

## COMMUNICATION

Supramolecular Assembly in a Janus-Type Urea System<sup>†</sup>

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**A pyrazolyl urea ligand adopts two possible conformations with the urea NH groups directed either outward or inward. Metal coordination enforces the outward conformation resulting in either anion complexation or self-association and hence extended supramolecular assemblies including a hexameric barrel that persists in solution.**

Ligands bearing hydrogen bonding functionality represent a powerful tool in the design of self-assembling systems.<sup>1-6</sup> Both coordination bonds and hydrogen bonds are strong, directional and synthetically versatile non-covalent interactions and in concert can give rise to stable, self-assembled aggregates with a high degree of complexity. Because ligand donor atoms that commonly bind to metal ions are also generally hydrogen bond acceptors, metal ion coordination can be used to mask a potential hydrogen bonding site and hence favour an alternative hydrogen bonding pattern, giving rise to metal-ion-switchable supramolecular assembly.<sup>7</sup> The proximity of a metal cation may also enhance hydrogen bond acidity as a result of inductive effects.<sup>8</sup> This approach has been used to good effect in a range of creative systems in which metal coordination compounds act as hosts for anion guests.<sup>9, 10</sup> Applications include, for example, anion sensing and medical diagnostic devices.<sup>11, 12</sup> We and others have produced a range of pyridyl ligands bearing urea functional groups exhibiting interesting self-assembly, anion binding and materials properties, particularly gelation behaviour.<sup>13-16</sup> The pyridyl ligand is relatively bulky, however, and hence we have turned our attention to urea derivatives bearing the smaller, strongly basic pyrazole<sup>17</sup> functionality which contains a 5-membered heterocyclic ring.

Ligand **1** possesses a total of three hydrogen bond donor groups on the urea functionalities as well as a basic pyrazole nitrogen atom. The compound is readily prepared as a mixture of the 1- and 2-substituted isomers by reaction of 3-amino-5-methylpyrazole with *p*-tolyl isocyanate. The isomerically pure compound is obtained by recrystallization from hot chloroform. The single crystal X-ray structure of free ligand **1** crystallized from hot

chloroform solution (form I) is shown in Figure 1(i). The disubstituted urea functionality adopts an *anti* conformation resulting from an intramolecular hydrogen bond from N(4)-H to the Lewis basic pyrazolyl nitrogen atom.<sup>18</sup> The carboxamide N(5)-H group also forms an intra-molecular hydrogen bond to the same pyrazolyl nitrogen atom. Such intramolecular hydrogen bonding is expected based on Etter's rules which state that intra- rather than intermolecular hydrogen bonding should dominate.<sup>19, 20</sup> It is in contrast to the structure of many disubstituted ureas, however, such as *N,N'*-diphenylurea which adopt a *syn* conformation forming the characteristic urea  $\alpha$ -tape hydrogen bonding motif in which the two NH groups interact with the carbonyl oxygen atom of an adjacent urea to give a hydrogen bonded polymer.<sup>21</sup> In this case compound **1** adopts an eight-membered hydrogen bonded ring motif ( $R_2^2(\mathbf{8})$  in graph set nomenclature<sup>18</sup>) There are only weak C-H...O interactions with the carbonyl of the carboxamide group leading to a 1D chain of these V-shaped molecules. This structure is interesting in that it adopts an *anti* conformation of the urea group with intramolecular hydrogen bonding, even though the pyrazolyl nitrogen atom is acting as a bifurcated acceptor. This means that the intramolecular interaction to the urea might be expected to be sterically hindered and hence the acceptor ability of the pyrazolyl nitrogen atom reduced by taking part in two different hydrogen bonds.

