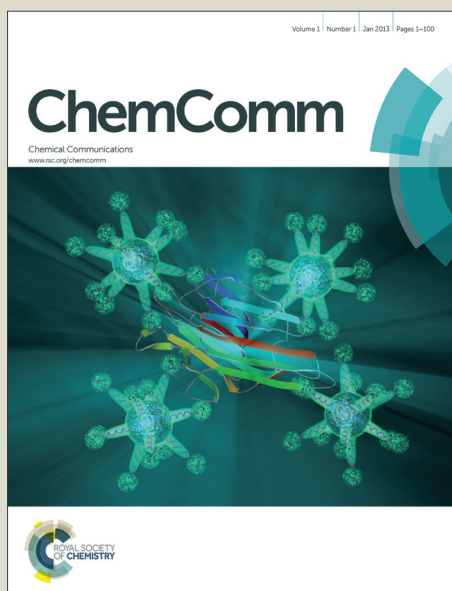


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Stacking interactions of hydrogen-bridged rings - stronger than stacking of benzene molecules

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Analysis of crystal structures from Cambridge Structural Database showed that 27% of all planar five-membered hydrogen-bridged rings, possessing only single bonds within the ring, form intermolecular stacking interactions. Interaction energy calculations show that interactions can be as strong as -4.9 kcal/mol, but dependent on ring structure.

Stacking interactions of aromatic rings are very important in many fields, like supramolecular chemistry, material design and biochemistry.¹ Although stacking interactions are typical for aromatic molecules, other planar rings can also participate in stacking interactions similar to those of aromatic organic molecules.²

Hydrogen-bridged quasi-rings often act as classical rings formed by covalent bonding. It was recently stated that quasi-chelates can participate in C-H... π interactions similar to these of organic molecules.³ Quasi-aromatic rings or any other chemical species possessing resonance-assisted intra- or intermolecular hydrogen bonds can also form stacking interactions.⁴⁻⁶

In this paper, intermolecular interactions of five-membered hydrogen-bridged rings, which possess only planar atoms and single bonds within the ring, are studied by searching Cambridge Structural Database (CSD) and by quantum chemical calculations, including very accurate CCSD(T)/CBS level. To the best of our knowledge this is the first study on stacking interactions of this kind of hydrogen-bridged rings. Interactions described in this work could be interesting from the viewpoint of the deeper understanding of the behaviour of cyclic structures formed by hydrogen bonding in supramolecular arrangements.

We studied planar rings formed by intramolecular hydrogen bonding, containing only single bonds, which are all parts of the acyclic systems. Planar systems conditioned by multiple bonding or rigid condensed systems are excluded.

A CSD search (CSD version 5.35, November 2013, and updates, May 2014) is performed by using ConQuest 1.16⁷. Constraints applied in search were: 1) distances between donor (D) and acceptor (A) atoms within the ring less than 4.0 Å; 2) angles between donor (D), hydrogen, and acceptor (A) atoms within the ring from 90° to 180°; 3) absolute torsions AX₁YD and XYD₁H (Fig. 1) from 0 to 10°; 4) donor and acceptor atoms include N, O, Cl, S and F atoms, due to their considerable electronegativities; 5) all covalent bonds within the ring are set to be single acyclic; 6) all atoms in the ring were planar (rings with nonplanar atoms; tetrahedral nitrogen, oxygen or carbon atoms, multivalent sulphur or metal atoms were excluded) 7) intermolecular contacts having distances between two centroids 4.5 Å or less are considered as interactions between rings. The criterion 6), for planar atoms in the ring was set in order to avoid side interactions or steric hindrances coming from atoms or groups which are situated in the region between the rings.

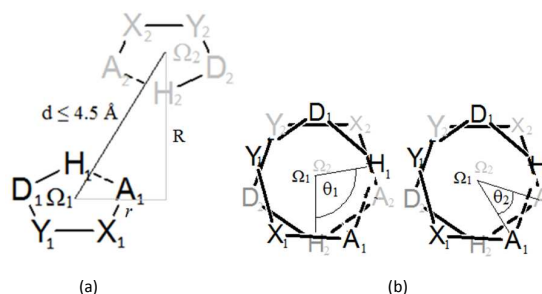


Fig. 1. Geometric parameters and atom labelling scheme used for the description of intermolecular interactions of hydrogen-bridged rings, studied in this work; a) Ω marks the centroid of the ring; X and Y are any atoms adjacent to hydrogen bond acceptor-A and donor-D atoms, respectively, R and r mark normal distance and offset value, respectively; b) θ_1 and θ_2 angle definition

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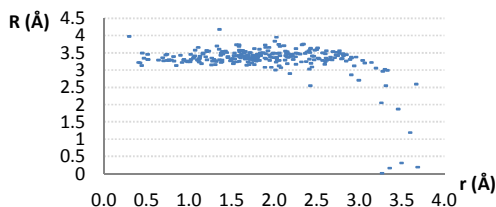


Fig. 2. Interplanar distance R for contacts having parallel ring planes ($\pi \leq 10^\circ$), plotted as a function of offset value r of the two centroids.

