Misassigned C–H···Cu agostic interaction in a copper(II) ephedrine derivative is actually a weak, multicentred hydrogen bond

Tejender S. Thakur and Gautam R. Desiraju*

Agostic interactions and weak hydrogen bonds to metal acceptors, M, are chemically and geometrically distinct, and this distinction must be maintained in the classification of new C–H···M interactions.

Castro et al., in a recent paper in this journal[1] have reported a close approach of a C–H group to Cu(II) in the coordination compound, **1**, [Cu(Hceph)$_2$] where (H$_2$ceph) is *N*-[2-hydroxy-1-(*S*)-methyl-2(*R*)-phenylethyl]-*N*-methylglycine. They have termed this approach a C–H···Cu agostic interaction based on their X-ray data and computational results. We show, in this communication, that this description is a misnomer and that the interaction is correctly designated as a weak hydrogen bond with the C–H group bifurcated between two acceptor sites, Cu and O.

The origin of the agostic interaction lies in the identification of hydridic H-atoms in transition metal complexes by Trofimenko in the 1960s.[2] The term agostic was proposed by Brookhart and Green in their seminal 1983 paper[3] for a situation in which a C–H group interacts with a transition metal with the formation of a two-electron three-centre bond (Scheme 1). The metal centre behaves like a Lewis acid: an early transition metal in a higher oxidation state (Ti, Zr) or a middle transition metal (Fe, Co) is typically involved. Crabtree and co-workers studied a number of these interactions by the method of structure correlation and proposed that the C–H bond initially approaches the metal atom with a C–H···M angle of around 130° resulting in a strong M–H interaction.[4] The C–H bond then rotates, bringing the C-atom close to the metal centre. The C–H distance lengthens significantly (to around 1.1 to 1.2 Å) and the M···C and M···H distances become comparable. A desirable though not sufficient condition for the formation of an agostic bond is that the metal atom has a 16e configuration. Indeed, and as stated by Brookhart and Green, "the minimal requirement is that the metal centre should have an empty orbital to receive the two electrons of the C–H bond".[3] The necessity of an electron deficient metal was further described by Braga et al. who used the CSD to study this phenomenon and
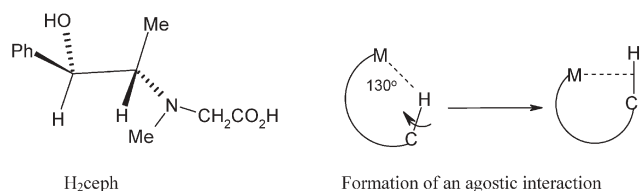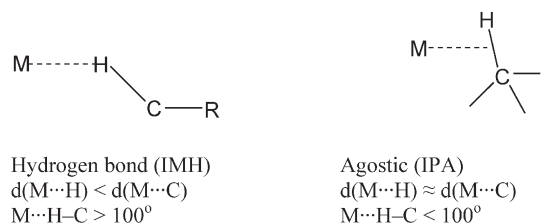
reviewed the behaviour of Li(I) in this context.[5] A recent summarizing review by Scherer and McGrady expands and generalizes the phenomenon: rather than use the 2e–3c concept, these authors state that the agostic interaction may be considered as a hyperconjugative delocalization of the M–C bond over the metal–alkyl fragment; instead of total acidity, they suggest that local Lewis acidity at the metal centre controls these interactions.[6] This review suggests that some agostic interactions may be rather weak—certainly weaker than the range (7 to 15 kcal mol^{-1}) given by Desiraju and Steiner in their book on hydrogen bonding.[7]

Most authors have, however, been clear that a distinction must be made between agostic interactions and three-centre four-electron X–H···M interactions which are properly considered as weak hydrogen bonds. A hydrogen bond is an interaction where an electropositive H-atom acts as a bridge between two electronegative centres.[8] Depending on the electronegativity of these centres, the hydrogen bond is classified as very strong, strong and weak.[7,9] Electron rich metal atoms, typically late transition metals in low oxidation states, can act as acceptors of hydrogen bonds[10] and this was first suggested in 1972 by Maitlis[11] with respect to Pd(II). Brammer et al. termed interactions of the type [R$_3$N–H$^+$···Co(CO)$_4^-$], wherein the metal has an 18e configuration, as hydrogen bonds.[12] All this is in contrast to agostic interactions which are associated with electron deficient metals and hydridic H-atoms. However, Crabtree and co-workers have cautioned that when C–H donors are involved, assignment of a C–H···M interaction as a hydrogen bond or an agostic bond could be difficult because of the weakness of the interaction.[13] The distinction between these situations was further clarified by Braga et al. and their schematic depictions of the intermolecular multicentre hetero-acceptor hydrogen bond, IMH, and the intermolecular pseudo-agostic bond, IPA, are given in Scheme 2 with their suggested geometrical ranges for lengths and angles in the two cases.[14] We note that hydrogen bond geometry tends to linearity because the protic H-atom screens the two electronegative centres most effectively in this geometry, whereas the agostic geometry (IPA) is bent severely at the H-atom.

