**Substituent Effects in the zinc(II) coordination chemistry of isomeric pyridylpyrazole ligands**

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**Abstract**

Pyrazoles with unsymmetric substitution are useful ligands in coordination chemistry, but are under-developed due to synthetic challenges in accessing the pure isomers. We have prepared four new structurally-related *N*-(2-pyridyl)-3,5-dialkylpyrazole ligands **L1** – **L4**, and probed their coordination chemistry in the crystalline phase and in solution to elucidate a relationship between steric influence of the alkyl substituents, the stability of the subsequent metal complexes, and their crystal packing influences. We find that the ligands **L1** and **L2**, bearing linear or branched alkyl substituents, show similar stabilities and crystal packing motifs featuring π···π and C-H···Cl interactions in the crystalline complexes **1** and **2,** respectively. The cyclohexyl-fused species **L3** and **L4** vary both in the solution stability of the complexes **3** and **4**, respectively, and in their crystal packing. Complex [ZnCl2(**L3**)] **3** is a mononuclear complex similar to **1** and **2**, albeit with π···π interactions disallowed by the bulk of the cyclohexyl ring. Reaction of the isomeric **L4** with ZnCl2 gives two polymorphic complexes **4α** and **4β** of the form [Zn2Cl2(μ2-Cl)2(**L4**)2], varying only in their long-range packing modes. These results show the importance of understanding the steric influences in substituted pyridylpyrazoles, which determine both stability in solution and speciation in the crystalline phase.

**Keywords**

Coordination chemistry, pyrazole, zinc, crystallography, fluorescence

1. **Introduction**

Pyrazole is a commonly used ligand in many aspects of coordination chemistry, which has been successfully employed in a wide variety of coordination compounds from discrete mononuclear complexes to multi-metallic systems and coordination polymers.1 Recently many elegant examples have been reported of substituted pyrazoles acting as linkers in cages, helicates, boxes and coordination polyhedra,2 where the ready functionalisation of the pyrazole ring gives access to a versatile assortment of substitution patterns, with many possible binding modes.3 Pyrazole is often also combined with pyridine to form polydentate ligands.4 The electronic properties of pyridylpyrazole chelates lend themselves perfectly to spin crossover systems, such as in the 2,6-bis(pyrazol-1-yl)pyridine ligands shown by Halcrow and others to favour room temperature spin crossover in Fe(II) complexes.5 Pyrazole is also becoming increasingly common in Metal-Organic Framework (MOF) chemistry.6 The excellent hydrolytic stability of metal pyrazolate complexes has been beneficial in designing water-stable MOFs,7 while the outer-sphere hydrogen bonding interactions which defines the coordination chemistry of *1H*-pyrazoles and indazoles has proven useful in structure direction for other pyrazole-based MOFs and related species.8

 A common issue in pyrazole chemistry is encountered in the preparation of N-substituted pyrazoles with inequivalent substituents at the 3- and 5-positions.9 Depending on the electronic and steric influences of the substituents, synthesis of such systems either by alkylation of the parent *1H*-pyrazole or by reaction of the precursor diketone with a substituted hydrazine often gives a mixture of isomers. As a result, while symmetrically substituted pyrazoles are commonly encountered as a component of chelating ligands,10 3,5-unsymmetric derivatives are much less common. Nonetheless, unsymmetrically substituted pyrazoles provide important means of steric control around metal binding sites, important for catalytic applications with chelating ligands, especially tris-pyrazolylborates.11 Here, we report the synthesis of four new structurally related pyridylpyrazole ligands, each containing either symmetric or unsymmetric alkyl substitution at the pyrazolyl 3- and 5-positions. These ligands were designed and prepared with the intention of not only establishing the selectivity of the ligand synthesis itself, but also to probe the influence of alkyl substituents of varying size, rigidity and symmetry on the nearby chelating pocket. Using ZnCl2 as a basis, we then examine the coordination behaviour of these four ligands both in the crystalline phase and in solution. The coordination geometry, crystal packing behaviour and stability constants of each complex is then related to the underlying substitution pattern of the parent ligands.

1. **Results and Discussion**

***2.1 Design and Synthesis of Ligands L1 – L4***

With the intention of developing N-(2-pyridyl)pyrazole chelating ligands containing unsymmetric substitution at the 3- and 5-positions, three β-diketones were selected. Ligand **L1** was designed as a control molecule, a ligand with similar steric bulk to the target compounds but without the possibility of isomer formation during the synthesis. Ligand **L2** contains a large isobutyl substituent and a small methyl substituent, and was expected to preferentially form as a single isomer, although a mixture of isomers is possible. Finally, isomers **L3** and **L4**, both containing methyl and fused-cyclohexyl functionalities, were expected to form in comparable yields. Initially all three reactions were carried out under the typical reaction conditions for the synthesis of disubstituted pyrazoles,12 by heating the appropriate diketone with 2-hydrazinopyridine in ethanol at reflux. This process gave **L1** in excellent yield (96%), while repeating the reaction to form **L2** gave 75% purified yield of the major isomer and no isolable quantities of the theoretical minor isomer. Both **L1** and **L2** were purified from residual starting materials by flash chromatography, giving the products as pale yellow liquids.

[Scheme 1]

In the case of the cyclohexyl-fused (4,5,6,7-tetrahydroindazole) derivatives **L3/L4**, the equivalent synthesis in ethanol gave poor conversion, which we ascribe to the kinetic barrier of the more hindered cyclic ketone. While **L3** and **L4** have been reported as part of a scope exploration in the use of heterogeneous zirconia catalysts in solvent-free systems,13 we elected to repeat the reaction in refluxing toluene with a Dean-Stark trap in the presence of catalytic *p*-toluenesulfonyl chloride. This gave a mixture of **L3** and **L4**, in an approximately 6:1 ratio. Although chemically very similar, the two isomers could be separated by flash chromatography in good purity to give crystalline solids. In order to confirm that the isomeric ratio was intrinsic to the starting materials and not an artefact of the reaction conditions, the synthesis of **L2** was repeated in toluene under Dean-Stark conditions, but again only the dominant isomer was observed. We were somewhat surprised to note the dominance of **L3** as the major isomer at the expense of **L4**; our expectation was for the initial reaction of the less sterically hindered acetyl carbonyl with the terminal hydrazine nitrogen atom, followed by the rate-determining ring closure, to give **L4** as the major isomer. However, the product distribution would indicate that the pathway involving initial attack at the cyclic ketone (with the release of *i*-strain to form the tetrahedral intermediate potentially acting as a driving force14) followed by ring closure *via* the acetyl carbonyl is dominant.

As a side note, a trace amount of crystalline material was observed to deposit from the isomeric mixture of **L3** and **L4** immediately following the reaction and removal of the solvent and prior to chromatography. These crystals analysed for 2-aminopyridinium *p*-toluenesulfonate, and give an insight to the fate of unreacted 2-hydrazinopyridine under these reaction conditions, where a decomposition process most likely involving oxidative cleavage of the hydrazine substituent takes place. The material is isostructural to a previously reported polymorph,15 although here we include the low-temperature data collection for posterity. An analysis of the crystal structure of this side product is given as Electronic Supporting Information.

