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Can Topological Analysis of Intermolecular Interactions Explain Differences in the Physico-Chemical Properties of Related Chiral Compounds? Sine Larsen^{a,b}, Henning Osholm Sorensen^a, Anders Østergaard Madsen^{a,b} and Robert F. Stewart^c, ^aCentre for Crystallographic Studies, University of Copenhagen, Denmark; ^bESRF, Grenoble, France; ^cCarnegie-Mellon University, Pittsburgh, USA. E-mail: sine@ccs.ki.ku.dk

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Interactions between chiral molecules play a fundamental role for the most biological and many chemical processes. Due to the complexity of the interactions that range from normal hydrogen bonds to weaker interactions like C-H—O hydrogen bonds and π - π stacking, it can be difficult to relate overall thermodynamic properties to the nature of the intermolecular interactions.

The topological analysis developed by R.W. Bader for theoretical electron densities has proven to be a powerful tool to analyse intermolecular interactions in crystals based on an analysis of experimental electron densities obtained from accurate high resolution X-ray diffraction data. Our recent investigations of the molecular crystal naphthalene revealed that the topological analysis could reveal and characterize unexpected interatomic interactions [1].

The two pentose epimers xylitol and ribitol differ in the physico-chemical properties, the acentric xylitol being the higher melting and the less dense than ribitol. All possible hydrogen bond donors participate in the hydrogen bond interactions in both compounds, and the topological analysis confirms the energetic similarity of these interactions. The investigations suggest that the origin of the differences in physico-chemical properties is related to differences in the weaker intermolecular interactions and in the entropy.

Crystallization of a racemate may lead to racemic compound composed of equal amounts of the two enantiomers or to a spontaneous resolution of crystals that are formed by the pure enantiomers, and the outcome of the process depends on differences in enthalpy and entropy. We have investigated the intermolecular interactions in closely related crystal structures, e.g. a racemic para-fluoromandelic acid and its corresponding enantiomer. The racemic para-fluoromandelic acid showing the unusual behaviour of being the higher melting. An earlier investigation showed that the two forms have an identical hydrogen bond pattern. This was confirmed by the topological analyses based on accurate X-ray diffraction data. Though additional features were revealed from the topological analysis it also showed the significance of supplementing the investigations with theoretical calculations.

[1] J. Oddershede and S. Larsen ; *J. Phys. Chem. A* (2004) **108** 1057-1063.

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Tuning Protons in Hydrogen Bonds: Diffraction + Temperature = Chemistry? Chick Wilson, Department of Chemistry, University of Glasgow, Glasgow G12 8QQ, UK, and ISIS Facility, CCLRC Rutherford Appleton Laboratory, Chilton, Didcot, Oxon OX11 0QX, UK. E-mail: C.C.Wilson@chem.gla.ac.uk

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We have been interested for several years in apparently "anomalous" behaviour of hydrogen atoms in molecular systems [1]. In particular we have been examining structural evolution, where we look for changes in a structure at a range of temperatures (or pressures), to allow us better to image, model and understand these changes. Using a combination of X-ray and neutron single crystal diffraction we have been able to identify many systems in which there is disorder of hydrogen atoms in hydrogen bonds, and have been able to characterise these successfully. In addition, we have identified a range of candidate systems where the position of a hydrogen atom in a hydrogen bond, particularly short, strong hydrogen bonds, appears to change as a function of temperature. A comprehensive multiple temperature/pressure study can allow this proton migration effect to be identified unambiguously (ideally by neutron diffraction, but also by careful X-ray diffraction) and to be followed as it evolves. In such cases, the nature of the hydrogen bond can be said to be changing as the position of the hydrogen atom changes, in essence changing the underlying chemistry of the system. Using neutron and X-ray diffraction, we will discuss examples in which the hydrogen atom migrates towards the mid-point of the hydrogen bond, and also in which the hydrogen atom moves from a position close to the "donor" atom, to a position closer to the "acceptor" atom, thus changing the nature of the hydrogen bond and thus the chemistry. In discussing these systems, we will emphasise: the added value of using both X-ray and neutron methods; the power of imaging through evolutionary Fourier maps; the caution required in using X-ray refinements in modelling subtle hydrogen atom behaviour in such cases; the vital complementary role of computation chemistry methods in understanding these effects.

[1] C C Wilson (2002). *Recent Res Devel Chem Phys*, **3**, 119-147