

# Interactions Steering Arrangement of Molecules in Crystals

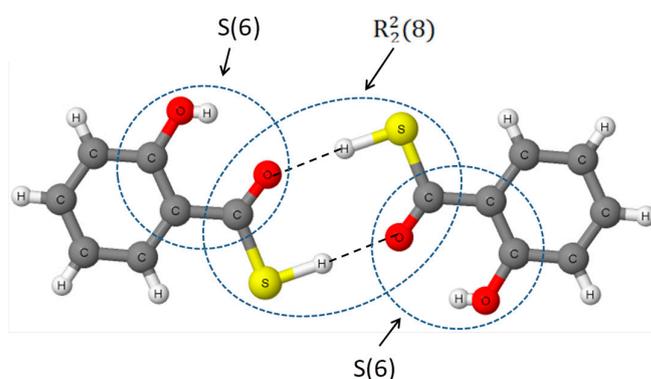
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It is well known that the hydrogen bond is an important interaction that influences an arrangement of molecules in numerous organic and metal-organic crystals [1,2]. There are various motifs containing hydrogen bond links in crystal structures; the method based on the graph theory was proposed to categorize them [3,4]. For example, the  $R_2^2(8)$  motif, according to the graph-set assignments, is among the most often occurring ones, it is typical for crystals of carboxylic acids, amides, and numerous other compounds [5]. Figure 1 presents the fragment of the crystal structure—the dimer of the 2-hydroxythiobenzoic acid [6] (RONVAR refcode in the Cambridge Structural Database, CSD [7,8]). One can see here the above-mentioned  $R_2^2(8)$  motif that corresponds to the eight-member ring formed by two thiocarboxylic groups linked by symmetrically equivalent S-H...O hydrogen bonds. There are also intramolecular O-H...O hydrogen bonds in this structure that close the six-member rings designated as S(6) in the graph set method [3,4]. The latter motifs occur very often in crystal structures and it was stated early on by Etter that the formation of such a type of intramolecular hydrogen bond is preferred in crystal structures to the formation of other interactions [5].

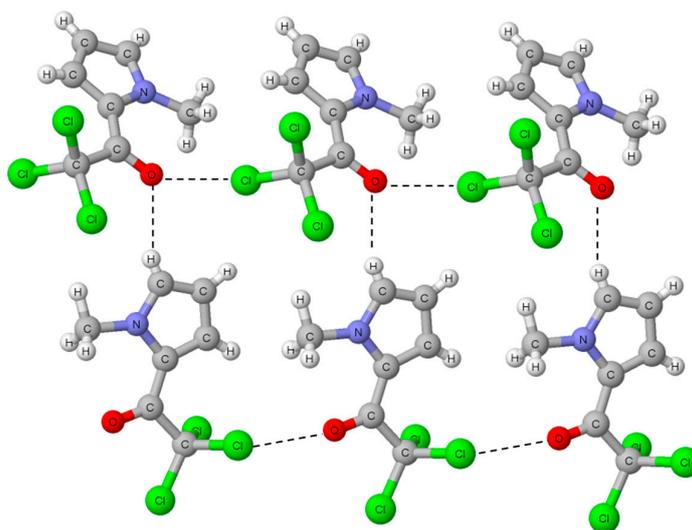


**Figure 1.** The dimer of 2-hydroxythiobenzoic acid [6] (RONVAR refcode in CSD). The  $R_2^2(8)$  and S(6) motifs are presented. This dimer is linked by the S-H...O hydrogen bonds (broken lines).

Thus, the S-H...O hydrogen bond that is classified as a rather weak interaction (the hydrogen bond energy calculated at the  $\omega$ B97XD/aug-cc-pVTZ level amounts  $\sim 3$  kcal/mol [9]) plays an important role in the arrangement of molecules in crystals; one can see that not only strong and moderate hydrogen bonds like O-H...O or N-H...O influence the architecture of crystal structures. It has been stated in numerous studies that such weak interactions as the C-H...O, C-H...S or C-H... $\pi$  hydrogen bonds [10,11], for example, play a crucial role in the arrangement of molecules.

Not only hydrogen bonds are important interactions in crystal engineering. It was analysed early that other ones are their counterparts in greater aggregates [12]. The halogen bond is the interaction

that similarly as the hydrogen bond was analysed as the factor that steers the orientation of molecules in crystals [13]. Figure 2 presents the fragment of the crystal structure of the 1-methylpyrrol-2-yl trichloromethyl ketone [14] (WEYYUV refcode in CSD [7,8]) where molecules are linked by the C-Cl ... O=C halogen bonds and the C-H ... O=C weak hydrogen bonds. In the case of both interactions, oxygen plays a role of the Lewis base centre while C-H and C-Cl bonds act as the electron acceptors.



**Figure 2.** The fragment of the crystal structure of 1-methylpyrrol-2-yl trichloromethyl ketone [14] (WEYYUV refcode in CSD). The C-Cl ... O=C and C-H ... O=C intermolecular halogen and hydrogen bonds, respectively, are marked by the broken lines.