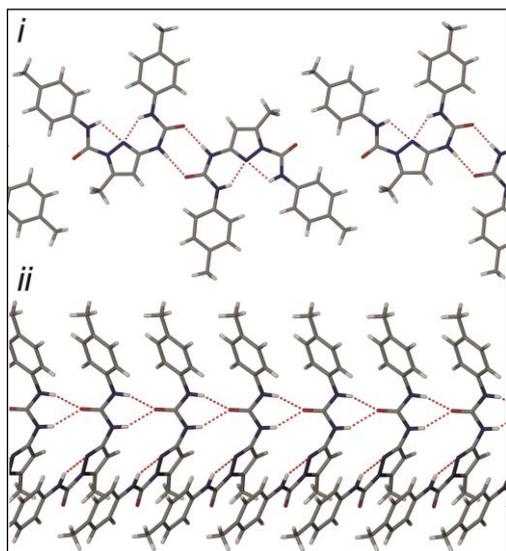


Fig. 1 Crystal packing of **1** in polymorphic forms i) I and ii) II.

Interestingly, when **1** is crystallised from methanol (or other polar solvents such as ethanol and acetonitrile), a conformational polymorph,<sup>22, 23</sup> form II results, Figure 1(ii). Form II retains the intramolecular hydrogen bonding of the carboxamide to the pyrazolyl nitrogen atom but the urea group adopts a *syn* conformation resulting in the formation of a conventional urea  $\alpha$ -tape hydrogen bonding motif. Ligand **1** is thus ‘Janus-like’,<sup>24, 25</sup> apparently finely poised between adopting an intra- or intermolecular hydrogen bonding behaviour and presents a more hydrophilic face in methanol and a more hydrophobic one in chloroform. Calculations using the UNI force field<sup>26</sup> implemented in Mercury<sup>27</sup> give a packing energy for form I of  $-165.6 \text{ kJ mol}^{-1}$  compared to a much more substantial  $-243.7 \text{ kJ mol}^{-1}$  for form II dominated by the urea  $\alpha$ -tape motif which allows an additional intermolecular hydrogen bonding interaction. This marked difference strongly suggests that form I is metastable and arises from the conformation adopted by the molecule in the non-polar crystallization medium.

The conformational behaviour of ligand **1** should be markedly influenced by metal ion coordination to the hydrogen bond acceptor pyrazolyl nitrogen atom, with metal cations both polarising the urea NH groups, enhancing hydrogen bond strength, as well as favouring the more polar conformer found in the structure of form II by blocking the hydrogen bond acceptor pyrazolyl nitrogen atom. We opted to try metal acetates because the acetate anion is likely to deprotonate the ligand and should hydrogen bond strongly to the urea groups. Reaction of **1** with copper(II) acetate in methanol resulted in the isolation of a remarkable hexameric, hexacationic assembly of formula  $[\{\text{Cu}(\mu\text{-}\kappa\text{-O}, \text{O}, \text{N}, \text{N}-\text{1-H})(\text{MeOH})\}_6](\text{MeCO}_2)_6 \cdot 6\text{MeOH}$  (Figure 2). The structure involves the deprotonation of **1** by the basic acetate counter anion. Deprotonated **1** acts as a tetradentate chelate and bridging ligand to the distorted trigonal bipyramidal copper(II) centre. There are two chelate rings present from the coordination of the deprotonated **1**; a five-membered ring involving the deprotonated carboxamide group and pyrazolyl nitrogen atom and a six-membered ring involving the carbonyl oxygen atom of the urea group and pyrazolyl nitrogen atom. The tridentate coordination by the deprotonated **1** is similar to some Schiff base ligands and similar ligands used in the supramolecular assembly of multi-metal centred grids.<sup>28</sup> The pentacoordination of the metal is completed by interactions to a molecule of coordinated methanol. Each metal centre bridges to an

