1—I2	2.590(2)	N1-Zn1-N2	99.7(5)
	Zn—N1	2.021(9)		
	Zn1—N2	2.004(14)		
	N1—C ^a	1.27(2)		
10	Zn1—I1	2.5937(7)	Cl1-Zn1-Cl2	112.18(2)
	Zn1—I2	2.5827(8)	N1-Zn1-N2	106.48(15)
	Zn1—N1	2.059(4)		
	Zn1—N2	2.074(4)		
	N1—C ^a	1.280(7)		
	N2—C ^a	1.268(6)		
11^b	Zn1—Cl1	2.2352(7)	Cl1-Zn1-Cl2	111.97(3)
	Zn1—Cl2	2.2432(7)	N1-Zn1-N2	103.70(7)
	Zn1—N1	2.026(2)		
	Zn1—N2	2.050(2)		
	N1—C ^a	1.282(3)		
12^b	Zn1—Br1	2.3712(7)	Br1-Zn1-Br2	108.61(3)
	Zn1—Br2	2.3712(6)	N1-Zn1-N2	104.59(12)
	Zn1—N1	2.053(3)		
	Zn1—N2	2.025(3)		
	N1—C ^a	1.285(4)		
13	Zn1—I1	2.5706(8)	I1-Zn1-I2	110.42(2)
	Zn1—I2	2.5937(7)	N1-Zn1-N2	107.51(13)
	Zn1—N1	2.052(3)		
	Zn1—N2	2.042(3)		
	N1—C ^a	1.282(5)		
15	Zn1—Br1	2.3905(5)	Br1 ^c -Zn1-Br1	112.92(3)
	Zn1—N1	2.076(3)	N1 ^c -Zn1-N1	119.07(14)
	N1—C ^a	1.269(4)		

^aRefers to the formal N=C of the oxazoline ligands containing N1.

^bTwo distinct molecules in the unit cell; values given for Zn1 complex only (see Supplementary data).

^cSymmetry code = $-x - 1/2, -y + 1/2, z$.

Conclusions

The treatment of ether solutions of ZnX₂ with oxazolines **1–4** results in the formation of mildly hygroscopic mononuclear bis-oxazoline complexes, except in the case of X = I and oxazoline **4**. Six derivatives have been characterized by single crystal X-ray diffraction. These materials represent the first series of mononuclear oxazoline complexes of Zn²⁺ to be fully characterized. The medicinal properties of these materials are currently under investigation and will be reported in a separate disclosure.

Experimental

General

All reactions were carried out in air, using commercially available, reagent-grade solvents. Zinc halides and ligands **1–4** (Fig. 1) were purchased commercially and used as received, with the exception of ZnCl₂. This material was dried by heating thrice to the melt under vacuum (approximately (approx.) 2000 Pa), and then the solid was cooled to RT under an atmosphere of dry argon gas. THF was stored over

4 Å molecular sieves. ¹H NMR spectra (CDCl₃ solution) were recorded at RT using a Bruker AC-250 NMR spectrometer located at the Atlantic Regional Magnetic Resonance Centre (ARMRC) (Halifax, N.S., Canada), operating at 250 MHz, or were recorded using a Bruker Avance 300 NMR spectrometer located at the Acadia Centre for Microstructural Analysis (ACMA) (Wolfville, N.S., Canada), operating at 300 MHz. Chemical shifts are reported in ppm using TMS (and (or) residual solvent resonance) as internal standard ($\delta_{\text{TMS}} = 0.00$ ppm). Coupling constants are reported in Hertz. IR spectra were recorded as nujol muls (except where noted) on a PerkinElmer 683 or 283B IR spectrometer; reported values are in units of cm⁻¹. Melting points were recorded in air on a Mel-Temp II apparatus and are uncorrected. Elemental analyses measurements were performed at the Lakehead University Centre for Analytical Services (LUCAS) located in Thunder Bay, Ont., Canada.

