Downloaded by York University on 05/05/2013 14:01:53.
Published on 19 October 2005 on http://pubs.rsc.org | doi:10.1039/B511944H

Charge density based classification of intermolecular interactions in molecular crystals†

Parthapratim Munshi and Tayur N. Guru Row*

Received 23rd August 2005, Accepted 5th October 2005
First published as an Advance Article on the web 19th October 2005
DOI: 10.1039/b511944h

Evaluation of intermolecular interactions in terms of both experimental and theoretical charge density analyses has produced a unified picture with which to classify strong and weak hydrogen bonds, along with van der Waals interactions, into three regions.

Ever since the description of bonding[1] between the atoms in a molecule, the association of the molecules in a crystal lattice has also been classified based on the strength of bonding. Among these associating interactions, hydrogen bonds (HBs) have been extensively studied in terms of geometry, energy, and other thermodynamic aspects.[2] In a recent review,[3] while giving a working definition of HB, Steiner remarks "there is no experimental indication that at a critical distance the nature of X–H···A interactions is switched from hydrogen bond to van der Waals type". The introduction of "synthons" as building blocks in crystal engineering[4] has provided a working definition to include all intermolecular interactions [HBs and van der Waals (vdW) interactions] in a general framework. The theory of "*Atoms in Molecules*" (AIM)[5] recognizes the importance of bonding densities and indeed provides a quantitative evaluation of HBs as per the criteria of Koch and Popelier (KP).[6] We have evaluated the charge density (CD) distribution in the intermolecular regions, which comprise both HBs and other weak interactions in terms of experimental (high-resolution X-ray diffraction data† at 90 K) and theoretical (periodic calculation,†[7] DFT, B3LYP/6-31G**) CD analyses. The results indicate a remarkable unified picture of the distribution of a variety of intermolecular interactions for the first time.

The present study consists of CD analysis of nine molecular crystals (Scheme S1†), comprising 15 types of interaction (for example O–H···O, N–H···O, C–H···O, π···π *etc.*) resulting in a total of 114 intermolecular interactions (Table 1). Among the molecular crystals included in the analyses, six are from the coumarin family;[8] coumarin, 1-thiocoumarin, 2-thiocoumarin, dithiocoumarin, and 3-acetylcoumarin (form A and form B), three are small bioactive molecules;[9] 2-thiouracil, cytosine monohydrate, and salicylic acid. Earlier reports involved either only theoretical[6*a*,10] estimates or purely experimentally[11] derived values. A couple of recent studies were based on either one type of interaction (C–H···O)[12] or a comparison between two types of interactions (C–H···O and C–H···π).[8*a*] In order to classify all types of interactions in molecular crystals and gain insights into the subtle features which distinguish HBs from vdW interactions, we have considered exclusively interactions involving aromatic systems (except in the case of cytosine monohydrate).

The multipole refinements are based on Hansen–Coppens formalism,[13] incorporated in the package XD.[14] The interactions have been characterized based on the first four KP of criteria, defined using the theory of AIM.

The topological properties, such as electron density, $\rho_{b(\mathbf{r})}$, Laplacian, $\nabla^2\rho_{b(\mathbf{r})}$, local kinetic $[G(\mathbf{r}_{CP})]$ and potential $[V(\mathbf{r}_{CP})]$ energy densities, and interpenetration of van der Waals spheres $[(\Delta r_D + \Delta r_A)]$[6] correlate well with the length of the interaction line, R_{ij} as can be seen from Fig. 1–4. Additionally, the negative values of $(\Delta r_D - \Delta r_A)$ (Table S1†) correspond to vdW interactions.[6] Based on the values of R_{ij} (~1.6 to 3.8 Å) and the corresponding values of ρ_b (~0.3 to 0.005 e Å^{-3}), the continuum of HBs to vdW interactions formed by these interactions can be classified into three regions (Fig. 1): *Region 1* consisting of HBs, O–H···O, N–H···O, and N–H···N, defining strong HBs (R_{ij} < 2.2 Å,