adjacent one *via* the carboxamide carbonyl oxygen atom. The Cu–O bond length in this bridging interaction is relatively short<sup>29</sup> at  $1.937(6) \text{ \AA}$ , reflecting the delocalization of the amidate negative charge onto the oxygen atom. These bridging interactions result in a remarkable hexameric, barrel-shaped assembly exhibiting crystallographic  $\bar{3}$  symmetry, supported by edge-to-face  $\pi$ -interactions involving the tolyl groups and linking to adjacent assemblies *via* hydrogen bonding to the coordinated methanol. The hexamers stack one on top of each other resulting in columns that are packed into the trigonal lattice. The urea group is in a *syn* conformation and directed away from the metal centre as in form II of the free ligand structure and hence is available to hydrogen bond to the acetate anion, forming the well-known  $R_2^2(\mathbf{8})$  hydrogen bonding motif.<sup>18, 30</sup> This anion binding mode resembles analogous exogenous complexation of anions by ruthenium(II) bound thiourea ligands.<sup>31</sup> The strength of the coordination interactions holding the assembly together, as well as its close-packed nature, suggest that it should be stable in solution as well as in the solid state. While the paramagnetism of copper(II) does not permit detailed study of the assembly by NMR spectroscopy, by ESI-MS of the crystals in MeOH solution showed clear evidence for the persistence of the hexamer. The mass spectrum exhibited a peak at  $1574 \text{ m/z}$  with half-integer isotopic progression consistent with the assembly  $[\{\text{Cu}(\text{1-H})(\text{MeOH})\}_6](\text{MeCO}_2)_6$  in conjunction with two  $\text{Na}^+$  cations. Further peaks assigned to fragments of the hexameric assembly were also observed (see supplementary material)

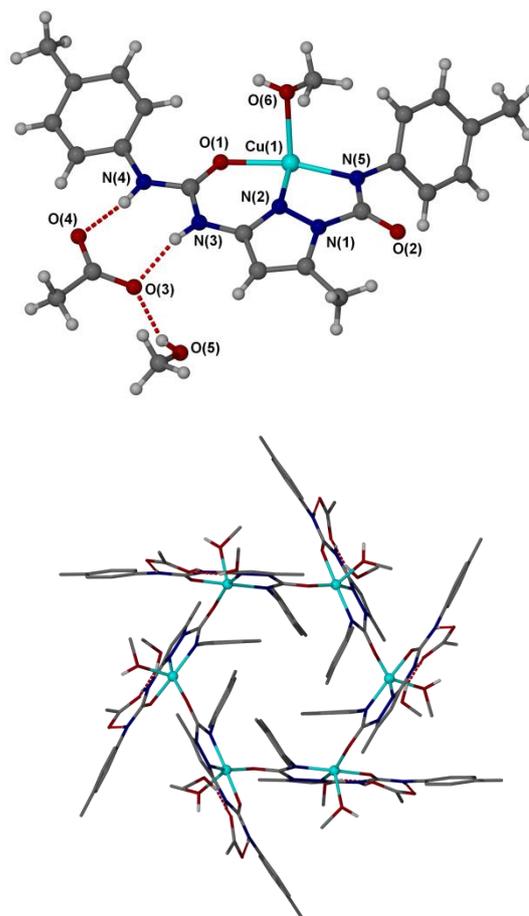
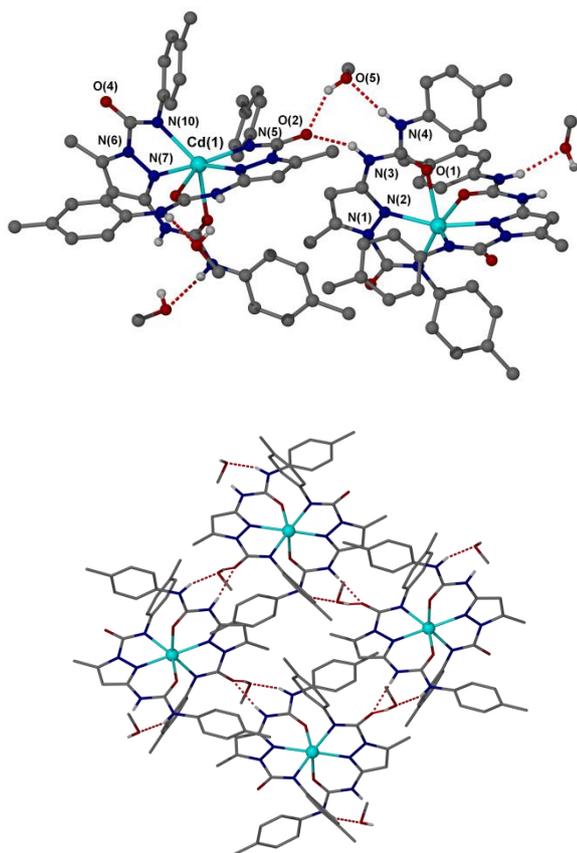