***2.2 Crystallographic Studies of L3 and L4***

While both products share the same chemical formula and very similar chemical structures, we noted that **L4** crystallised much more readily than **L3**, which slowly crystallised on standing. This and the *ca.* 25 K difference in melting point between the two compounds would seem to implicate differences in the crystal packing behaviour of the two solids. Both compounds were subjected to single crystal X-ray diffraction to elucidate the differences in geometry and packing behaviour between the isomers. The diffraction data for **L3** were solved and refined in the orthorhombic space group *P*212121, to give a structural model containing three unique **L3** molecules within the asymmetric unit. All three discrete species adopt the expected conformation; a *trans* oriented pyridyl-pyrazole torsion angle, and a half-chair conformation for the fused cyclohexyl group. Minor geometrical differences are manifest in these conformations between the three residues, however; the pyridyl-pyrazolyl torsion angles (measured N­py-Cpy-Npz-Npz) of 162.8(2)°, 157.9(2)° and 166.7(2)° show statistically significant differences. The representative structure of **L3** is shown in Figure 1.

[Figure 1]

The extended structure of **L3** contains relatively few well-defined intermolecular contacts. Two of the three residues engage in C-H···N interactions originating at the pyridyl 6-position donating to an adjacent pyrazolyl nitrogen atom, with C···N distances 3.462(3) and 3.475(3) Å for the two unique interactions. One example of a C-H···N interaction originating from a cyclohexyl CH2 group is also evident (C···N distance 3.473(3) for C10···N6). While various C-H···π contacts are evident involving the cyclohexyl and pyridyl groups, these exhibit long C···π distances more consistent with diffuse crystal packing interactions rather than directed forces. The key intermolecular contacts can be more easily visualised by examination of the Hirshfeld isosurface mapped with intermolecular contacts.16 As shown in Figure 1 (bottom), the short C-H···N contacts described above are the only notable features on the normalized contact mapping. Surprisingly, the significant face-to-face π-π interactions which might be expected based on the polarity of the pyridylpyrazole conjugated system seem to be prohibited by the steric bulk of the cyclohexyl groups.

Examination of the structure of **L4**, solved and refined in the triclinic space group *P*-1, allows direct comparison between the two compounds. Crystalline **L4** exhibits a slightly higher calculated density (1.292 g·cm‑3) than **L3** (1.280 g·cm‑3), which tends to support the expectation of a more efficient crystal packing mode.The asymmetric unit of **L4** contains a single molecule of the compound, which exhibits a similar half-chair conformation for the cyclohexyl ring and *trans* orientation of the pyridylpyrazole system (with an Npy-Cpy-Npz-Npz torsion angle of 164.09(13)°), as shown in Figure 2. However, the more angular geometry of the overall molecule compared to the linear **L3** enforces differences in crystal packing. In the case of **L4**, C-H···N contacts involving the pyrazole nitrogen atom exhibit much greater distances, and originate at the 4-pyridyl position of the adjacent molecule. The C···N distance of 3.693(3) Å is considerably longer than the similar interactions in the structure of **L3**. Unlike **L3**, however, in the structure of **L4** a defined offset face-to-face (OFF)17 π-π interaction is observed between two antiparallel pyridyl groups, with a mean interplanar distance of 3.54 Å and a 1.08 Å slip distance. The methyl group also engages in more directed C-H···π interactions with the pyrazole π-system, exhibiting a C···π(mean plane) distance of 3.44 Å. Nonetheless, somewhat counterintuitively, the crystal packing interactions in **L4** would appear to be more diffuse in nature than **L3**. This observation is supported by a largely featureless Hirshfeld surface mapping of normalized contact distance (Figure 2), visualised at the same rendering level, as for **L3** above. This implies the differences in molecular geometry between the two ligands play a larger role in dictating packing efficiency than the presence of defined interactions in these systems.

[Figure 2]

***2.3 Coordination Chemistry of L1 – L4***

*Structure of Complexes* ***1*** *and* ***2***

With the four ligands **L1** – **L4** in hand, we turned our attention to studying their coordination chemistry. With the intention of providing limited structure direction from the metal ion, we chose zinc chloride as the appropriate metal salt for these studies, as the lack of strictly enforced coordination geometry from the metal allows better insight into the coordination preferences of the ligands themselves. Our goal was to elucidate the impact of the unsymmetric alkyl substituents on the coordination behaviour of the pyridylpyrazole chelate, and particularly any differences based on the size or rigidity of the alkyl functionality. Reacting each of the four ligands with one equivalent of zinc chloride in acetonitrile, followed by slow diffusion of toluene vapour, gave colourless crystals of the (empirical) formula [ZnCl2(**L**)] over the course of two weeks.

The diffraction data for [ZnCl2(**L1**)] **1** were solved and refined in the monoclinic space group *P*21/*n*, and the structural model contains the complex in its entirety within the asymmetric unit. Crystals of **1** were observed to shatter at low temperature, and so data collection was carried out at 230 K. One of the two ethyl groups (proximal to the metal binding site) exhibits conformational disorder over two orientations. The pyridylpyrazole unit exhibits a planar *cis* conformation (Npy-Cpy-Npz-Npz angle 6.8(4)°) and coordinates to the zinc ion with a bite angle of 78.08(10)°. The coordination sphere of the zinc ion is completed by two chlorido ligands in a distorted tetrahedral fashion, with a Cl-Zn-Cl angle of 117.08(4)°. The pyrazolyl N-Zn bond (N3-Zn1, 2.020(3) Å) is marginally shorter than the pyridyl equivalent (N1-Zn1, 2.085(2) Å). The structure of complex **1** is shown in Figure 3.

[Figure 3]

The most obvious intermolecular interaction in the extended structure of **1** is a centrosymmetric dimer involving OFF π-π interactions between two parallel pyridylpyrazole units (mean interplanar distance 3.41 Å). This interaction also involves two reciprocated sets of chelating C-H···Cl interactions originating from the pyridyl 3-position and the CH2 substituent of the distal ethyl chain, with C···Cl distances of 3.640(3) and 3.884(5) Å, respectively. These stacked dimers undergo further C-H···π interactions on their outer faces with the disordered ends of the proximal ethyl chain.

The diffraction data for [ZnCl2(**L2**)] **2** were solved and refined in the monoclinic space group *P*21/*n*, and similarly to **1**, contained a single mononuclear complex in the asymmetric unit. Minor crystallographic disorder was observed in the CH and CH2 groups of the isobutyl side chain, although the terminal methyl groups are localised. The geometry of the coordination sphere itself is closely related to complex **1**; the N-Zn bond lengths of 2.030(2) and 2.079(2) Å for N3 and N1, respectively, are equivalent within error to those in **1**, as is the bite angle (78.08(6)°), while the Npy-Cpy-Npz-Npz torsion angle (4.0(2)°) is marginally smaller. Both disordered conformers of the isobutyl group are directed towards the same face of the pyridylpyrazole π system, giving the molecule a somewhat hooked geometry, as shown in Figure 4.