Table 1 Variety of hydrogen bonds and van der Waals interactions

Compound	O–H···O	N–H···O	N–H···N	N–H···S	C–H···O	C–H···π	C–H···S	O···C	N···N	C···C	O···O	N···C	S···S	S···C	S···N	Total
Coumarin	—	—	—	—	4	9	—	—	—	1	—	—	—	—	—	14
Form A	—	—	—	—	8	9	—	5	—	9	—	—	—	—	—	31
Form B	—	—	—	—	3	—	—	2	—	2	—	—	—	—	—	7
1-Thiocoumarin	—	—	—	—	3	3	2	1	—	2	—	—	—	1	—	12
2-Thiocoumarin	—	—	—	—	1	—	3	1	—	2	—	—	—	—	—	7
Dithiocoumarin	—	—	—	—	—	—	2	—	—	4	—		2	2	—	10
2-Thiouracil	—	1	—	1	1	—	2	1	1	1	1	—	1	—	1	11
Cytosine	1	2	1	—	3	—	—	1	1	—	—	2	—	—	—	11
Salicylic acid	1	—	—	—	2	—	—	5	—	1	2	—	—	—	—	11
Total	2	3	1	1	25	21	9	16	2	22	3	2	3	3	1	114

Solid State and Structural Chemistry Unit, Indian Institute of Science, Bangalore-560012, India. E-mail: ssctng@sscu.iisc.ernet.in; Fax: +91 80 23601310; Tel: +91 80 22932796

† Electronic supplementary information (ESI) available: (i) all the molecular diagrams as Scheme S1, (ii) all the parameters characterizing the interactions as Table S1, (iii) experimental and theoretical sections. See DOI: 10.1039/b511944h

This journal is © The Royal Society of Chemistry 2005

Downloaded by York University on 05/05/2013 14:01:53.
Published on 19 October 2005 on http://pubs.rsc.org | doi:10.1039/B511944H

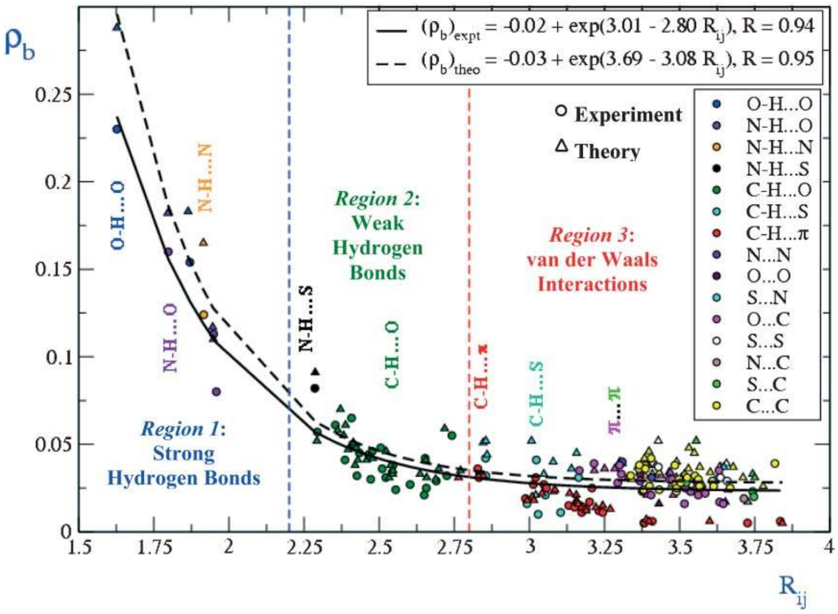

Fig. 1 Exponential dependence of $\rho_{b(\mathbf{r})}$ [e Å^{-3}] on R_{ij} [Å], the circles and triangles represent experimental and theoretical values respectively and the solid and dashed black lines represent the corresponding fittings. The inset gives the details of the fitting models along with correlation coefficients R and the color code for each type of interaction.

$\rho_b > 0.1$ e Å^{-3}), *Region 2* involves N–H···S and C–H···O interactions (2.2 Å $< R_{ij} <$ 2.8 Å, 0.08 e Å$^{-3} > \rho_b >$ 0.02 e Å^{-3}), defining weak HBs, and *Region 3* defining the regime of vdW interactions such as, C–H···π, C–H···S, and π···π (O···C, N···N, C···C, O···O, S···S, S···C, S···N, and N···C) with $R_{ij} >$ 2.8 Å and $\rho_b <$ 0.05 e Å^{-3}.