Scheme 1

Hydrogen bond (IMH)
d(M···H) < d(M···C)
M···H–C > 100°

Agostic (IPA)
d(M···H) ≈ d(M···C)
M···H–C < 100°

Scheme 2

School of Chemistry, University of Hyderabad, Hyderabad 500 046, India. E-mail: gautam_desiraju@yahoo.com

With this background let us consider compound **1** which is given in Fig. 1. The accuracy and precision of the crystal structure published by Castro *et al.* is satisfactory and all experimental values refer to their work.[1] The Cu(II) ion may be considered as being octahedral, if the C–H group is taken as a ligand, or as being square pyramidal, if it is not. The latter option may be more realistic if we note that the Cu-atom is displaced 0.15 Å towards the β-OH group *trans* to the C–H group and above the square plane of O, O, N and N. Such a displacement is characteristic of pentacoordinate square pyramidal Cu(II).† Accordingly, we conclude that whatever be the nature of the interaction between Cu(II) and the C–H group, it is very weak. Cu(II) in a square pyramidal configuration is a 19e species and the geometry of **1** fails three other tests for an agostic interaction: (1) the M···H (2.45 Å) and M···C (3.08 Å) distances are not comparable; (2) the C–H···M angle (121°) is greater than 100° and; (3) the C–H distance (0.98 Å) is not elongated. Qualitatively, Cu(II) cannot be considered as a particularly good Lewis acid, and there is no empty orbital on the metal atom which can interact with the C–H bond, the *sine qua non* of the agostic interaction.

These observations are supported by computation. DFT calculations[15] on **1** were performed at the 6-31G(d,p)/B3LYP level. In the calculated geometry, the intramolecular parameters are largely unchanged from the experimental values. In a true agostic interaction, the charge of the H-atom should show a hydride shift, in other words, it should be less positive when compared to the interaction-free species in which the metal centre is isolated from the C–H group. However, the natural population analysis (NPA) charge on the pertinent H-atom in **1** actually becomes more positive (+0.007e) suggesting a hydrogen bond type interaction. In contrast, we obtained charge differences of $-0.058e$ for $[FeP(OMe)_3(C_8H_{13})]^+$ and $-0.007e$ for $[Co(\eta^5-C_5Me_5)PPh_3Et]$ both of which are well established cases of an agostic interaction.[16,17]

An important distinguishing feature of an agostic interaction is the dative interaction from the $\sigma_{C–H}$ orbital to the low lying empty metal orbital. This interaction is not seen in the case of hydrogen bonding. Natural bond orbital (NBO) analysis[18] gives a quantitative picture of this Lewis acid–base interaction in terms of the second order delocalization energy correction. The difference
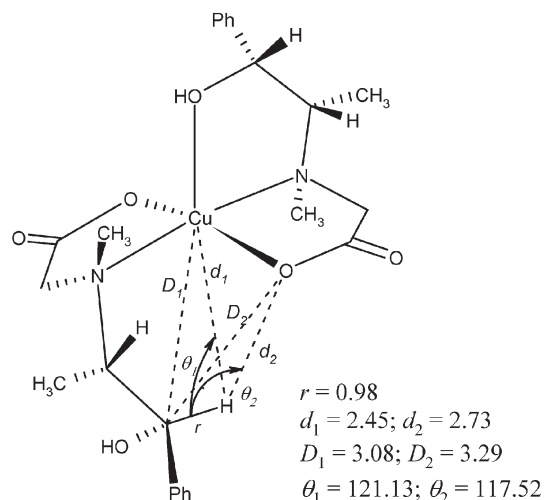
between an agostic interaction and a hydrogen bond can be clearly seen using this approach. For complex **1**, the net $\sigma_{C–H}$ to metal delocalization energy is 1.50 kcal mol^{-1}; this value goes up to as much as 56.66 kcal mol^{-1} for a strongly agostic interaction as in the case of the $[Co(\eta^5-C_5Me_5)PPh_3Et]$ complex.[17]