[Figure 4]

Further parallels to the structure of **1** are observed when considering the intermolecular interactions in complex **2**. A similar antiparallel OFF π-π-stacked dimer is the dominant mode of association, although the mean interplanar distance of 3.38 Å in **2** is marginally smaller than that observed in **1**. This interaction again supports C-H···Cl interactions originating at the pyridyl 3-position (with C···Cl distance 3.536(2) Å), with longer contacts originating from the CH2 and CH3 groups of the isobutyl side chain, although these are somewhat obscured by crystallographic disorder. On the outer faces of this dimer, C-H···π interactions are evident from an isobutyl CH3 group to the pyridine face, with a C···π(mean plane) distance of 3.63 Å. The contributions of the proximal methyl group, in contrast, generally involve longer contact distances and are difficult to meaningfully delineate from diffuse crystal packing interactions.

*Crystal Structures of complexes* ***3****,* ***4α*** *and* ***4β***

The isomeric ligands **L3** and **L4** also gave colourless crystalline material on reaction with ZnCl2 in acetonitrile following toluene diffusion, and being structural isomers, provide more opportunity for direct comparison between coordination modes and intermolecular interactions. The diffraction data for [ZnCl2(**L3**)] **3** were solved and refined in the monoclinic space group *C*2/*c*, and the asymmetric unit of **3** contains the complete mononuclear complex with no solvent or guest species. The half-chair conformation of the cyclohexyl ring is maintained as expected, while the pyridylpyrazole torsion angle of 10.8(3)° is further from planarity than those of complexes **1** and **2**, but slightly closer to planarity than observed in the *trans* orientation of the free ligand. The bite angle of 79.06(7)° is closely comparable to complexes **1** and **2**, as are the Zn-N bond lengths (2.069(2) and 2.022(2) Å for N1 and N3, respectively). With essentially no freely rotatable atoms within the structure besides the CH3 group, the molecular structure of **3**, as shown in Figure 5, can be considered comparably rigid.

[Figure 5]

While the prevalence of OFF π-π interactions in complexes **1** and **2** had major impact on the crystal packing of these species, equivalent interactions are not observed in complex **3**, despite its more planar geometry. Molecules of **3** align in infinite columns parallel to the [110] vector, and although similar antiparallel stacking arrangements are observed, the axial bulk of the cyclohexyl group enforces a much larger interplanar distance between the ligand mean planes. The ligand mean planes of adjacent groups are separated by 4.06 or 4.14 Å, with slip between the conjugated pyridylpyrazole groups of approximately 3.9 or 4.7 Å, respectively, for the two unique interactions. The closest C-H···π contact involved in each column is 3.51 Å involving a non-coplanar cyclohexyl CH2 group and the pyridyl group of the adjacent molecule. This contact, as well as a short C-H···Cl contact from a cyclohexyl CH2 hydrogen atom within the same column (distance C13···Cl2 3.688(2)), are the most significant intermolecular contacts in the structure. Adjacent columns interact through myriad weak C-H···Cl interactions originating from the cyclohexyl methylene hydrogen atoms and the pyridyl 3-position.

When subjected to the same crystallisation conditions, **L4** initially appeared to show similar coordination behaviour. However, careful analysis of the X-ray powder diffraction pattern revealed the presence of two crystalline phases, the dominant phase **4α** (monoclinic *P*21/*n*) and a minor phase **4β** (triclinic *P*-1). Both phases are similar in calculated density (1.688 g·cm-3 for the major phase **4α** and 1.661 g·cm-3 for the minor form **4β**). Single crystal X-ray diffraction was carried out on each phase separately, and revealed identical formulations for both polymorphs, which differ only in their crystal packing behaviour. Interestingly, and in contrast to complexes **1** – **3**, both polymorphs of complex **4** exhibit a dimeric centrosymmetric [Zn2Cl2(μ2-Cl)2(**L4**)2] speciation in the crystalline phase, with the asymmetric unit of each containing half of the molecule. This coordination behaviour is clearly closely related to the monomeric forms observed for the other complexes. Given the lack of a strong energetic preference for coordination geometry in zinc(II), from considering the crystal structure alone it is difficult to ascribe the existence of the dimer to either a ligand-directed coordination preference or simply a dimerization in the crystalline phase as a result of crystal packing influences. For both polymorphs, the zinc ion adopts a five-coordinate geometry intermediate between square pyramidal and trigonal bipyramidal (τ5 = 0.33 for **4α**, 0.64 for **4β**).18 In both cases, the major axis is defined by the pyrazole nitrogen atom and the *trans*-oriented μ2 chlorido ligand. The Npz-Zn bond lengths of 2.092(2) and 2.1004(12) Å, and the Npy-Zn bond lengths of 2.152(2) and 2.1455(12) Å, for **4α** and **4β**, respectively, are considerably longer than those observed in complexes **1** – **3**, which is consistent with the increased coordination number in **4**. Unsurprisingly, the bridging chlorido ligand exhibits longer Zn-Cl bond lengths (all falling in the range 2.3548(4) to 2.5234(4) Å) than the terminal chlorido ligand (2.2373(6) Å for **4α** and 2.2315(4) Å for **4β**). With pyridyl-pyrazole torsion angles of 5.8(3) and 4.4(2)°, respectively, **4α** and **4β** exhibit similar planarity to the other compounds studied, and regular half-chair conformations are observed for the cyclohexyl rings. The molecular structure of **4α** (also representative of **4β**) is shown in Figure 6.

[Figure 6]

The main mode of intermolecular interaction in both **4α** and **4β** is an antiparallel OFF π-π interaction. The overlap of π-systems is mostly restricted to the pyridyl rings, with mean interplanar distance 3.41 Å and centroid···centroid slip distance of 1.34 Å in **4α** and similar values (3.46 and 1.23 Å, respectively) for **4β**. Propagating this interaction leads to one-dimensional stacks in both structures. In both cases, these stacks associate in the orthogonal direction, in an arrangement which leads to overlap of the cyclohexyl CH2 groups with the pyrazole π systems of adjacent complexes. The C···π (mean plane) distances involved, of 3.52 Å for **4α** and 3.56 Å for **4β** are consistent between the two polymorphs and in line with expectations from complexes **1 – 3**. Considering the association of the dinuclear complex **4** into sheets in both polymorphs through these weak interactions, association in the third dimension is the source of variation in the two packing modes. Phase **4α** exhibits the classic monoclinic “herringbone”-type packing motif for these sheets where the tilting of alternate sheets in the *b* direction is inverted through a glide plane. In **4β**, adjacent sheets are aligned in register, as shown in Figure 7. In neither packing mode are any prominent intermolecular interactions obvious. Given the similarities in molecular geometry and packing modes in the other directions, these observations may rationalise the apparent energetic similarity of the two forms.

[Figure 7]

***2.4 Solution Studies***

With each ligand forming discrete coordination compounds on reaction with ZnCl2, UV-Visible and fluorescence spectroscopy were employed to ascertain the speciation and nature of the bonding in acetonitrile solution. Each of the four ligands in acetonitrile was titrated with ZnCl2 solution in acetonitrile, which in all cases led to significant changes in both the absorbance and emission profiles. UV-Visible and fluorescence data were measured in the initial concentration ranges [L]init = 9 – 11 μM, and pure UV-Visible titrations were also carried out at higher concentrations (up to [L]init = 64 μM), with statistically equivalent binding constants observed irrespective of concentration. Representative UV-Visible and fluorescence titration plots are shown in Figure 8, with additional data provided as Supporting Information. Both **L1** and **L2** exhibit near-identical photophysical properties, with two absorbance bands in the UV region (λmax = 278, 254 nm) ascribed to π-π\* or n-π\* transitions. Excitation (at either wavelength) gives a weak emission band with λmax = 315 nm. Sequential addition of ZnCl2 aliquots leads to the growth of a new absorbance with λmax  = 288 nm, with reduction of the nearby free ligand band, and a slight blue-shift of the higher energy absorbance, to λmax = 251 nm. Excitation at the isosbestic point for the lower-energy absorbance (283 nm) reveals a significant increase in emission intensity accompanying complex formation, with the peak intensity increasing by a factor of 6, and a red-shift in the emission band to 328 nm.

