Timmins,[d] [a]*School of Life & Health Sciences, Aston University, Birmingham B4 7ET, (UK).* [b]*Cambridge Crystallographic Data Centre, 12 Union Rd, Cambridge CB2 1EZ, (UK).* [c]*School of Applied Sciences, University of Huddersfield, Huddersfield HD1 3DH, UK.* [d]*Bristol-Myers Squibb, Reeds Lane, Moreton, Cheshire CH46 1QW, (UK).* E-mail: c.h.schwalbe@aston.ac.uk

We report four structures of primary ammonium salts of the anti-inflammatory agent diclofenac (D), and we complete the salt sequences from t-butylammonium to Tris and mono- to triethanolammonium, seeking to optimize formulation properties.

Primary ammonium salts form columns made from hydrogen bonded (HB) rings. The highest-melting primary ammonium salts have $R_4^3(10)$ columns (melting points by DSC in triplicate; estimated errors in parentheses). The six independent ion pairs of the cyclohexylammonium salt are related by pseudosymmetry.

R group	Z'	Graph set for HB ring(s)	M. p. /°C
t-butyl	1	$R_4^2(8)$ & $R_4^4(12)$	166(2)
cyclohexyl	6	2 independent $R_4^3(10)$	191(2)
benzyl	1	$R_4^4(12)$	108(2)
adamantyl	1	$R_4^3(10)$	242(2)

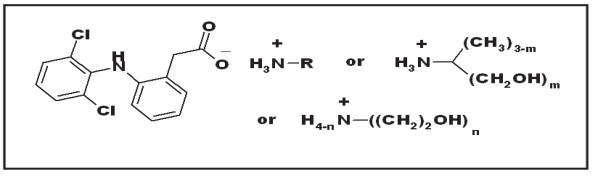
Hydroxymethyl derivatives have HB to OCO^- from OH as well as NH^+. Although $R_4^3(10)$ columns persist when m=1, they are distorted and presumably bring less stability.

m	Z'	H bond donors to OCO^-	M. p. /°C
1	1	$R_4^3(10)$, $R_2^2(9)$ NH^+&OH...O^-	143.7(6)
2	1	$R_3^3(8)$ NH^+&OH...O^-; $R_4^2(14)$	179(2)
3 (TUDPIR)	1	$R_3^3(8)$ NH^+&OH...O^-; $R_4^2(14)$	207.2(3)

Hydroxyethyl derivatives with n=1 or 2 also use these groups, but when n=3 the NH^+ is blocked [1]. Two ion pairs of the mono-hydroxyethyl compound differ in their HB: one D lacks the ubiquitous $S_1^1(7)$ intramolecular N-H…O^-, and only one pair has cation-cation NH^+…OH. Pseudosymmetry relates the other two.

n	Z'	H bond donors to OCO^-	M. p. /°C
1	4	$R_4^2(8)$ NH^+...O^-; $R_2^2(9)$	140.3(2)
2 (ZIKPOY)	1	$R_4^2(8)$ NH^+...O^-; $C_2^2(9)$	131.2(3)
3 (TEKVAG)	1	$C_2^2(12)$ OH...O^-	135(2)

HB motifs but not Z' obviously affect stability. We thank the NCS, Southampton, for data on these often difficult specimens.



[1] C. Castellari, S. Ottani, *Acta Cryst.* **1996**, *C52*, 2619-2622.

Keywords: diclofenac, H-bond, stability

MS73.P04

Acta Cryst. (2011) A**67,** C662

Halogen Interactions Using Variable Temperature Single Crystal X-ray Diffraction

Angshuman Roy Choudhury,[a] Piyush Panini,[b] Gurpreet Kaur,[a] and Deepak Chopra,[b] [a]*Indian Institute of Science Education and Research Mohali, Sector 81, S.A.S. Nagar, Manauli PO, Punjab, (India), 140306.* [b]*Indian Institute of Science Education and research Bhopal, Govindpura, Bhopal, (India), 462023*. E-mail: angshurc@iisermohali.ac.in.