The atoms in molecule (AIM) theory[19] may also be used to probe the distinction between agostic and hydrogen bond interactions. Popelier[20] and Coppens[21] have pointed out that for the weaker agostic interactions, it is sometimes difficult to identify the BCP and bond path. The consensus seems to be that ρ_{BCP} lies between 0.002 and 0.035 a.u. for a hydrogen bonded system,[22] whereas for an agostic system[20] it lies outside this range. Further, $\nabla^2\rho_{BCP}$ lies between 0.024 and 0.139 a.u. for a hydrogen bonded system and between 0.15 and 0.25 a.u. for the agostic case. For complex **1**, Castro *et al.* have reported a ρ_{BCP} value of 0.012 and a $\nabla^2\rho_{BCP}$ value of -0.012 suggesting an open shell shared interaction. However, this value should be positive for both agostic interactions and hydrogen bonds. The above results of Castro *et al.* therefore do not permit a clear identification of the interaction type.

What then is the nature of this weak C–H···Cu interaction in the example of Castro *et al.*? The discussion above shows that it is certainly not an agostic interaction. The values of d_1, d_2, D_1, D_2, θ_1 and θ_2 (Fig. 1) are suggestive of a weak intramolecular hydrogen bond of the IMH type from the C–H group to the two acceptors Cu(II) and the carboxylate O-atom. This would be termed as a multi-centred interaction involving a bifurcated donor (more than one acceptor).‡ A nearly identical situation prevails in crystalline CELWOF, CuL_2 (L = cyclodecane-1,3-dionato)[23] shown in Fig. 2. Here, the C–H group points towards the Cu-atom and the two nearby O-atoms of the ligand with a typical weak hydrogen bond geometry (H···Cu 2.289 Å, H···O 2.643 and 2.694 Å). This interaction has been described as being of the IMH type,[14] and this depiction is also chemically more reasonable.

In conclusion, we caution workers that designations like *agostic interaction* or *weak hydrogen bond* be carried out with care for C–H···M interactions. There is much current emphasis on the identification and characterization of new intermolecular
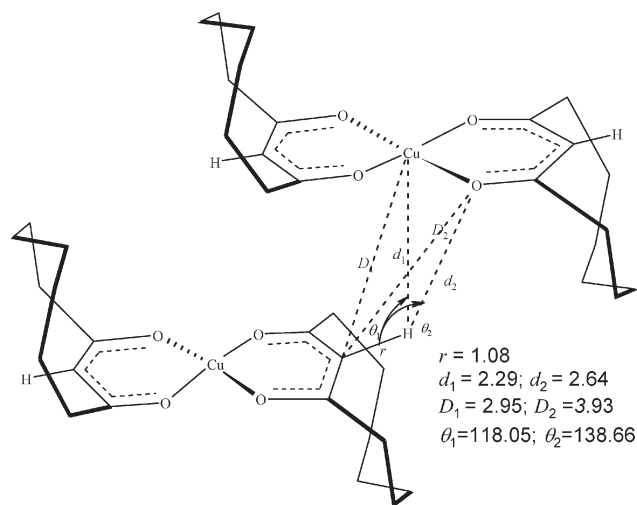

$r = 0.98$
$d_1 = 2.45; d_2 = 2.73$
$D_1 = 3.08; D_2 = 3.29$
$\theta_1 = 121.13; \theta_2 = 117.52$

Fig. 1 [Cu(Hceph)$_2$] complex **1** showing C–H···Cu interaction.

$r = 1.08$
$d_1 = 2.29; d_2 = 2.64$
$D_1 = 2.95; D_2 = 3.93$
$\theta_1 = 118.05; \theta_2 = 138.66$

Fig. 2 Intermolecular multicentre hetero-acceptor (IMH) interaction in crystalline CELWOF.[23] An additional H···O contact of 2.69 Å to the second O-atom of the ligand is not shown for clarity.

interactions, especially in the context of crystal engineering and solid state supramolecular chemistry. Many of these interactions are borderline to weak, and there is debate on their role and significance in maintaining stable crystal structures. In such a scenario, there is a particular responsibility on experimental scientists to classify these weak interactions correctly.

Notes and references

† A CSD survey of 6053 of these pentacoordinate structures shows that the median displacement of Cu(II) above the square plane of the ligand atoms is 0.19 Å.
‡ The smaller values of θ_1 and θ_2 arise because the interaction is intramolecular.