[Figure 8]

In the case of **L3** and **L4**, again very similar spectroscopic profiles were observed between the two related ligands, although these were quite distinct from the observations for **L1** and **L2**. The free ligands exhibit absorbance bands at 283 and 264 nm (with the 264 nm band being slightly suppressed in **L3** compared to **L4**), and both show weak emission at 328 nm upon excitation into either absorbance band. Addition of aliquots of ZnCl2 to these ligands causes a more pronounced splitting of the two absorbance features compared to **L1**/**L2**; the 283 nm absorbance undergoes a red-shift to 299 nm, while the 264 nm absorbance is reduced in intensity compared to a new absorbance at 244 nm. Well-defined isosbestic points are evident at 253 and 291 nm. Excitation at 291 nm reveals a red-shift in emission as a function of ZnCl2 concentration, with the emission maxima shifting from 328 nm to 370 nm. Interestingly, however, while both **L3** and **L4** undergo this transition, neither compound experiences the drastic increase in fluorescence intensity observed in the zinc complexes of **L1** and **L2**, with the emission intensity at λmax increasing by only a factor of 1.5. The suppression of the emission in complex **3** and **4** may be a result of several factors, but the most obvious difference in **L3** and **L4** is the fusion of the cyclohexyl ring to the pyrazole 3- and 4-positions. It is well known that molecular vibrations can play a key role in suppressing emission from singlet excited states by providing non-radiative decay pathways.19 Given **L3** and **L4** both have access to additional ring-based intramolecular motions, such as half-chair-to-half-boat transitions, as well as an additional attachment point to the conjugated system in the pyrazole 4-position, this seems a possible candidate for the origin of the diminished fluorescence in these instances.

In order to better determine any differences in speciation or stability constants, the UV-Visible titration data were modelled with a global non-linear regression method using ReactLab Equilibria software.20 In every case, sensible fits were only obtained for a single speciation, the expected 1M:1L stoichiometry, and no obvious additional inflection points were visible from the data (Supporting Information). The stability constants, expressed as logK1:1 and presented as an average value calculated from three independent titrations (Table 1), are largely in line with the observations from the titrations themselves. Ligands **L1** and **L2** are inseparable in their binding affinity, and **L3** and **L4** also show statistically equivalent stability constants. However, **L3** and **L4** uniformly showed stronger binding affinities for Zn than **L1** and **L2**.

[Table 1]

The discrepancies in stability constants between the two classes of ligand cannot necessarily be ascribed to any differences in the actual binding site geometry or “preorganization”, which as shown in the crystal structures is fairly uniform for the mononuclear complexes **1** – **3**. Instead, a likely cause for the higher binding affinity of **L3** and **L4** is simply the reduced steric bulk of the alkyl chains in the vicinity of the binding site. In both **L3** and **L4**, the alkyl substituents are more compactly arranged without the opportunity to either restrict access directly to the binding site or hinder the necessary *trans*-*cis* conversion of the conjugated pyridylpyrazole system. Re-dissolving the crystalline complexes in deuterated acetonitrile gave 1H NMR spectra which showed only monotonic downfield shifts of all aromatic signals compared to the free ligands in CDCl3, consistent with coordination and with no ring current shielding effects to suggest any higher-order speciation or aggregation at higher concentrations. Unfortunately, none of the four complexes could be detected by mass spectrometry, presumably due to the ready dissociation of the complexes at very low concentrations. The near-identical behaviour of **L3** and **L4** in solution in the presence of zinc(II) lends support to the notion that the variations in the crystalline structures of complexes **3** and **4** include a strong component of crystal packing forces, rather than any intrinsic preference for the dimeric form in solution.

1. **Conclusions**

Here we have shown the convenient synthesis of four *N*-(2-pyridyl)pyrazole ligands containing alkyl substitution at their 3- and 5-positions, and the fascinating influences of these substituents on their isomer distributions, solution stability of their zinc(II) complexes, and crystal packing influences both of the free ligands and of their metal complexes. Ligands **L1** and **L2**, bearing linear or branched alkyl substituents, exhibited similar capacity for coordination to zinc in solution, and their crystal packing was largely influenced by π-π stacking synthons. In contrast, the isomeric species **L3** and **L4**, bearing fused cyclohexyl substitution, exhibited higher stability constants for their zinc complexes in acetonitrile solution, and exhibited diverse crystal packing behaviours. In complex [ZnCl2(**L3**)] **3**, π-π stacking interactions appear disfavoured by the steric bulk of the cyclohexyl group and the bent geometry of the molecule. Ligand **L4**, however, forms two polymorphic zinc complexes **4α** and **4β** in the crystalline phase, each with the formula [Zn2Cl2(μ2-Cl)2(**L4**)2], which we ascribe to crystal packing influences bought about by the differences in ligand geometry compared to **L3**. These results show the importance of even relatively small and remote functional groups on the coordination chemistry of these systems, and the utility of the pyrazole ring in generating closely related families to study these effects.

1. **Experimental**

*Materials and Methods*

All reagents, solvents and starting materials were purchased from Sigma Aldrich, Fisher Scientific or Fluorochem, were of reagent grade or better, and were used as received. NMR spectra were collected on a Bruker Avance III HD 400 spectrometer operating at 400 MHz for 1H and 100 MHz for 13C. Spectra were referenced to TMS and/or the residual solvent signal. Infrared spectra were recorded using a Thermo Scientific Nicolet iS10 instrument operating in ATR sampling mode. UV-Visible absorbance spectra were recorded in spectrophotometric grade solvents using quartz cuvettes from Starna on a Varian Cary 50 Bio spectrophotometer. The data series were fitted with ReactLab Equilibria software in the wavelength range 200 – 350 nm.20 The presented stability constants are averaged fitted stability constants of three independent titrations, with standard deviations. Fluorescence spectra were measured using a Varian Cary Eclipse fluorimeter. Elemental analysis was performed using a Thermo Flash 2000 CHNS analyser. High resolution mass spectra were measured using an Agilent 6530B Q-TOF LC/MS instrument with samples dissolved in acetonitrile. X-ray powder diffraction patterns were measured using a Bruker D8 Advance powder diffractometer using Cu Kα radiation (λ = 1.54178 Å). Samples were finely ground and applied to a zero-background silicon single crystal sample holder. All measurements were carried out at room temperature, and patterns were compared to the simulated patterns calculated from the single crystal data collected at 150 or 230 K.