Synthesis of [dichlorobis(η¹-N-(2-methyl-2-oxazoline))zinc] (**5**)

Solid zinc chloride (4.2 g, 31 mmol) was dissolved in 150 mL of diethylether by stirring the mixture at RT for

15 min. This mixture was then filtered to remove any undissolved material. To the rapidly stirring (clear and colourless) solution was added (via syringe) 8.0 mL (94 mmol) of **1** in a single portion. A white precipitate began to form almost immediately. Stirring was continued for a further 12 h at RT, and the resulting solid was isolated by filtration. This material was then washed thrice with Et₂O (35 mL) and then allowed to dry in air. Yield 8.0 g (84%) of a white, slightly hygroscopic solid. Crystals of **5**, suitable for X-ray diffraction, grew after a CH₂Cl₂ solution of **5**, layered with Et₂O, was left standing for several days at RT. mp > 105 °C (decomposition temperature (decomp.)). IR: 1650 (st). ¹H NMR (250 MHz) δ: 4.50 (t, 2H, *J* = 9.8, CH₂O), 3.98 (t, 2H, *J* = 9.8, CH₂N), 2.27 (s, 3H, CH₃). Calcd. for C₈H₁₄N₂O₂Cl₂Zn·(H₂O) (%): C 29.72, H 4.55, N 8.67; found: C 29.72, H 4.97, N 8.63.

Synthesis of [dibromobis{η¹-N-(2-methyl-2-oxazoline)}zinc] (**6**)

In a reaction analogous to that used to produce **5**, zinc bromide (1.0 g, 4.4 mmol) in Et₂O was treated with **1** (2.1 equiv). Yield 1.6 g (92%, hygroscopic solid). mp > 72 °C (decomp.). IR: 1650 (st). ¹H NMR (250 MHz) δ: 4.50 (t, 2H, *J* = 9.8, CH₂O), 4.00 (t, 2H, *J* = 9.8, CH₂N), 2.29 (s, 3H, CH₃). Calcd. for C₈H₁₄N₂O₂ZnBr₂·0.5(H₂O): C 23.76, H 3.74, N 6.93; found: C 23.53, H 3.63, N 6.85.

Synthesis of [diiodobis{η¹-N-(2-methyl-2-oxazoline)}zinc] (**7**)

As for **5**, zinc iodide (3.0 g, 9.4 mmol), suspended in Et₂O–THF (60 mL : 10 mL), was treated with 2.4 mL (28 mmol) of **1**. Yield 4.0 g (87%, hygroscopic white solid). Crystals, suitable for X-ray diffraction, were grown from a solution of **3** (CH₂Cl₂ layered with Et₂O) that had been left standing at RT for several days. mp > 94 °C (decomp.). IR: 1650 (st). ¹H NMR (250 MHz) δ: 4.50 (t, 2H, *J* = 9.8, CH₂O), 4.02 (t, 2H, *J* = 9.8, CH₂N), 2.29 (s, 3H, CH₃). Calcd. for C₈H₁₄N₂O₂ZnI₂·0.25(H₂O): C 19.45, H 2.96, N 5.67; found: C 19.21, H 2.76, N 5.57.

Synthesis of [dichlorobis{η¹-N-(2,4,4-trimethyl-2-oxazoline)}zinc] (**8**)

As for **5**, zinc chloride (1.2 g, 8.8 mmol) in Et₂O was treated with **2** (2.2 mL, 17 mmol), and the solid was washed with Et₂O (2 × 35 mL) and petroleum ether (50 mL); the product can be further recrystallized from a 1:1 mixture of CH₂Cl₂–Et₂O. Yield 2.0 g (65%). mp > 124 °C (decomp.). IR: 1635 (st). ¹H NMR (250 MHz) δ: 4.17 (s, 2H, CH₂O), 2.27 (s, 3H, N=C–CH₃), 1.61 (s, 6H, CH₃). Calcd. for C₁₂H₂₂N₂O₂Cl₂Zn·0.5(CH₂Cl₂): C 37.06, H 5.72, N 6.92; found: C 37.29, H 5.86, N 6.92.

