Preface

Crystal engineering is defined as *"the understanding of intermolecular interactions in the context of crystal packing and in the utilisation of such understanding in the design of new solids with desired physical and chemical properties"*. If crystals are the supramolecular equivalents of molecules, then crystal engineering is the supramolecular equivalent of organic synthesis. The subject considers both crystal structure analysis and design of new structures with targeted properties. The concept of "Supramolecular Synthons" was introduced by G. R. Desiraju in this context, for the rational design of structures. Supramolecular synthons are the smallest reducible structural units that contain geometrical and chemical information required for recognition between functional groups in molecular solids. Crystal engineering has grown very fast after the introduction of this idea in 1995 and engineered solids were found to be useful for application in many diverse fields, from structural chemistry to drug design. Because of the great significance of supramolecular synthons, their identification and analysis in terms of crystallographic, spectroscopic, and computational methods is essential. Single crystal X-ray diffraction (SCXRD) is a widely used technique for the identification of synthon structure. But the technique has its own limitations like requirement of good quality, suitably sized single crystals, longer times associated with the process which further restricts high throughput analysis. Practically, there is no other way for identification of synthons on a regular basis. In this situation a simple, accurate, and fast method will be of significance; not only for basic studies, but also to scan different solid state phases in pharmaceutical industries. Due to this reason, I have studied IR spectroscopy to find marker bands for different synthons in the first part of the thesis.

In chapter 2, I have analyzed a variety of C–H···X based weak synthons. For identification of each synthon, two sets of compounds were taken. In one set the synthon exists and in the other set it does not. Comparison and verification of IR characteristics helps to establish marker bands. Such markers are used to get information on synthon patterns in compounds with unknown crystal structures. The next challenge is whether or not such an IR method can distinguish different geometries of a same interaction.

To address this question, different geometries of $NO_2\cdots I$ halogen bonded synthons are investigated in chapter 3. This synthon exists in three geometries **P**, **Q** and **R** based on angular and distance criteria. The identification process is divided into five steps. The first step identifies IR signatures from very similar compounds, but with different topologies. The second step verifies earlier features and establishes IR marker bands. In the next step a graded IR protocol is formulated for stepwise discrimination of unknown systems. Such a graded method is applied for clarification of synthon ambiguities and in the identification of synthons in new compounds. Till now synthon information from crystal structures is used as a basis for IR study. Spectroscopy provides chemical information on intermolecular interactions. Is it possible to use such chemical information for crystal engineering?

Chapter 4 deals with this aspect. Here, IR investigation is performed on the acid···amide heterodimer synthon. The initial analysis shows contradictory outcomes for synthon formation. According to IR, the N–H···O interaction is significantly destabilized in this synthon. Why then does the acid···amide synthon form? It is found that the answer lies in the higher stability of the other interaction, O–H···O, in the synthon. In other words, dimer formation will be preferred when the O–H···O interaction is favoured. This is possible when the acidity of H-atom and the basicity of carbonyl O-atom is high. Based on this, a combinatorial study is performed varying the chemical nature of molecules, electron donating or withdrawing. Four quadrants are generated with different combinations of the molecular nature. The result of the combinatorial study shows different acid–amide oriented synthon preferences from different quadrants. A combination of all the observed synthons creates a structural landscape for the acid–amide system. A particular synthon associated with a specific quadrant is found to be responsible for the mechanical property of the synthesized cocrystals. Analysis on the structural aspects of mechanical properties allows for the formulation of models for property engineering. Can it be possible to use these models for targeted property design, other than serendipitous results?

Crystal engineering is associated with three aspects, structure analysis, structure design and property engineering. Structure analysis is the first step in any crystal engineering exercise. It also explains the way by which the subject was started in the early days to correlate structure with property. This is the first phase or generation of crystal engineering. The second generation considers rational design of crystal structure which is facilitated by the concept of the supramolecular synthon. This phase has seen in the incorporation of different synthon based strategies to build a variety of supramolecular architectures. However, there is no prediction of a property which is the ultimate aim of crystal engineering. If one can achieve a desired property by predesign, then crystal engineering will see the final and higher stage which is termed *third generation crystal engineering* in chapter 5. The second part of the thesis discusses work is this direction, where mechanical properties are targeted and achieved by design using models from previous work.

Chapter 6 discusses the engineering of elastic crystals from initial brittle precursors. A capping based model is proposed and used to prepare systems that can adopt the desired structure type. Among many other requirements, the crystals need some structurally buffering regions to show elasticity. Type-II electrostatic halogen bonds are used to construct such buffering regions. When the crystals are obtained according to the model type, they show reversible elastic deformation. σ-Hole based halogen bonds are crucial to the synthesis. But, during the project some adverse effects were noticed/realized for the use of halogen bonds. This suggests the need for an alternative methodology.

A synthon that can mimic both the geometrical and chemical nature of σ-hole based halogen bonds would be useful to replace the earlier one. A search in this respect results in π-hole oriented orthogonal synthons based on $C{=}O\cdots C{=}O$ and $NO_2\cdots NO_2$ interactions. A stepwise replacement procedure is applied to see and carry forward structural modularity in the new systems. Cocrystal systems are chosen for easy replacement by changing the constituents. Halogen bonds in cocrystals of the first step are partially substituted by a π-hole mimicking synthon in the second step and completely substituted in the third step. All the structures in the different steps are found to retain the same property, namely elasticity, although they possess dissimilar synthons. These aspects are discussed in chapter 7.

Chapter 8 deals with the design of hand twistable helical crystals which are known to result during natural growth. Helical shape crystals are highly impactful for application in metamaterials and lithographic techniques, but at the same time occurrence of such morphology is unpredictable. Such shape generates from the periodic bending of crystals and thus needs multiple deformation directions. Here, a multistep crystal engineering procedure is adopted to get two directionally (2D) plastically bendable crystals, starting from one directional (1D) plastic crystals. Halogen bonds again play a major role in the design. The route follows the order 1D plastic crystals → 1D elastic crystals → 2D elastic crystals → 2D plastic crystals. These 2D plastic crystals are used to obtain hand-twisted helical crystals. Here, different properties namely elastic and plastic are seen in identically structured compounds. Once again, problems in using halogens are noticed.

To address the issue of halogens, chapter 9 uses halogen bond/hydrogen bond equivalence to replace halogen bonds by geometrically and chemically similar hydrogen bonds. However, the first designed molecule in this respect did not result in the desired structure. The obligations are removed by applying the molecular/supramolecular equivalence strategy on the earlier molecule. Such an attempt gives another completely hydrogen bonded system that can now adopt the model structure and show a similar 2D plasticity. Crystals of this compound are also hand twistable.

Third generation crystal engineering needs predesign models for targeted property engineering. In this context some differently structured elastic crystals are compared with common brittle crystals to identify and ascertain the structural requirements. This analysis helps in constructing different models for future engineering of elastic crystals. It also tabulates the structural and interaction differences in obtaining different mechanical properties namely shearing, plastic, elastic and brittle.

In summary, these two major aspects for doing crystal engineering are highlighted in my thesis. One is the identification of robust synthons and the other is the use of synthon based structure design for property engineering. The first part of the thesis discusses the IR spectroscopic method for identification of synthons and then uses the spectral information for crystal structure engineering. The second part is related to deliberate crystal property engineering and uses structure-property relationships from the previous chapters and the literature to formulate predesign models and strategy. Achieving crystal properties in this way is expected to initiate the fast progress of the third generation crystal engineering.