*Single Crystal X-ray Diffraction*

Crystal and refinement parameters are given in Tables 2 and 3. All data were collected on a Bruker D8 Quest ECO with graphite-monochromated Mo Kα radiation (λ = 0.71073 Å). All samples were mounted on Mitegen micromounts in NVH immersion oil, and collections were carried out at 150 K except for complex **1**, crystals of which shattered at low temperatures, and so this collection was performed at 230 K. Data collections were carried out using φ and ω scans, with collections and data reductions carried out in the Bruker APEX-3 suite of programs.21 Multi-scan absorption corrections were applied for all datasets using SADABS.22 The data were solved with the intrinsic phasing routine in SHELXT,23 and all data were refined on F2 with full-matrix least squares procedures in SHELXL,24 operating within the OLEX-2 GUI.25 All non-hydrogen atoms were refined with anisotropic displacement parameters, while hydrogen atoms were placed in riding positions and refined with isotropic displacement parameters equal to 1.2 or 1.5 times the isotropic equivalent of their carrier atom. Specific collection and refinement strategies are further outlined in the combined crystallographic information file (cif). While most datasets were refined to full convergence without the need for additional restraints, the side chain disorder in complexes **1** and **2** required SADI and RIGU restraints to maintain sensible chemical geometries. Occupancies of the disordered contributors were determined with free variable refinement and subsequently fixed to rounded values. CCDC 1885087-1885094.

*Synthesis of 1-(2-pyridyl)-3,5-diethylpyrazole* ***L1***

Heptane-3,5-dione (1.60 mL, 1.42 g, 11.8 mmol) and 2-hydrazinopyridine (1.35 g, 12.4 mmol) were combined in ethanol (15 mL) and heated at reflux in air for 16 hours. On cooling to room temperature, the reaction mixture was concentrated *in vacuo*, giving a light brown oil. Purification by flash chromatography (silica, 3:1 hexane:ethyl acetate) gave the product as a pale yellow oil. Yield 2.281 g (96%). δH(400 MHz, CDCl3) 8.41 (ddd, 1H, *J*1 = 4.8 Hz, *J*2 = 1.9 Hz, *J*3 = 0.9 Hz, 6-py), 7.82-7.85 (m, 1H, 3-py), 7.74 – 7.78 (m, 1H, 4-py), 7.13 (ddd, 1H, *J*­1 = 7.2 Hz, *J*2 = 4.9 Hz, *J*3 = 1.1 Hz, 5-py), 6.08 (s, 1H, 4-pz), 3.13 (qd, 2H, *J*1 = 7.5 Hz, *J*2 = 0.7 Hz, CH2), 2.69 (q, 2H, *J* = 7.7 Hz, CH2), 1.25 – 1.31 (m, 6H, 2×CH3); δC(100 MHz, CDCl3) 155.68, 153.66, 147.71, 147.43, 138.06, 120.65, 116.21, 105.28, 21.59, 21.40, 13.66, 13.08; *m/z* (HR-ESI+) 202.1340 ([M+H+], calculated for C12H16N3+202.1344). νmax(ATR, cm-1) 3061w, 3016w, 2968s, 2935m, 2874m, 1589s, 1577s, 1556s, 1476s, 1457m, 1428s, 1373s, 1328w, 1311m, 1257w, 1233w, 1140m, 1090w, 1047m sh, 1034m, 1007m, 992m, 972w, 953m, 881w, 807m, 777s, 737m, 698m sh, 622m.

*Synthesis of 1-(2-pyridyl)-3-methyl-5-isobutylpyrazole* ***L2***

6-Methyl heptane-2,4-dione (1.91 mL, 1.76g, 12.4 mmol) and 2-hydrazinopyridine (1.35g, 12.4 mmol) were combined in ethanol (15 mL) and heated at reflux in air for 16 hours. Cooling the reaction to room temperature and concentration *in vacuo* gave a light brown oil. Purification by flash chromatography (silica, 4:1 petroleum ether: ethyl acetate) yielded the product as a pale yellow oil. Yield 2.014 g (75%). δH(400 MHz, CDCl3) 8.43 (ddd, 1H, *J*1 = 4.9 Hz, *J*2 = 1.8 Hz, *J*3 = 0.7 Hz, 6-py), 7.75 – 7.82 (m, 2H, 3-py + 4-py), 7.15 (ddd, 1H, *J*1 = 6.7 Hz, *J*2 = 4.9 Hz, *J*3 = 1.8 Hz, 5-py), 6.01 (s, 1H, 4-pz), 2.97 (d, 2H, *J* = 7.1 Hz, CH2), 1.87-2.00 (m, 1H, CH), 2.32 (s, 3H, CH3), 0.92 (d, 6H, *J* = 6.6 Hz, 2×CH3); δC(100 MHz, CDCl3) 153.70, 149.66, 147.51, 145.25, 138.11, 120.83, 116.50, 108.65, 36.41, 28.08, 22.45, 13.65; *m/z* (HR-ESI+) 216.1495 ([M+H+], calculated for C13H18N3+ 216.1501). νmax(ATR, cm-1) 3062w, 3014w, 2954m, 2926w, 2868m, 1590s, 1578s, 1557m, 1473s, 1436s sh, 1381s, 1360s sh, 1217w, 1166w, 1142m, 1093m sh, 1053w, 1034m, 1014m, 990m, 974m, 957w, 942w, 879m, 826w, 774s sh, 737s, 714s, 701m, 680m, 657m, 620m.

*Synthesis of 2-(2-pyridyl)-3-methyl-4,5,6,7-tetrahydroindazole* ***L3*** *and 1-(2-pyridyl)-3-methyl-4,5,6,7-tetrahydroindazole* ***L4***

2-Acetylcyclohexanone (1.61 mL, 1.74g 12.4 mmol) was added to 2-hydrazinopyridine (1.35g, 12.4 mmol) and a catalytic amount (10 mg) of *p*-toluenesulfonic acid in toluene (50 mL). The mixture was heated at reflux for 8 hours with a Dean-Stark condenser. After cooling to room temperature the orange solution was decanted and concentrated *in vacuo* to give a brown oil. A small crop of crystals which analysed for 2-aminopyridinium toluenesulfonate were also isolated from this oil. Purification by flash chromatography (silica, 4:1 petroleum ether:ethyl acetate) gave **L3** as the major product, as a yellow oil which slowly crystallised on standing, and **L4** as the minor product, as a colourless crystalline solid. Yields: **L3** 1.608 g (61%); **L4** 238 mg (9%).

*Characterisation data for* ***L3****:*

m.p. 48-49 °C; δH(400 MHz, CDCl3) 8.40 (ddd, 1H, *J*1 = 4.9 Hz, *J*2 = 1.8 Hz, *J*3 = 0.9 Hz, 6-py), 7.82 (dt, 1H, *J*1 = 8.3 Hz, *J*2 = 1 Hz, 3-py), 7.72-7.77 (m, 1H, 4-py), 7.11 (ddd, 1H, *J*1 = 7.2 Hz, *J*2 = 4.9 Hz, *J*3 = 1.1 Hz, 5-py), 2.73 (t, 2H, *J* = 6.2 Hz, CH2), 2.54 (s, 3H, CH3), 2.48 (t, 2H, *J* = 6.1 Hz, CH2), 1.75 – 1.86 (m, 4H, 2×CH2); δC(100 MHz, CDCl3) 153.83, 150.89, 147.39, 138.01, 136.36, 120.36, 116.92, 115.69, 23.54, 23.35, 23.28, 20.32, 12.49; *m/z* (HR-ESI+) 214.1343 ([M+H+], calculated for C13H16N3+ 214.1344). νmax(ATR, cm-1) 3056w, 2930s, 2883w, 2851m, 2837m, 1582s, 1489s, 1474s, 1367s, 1345s, 1331w, 1271w, 1254w, 1238w, 1144m, 1088m, 1064m, 1055m, 1046m, 1016w, 987m, 971w, 959m, 928m, 908w, 881w, 852w, 821w, 773s sh, 737m, 725s, 710w, 687w, 661w, 629w, 615w. Phase purity was confirmed by X-ray powder diffraction (Supporting Information).