It is noteworthy that all the interactions follow a Morse-like dependence of $\nabla^2\rho_b$, on R_{ij} (Fig. 2), which emphasizes the separation between the different types of interactions. For $R_{ij} <$ 2.2 Å, $\nabla^2\rho_b$ has higher values (>2.5 e Å^{-5}) which define *Region 1*. In *Region 2*, the value of $\nabla^2\rho_b$ varies in the range 1.7 to 0.4 e Å^{-5} (2.2 Å $< R_{ij} <$ 2.8 Å). The values of $\nabla^2\rho_b <$ 0.5 eÅ^{-5} define *Region 3*.

Fig. 3 clearly distinguishes the variation in the strengths of the interactions. The positive values of $G(\mathbf{r}_{CP}) >$ 50 kJ mol^{-1} bohr^{-3} and the negative values of $V(\mathbf{r}_{CP}) <$ 35 kJ mol^{-1} bohr^{-3} form *Region 1*. The $G(\mathbf{r}_{CP})$ values (10 to 35 kJ mol^{-1} bohr^{-3}) and $V(\mathbf{r}_{CP})$ values (−25 to −7 kJ mol^{-1} bohr^{-3}) define *Region 2*. The lower magnitude of $G(\mathbf{r}_{CP})$ (< 12 kJ mol^{-1} bohr^{-3}) and $V(\mathbf{r}_{CP})$ (> −8 kJ mol^{-1} bohr^{-3}) lie in *Region 3*.

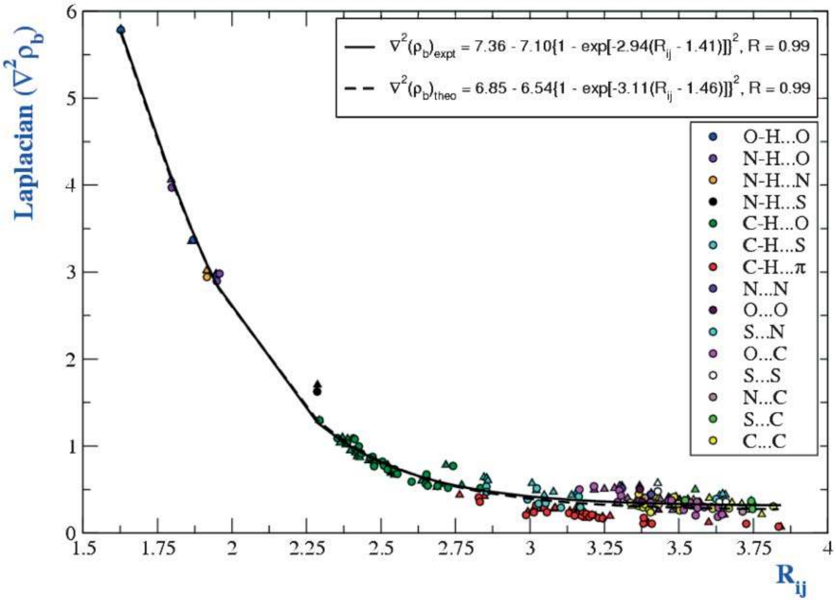

Fig. 2 Morse-like dependence of Laplacian [$\nabla^2\rho_{b(\mathbf{r})}$] (e Å^{-5}) on R_{ij} [Å] for 114 data points, the inset gives the details of the fitting models along with correlation coefficients R and the color code for each type of interaction.

Published on 19 October 2005 on http://pubs.rsc.org | doi:10.1039/B511944H
Downloaded by York University on 05/05/2013 14:01:53.

