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## Investigation of putative arene-C–H $\cdots$ $\pi$ (quasi-chelate ring) interactions in copper(I) crystal structures<sup>†</sup>

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Evidence for  $C-H\cdots\pi(CuCl\cdots HNCS)$  interactions, *i.e.*  $C-H\cdots\pi(quasi-chelate ring)$  where a six-membered quasi-chelate ring is closed by an  $N-H\cdots Cl$  hydrogen bond, is presented based on crystal structure analyses of  $(Ph_3P)_2Cu[ROC(\Longrightarrow)N(H)Ph]Cl$ . Similar intramolecular interactions are identified in related literature structures. Calculations suggest that the energy of attraction provided by such interactions approximates 3.5 kcal mol<sup>-1</sup>.

Complementing supramolecular synthons based on conventional hydrogen bonding and coordinate bonds, which remain crucial in crystal engineering studies, is a myriad of other intermolecular interactions coming to the fore with the notable example being halogen bonding.<sup>1</sup> Supramolecular association based on  $\pi$ -systems is also well established in all-organic crystal structures and increasingly, chelate rings are being recognised as being capable of forming analogous interactions,<sup>2</sup> reflecting their metalloaromatic nature.<sup>3</sup> Thus, just as arene rings can associate via  $\pi \cdots \pi$  interactions, mixed  $\pi$ (arene) $\cdots \pi$ (chelate) interactions can occur,<sup>4*a*</sup> as well as  $\pi$ (chelate) $\cdots \pi$ (chelate) interactions which are found in up to 40% of certain square planar transition metal complexes and exhibit the same attributes as  $\pi \cdots \pi$  interactions involving arene rings, such as cooperativity, separation and orientation, i.e. parallel and antiparallel.<sup>4b</sup> As demonstrated by Zarić et al. in their systematic evaluation of transition metal acetylacetonate crystal structures, chelate rings may also function as donors and acceptors of C-H··· $\pi$  interactions and impart approximately the same energy of stabilisation as for C-H··· $\pi$  interactions occurring between organic residues.<sup>5</sup> While

work continues on this phenomenon,<sup>6</sup> the role of conjugated or resonance-assisted hydrogen bonded systems, where one of the links within the organic ring is a hydrogen bond rather than a formal covalent bond, giving rise to quasi-aromatic rings, is less well understood.<sup>7</sup> Analogous quasi-aromatic rings where one of the constituent atoms is a metal have received considerably less attention and their putative formation forms the focus of the present communication. Herein, the observation and theoretical investigation of intra-molecular arene-C-H… $\pi$ (quasi-chelate rings) interactions in some (Ph<sub>3</sub>P)<sub>2</sub>Cu[ROC(=S)N(H)Ph]Cl complexes are described, as is the prevalence of analogous interactions in the crystallographic literature.

The new copper(I) complexes were prepared in response to the recently demonstrated anti-cancer potential of platinum<sup>8a</sup> and gold<sup>8b</sup> complexes of thiocarbamides, ROC(=S)N(H)Ar, and the remarkable and selective anti-microbial activity against four Gram-positive bacteria exhibited by phosphanegold(1) derivatives.<sup>8c</sup> The potential of copper(1) complexes as therapeutic agents has been reviewed recently,9 and so attention was naturally directed to investigating related phosphanecopper(I) derivatives during which the title complexes, (Ph<sub>3</sub>P)<sub>2</sub>Cu[ROC(=S)N(H)Ph]Cl, R = Me (1), Et (2) and iPr (3), were synthesised and characterised, including by single crystal X-ray crystallography; see the ESI† for details. Spectroscopy showed the expected characteristics, with the only feature worth highlighting being the downfield shift of the <sup>1</sup>H resonance due to the acidic proton as the concentration of the solution was increased, consistent with retention of the N-H...Cl hydrogen bond in solution (see below), see ESI,† Fig. S1.

The molecular structure of 2 is shown in Fig. 1 and features a tetrahedrally coordinated Cu(i) centre with the environment defined by one chlorido, a thione-S and two phosphane-P atoms; the maximum deviation from regular tetrahedral is found in the P1–Cu–P2 angle of 125.099(19)°. An intramolecular N–H···Cl hydrogen bond is formed closing a (CuCl···HNCS) quasi-chelate ring, see the ESI,† Table S2 for geometric details. The interesting feature of the structure is the relative orientation of one of the phenyl-H atoms which appears to be directed toward the centre of the aforementioned ring. The separations between the phenyl-H atom and each of the constituent atoms of the ring are given in the caption of Fig. 1, and from these data it is evident that the

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Fig. 1 Molecular structure of **2** showing atom labelling and 70% displacement ellipsoids. The C-H\*···Cu, Cl1, S1, N1, C1 and H1n separations are 3.12, 3.41, 2.99, 2.63, 2.88 and 2.48 Å, respectively.

phenyl-H atom is not orientated toward any one atom of the ring but rather to the centre of the quasi-chelate ring. The distance between phenyl-H and the centroid of the quasi-ring is 2.31 Å and the angle is  $147^{\circ}$ . By analogy with a C–H··· $\pi$ (arene) interaction, this contact can be represented as C–H··· $\pi$ (CuCl···HNCS).