The crystallographic R factor is set to be less than 10%, the error-free coordinates according to the criteria used in the CSD, the H-atom positions were normalized using the CSD default X-H bond lengths (O-H = 0.983 Å; C-H = 1.083 Å and N-H = 1.009 Å), no polymer structures and no powder structures were included.

Searching the CSD 978 rings satisfying criteria 1-6 were found; these rings form 307 (31 %) contacts that have the distance between two centroids less than 4.5 Å, while 27% (264 contacts) form parallel interactions (angle between planes of the two rings less than 10°). Hence, most of the contacts with the distance between two centroids less than 4.5 Å (307 contacts), have parallel orientations of the rings (264 contacts, 86 %) (Fig. S1).

The data in Fig. 2 show that most of contacts have normal distance in the range between 3.0 Å and 3.5 Å, similar to those in stacking interactions of organic aromatic rings (3-4 Å),^{8,9} and that offset values are mostly between 1.0 and 3.0 Å, indicating slipped parallel orientations, again similar to aromatic rings.^{8,9}

Analysis of the distributions of absolute values of torsion angles $H_1\Omega_1\Omega_2H_2$ (θ_1) and $A_1\Omega_1\Omega_2A_2$ (θ_2) (Fig. 1) showed that large majority of contacts have both torsion angles around 180° , indicating that the "head to tail" orientations are preferred (Fig. S2).

In order to evaluate strength of the interaction between two stacked hydrogen-bridged rings, the interaction energies were calculated on structures presented in the Fig. 3. These structures were chosen since their derivatives occur quite frequently in crystal structures. Namely, 94% of 307 contacts

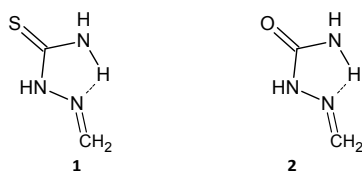


Fig. 3. Molecules used for the model systems for quantum chemical calculations of parallel interaction energies

(or 288 contacts) have N, C, N and N atoms as D, Y, X and A atoms, respectively, in the ring (Fig. 1). Moreover, in 75% (or 217 contacts) sulphur atom is a substituent on carbon atom, while in 20% (or 59 contacts) oxygen atom is a substituent on carbon atom.

Model systems used for calculations are composed of two hydrogen-bridged rings in the antiparallel position (Fig. 4 and 5). Optimizations of monomers are done at MP2/cc-pVTZ level. Stacking interaction energies between two rings were calculated by single-point calculations at CCSD(T)/CBS method.¹⁰ Interaction energy was determined as a difference of the dimer energy and the sum of energies of monomers, including correction of basis set superposition error (BSSE).¹¹ All calculations are done by using Gaussian09 series of programs.¹²

Calculated interaction energies are significantly strong; energies at CCSD(T)/CBS level for sandwich geometries ($r = 0.0$ Å Fig. 4) for **1** and **2** are -4.84 kcal/mol and -2.95 kcal/mol, respectively. Stronger interaction energy in case of **1** is probably a consequence of higher dispersion energy component. Maps of electrostatic potentials indicate larger delocalisation of electronic density in case of **1** (Fig. S7 ESI).

Moving molecules along Ω -C direction, where Ω represents the centroid of the molecule, while C represents the centroid of the hydrogen-acceptor bond (Fig. 4) we calculated potential curves. Molecules are also moved along the orthogonal direction to the Ω -C (Fig. 5). Both potential curves are presented in Fig. S5 Offset values were varied from -2.5 to 2.5 Å in steps of 0.5 Å, while normal distances were varied for every particular offset value in order to obtain the strongest energy. The potential curves are obtained by using DFT methods that were chosen by careful benchmarking for each system against very accurate CCSD(T)/CBS values (ESI).