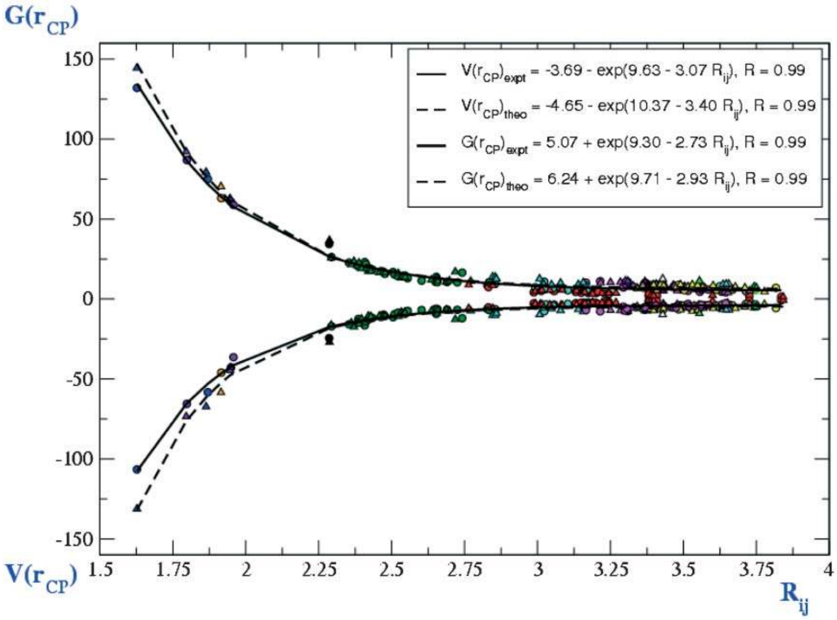

Fig. 3 Exponential fitting of $V(\mathbf{r}_{CP})$ [kJ mol^{-1} bohr^{-3}] and $G(\mathbf{r}_{CP})$ [kJ mol^{-1} bohr^{-3}] values on R_{ij} [Å].

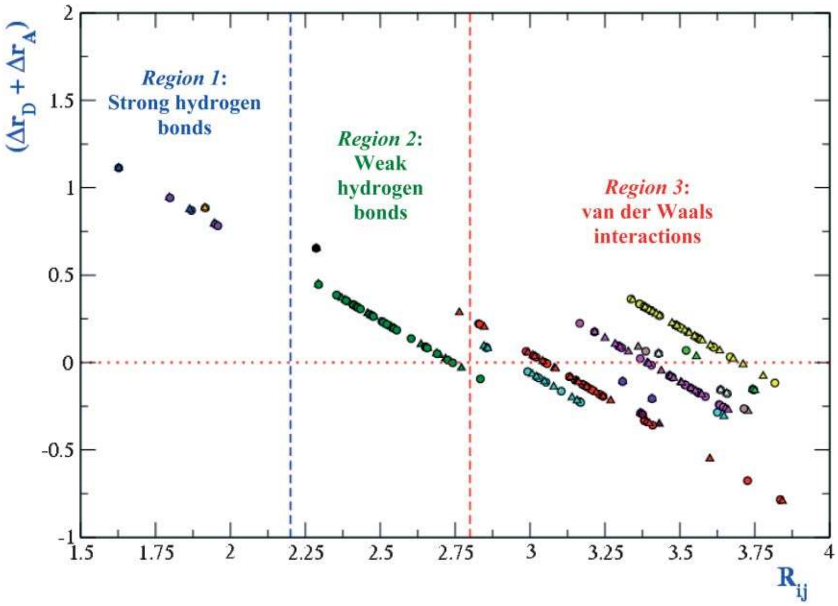

Fig. 4 Linear dependence of $(\Delta r_D + \Delta r_A)$ [Å] on R_{ij} [Å], dotted red lines corresponds to $(\Delta r_D + \Delta r_A) = 0$.

Fig. 4 is an evaluation of the fourth criterion of KP, which emphasizes the distinction between the HBs and the vdW interactions. The linear dependence of $(\Delta r_D + \Delta r_A)$ in both the regions is strikingly clear. Further, each vdW interaction is separated and it is noteworthy that $\pi\cdots\pi$ interactions, where no H atoms are involved, show positive as well as negative values of interpenetration and do not blend with interactions involving H atoms.