The studies of intermolecular interactions involving halogen atoms in small organic molecules have been a controversial topic in contemporary research [1]. While a number of research groups have indicated that F behaves differently than Cl and Br in building crystal lattices [2]. mostly using Cambridge Structural Database; many other research groups have shown significant amount of experimental evidence of the active role of weak interactions such as C-H···F, C-F···F and C-F···π like C-H···X, C-X···X, C-X···π (X = Cl and Br) in crystal packing [3]. The natures of these interactions are yet to be well understood. The importance of fluorine in pharmaceutical industry, especially in medicinal application of small fluorinated organic molecules have gained significant interest in scientific literature [4]. We have been interested in this field as fluorine is one of the major substitutions found in drugs and drug intermediates and the C-F group in these play a major role in their biological activity [4b,c].In order to understand the nature and modes of weak interactions offered by a C-F group, we have chosen few model molecules such that these interactions can be studied both in the presence and absence of stronger hydrogen bonding interactions. We have also studied the crystal structures of the same set of compounds where F is replaced by Br or Cl. The altered packing modes of these molecules show that aromatic C-F groups provide significant interactions to stabilize crystal packing. These crystal structures have been studied at different temperatures to get an indication about the nature (attractive or repulsive) of these interactions. The salient features of our recent studies will be presented and the significance of weak interactions offered by the so called "organic fluorine" will be highlighted.

[1] (a) J.D. Dunitz, R. Taylor. *Chem. Eur. J.* **1997**, *3*, 89-98, (b) J A.K. Howard, V.J. Hoy, D. O'Hagan, G.T. Smith, *Tetrahedron* **1996**, *52*, 12613-12622, (c) V.R. Thalladi, H.C. Weiss, D. Bläser, R. Boese, A. Nangia, G.R. Desiraju, *J. Am. Chem. Soc.* **1998**, *120*, 8702-8710. [2] (a) G.R. Desiraju, R. Partasarathy, *J. Am. Chem. Soc.* **1989**, *111*, 8725-8726, (b) L. Shimoni, J.P. Glusker, *Struct. Chem*. **1994**, *5*, 383397. [3] (a) A.R. Choudhury, U.K. Urs, P.S. Smith, R. Goddard, J.A.K. Howard, T.N. Guru Row, *J. Mol. Struct*. **2002**, *641*, 225-232. (b) A.R. Choudhury, T.N. Guru Row, *Cryst. Growth Des.* **2004**, *4*, 47-52. (c) D. Chopra, T.N. Guru Row, *CrystEngComm* **2008**, *10*, 54-67. (d) D. Chopra, T.N. Guru Row, *CrystEngComm*, **2011**, *13*, 2175-2186, [4] (a) S. Purser, P.R. Moore, S. Swallow, V. Gouverneur, *Chem. Soc. Rev.* **2008**, *37*, 320-330, (b) Y. Benitex, A.M. Baranger, *J. Am. Chem. Soc.* **2011**, *133*, 3687-3689, (c) N.H. Campbell, D.L. Smith, A.P. Reszka, S. Neidle, D. O'Hagan, *Org. Biomol. Chem.* **2011**, *9*, 1328-1331, (d) C. Dalvit, A. Vulpetti, *ChemMedChem*, **2011**, *6*, 104-14.

Keywords: halogen interactions, disorder, crystal engineering

MS73.P05

Acta Cryst. (2011) A**67,** C662-C663

Subtle Interplay of Hydrogen Bonds and Weak Interactions in Drugs

Maheswararao Karanam and Angshuman Roy Choudhury, *Indian Institute of Science Education and Research Mohali, Sector 81, S. A. S. Nagar, Manauli PO, Punjab, (India), 140306.* E-mail: maheswararao@iisermohali.ac.in.