Synthesis of [dibromobis{η¹-N-(2,4,4-trimethyl-2-oxazoline)}zinc] (**9**)

As for **5**, using ZnBr₂ (1.4 g, 6.2 mmol; ether suspension) and **2** (1.7 mL, 13 mmol). Yield 2.7 g (96%). mp > 172 °C (decomp.). IR: 1625 (st). ¹H NMR (250 MHz) δ: 4.18 (s, 2H, CH₂O), 2.29 (s, 3H, N=C–CH₃), 1.68 (s, 6H, CH₃). Calcd. for C₁₂H₂₂N₂O₂Br₂Zn: C 31.92, H 4.91, N 6.20; found: C 32.16, H 4.59, N 6.21.

Synthesis of [diiodobis{η¹-N-(2,4,4-methyl-2-oxazoline)}zinc] (**10**)

As for **5**, ZnI₂ (3.3 g, 10 mmol; ether suspension) was treated with **2** (2.7 mL, 21 mmol). Yield 4.9 g (90%). Crystals, suitable for X-ray diffraction, grew from a sealed solution of **10** (CH₂Cl₂) layered with Et₂O, after standing at RT for several days. mp > 159 °C (decomp.). IR: 1630 (st). ¹H NMR (250 MHz) δ: 4.17 (s, 2H, CH₂O), 2.27 (s, 3H, N=C–CH₃), 1.61 (s, 6H, CH₃). Calcd. for C₁₆H₁₈N₂O₂ZnI₂ (%): C 26.42, H 4.06, N 5.14, found: C 26.27, H 3.86, N 5.02.

Synthesis of [dichlorobis{η¹-N-(2-phenyl-2-oxazoline)}zinc] (**11**)

As for **5**, ZnCl₂ (2.0 g, 15 mmol) in Et₂O (125 mL) was treated with **3** (3.9 mL, 30 mmol), and the resulting white solid was washed with Et₂O (2 × 15 mL) and then air-dried. Yield 4.77 g (74%). mp > 179 °C (decomp.). IR: 1618 (st). ¹H NMR δ: 7.78 (d, 2H, *J* = 7.5, ArH), 7.61 (t, 1H, ArH), 7.41 (t, 2H, *J* = 7.6, ArH), 4.33 (m, 4H, CH₂CH₂). Calcd. for C₁₆H₁₈N₂O₂Cl₂Zn: C 50.20, H 4.21, N 6.51; found: C 50.47, H 4.26, N 6.68.

Synthesis of [dibromobis{η¹-N-(2-phenyl-2-oxazoline)}zinc] (**12**)

As for **5**, ZnBr₂ (2.1 g, 9.3 mmol) in Et₂O (100 mL) was treated with **3** (2.5 mL, 19 mmol), and the solid was washed with Et₂O (2 × 15 mL) and then air-dried. Yield 4.71 g (48%). mp > 170 °C (decomp.). IR: 1620 (st). ¹H NMR δ: 7.76 (d, 2H, *J* = 8.0, ArH), 7.58 (t, 1H, ArH), 7.35 (t, 2H, *J* = 7.9, ArH), 4.47 (m, 4H, CH₂CH₂). Calcd. for C₁₆H₁₈N₂O₂ZnBr₂: C 41.61, H 3.49, N 5.39; found: C 41.66, H 3.49, N 5.30.