It may be pointed out that as far as the molecular crystals are concerned, there is a remarkable agreement between the experimental and theoretical results based on the charge density and further in a unique classification of HBs. Also, the choice of molecular crystals analyzed here provides the classification of a large number of interactions under one paradigm. Thus, it is imperative that the plot in Fig. 1 is a unified picture of all intermolecular interactions in molecular crystals. Understanding of crystal engineering based purely on distance–angle criteria is inadequate, thus the unified picture emphasizes the quantitative features of strong and weak HBs as well as vdW interactions. This approach to characterizing and fine-tuning intermolecular interactions has opened a new area, "*quantitative crystal engineering*",[11] which will have remarkable contributions to the future impact of supramolecular chemistry and further towards the design of new materials and molecular machines.

This journal is © The Royal Society of Chemistry 2005

Published on 19 October 2005 on http://pubs.rsc.org | doi:10.1039/B511944H
Downloaded by York University on 05/05/2013 14:01:53.

Acknowledgements

PM thanks the CSIR, India for a senior research fellowship. We thank DST-IRHPA, India for the CCD facility at IISc, Bangalore.

Notes and references

1 L. Pauling, *The Nature of the Chemical Bond*, Cornell University Press, Ithaca, New York, 3rd edn, 1960.

2 (*a*) G. R. Desiraju and T. Steiner, The Weak Hydrogen Bond, in *Structural Chemistry and Biology*, Oxford University Press, Oxford, New York, 1999; (*b*) G. A. Jeffrey, *An Introduction to hydrogen bonding*, Oxford University Press, New York, 1997; (*c*) G. A. Jeffrey and W. Saenger, *Hydrogen bonding in biological structures*, Springer-Verlang, Berlin, 1991.

3 T. Steiner, *Crystallogr. Rev.*, 2003, **9**, 177.

4 G. R. Desiraju, *Angew. Chem., Int. Ed. Engl.*, 1995, **34**, 2311.

5 R. F. W. Bader, *Atoms in Molecules–A Quantum Theory*, Clarendon, Oxford, 1990.

6 (*a*) U. Koch and P. L. A. Popelier, *J. Phys. Chem.*, 1995, **99**, 9747; (*b*) P. L. A. Popelier, *Atoms in Molecules. An Introduction*, Pearson Education, Harlow, 2000, pp. 150–153.

7 V. R. Saunders, R. Dovesi, C. Roetti, R. Orlando, C. M. Zicovich-Wilson, N. M. Harrison, K. Doll, B. Civalleri, I. Bush, Ph. D'Arco and M. Llunell, *CRYSTAL2003 User's Manual*, University of Torino, Torino, 2003.

8 (*a*) P. Munshi and T. N. Guru Row, *J. Phys. Chem. A*, 2005, **109**, 659; (*b*) P. Munshi and T. N. Guru Row, *Acta Crystallogr., Sect. B*, 2002, **58**, 1011; P. Munshi and T. N. Guru Row, *Acta Crystallogr., Sect. B*, 2003, **59**, 159; (*c*) P. Munshi and T. N. Guru Row, *Crystallogr. Rev.*, 2005, **11**, 199; (*d*) P. Munshi and T. N. Guru Row, *Cryst. Growth Des.*, 2004, **4**, 6, 1105.

9 P. Munshi and T. N. Guru Row, *Chem. Eur. J.*, 2005, submitted.

10 P. L. A. Popelier, *J. Phys. Chem. A*, 1998, **102**, 1873.

11 P. R. Mallinson, G. T. Smith, C. C. Wilson, E. Grech and K. Wozniak, *J. Am. Chem. Soc.*, 2003, **125**, 4259.

12 C. Gatti, E. May, R. Destro and F. Cargnoni, *J. Phys. Chem. A*, 2002, **106**, 2707.

13 N. K. Hansen and P. Coppens, *Acta Crystallogr., Sect. A*, 1978, **34**, 909.

14 T. S. Koritsanszky, S. Howard, P. Macchi, C. Gatti, L. J. Farrugia, P. R. Mallinson, A. Volkov, Z. Su, T. Richter and N. K. Hansen, *XD (version 4.10, July 2003)*, Free University of Berlin, Germany; University of Wales, Cardiff, UK; Università di Milano, UK; CNR-ISTM, Milano, UK; University of Glasgow, UK; State University of New York, Buffalo, USA; University of Nancy, France, 2003.