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Close packing *vs*. specific interactions: para-disubstituted benzene derivatives

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Keywords: intermolecular interactions and packing in small-molecule crystals, structural databases, statistical analysis

In order to assess the relative importance and the structure defining role of close packing interactions (molecular shape) and specific directional interactions (*e.g.* hydrogen bonds, halogen-halogen interactions), a systematic study of the crystal structures of *para*-disubstituted benzene derivatives was started. The molecular shapes and possible p-p interactions are similar for each of these compounds, while different specific interactions may arise between the various functional groups.

198 unique crystal structures were retrieved from the Cambridge Structural Database [1]. The molecular arrangements in these structures were classified using the Compack algorithm [2], which tests the similarity of the coordination shell of 12-16 molecules packed around a reference molecule. Molecules were assigned to sets so that each molecule in a set had at least one partner in the same set for which a match of 15 molecules with a 20% distance tolerance was found. These sets provide a broad, general classification of the crystal packing arrangements.

Since some geometrical distortions were observed between the structures belonging to the same set, another method of classification was also applied. The 198 structures were searched by Conquest for short intermolecular contacts between the benzene rings (with any pair of atoms being closer than the sum of their van der Waals radii + 0.3 Å). The resulting dataset defines the spatial relationship between immediately neighbouring molecules in terms of centroid-centroid distances and interplanar angles. The contacts in the dataset were classified using the cluster analysis program Tanagra [3]. Four clusters representing distinct interaction modes between the aromatic moieties were identified. The occurrence of the different interaction modes between immediate neighbours in the crystal structures correlates with the grouping of the packing arrangements. This correlation confirms the significance of the packing sets deduced from Compack based comparisons.

It was found that there are popular arrangements, which are exhibited by compounds having completely different substituents (*e.g.* OH, SO_2Me, Br, $B(OH)_2$, Me), some hydrogen bonding and some hydrophobic. A description of these arrangements will be given, and they will be compared with the packing arrangements of aromatic hydrocarbons [4]. The role of the functional groups in the formation of the patterns will be discussed.

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[1] Allen, F. H. *Acta Cryst.*, 2002, B58, 380.
[2] Chisholm, J. A., Motherwell, S. *J. Appl. Cryst.*, 2005, 38, 228.
[3] Rakotomalala, R. *TANAGRA: free software for research and academic purposes*, in *Proceedings of EGC'2005, RNTI-E-3*, 2005, vol. 2, pp. 697-702 (in French); Web site: *http://eric.univ-lyon2.fr/~ricco/tanagra/en/tanagra.html*
[4] Desiraju, G. R., Gavezzotti, A. *Acta Cryst.*, 1989, B45, 473.

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Pi-Bond Cooperativity and Anticooperativity Effects in Resonance-Assisted Hydrogen Bonds (RAHBs)

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Keywords: resonance-assisted hydrogen bonding (RAHB), prototropic tautomerism, crystal structure databases

Bond cooperativity effects, which are typical of ”resonant” chains or rings of π-conjugated hydrocarbons, can also occur in H-bonded systems in form of *s-bond* and *p-bond cooperativity* or *anticooperativity*.

Σ*-bond cooperativity* is associated with the long chains of O-H...O bonds in water and alcohols, while α*-bond anticooperativity* occurs when the cooperative chain is interrupted by a local defect reversing the bond polarity. Both effects are known to play an important role in nature by controlling proton transmission in water and water flow without proton transmission in aquaporins.

Π*-bond cooperativity* is the driving force controlling resonance-assisted H-bonds (RAHBs). In typical intamolecular RAHBs enolones (...O=C-C=C-OH...) and enaminones (...O=C-C=C-NH...) form p-cooperative 6-membered rings closed by strong O-H...O or N-H...O bonds [1-4].

Π*-bond anticooperativity* has never been considered so far and it is investigated here by studying couples of H-bonded β-enolone and/or β-enaminone 6-membered rings fused through a common C=O or C-C bond. The effect is studied by X-ray crystal structure determination of five compounds and by extensive CSD [5] search of related fragments. It is shown that fusion through the C=O bond is always anticooperative and such to weaken the symmetric O-H...O...H-O and N-H...O...H-N bonds formed but not the asymmetric O-H...O...H-N one, a fact that is interpreted in terms of equal or different proton affinities of the H-bond donor and acceptor atoms. Fusion through the C-C bond may produce either cooperative or anticooperative H-bonds, the former being more stable than the latter and giving rise to a unique resonance-assisted 10-membered ring running all around the two fused 6-membered ones that can be considered *a type of prototropic tautomerism never described before*. The possible applications of these fused rings as two-state centers in potentially ferro/ antiferroelectric systems are finally discussed.

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[1] Gilli G., Bellucci F., Ferretti V., Bertolasi V., *J. Am. Chem. Soc.*, 1989, 111, 1023.
[2] Bertolasi V., Gilli P., Ferretti V., Gilli G., *J. Am. Chem. Soc.*, 1991, 113, 4917.
[3] Gilli P., Bertolasi V., Ferretti V., Gilli G., *J. Am. Chem. Soc.*, 1994, 116, 909.
[4] Gilli P., Bertolasi V., Ferretti V., Gilli G., *J. Am. Chem. Soc.,* 2000, 122, 10405.
[5] Allen F.H., *Acta Cryst.*, 2002, B58, 380.