1 M. Castro, J. Cruz, H. Lopez-Sandoval and N. Barba-Behrens, *Chem. Commun.*, 2005, 3779.
2 S. Trofimenko, *J. Am. Chem. Soc.*, 1968, **90**, 4754; S. Trofimenko, *Inorg. Chem.*, 1970, **9**, 2493.
3 M. Brookhart and M. L. H. Green, *J. Organomet. Chem.*, 1983, **250**, 395.
4 R. H. Crabtree and D. G. Hamilton, *Adv. Organomet. Chem.*, 1988, **28**, 299.
5 D. Braga, F. Grepioni, K. Biradha and G. R. Desiraju, *J. Chem. Soc., Dalton Trans.*, 1996, 3925.
6 W. Scherer and G. S. McGrady, *Angew. Chem., Int. Ed.*, 2004, **43**, 1782.
7 G. R. Desiraju and T. Steiner, *The Weak Hydrogen Bond in Structural Chemistry and Biology*, Oxford University Press, Oxford, 1999.
8 G. C. Pimentel and A. L. McClellan, *The Hydrogen Bond*, W. H. Freeman, San Franscisco, 1960.
9 G. A. Jeffrey, *An Introduction to Hydrogen Bonding*, Oxford University Press, Oxford, 1997.
10 D. Braga, F. Grepioni and G. R. Desiraju, *Chem. Rev.*, 1998, **98**, 1375; D. Braga, F. Grepioni and G. R. Desiraju, *J. Organomet. Chem.*, 1997, **548**, 33.
11 D. M. Roe, P. M. Bailey, K. Moseley and P. M. Maitlis, *J. Chem. Soc., Chem. Commun.*, 1972, 1273.
12 L. Brammer, M. C. McCann, R. M. Bullock, R. K. McMullan and P. Sherwood, *Organometallics*, 1992, **11**, 2339.
13 W. Yao, O. Eisenstein and R. H. Crabtree, *Inorg. Chim. Acta*, 1997, **254**, 105.
14 D. Braga, F. Grepioni, E. Tedesco, K. Biradha and G. R. Desiraju, *Organometallics*, 1997, **16**, 1846.
15 Gaussian 03, Revision B.05, M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, J. A. Montgomery, Jr., T. Vreven, K. N. Kudin, J. C. Burant, J. M. Millam, S. S. Iyengar, J. Tomasi, V. Barone, B. Mennucci, M. Cossi, G. Scalmani, N. Rega, G. A. Petersson, H. Nakatsuji, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, M. Klene, X. Li, J. E. Knox, H. P. Hratchian, J. B. Cross, C. Adamo, J. Jaramillo, R. Gomperts, R. E. Stratmann, O. Yazyev, A. J. Austin, R. Cammi, C. Pomelli, J. W. Ochterski, P. Y. Ayala, K. Morokuma, G. A. Voth, P. Salvador, J. J. Dannenberg, V. G. Zakrzewski, S. Dapprich, A. D. Daniels, M. C. Strain, O. Farkas, D. K. Malick, A. D. Rabuck, K. Raghavachari, J. B. Foresman, J. V. Ortiz, Q. Cui, A. G. Baboul, S. Clifford, J. Cioslowski, B. B. Stefanov, G. Liu, A. Liashenko, P. Piskorz, I. Komaromi, R. L. Martin, D. J. Fox, T. Keith, M. A. Al-Laham, C. Y. Peng, A. Nanayakkara, M. Challacombe, P. M. W. Gill, B. Johnson, W. Chen, M. W. Wong, C. Gonzalez, and J. A. Pople, Gaussian, Inc., Pittsburgh PA, 2003.
16 R. K. Brown, J. M. Williams, A. J. Schultz, G. D. Stucky, S. D. Ittel and R. L. Harlow, *J. Am. Chem. Soc.*, 1980, **102**, 981.
17 R. B. Cracknell, A. G. Orpen and J. L. Spencer, *J. Chem. Soc., Chem. Commun.*, 1984, 326.
18 A. E. Reed, L. A. Curtiss and F. Weinhold, *Chem. Rev.*, 1988, **88**, 899.
19 R. F. W. Bader, *Atom in Molecules. A Quantum Theory*, The Clarendon Press, Oxford, 1990; R. F. W. Bader, *Chem. Rev.*, 1991, **91**, 893.
20 P. L. A. Popelier and G. Logothetis, *J. Organomet. Chem.*, 1998, **555**, 101.
21 S. Pillet, G. Wu, V. Kulsomphob, B. G. Harvey, R. D. Ernst and P. Coppens, *J. Am. Chem. Soc.*, 2003, **125**, 1937.
22 U. Koch and P. L. A. Popelier, *J. Phys. Chem.*, 1995, **99**, 9747.
23 C. L. Modenbach, F. R. Fronczek, E. W. Berg and T. C. Taylor, *Inorg. Chem.*, 1983, **22**, 4083.