Synthesis of [diiodobis{η¹-N-(2-phenyl-2-oxazoline)}zinc] (**13**)

As for **5**, ZnI₂ (1.4 g, 4.4 mmol) was suspended in Et₂O (25 mL), and the mixture was then treated with **3** (1.1 mL, 8.4 mmol), and the light yellow solid was washed with Et₂O (2 × 10 mL) and then air-dried. Yield 2.55 g (99%). mp > 193 °C (decomp.). IR: 1620 (st). ¹H NMR δ: 7.76 (d, *J* = 7.9, 2H, ArH), 7.61 (t, 1H, ArH), 7.38 (t, 2H, *J* = 8.0, ArH), 4.43 (m, 4H, CH₂CH₂). Calcd. for C₁₆H₁₈N₂O₂ZnI₂ (%): C 35.24, H 2.96, N 4.57; found: C 34.90, H 2.97, N 4.43.

Synthesis of [dichlorobis{η¹-N-(4,4-dimethyl-2-phenyl-2-oxazoline)}zinc] (**14**)

A sample of ZnCl₂ (2.25 g, 16.5 mmol) was dissolved in 100 mL of Et₂O, and the solution was then filtered. Compound **4** (5.6 mL, 33 mmol) was added, and the mixture was then stirred at RT for 2 h. The resulting white solid was collected by filtration and washed with Et₂O (2 × 25 mL). Yield 4.2 g (58%). mp > 174 °C (decomp.). IR: 1620 (st). ¹H NMR δ: 7.86 (m, 2H, ArH), 7.28 (m, 3H, ArH), 3.95 (s, 2H, CH₂), 1.25 (s, 6H, CH₃). Calcd. for C₂₂H₂₆N₂O₂Cl₂Zn: C 54.29, H 5.38, N 5.76; found: a reproducible elemental analysis (±0.4%) could not be obtained for this material.

Synthesis of [dibromobis{η¹-N-(4,4-dimethyl-2-phenyl-2-oxazoline)}zinc] (**15**)

As for **5**, ZnBr₂ (2.0 g, 8.9 mmol) in Et₂O (100 mL) was treated with **4** (3.0 mL, 18 mmol), then stirred for 2 h, and

then evaporated at RT. Yield 2.0 g (65%). mp > 168 °C (decomp.). IR: 1618 (st). ¹H NMR δ: 7.86 (m, 2H, ArH), 7.28 (m, 3H, ArH), 3.95 (s, 2H, CH₂), 1.25 (s, 6H, CH₃). Calcd. for C₂₂H₂₆N₂O₂ZnBr₂: C 45.90, H 4.55, N 4.87; found: C 45.68, H 4.46, N 4.84.

Single crystal X-ray structure determinations

X-ray structure of 7

Suitable white crystals were obtained by slow diffusion of Et₂O into a CHCl₃ solution of the complex. Diffraction data were collected on a Nonius Kappa-CCD diffractometer equipped with a 95 mm CCD camera and a k-goniostat, using graphite-monochromated Cu Kα radiation. Data were reduced to F_o² values. A numerical absorption correction was applied using Gaussian integration (27), with max and min transmission factors of 0.024 and 0.009, respectively. The structure was solved by Patterson interpretation, using the program DIRDIF-96 (28). Isotropic and full matrix anisotropic least-squares refinements were carried out using SHELXL-97 (29). All non-H atoms were refined anisotropically, except N2, C5, and O2, which were isotropically refined. All the hydrogen atom positions were geometrically calculated and refined riding on their parent atoms. The molecular plots were made with the EUCLID program package (30). The WINGX program system (31) was used throughout the structure determinations.

X-ray structures of 10–13 and 15

Suitable crystals were grown from solutions of the complexes in dichloromethane that had been layered with Et₂O and allowed to stand at RT (or at –10 °C) for several days. Crystals were mounted on a glass fibre, covered in epoxy, and data was collected on a Smart 1000 CCD diffractometer using Mo Kα radiation (graphite monochromated). Isotropic and full matrix anisotropic least-squares refinements were carried out using SHELXL-97 (29). It should be noted that complex 15 has twofold imposed crystallographic symmetry.

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