A similar interaction is found in the R = iPr derivative, 3 [phenyl-H...quasi-ring centroid = 2.56 Å and angle at H =  $124^{\circ}$ ; see the ESI,† Fig. S2 for details], but not in the R = Me analogue, 1, where the shortest H...quasi-ring centroid distance is 3.41 Å. An overlay diagram, ESI,† Fig. S2c, shows that while the overall molecular structures are similar, the phenyl ring forming the C-H $\cdots$  $\pi$ (CuCl $\cdots$ HNCS) interaction in 2 and 3 is somewhat splayed in 1; the dihedral angles between the relevant phenyl ring and the least-squares plane through the non-hydrogen atoms of the quasi-chelate ring are 36.5(5), 64.02(5) and 55.25(5)° for 1, 2 and 3, respectively. It is noted that the quasi-ring in 1 (r.m.s. deviation of the five non-hydrogen atoms = 0.1902 Å) is less planar than the equivalent rings in 2 and 3 (r.m.s. = 0.0997 and 0.0898 Å, respectively). In fact the ring in 1 has a distinct envelope conformation with the Cu atom lying 0.6751(11) Å above the leastsquares plane defined by the remaining four non-hydrogen atoms; see ESI,† Table S3. The other difference between the structures is found in the pattern of Cu-ligand bond lengths (see ESI,† Table S4) so that in 1, the Cu-Cl1 bond length is significantly longer, by 0.03 Å, than those in 2 and 3, and the remaining bond lengths in 1 are concomitantly shorter cf. to the equivalent bonds in 2 and 3. This is not related to the nature of the supramolecular aggregation as C-H···Cl interactions are formed in each of the crystal structures; ESI,<sup>†</sup> Fig. S3–S5. In 1 and 2 C–H···Cl along with C–H··· $\pi$ (arene) contacts lead to a supramolecular layer and a double chain, respectively. In 3, C-H···Cl, C-H···S and C-H··· $\pi$ (arene) interactions lead to a supramolecular chain. The crystal packing in 1-3 was also evaluated for phenyl embraces (PE), known to be important in stabilising the crystal structures of phenyl-rich molecules.<sup>10</sup> As summarised in the figure captions, ESI,† Fig. S3-S5, the P1-phosphane, *i.e.* not involved in forming the putative C-H··· $\pi$ (CuCl···HNCS) interactions, participates in sextuple PE whereas the P2-phosphane ligand forms parallel quadruple PE interactions in 1, double PE in 2 but no recognisable pattern is observed in 3.

The unusual nature of the C–H··· $\pi$ (CuCl···HNCS) contact prompted a search of the Cambridge Structural Database (CSD version 5.33)<sup>11*a*</sup> for analogous interactions using CONQUEST.<sup>11*b*</sup> The initial search comprised seeking a specific arrangement of the Cu, Cl, H, N, C and S atoms as well as the presence of a N–H···Cl hydrogen bond to close the ring: this gave rise to a total of 91 hits. This sub-set was



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**Fig. 2** Search protocols for  $C-H\cdots\pi(CuCl\cdots HNCS)$  interactions: *d* is the distance between the ring centroid (Cg) of the quasi-chelate ring and the H atom;  $V_1$  is the vector normal to the plane through the ring;  $\alpha$  is the C-H···Cg angle;  $\beta$  is the angle between the  $V_1$  and  $V_2$  vectors.

further probed to seek intramolecular C–H···π(CuCl···HNCS) contacts by adding the following restrictions, Fig. 2. The distance, *d*, from the ring centroid (Cg) to the H atom is  $\leq 3.6$  Å<sup>6a</sup> and the C–H···Cg angle is in the range  $110 \leq \alpha \leq 180^{\circ}$ . Although the quasi-ring was not restricted to be planar, the angle between the normal of the leastsquares plane through the six atoms and the C–H vector was restricted to  $\leq 15^{\circ}$  to ensure that the C-bound H atom was approximately plumb to the ring. There were 14 structures,<sup>11</sup> out of a possible 91, that satisfied these criteria; details are summarised in the ESI,† Table S5.