*Characterisation data for* ***L4****:*

m.p. 72-74 °C; δH(400 MHz, CDCl3) 8.35-8.39 (m, 1H, 6-py), 7.85 (d, 1H, *J* = 8.3 Hz, 3-py), 7.71-7.77 (m, 1H, 4-py), 7.06-7.10 (m, 1H, 5-py), 3.14 (t, 2H, *J* = 5.6 Hz, CH2), 2.45 (t, 2H, *J* = 5.5 Hz, CH2), 2.25 (s, 3H, CH3), 1.73-1.86 (m, 4H, 2×CH2); δC(100 MHz, CDCl3) 153.58,HH 148.35, 147.44, 140.48, 138.03, 119.93, 117.71, 114.33, 25.49, 23.05, 22.67, 20.47, 11.89; *m/z* (HR-ESI+) 214.1337 ([M+H+], calculated for C13H16N3+ 214.1344). νmax(ATR, cm-1) 3006w, 2971w, 2939m, 2922m, 2858m, 2843m, 1582s sh, 1486s, 1470s, 1442s, 1425s, 1382s, 1367m, 1325m, 1268w, 1236w, 1190w, 1151m, 1139w, 1087m, 1068m, 1049s, 1009w, 991m, 967m, 946m, 876w, 852m, 823w, 802w, 772s, 737s, 710s, 687m, 665m, 644w, 610m. Phase purity was confirmed by X-ray powder diffraction (Supporting Information).

*Synthesis of [dichlorido(1-(2-pyridyl)-3,5-diethylpyrazolyl)zinc]* ***1***

To a suspension of zinc chloride (18 mg, 130 μmol) in acetonitrile (2 mL) was added a solution of **L1** (27 mg, 130 μmol) in acetonitrile (2 mL). The resulting mixture was dispersed by sonication, heated briefly and filtered, and the filtrate was subjected to slow diffusion of toluene vapour, yielding colourless crystals of **1** within one week. Yield 26.9 mg (62%). m.p. 216-218 °C; Anal. Calcd. for C12H15N3ZnCl2(%): C, 42.70; H, 4.48; N, 12.45. Found C, 42.76; H, 4.36; N, 12.17; δH(400 MHz, CD3CN) 8.53 (dd, 1H, *J*1 = 5.3 Hz, *J*2 = 1.1 Hz, 6-py), 8.24 (ddd, 1H, *J*1 = 9.0 Hz, *J*2 = 7.7 Hz, *J*3 = 1.3 Hz, 4-py), 7.88 (d, 1H, *J* = 8.8 Hz, 3-py), 7.60 (dd, 1H, *J*1 = 7.5 Hz, *J*2 = 5.4 Hz, 5-py), 6.53 (s, 1H, 3-pz), 3.07 (dq, 2H, *J*1 = 7.3 Hz, *J*2 = 0.7 Hz), 2.81 (q, 2H, *J*= 7.6 Hz, CH2), 1.34-1.41 (m, 6H, 2×CH3); νmax(ATR, cm-1) 3147w, 3091w, 2975m, 2940w, 2883w, 1607s, 1577w, 1556m, 1484m, 1466m, 1444s, 1376s sh, 1314s, 1263w, 1244w, 1174w, 1162w, 1137m, 1083m, 1056m, 1037m sh, 1016m, 833m, 800m, 779s, 704w, 687w, 645m, 619w. Phase purity was confirmed by X-ray powder diffraction (Supporting Information).

*Synthesis of [dichlorido(1-(2-pyridyl)-3-methyl-5-isobutylpyrazolyl)zinc]* ***2***

An equivalent procedure to complex **1** was performed using 27 mg (130 μmol) of L2. Yield 24.6 mg (54%). m.p. 230-234 °C; Anal. Calcd. for C13H17N3ZnCl2(%): C, 44.41; H, 4.87; N, 11.95. Found C, 44.82; H, 4.82; N, 11.68; δH(400 MHz, CD3CN) 8.53 (d, 1H, *J* = 5.3 Hz, 6-py), 8.24 (ddd, 1H, *J*1 = 9.1 Hz, *J*2 = 7.2 Hz, *J*3 = 1.4 Hz, 4-py), 7.84 (d, 1H, *J* = 8.6 Hz, 3-py), 7.59 (dd, 1H, *J*1 = 7.1 Hz, *J*2 = 5.6 Hz, 5-py), 6.46 (s, 1H, 3-pz), 1.04 (d, 6H, *J* = 6.6 Hz, 2×CH3), 2.93 (d, 2H, *J* = 6.9 Hz, CH2), 2.43 (s, 3H, CH3), 2.03 - 2.13 (m, 1H, CH); νmax(ATR, cm-1) 3142w sh, 3065w, 2959m sh, 2935m, 2873m, 1607s, 1579w, 1558m, 1482s sh, 1444s, 1340s, 1364s, 1316s, 1220w, 1166w, 1146m, 1111w, 1064m, 1038m sh, 1014w, 992w, 972w, 881w, 831m, 818m, 808m, 780s, 714m, 702m, 682m, 644m. Phase purity was confirmed by X-ray powder diffraction (Supporting Information).

*Synthesis of [dichlorido(2-(2-pyridyl)-3-methyl-4,5,6,7-tetrahydroindazolyl)zinc]* ***3***

To a suspension of zinc chloride (9 mg, 65 μmol) in acetonitrile (2 mL) was added a solution of **L3** (15 mg, 70 μmol) in acetonitrile (1 mL). The mixture was dispersed by sonication and heated briefly, filtered, and the filtrate was subjected to diffusion of toluene vapour yielding colourless crystals of **3** within two weeks. Yield 13.6 mg (60%). m.p. 221-223 °C; Anal. Calcd. for C13H15N3ZnCl2(%): C, 44.67; H, 4.33; N, 12.02. Found C, 45.27; H, 4.34; N, 11.66; δH(400 MHz, CD3CN) 8.51 (d, 1H, *J* = 5.1 Hz, 6-py), 8.20-8.24 (m, 1H, 4-py), 7.91 (d, 1H, *J* = 8.6 Hz, 3-py), 7.56 (dd, 1H, *J*1 = 7.2 Hz, *J*2 = 5.4 Hz, 5-py), 2.76 (t, 2H, *J* = 6.1 Hz, CH2), 2.60 (s, 3H, CH3), 2.54 (t, 2H, *J* = 6.0 Hz, CH2), 1.77-1.90 (m, 4H, 2×CH2); νmax (ATR, cm-1) 3142w, 3097w, 2938m sh, 2859w, 1607s, 1569m, 1488s, 1463m, 1443s, 1428m, 1373s, 1338w, 1312m, 1279m, 1260w, 1239w, 1187m, 1146s sh, 1106m, 1080w, 1069w, 1061w, 1051m, 1026m, 1014w, 963m, 938m, 853w, 817w, 782s, 749s sh, 697w, 683w, 668w, 658m, 646w. Phase purity was confirmed by X-ray powder diffraction (Supporting Information).