Classical hydrogen bonds [1] are known to take the leading role in generating the supramolecular assemblies, both in the solution and in the solid state and influence the formation of various crystal lattices of all organic, organometallic and biological macromolecules [2]. Weak

hydrogen bonds of the type C-H···O/N and weaker interactions of the type C-H···F and C-H···π are also considered to have important role in the building of a crystal lattice in the presence of strong hydrogen bonds [3]. Different altered modes of hydrogen bonds and weak interactions are known to generate a number of polymorphs of many compounds [4]. Polymorphism is a phenomenon of immense importance in pharmaceutical industry [5] and generation of new polymorphs, [5] cocrystals [6] and salts [7] of known APIs are possible using different modes of hydrogen bonds and weaker interactions. Study of polymorphism and cocrystal formation have gained momentum in recent years in the view of intellectual property rights (IPR) as well as in the enhancement of physicochemical properties of the drug molecules for their batter formulations [8]. We are interested to investigate the possibility of the formation of new polymorphs and cocrystals of a number of well-known Active Pharmaceutical Ingradients (APIs). Our recent experiments using Fluconazole, Ciprofloxacin, Lamivudine, Lamotrigine and Voriconazole revel that these APIs form new polymorphs or cocrystals or salts when crystallized in the presence of stoichimetric amount of a cocrystal former. The cocrystallization screening experiments have been performed by using both single crystal and powder X-ray diffraction techniques and solid state Raman spectroscopy. We shall highlight our recent results of these experiments and elucidate the crystal structures of new polymorphs of Fluconazole and Lamivudine, new salts of Fluconazole, Ciprofloxacin, Lamivudine and Lamotrigine and a new cocrystal of Voriconazole. Our studies indicate that the presence of a number of weak hydrogen bonds or weaker intermolecular interactions collectively can alter the mode of strong hydrogen bonds and generate new polymorphs, cocrystals and salts of the known APIs.

[1] L. Pauling, *The Nature of Chemical* Bond, Cornell Univ, Press, Ithaka, **1939**. [2] G.R. Desiraju, *Angew. Chem. Int. Ed.* **2010**, *49*, 2-10. [3] G.R. Desiraju, T. Steiner, *The Weak Hydrogen Bond in Chemistry and Biology*, Oxford University Press, Oxford, **1999**. [4] J. Bernstein, *Polymorphism in Molecular Crystals*, Oxford University Press, Oxford, **2002**. [5] S.M. Reutzel-Edens, J.K. Bush, P.A. Magee, G.A. Stephenson, S.R. Byrn, *Crystal Growth & Design*, **2003**, *3*, 897–907. [6] J. Kastelic, I. Hodnik, P. ket, J.Plavec, N. Lah, I. Leban, M. Pajk, O. Planinek, D. Kikelj, *Cryst. G rowth Des.* **2010**, *10*, 4943-4953. [7] J. McMahon, M. Peterson, M.J. Zaworotko, T. Shattock, M.B. Hickey, WO patent, WO 2006/007448 A2, **2006**. [8] P. Vishweshwar, J.A. McMahon, J.A. Bis, M J. Zaworotko, *J. Pharm. Sci.* **2006**, *95*, 499-516.

Keywords: polymorphism, cocrystals, hydrogen bond

MS73.P06

Acta Cryst. (2011) A**67,** C663

Geometry of C–H···O interactions: case of aromatic CH donors.

D.Ž. Veljković,[a] G.V. Janjić,[a] V.B. Medaković,[b] S.D.Zarić,[b] [a]*Institut of Chemistry, Technology and Metallurgy, University of Belgrade Njegoševa 12, Belgrade, (Serbia).* [b] *Department of Chemistry, University of Belgrade (Serbia).* E-mail: vdusan@chem.bg.ac.rs

C–H···O interactions play important role in biological systems, especially in biomolecules, in stabilizing structures of proteins, in interactions with the ligands, and in recognition of host-guest systems [1,2]. Based on directionality it was shown that C–H···O interactions, although can be weak, are hydrogen bonds and not the van der Waals interaction. Directionality is one of the most important properties of hydrogen bonds [3]. Hydrogen bonds with linear or close to linear geometries are energetically more stable than bent ones.