Twelve of the hits contain phosphane ligands, with seven having very similar mononuclear structures with  $\text{ClP}_2\text{S}$  donor sets as found for **2** and **3**;<sup>12*b*-*e*,*h\_j*-*l*,*o*</sup> a simple variation is found in one binuclear example having bridging bidentate phosphanes.<sup>12*f*</sup> Four binuclear structures with monodentate phosphane ligands have  $\text{S}^{12g,n}$  or  $\text{Cl}^{12i}$  bridges. The remaining two structures are thione adducts of CuCl.<sup>12*a*,*m*</sup> In each case the donor H atom was connected to an aromatic ring. Values of *d* were in the range 2.28 to 2.92 Å and the  $\alpha$  angles varied from 114 to 163°. The planarity of the quasi-chelate ring is not a factor in the formation of C–H··· $\pi$ (quasi-chelate ring) interactions as rms deviations of the five non-hydrogen atoms from their least-squares plane vary from a low 0.0297 to 0.3374 Å (ESI,† Table S5). Nor there is a correlation between the planarity of the quasi-chelate ring and the values of *d* or  $\alpha$ . This is hardly surprising as correlations involving weak interactions are notoriously unreliable.<sup>13</sup>

In order to investigate the nature of the C-H $\cdots\pi$ (CuCl $\cdots$ HNCS) interaction, DFT-D calculations were performed based on the coordinates of one of the literature crystal structures that feature an intramolecular contact, i.e. 4,120 Fig. 3a. As detailed in the ESI,† Gaussian09 was used employing the BP86 functional,<sup>14a,b</sup> including the D3 version of Grimme's dispersion correction,<sup>14c</sup> and the secondorder perturbation theory<sup>14d</sup> with the def2-TZVP basis set.<sup>14e,f</sup> Initially, the non-covalent interactions were calculated in real space based on the electron density and its reduced gradient using the NCI approach of Yang et al.15 Referring to Fig. 3b and c, the surfaces are coloured blue, green and red, correlating with strong attractive, weak attractive and strong non-bonded overlap, respectively. The NCI analysis<sup>15</sup> gives a conical surface pointing to the mass-centre of the ring, representing unambiguously the  $\pi$ -type interaction. An example of the T-shaped benzene-dimer can be seen in Fig. 3b. A similar situation was observed for 4, in which the green region indicates a weak attractive interaction as commonly presented in  $\pi$ -stacking interactions.

Additional calculations were conducted to elucidate the metalloaromaticity of the quasi-chelate ring by calculation of



**Fig. 3** (a) Chemical structure of **4**, (b) the gradient isosurface of a T-shaped benzene-dimer (adapted with permission from Yang *et al., J. Chem. Theory Comput.* 2011, **7**, 625. Copyright 2014 American Chemical Society), and (c) the gradient isosurface of **4**.

isotropic nucleus-independent chemical shifts  $(NICS(-1)_{ISO})$ NICS(0)<sub>ISO</sub> and NICS(1)<sub>ISO</sub>) at the centroid of 4, using the BP86, B3LYP and B3PW91 functionals.<sup>16a,b</sup> The magnetic criterion of aromaticity was not satisfied, with values in the range of -1.32 to 0.32 Å. The model complex 4', *i.e.* without any phenyl rings, and fully optimized at BP86-D/def2-TZVP, leads to a similar conclusion (ESI,† Fig. S6). Despite their non-aromatic character, these new synthons can form non-covalent interactions in a similar fashion to truly aromatic rings. Support for this is found in the analysis of the molecular orbitals (MO) of both 4 and 4'. As seen in ESI,† Fig. S7, three MOs present an alignment between the p orbitals of N, C, Cl and S, and the d orbital of Cu, forming a quasi-π-system. Furthermore, estimation of the interaction energy of C-H $\cdots\pi$ (CuCl $\cdots$ HNCS) was made using the optimal geometries (BP86-D/def2-TZVP) for a model system,  $C_2H_2\cdots 4'$ , removing the basis set superposition error (BSSE) by counterpoise (CP) correction.<sup>16c</sup> Referring to the ESI,† Fig. S8, single point calculations were performed at  $r(H \cdots \Omega)$  distances between 2.2 and 3.0 Å, for three positions in the ring, presenting an average energy at the optimal separation of 3.5 kcal mol<sup>-1</sup> at MP2 and M062X-D, and 4 to 5 kcal mol<sup>-1</sup> at B3LYP-D and B3PW91-D. For all calculated positions, the interactions are attractive.

In summary, experimental and theoretical evidence has been presented for attractive (*ca.* 3.5 kcal mol<sup>-1</sup>) intramolecular C-H··· $\pi$ (CuCl···HNCS) interactions which occur in approximately 15% of the copper(i) structures where they may potentially form.

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