*Synthesis of di-μ-chlorido-bis[chlorido(1-(2-pyridyl)-3-methyl-4,5,6,7-tetrahydroindazolyl)zinc]* ***4***

An equivalent procedure to complex **3** was performed, yielding 11.4 mg of complex **4** (50%) as a mixture of two polymorphic crystalline phases **4α** and **4β.** m.p.206-209 °C; Anal. Calcd. for C13H15N3ZnCl2(%): C, 44.67; H, 4.33; N, 12.02. Found C, 45.10; H, 4.31; N, 11.81; δH(400 MHz, CD3CN) 8.45 – 8.50 (br m, 2H, 6-py), 8.20 (ddd, 1H, *J*1 = 8.8 Hz, *J*2 = 7.3 Hz, *J*3 = 2.0 Hz, 4-py), 7.79 (d, 1H, *J* = 8.8 Hz, 3-py), 7.54 (dd, 1H, *J*1 = 7.2 Hz, *J*2 = 5.7 Hz, 5-py), 3.05 (t, 2H, *J* = 6.2 Hz, CH2), 2.52 (t, 2H, *J* = 6.2 Hz, CH2), 1.89 – 1.96 (m, 2H, CH2, overlapping solvent signal), 2.36 (s, 3H, CH3), 1.77-1.83 (m, 2H, CH2), νmax(ATR, cm-1) 3128w sh, 3070w sh, 2980m, 2949m, 2934m, 2907w, 2851w, 1607s sh, 1569m, 1491s, 1465m, 1451s sh, 1392s, 1378s, 1342w, 1319m, 1277w, 1255m sh, 1199w, 1167m, 1132m, 1120w, 1084m, 1071s sh, 1032w, 1011m, 972w, 885w, 858w, 830w, 801w, 784s, 726s, 689m, 667w, 637m, 615m. Phase purity was confirmed by X-ray powder diffraction (Supporting Information).

1. **Supplementary Information**

X-ray powder diffraction data, all NMR spectra, ellipsoid plots for all crystal structures, additional spectroscopic data, and structure of 2-aminopyridinium *p*-toluenesulfonate. CCDC 1885087-1885094.

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**Tables**

**Table 1** Calculated logK values for binding of ligands **L1** – **L4** to ZnCl2 in MeCN at room temperature

|  |  |
| --- | --- |
| Ligand | logK |
| **L1** | 4.64(8)a |
| **L2** | 4.43(13)a |
| **L3** | 4.99(10)a |
| **L4** | 4.92(6)a |

**a**Average calculated logK value (1:1 binding model) from three independent titration experiments, with standard deviations given in parentheses.

**Table 2:** Crystallographic and refinement parameters for **L3**, **L4**, **1** and **2**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Identification code | **L3** | **L4** | **1** | **2** |
| Empirical formula | C13H15N3 | C13H15N3 | C12H15Cl2N3Zn | C13H17Cl2N3Zn |
| Formula weight | 213.28 | 213.28 | 337.54 | 351.56 |
| Temperature/K | 150(2) | 150(2) | 230(2) | 150(2) |
| Crystal system | orthorhombic | triclinic | monoclinic | monoclinic |
| Space group | *P*212121 | *P*-1 | *P*21/*n* | *P*21/*n* |
| a/Å | 11.2059(4) | 7.6656(7) | 12.5735(7) | 9.1857(3) |
| b/Å | 12.6068(4) | 8.5793(8) | 8.4362(5) | 18.4036(6) |
| c/Å | 23.5081(9) | 9.3250(8) | 14.4563(8) | 9.9321(3) |
| α/° | 90 | 72.093(3) | 90 | 90 |
| β/° | 90 | 70.738(3) | 106.463(2) | 108.3160(10) |
| γ/° | 90 | 89.180(3) | 90 | 90 |
| Volume/Å3 | 3321.0(2) | 548.29(9) | 1470.55(15) | 1593.96(9) |
| Z | 12 | 2 | 4 | 4 |
| ρcalcg/cm3 | 1.28 | 1.292 | 1.525 | 1.465 |
| μ/mm‑1 | 0.079 | 0.079 | 2.019 | 1.866 |
| F(000) | 1368 | 228 | 688 | 720 |
| Crystal size/mm3 | 0.32 × 0.29 × 0.11 | 0.3 × 0.14 × 0.05 | 0.43 × 0.37 × 0.21 | 0.48 × 0.15 × 0.05 |
| Radiation | MoKα (λ = 0.71073) | MoKα (λ = 0.71073) | MoKα (λ = 0.71073) | MoKα (λ = 0.71073) |
| 2Θ range for data collection/° | 5.164 to 61.25 | 5.656 to 56.776 | 7.608 to 59.266 | 5.718 to 61.176 |
| Index ranges | -15 ≤ h ≤ 16, -18 ≤ k ≤ 17, -30 ≤ l ≤ 33 | -10 ≤ h ≤ 10, -11 ≤ k ≤ 11, -12 ≤ l ≤ 12 | -17 ≤ h ≤ 17, -11 ≤ k ≤ 11, -20 ≤ l ≤ 20 | -11 ≤ h ≤ 13, -26 ≤ k ≤ 26, -14 ≤ l ≤ 14 |
| Reflections collected | 41694 | 8541 | 23520 | 21185 |
| Independent reflections | 10197 [Rint = 0.0834, Rsigma = 0.0649] | 2747 [Rint = 0.0534, Rsigma = 0.0560] | 4128 [Rint = 0.0306, Rsigma = 0.0220] | 4889 [Rint = 0.0304, Rsigma = 0.0242] |
| Reflections Observed [I>=2σ (I)] | 7682 | 1960 | 3190 | 4136 |
| Data/restraints/parameters | 10197/0/436 | 2747/0/146 | 4128/2/184 | 4889/16/193 |
| Goodness-of-fit on F2 | 1.065 | 1.029 | 1.058 | 1.086 |
| Final R indexes [I>=2σ (I)] | R1 = 0.0548, wR2 = 0.1073 | R1 = 0.0506, wR2 = 0.1057 | R1 = 0.0446, wR2 = 0.0983 | R1 = 0.0361, wR2 = 0.0734 |
| Final R indexes [all data] | R1 = 0.0858, wR2 = 0.1187 | R1 = 0.0833, wR2 = 0.1181 | R1 = 0.0646, wR2 = 0.1149 | R1 = 0.0476, wR2 = 0.0780 |
| Largest diff. peak/hole / e Å-3 | 0.25/-0.26 | 0.29/-0.29 | 0.71/-0.74 | 0.77/-0.59 |
| Flack parameter | -0.1(9) | n/a | n/a | n/a |
| CCDC | 1885087 | 1885088 | 1885089 | 1885090 |