It may be surprising that the electrophilic chlorine centres are observed for this structure. The Lewis acid properties of halogen atoms were a subject of numerous earlier and recent studies and a subject of debates and controversies [15]. Various concepts were presented to explain the dual role of halogens since very often they may act as the Lewis acid and Lewis base centres simultaneously. It seems that the concept proposed by Politzer, Murray, and Clark explains the halogen atoms' properties [16,17]. It was explained that numerous electronegative atoms, not only halogens, but also elements of other groups, including noble gases [18], may act as the Lewis acid centres through the so-called  $\sigma$ -holes characterized by the depletion of the electron density and consequently the increase of the electrostatic potential, up to the positive values. The  $\sigma$ -hole is situated in the elongation of the bond to the centre considered. Numerous kinds of interactions named as the  $\sigma$ -hole bonds were analysed; these are: tetrel, pnictogen, chalcogen, halogen (discussed above here) and aerogen bonds, for the 14, 15, 16, 17 and 18th groups, respectively. The mentioned here centres possess usually dual acidic and basic character, except of tetrel centres probably [19]. There are other kinds of the regions of atoms that are characterized by the outflow of the electron charge and that they act as electrophiles, they are named  $\pi$ -holes [16,17]. The atoms of the 13th group often possess such regions and the corresponding interactions are named triel bonds [20]. Very recently, the analysis of bifurcated triel bonds was presented which seem to regard to new type of interactions where hydride and halide anions are "locked up" between Lewis acid triel centres [21].

Thus one can see that there are various kinds of interactions which steer the arrangement of molecules in crystals and which are important factors in crystal engineering. Such interactions are observed in crystal structures; the Cambridge Structural Database [7,8] is a source of information on crystal structures, on the geometry of molecules forming crystals, as well as on interactions that link molecules. The most important is that these interactions are often preliminary stages of the chemical reactions and processes [19]. The hydrogen bond interaction may be a preliminary stage of the proton transfer process [1,22]; the tetrel bond may initiate the  $S_N2$  reaction [19], the dihydrogen bond is an

important interaction for hydrogen storage materials, this interaction leads often to the release of the molecular hydrogen [23,24]. There are numerous studies concerning so-called low barrier hydrogen bonds and analyses of whether they play an important role in enzymatic catalysis [25–27]. There are other numerous examples.

This is why the analysis of crystal structures is a very important topic, especially if it is not restricted only to their presentation, but if it concerns the deeper insight into the kind of interactions and their architecture.

**Conflicts of Interest:** The author declares no conflict of interest.

## References

1. Jeffrey, G.A. *An Introduction to Hydrogen Bonding*; Oxford University Press: New York, NY, USA, 1997.
2. *Analysis of Hydrogen Bonds in Crystals (Printed Edition of the Special Issue Published in Crystals)*; Grabowski, S.J., Ed.; MDPI: Basel, Switzerland, 2016.
3. Etter, M.C.; MacDonald, J.C.; Bernstein, J. Graph-set analysis of hydrogen-bond patterns in organic crystals. *Acta Cryst.* **1990**, *B46*, 256–262. [[CrossRef](#)] [[PubMed](#)]
4. Bernstein, J.; Davis, R.E.; Shimoni, L.; Cheng, N.-L. Patterns in Hydrogen Bonding: Functionality and Graph Set Analysis in Crystals. *Angew. Chem. Int. Ed.* **1995**, *34*, 1555–1573. [[CrossRef](#)]
5. Etter, M.C. Encoding and Decoding Hydrogen-Bond Patterns of Organic Compounds. *Acc. Chem. Res.* **1990**, *23*, 120–126. [[CrossRef](#)]
6. Mikenda, W.; Steinwender, E.; Mereiter, K. Hydrogen Bonding in 2-Hydroxybenzoic, 2-Hydroxythiobenzoic, and 2-Hydroxydithiobenzoic Acid. A Structural and Spectroscopic Study. *Monatsh. für Chemie* **1995**, *126*, 495–504. [[CrossRef](#)]
7. Groom, C.R.; Bruno, I.J.; Lightfoot, M.P.; Ward, S.C. The Cambridge structural database. *Acta Cryst.* **2016**, *B72*, 171–179. [[CrossRef](#)]
8. Wong, R.; Allen, F.H.; Willett, P. The scientific impact of the Cambridge Structural Database: A citation-based study. *J. Appl. Cryst.* **2010**, *43*, 811–824. [[CrossRef](#)]
9. Aarabi, M.; Gholami, S.; Grabowski, S.J. S-H . . . O and O-H...O hydrogen bonds—Comparison of dimers of thiocarboxylic and carboxylic acids. *ChemPhysChem* **2020**. submitted for publication.
10. Desiraju, G.R.; Steiner, T. *The Weak Hydrogen Bond in Structural Chemistry and Biology*; Oxford University Press Inc.: New York, NY, USA, 1999.
11. Nishio, M.; Hirota, M.; Umezawa, Y. *The CH/π Interaction: Evidence, Nature and Consequences*; Wiley-VCH, Inc.: New York, NY, USA, 1998.
12. *Molecular Interactions. From van der Waals to Strongly Bound Complexes*; Scheiner, S., Ed.; John Wiley & Sons: Chichester, UK, 1997.
13. Metrangolo, P.; Meyer, F.; Pilati, T.; Proserpio, D.M.; Resnati, G. Highly Interpenetrated Supramolecular Networks Supported by N...I Halogen Bonding. *Chem. Eur. J.* **2007**, *13*, 5765–5772. [[CrossRef](#)]
14. Bilewicz, E.; Rybarczyk-Pirek, A.J.; Dubis, A.T.; Grabowski, S.J. Halogen bonding in crystal structure of 1-methylpyrrol-2-yl trichloromethyl ketone. *J. Mol. Struct.* **2007**, *829*, 208–211. [[CrossRef](#)]
15. Cavallo, G.; Metrangolo, P.; Milani, R.; Pilati, T.; Priimagi, A.; Resnati, G.; Terraneo, G. The Halogen Bond. *Chem. Rev.* **2016**, *116*, 2478–2601. [[CrossRef](#)]
16. Politzer, P.; Murray, J.S.; Clark, T. Halogen bonding: An electrostatically-driven highly directional noncovalent interaction. *Phys. Chem. Chem. Phys.* **2010**, *12*, 7748–7758. [[CrossRef](#)] [[PubMed](#)]
17. Politzer, P.; Murray, J.S.; Clark, T. Halogen bonding and other  $\sigma$ -hole interactions: A perspective. *Phys. Chem. Chem. Phys.* **2013**, *15*, 11178–11189. [[CrossRef](#)] [[PubMed](#)]
18. Bauzá, A.; Frontera, A. Aerogen Bonding Interaction: A New Supramolecular Force. *Angew. Chem. Int. Ed.* **2015**, *54*, 7340–7343. [[CrossRef](#)]
19. Grabowski, S.J. Hydrogen bonds, and  $\sigma$ -hole and  $\pi$ -hole bonds – mechanisms protecting doublet and octet electron structures. *Phys. Chem. Chem. Phys.* **2017**, *19*, 29742–29759. [[CrossRef](#)]
20. Grabowski, S.J. Boron and other Triel Lewis Acid Centers: From Hypovalency to Hypervalency. *ChemPhysChem* **2014**, *15*, 2985–2993. [[CrossRef](#)]