In this paper, angular distribution of C–H···O interactions of aromatic C-H donor was studied by *ab initio* calculations and by analyzing data in the Cambridge Structural Database (CSD). Crystal structures involving C_6-H aromatic groups and oxygen atoms were screened for intermolecular contacts. Following systems with oxygen atom were taken: HOH (non-coordinated), HOZ, Z_1OZ_2, O=CZ and O=YZ (Z, Z_1, and Z_2 are not hydrogen atoms, Y is not carbon atom). High level *ab initio* calculations were performed on three model systems: benzene-water, benzene-methanol, and benzene-acetone.

The analysis of the C–H···O interactions in crystal structures indicate that aromatic C-H donors do not show strong preference for linear contacts and that the preference depend on the type of the atom or group in o-position to the interacting C-H group. The acceptor oxygen atom has possibility for simultaneous C–H···O interactions with the hydrogen atom in o-position to the interacting C-H group. The C–H···O interactions of aromatic molecules with two hydrogen atoms in o-positions do not show preference for linear contacts. Bifurcated interactions are observed in substantial number of structures. Moreover, in the structures with a supstituent in o-position there is possibility for simultaneous hydrogen bonds, depending on the nature of the supstituent. The calculated energies for linear C–H···O interactions of benzene with water, methanol, and acetone are 1.28, 1.47, 1.45 kcal/mol; while for bifurcated interactions are 1.38, 1.63, and 1.70 kcal/mol, respectively. The calculations are in agreement with the results obtained by analysing crystal structure data from the CSD and show that stabilization energy is larger for bifurcated that for linear interactions. Analysis of the data in the CSD and the *ab initio* calculations indicate that the vicinity of the other possible hydrogen donors in the aromatic molecules cause small tendency for the linear contact the in C–H···O interactions. The result shows that nonlinear interactions are not energetically disfavoured because of the possibility for simultaneous interactions. This can be very important for recognizing C–H···O interaction in biomolecules containing aromatic groups, like proteins. It can also help in recognizing important C–H···O interactions, showing that nonlinear interactions are not energetically disfavored, because of the possibility for simultaneous interactions.

[1] R.K. Castellano, *Current Organic Chemistry*, **2004**, *8,* 845-865. [2] S. Scheiner, T. Kar, *J. Phys. Chem. B*, **2005**, *109***,** 3681-3689. [3] G.R. Desiraju, *Angew. Chem. Int. Ed.,* **2010**, *49*, 2–10.

Keywords: intermolecular interactions, crystallographic, calculations

MS73.P07

Acta Cryst. (2011) A**67,** C663-C664

Synthesis, structural characterization and hydrogen bond of new hybrid compound based on indium.

Sofiane Bouacida,[a,b] Ratiba Belhouas,[b] Boubakeur Fantazi, Chaouki Boudren,[b] Thierry roisnel,[c,] [a]*Département SM, Université LBM, Oum El Bouaghi, (Alegria).* [b]*Unité de recherche CHEMS, Université Constantine, (Alegria). c)Centre de difractométrie X ,UMR 6226,Université de Rennes I, (France).* E-mail: *Bouacida_sofiane@yahoo.fr*

The Tris(piperazine-1,4-diium) bis[hexachloridoindate(III)] tetrahydrate, $2[InCl_6]^{3-}$ $3[C_4H_{12}N_2]^{2+}$ $4H_2O$ was prepared as part of our ongoing studies of hydrogen-bonding interaction in the crystal structures of protonated amines and imines (Bouacida, 2008; Bouacida et al., 2005; 2007). we report here the synthesis and crystal structure of new hybrid compound based on indium with piperazine-1,4-diium that promises both the superior carrier mobility of inorganic semiconductors and the processability of organic materials.

It has been prepared by slow evaporation of an aqueous solution of piperazine, indium(III) chloride and hydrochloric acid in a molar ratio of 10:5:1.

The asymmetric unit consists of one and half independent piperazinium cations, an hexachloridoindiumate anion and two