**Table 3:** Crystallographic and refinement parameters for **3**, **4α**, **4β** and 2-aminopyridinium *p*-toluenesulfonate

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Identification code | **3** | **4α** | **4β** | **HPyNH2-OTs** |
| Empirical formula | C13H15Cl2N3Zn | C26H30Cl4N6Zn2 | C26H30Cl4N6Zn2 | C12H14N2O3S |
| Formula weight | 349.55 | 699.1 | 699.1 | 266.31 |
| Temperature/K | 150(2) | 150(2) | 150(2) | 150(2) |
| Crystal system | monoclinic | monoclinic | triclinic | monoclinic |
| Space group | *C*2/*c* | *P*21/*n* | *P*-1 | *P*21/*c* |
| a/Å | 12.6924(4) | 8.7841(3) | 8.1626(3) | 11.3994(4) |
| b/Å | 11.1515(3) | 15.4385(5) | 8.9428(3) | 8.5557(3) |
| c/Å | 21.3037(7) | 10.3172(3) | 10.6348(4) | 13.2976(5) |
| α/° | 90 | 90 | 84.3120(10) | 90 |
| β/° | 102.9820(10) | 92.8520(10) | 72.4520(10) | 91.4580(10) |
| γ/° | 90 | 90 | 68.3520(10) | 90 |
| Volume/Å3 | 2938.24(16) | 1397.42(8) | 687.91(4) | 1296.49(8) |
| Z | 8 | 2 | 1 | 4 |
| ρcalcg/cm3 | 1.58 | 1.661 | 1.688 | 1.364 |
| μ/mm‑1 | 2.024 | 2.128 | 2.161 | 0.252 |
| F(000) | 1424 | 712 | 356 | 560 |
| Crystal size/mm3 | 0.15 × 0.12 × 0.09 | 0.24 × 0.16 × 0.04 | 0.25 × 0.13 × 0.08 | 0.27 × 0.16 × 0.15 |
| Radiation | MoKα (λ = 0.71073) | MoKα (λ = 0.71073) | MoKα (λ = 0.71073) | MoKα (λ = 0.71073) |
| 2Θ range for data collection/° | 5.014 to 61.182 | 5.948 to 63.234 | 5.886 to 60.276 | 5.662 to 61.248 |
| Index ranges | -18 ≤ h ≤ 18, -15 ≤ k ≤ 15, -28 ≤ l ≤ 30 | -12 ≤ h ≤ 12, -22 ≤ k ≤ 22, -15 ≤ l ≤ 15 | -11 ≤ h ≤ 11, -12 ≤ k ≤ 12, -15 ≤ l ≤ 14 | -16 ≤ h ≤ 16, -12 ≤ k ≤ 12, -18 ≤ l ≤ 19 |
| Reflections collected | 25400 | 25810 | 18013 | 27762 |
| Independent reflections | 4505 [Rint = 0.0485, Rsigma = 0.0336] | 4678 [Rint = 0.0695, Rsigma = 0.0482] | 4054 [Rint = 0.0244, Rsigma = 0.0193] | 3990 [Rint = 0.0380, Rsigma = 0.0220] |
| Reflections Observed [I>=2σ (I)] | 3633 | 3532 | 3625 | 3180 |
| Data/restraints/parameters | 4505/0/173 | 4678/0/173 | 4054/0/173 | 3990/3/173 |
| Goodness-of-fit on F2 | 1.069 | 1.024 | 1.038 | 1.061 |
| Final R indexes [I>=2σ (I)] | R1 = 0.0356, wR2 = 0.0666 | R1 = 0.0359, wR2 = 0.0625 | R1 = 0.0233, wR2 = 0.0521 | R1 = 0.0398, wR2 = 0.1009 |
| Final R indexes [all data] | R1 = 0.0525, wR2 = 0.0714 | R1 = 0.0630, wR2 = 0.0700 | R1 = 0.0293, wR2 = 0.0549 | R1 = 0.0552, wR2 = 0.1108 |
| Largest diff. peak/hole / e Å-3 | 0.71/-0.45 | 0.61/-0.44 | 0.45/-0.43 | 0.47/-0.40 |
| CCDC | 1885091 | 1885092 | 1885093 | 1885094 |

**Figure Captions**

**Scheme 1** Synthesis and structure of **L1** – **L4**. Reagents and conditions: (i) 2-hydrazinopyridine, EtOH, reflux 16 hr; (ii) 2-hydrazinopyridine, TsOH (cat.), PhMe, reflux 8 hr.

**Figure 1** (Top) Structure of **L3** with heteroatom labelling scheme for one of the three unique residues within the asymmetric unit. Hydrogen atoms are omitted for clarity, and ellipsoids are rendered at 50% probability level. (Bottom) The major intermolecular contact in the structure of **L3** with Hirshfeld surface, mapped withnormalized contact distances (surface property scaled to -0.200 / +1.300).

**Figure 2** (Top) Structure of **L4** with heteroatom labelling scheme. Hydrogen atoms are omitted for clarity, and ellipsoids are rendered at 50% probability level. (Bottom) The major intermolecular contacts in the structure of **L4,** showing both the pyridyl-pyridyl π···π interaction and the directional CH3···π contacts, with Hirshfeld surface mapped withnormalized contact distances (surface property scaled to -0.200 / +1.300, equivalent to Figure 1).

**Figure 3** (Top) Structure of complex **1** with heteroatom labelling scheme. Hydrogen atoms are omitted for clarity, and ellipsoids are rendered at 50% probability level. (Bottom) Intermolecular interactions in the structure of **1** showing theOFFπ···π interactions between adjacent complexes, with side chain disorder omitted for clarity.

**Figure 4** (Top) Structure of complex **2** with heteroatom labelling scheme. Hydrogen atoms are omitted for clarity, and ellipsoids are rendered at 50% probability level. (Bottom) TheOFFπ···π interactions between adjacent complexes in the structure of complex **2**, with side chain disorder omitted for clarity

**Figure 5** (Top) Structure of complex **3** with heteroatom labelling scheme. All hydrogen atoms are omitted for clarity, and ellipsoids are rendered at 50% probability level. (Bottom) Intermolecular contacts in the structure of complex **3**, showing the closest contact between cyclohexyl CH2 groups and the adjacent π system. Selected hydrogen atoms are omitted for clarity.

**Figure 6** Structure of complexes **4α** (top)and **4β** (middle)with labelling scheme for unique heteroatoms, and ellipsoids rendered at 50% probability level. Hydrogen atoms are omitted for clarity. (Bottom) The primary association mode of adjacent complexes for both **4α** and **4β** (exemplified with **4α**) showing the two-dimensional sheet arrangement of adjacent complexes.

**Figure 7** Comparison of the extended packing modes of **4α** (Top)and **4β** (Bottom), viewed parallel to the common 2-dimensional sheet arrangement.

**Figure 8** (A) & (B): UV-Visible absorption and fluorescence emission spectra, respectively, for the addition of ZnCl2 to **L2** (9 μM, MeCN). Each addition represents 0.1 equivalents to a maximum of 2.9 equivalents; (C) & (D): UV-Visible absorption and fluorescence emission spectra, respectively, for the addition of ZnCl2 to **L4** (11 μM, MeCN). Each addition represents 0.11 equivalents to a maximum of 3.2 equivalents.