The data in Fig. S5a (ESI) show that minimum on potential curve along Ω -C direction occurs at 0.0 Å, for both molecules. Energies are only slightly weaker for small negative offsets. At small negative offsets double bonds of carboxyl and groups overlap with the rings (Fig. 4), however, these overlaps do not make interactions particularly strong. The potential curves along the direction orthogonal to Ω -C direction have one minima at -1.0 Å and the strongest interaction at offsets of 2.5 Å for both molecules (Fig. S5b, ESI). Strong interactions at 2.5 Å correspond to interactions of the ring with doubly bonded methyldene group (Fig. 5). Neglecting these interactions where side groups are dominant, the minima on the curves are at $r = -1.0$ Å (Fig. S5b, ESI), with the interaction energies of -

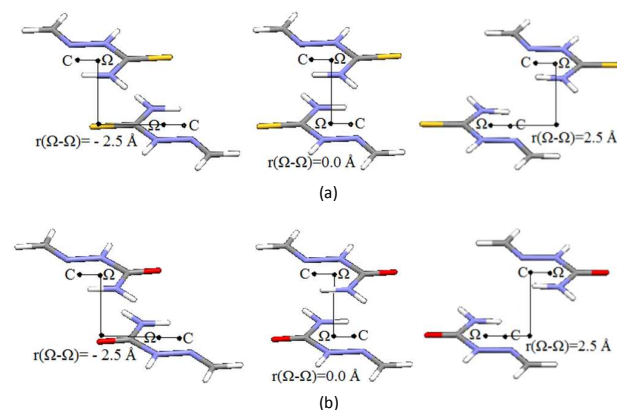


Fig. 4. Parallel interactions of (a) **1** and (b) **2** at three offset values along Ω -C direction

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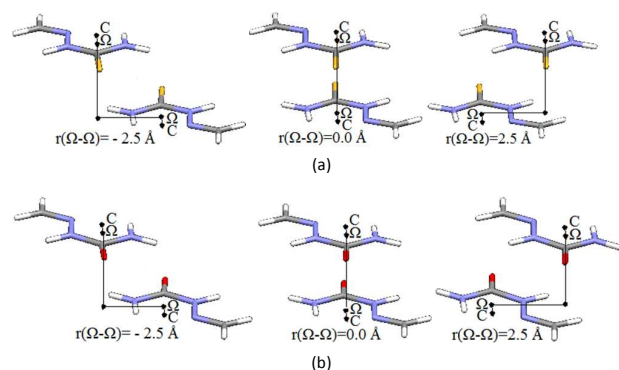


Fig. 5. Parallel interactions of (a) **1** and (b) **2** at three offset values along the direction orthogonal to Ω -C

Table 1 Energies on potential curves minima. Energies (in kcal/mol) are at CCSD(T) level, distances are in Å.

	Offset (r)	1	2
Potential curves			
Along Ω -C direction	0.0	-4.84	-2.95
Orthogonal to Ω -C direction	-1.0	-4.89	-2.95

4.89 kcal/mol for **1** and -2.95 kcal/mol, for **2**, calculated at CCSD(T)/CBS level. For comparison, the strongest benzene stacking interaction is -2.73 kcal/mol at CCSD(T)/CBS level.^{9e}

Significantly strong interactions indicate the importance of parallel interactions of hydrogen-bridged rings, that have single bonds in the ring, and show that the parallel alignment is not just the consequence of crystal packing.

In summary, analysis of planar five-membered hydrogen-bridged rings, possessing only single bonds, contained in Cambridge Structural Database (CSD), showed that 27% of these rings form intermolecular parallel interactions. The interactions have the distance between the planes in the range from 3.0 Å to 4.0 Å, that is typical for aromatic stacking interactions.^{8,9} Interaction energies were calculated at very accurate CCSD(T)/CBS level; the energies are -4.89 kcal/mol and -2.95 kcal/mol, for rings with sulphur and oxygen substituents respectively. These interactions are stronger than stacking between two benzene molecules (-2.73 kcal/mol).^{9e} The calculated energies suggest that parallel alignment of five-membered hydrogen-bridged rings, that have only single bonds in the ring, in crystal structures is not just a side effect of crystal packing. The results indicate that stacking of hydrogen-bridged rings, a phenomenon neglected until now, can be as important as aromatic ring stacking in various supramolecular systems.

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‡ Footnotes relating to the main text should appear here. These might include comments relevant to but not central to the matter under discussion, limited experimental and spectral data, and crystallographic data.

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