Fig. 2 (a) Asymmetric unit in  $[\{\text{Cu}(\mu\text{-}\kappa\text{-O}, \text{O}, \text{N}, \text{N}-\text{1-H})(\text{MeOH})\}_6](\text{MeCO}_2)_6 \cdot 6\text{MeOH}$  showing hydrogen bonding of the acetate anion to the urea group, and (b) hexameric barrel-shaped

assembly based on Cu–O bridges and in C–H $\cdots$  $\pi$  interactions between tolyl groups. Each barrel is linked to its neighbours by hydrogen bonding from the coordinated methanol to acetate anions, and hence the urea groups of the adjacent assembly.

Formation of this 1:1 complex between deprotonated ligand **1** and a divalent metal ion naturally leads to anion binding by the *syn* urea group, given the strong hydrogen bond acceptor nature of the acetate anion.<sup>32</sup> In contrast, reaction of **1** with cadmium(II) acetate hexahydrate in methanol results in the isolation of an overall neutral 2:1 complex between deprotonated **1** and Cd(II). The resultant complex, *mer*-[Cd( $\kappa$ -O,N,N,N-1-H)<sub>2</sub>], was isolated as a methanol water solvate of formula in the crystalline form [Cd( $\kappa$ -O,N,N,N-1)<sub>2</sub>] $\cdot$ 2MeOH $\cdot$ 2H<sub>2</sub>O. The two deprotonated ligands chelate to the cadmium through the same mode as seen in the copper structure. The *mer* geometry is a direct consequence of the planar tridentate binding domain of the ligand. The urea groups again adopt the *syn* conformation seen in form II of the free ligand and because the complex is neutral the urea groups form a fascinating variation on the urea tape motif observed for the free ligand form II involving interaction of one urea NH group to a urea carbonyl oxygen atom on an adjacent molecule and the other to an included methanol solvent molecule to give an unusual R<sub>2</sub><sup>3</sup>(**8**) motif which closes into a ring by the hydrogen bonding of the methanol to the same urea carbonyl, Figure 3b. The result is a cyclic tetrameric supramolecular assembly that links to adjacent complexes to give an infinite 2D sheet. The disordered water molecules reside within the interstitial space created between the mismatching of 2D layers.



**Fig. 3** (a) *mer*-[Cd( $\kappa$ -O,N,N,N-1-H)<sub>2</sub>] showing the unusual self-association via an unusual R<sub>2</sub><sup>3</sup>(**8**) hydrogen bonded motif incorporating methanol solvent, and (b) cyclic tetrameric fragment of the 2D sheet assembly.

## Conclusions

A combination of hydrogen bonding and metal coordination results in the formation of robust supramolecular assemblies in which the hydrogen bond donor abilities and conformation of the ligand are modulated by coordination to the metal centre. In the case of pyrazolyl urea ligand **1**, the ligand's Janus-like conformational polymorphism is easy to rationalise as a response to the crystallization medium in conjunction with the finely balanced nature of the intramolecular and intermolecular hydrogen bonding interactions. The ligand allows the formation of metallosupramolecular assemblies held together by a synergic combination of coordination, hydrogen bonding and aromatic interactions which in the case of the copper(II) hexameric cluster, forms a robust anion-binding complex in solution as well as the solid state.

## Notes and references

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Electronic Supplementary Information (ESI) available: experimental details for the preparation of ligand **1**, crystallography and experimental data. See DOI: 10.1039/c000000x/

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Graphical Abstract