21. Grabowski, S.J. Bifurcated Triel Bonds – Hydrides and Halides of 1,2-Bis(Dichloroboryl)Benzene and 1,8-Bis(Dichloroboryl)Naphthalene. *Crystals* **2019**, *9*, 503. [[CrossRef](#)]
22. Denisov, G.D.; Mavri, J.; Sobczyk, L. Potential Energy Shape for the Proton Motion in Hydrogen Bonds Reflected in Infrared and NMR Spectra, chapter in the book. In *Hydrogen Bonding—New Insights*; Grabowski, S.J., Ed.; Springer: Dordrecht, The Netherlands, 2006.
23. Belkova, N.V.; Shubina, E.S.; Gutsul, E.I.; Epstein, L.M.; Eremenko, I.L.; Nefedov, S.E. Structural and energetic aspects of hydrogen bonding and proton transfer to  $\text{ReH}_2(\text{CO})(\text{NO})(\text{PR}_3)_2$  and  $\text{ReHCl}(\text{CO})(\text{NO})(\text{PMe}_3)_2$  by IR and X-ray studies. *J. Organomet. Chem.* **2000**, *610*, 58–70. [[CrossRef](#)]
24. Custelcean, R.; Jackson, J.E. Topochemical Control of Covalent Bond Formation by Dihydrogen Bonding. *J. Am. Chem. Soc.* **1998**, *120*, 12935–12941. [[CrossRef](#)]
25. Benedict, H.; Limbach, H.-H.; Wehlan, M.; Fehlhammer, W.-P.; Golubev, N.S.; Janoschek, R. Solid State  $^{15}\text{N}$  NMR and Theoretical Studies of Primary and Secondary Geometric H/D Isotope Effects on Low-Barrier NHN—Hydrogen Bonds. *J. Am. Chem. Soc.* **1998**, *120*, 2939–2950. [[CrossRef](#)]
26. Shenderovich, I.G.; Tolstoy, P.M.; Golubev, N.S.; Smirnov, S.N.; Denisov, G.S.; Limbach, H.-H. Low-Temperature NMR Studies of the Structure and Dynamics of a Novel Series of Acid-Base Complexes of HF with Collidine Exhibiting Scalar Couplings Across Hydrogen Bonds. *J. Am. Chem. Soc.* **2003**, *125*, 11710–11720. [[CrossRef](#)]
27. Graham, J.D.; Buytendyk, A.M.; Wang, D.; Bowen, K.H.; Collins, K.D. Strong, Low-Barrier Hydrogen Bonds May Be Available to Enzymes. *Biochemistry* **2014**, *53*, 344–349. [[CrossRef](#)]



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