Chapter Three

Effects of C-H...O Hydrogen Bonding on O-H...O Hydrogen Bonded Networks: Some Anomalous Crystal Structures
3.1 Introduction

The ever-growing demand for the construction of supermolecules\textsuperscript{1} with high precision, that is with a control of secondary and tertiary structural features, has been largely unfulfilled, because such construction requires a subtle and simultaneous manipulation of strong and weak intermolecular interactions.\textsuperscript{2} This is quite a difficult task, at least at present, as our knowledge of weak intermolecular interactions has not yet reached a stage where they may be used reliably for molecular recognition.\textsuperscript{3}

In the preceding chapter we have seen how molecules organise themselves selectively using weak C-H...O hydrogen bonds. It is apparent from the earlier discussion that these weak interactions operate within the framework of strong hydrogen bonds.\textsuperscript{3,4} In other words, these interactions are formed in consonance with strong interactions and cannot compete with stronger hydrogen bonds in establishing stable crystal packings. But such an assumption need not always be valid. Sometimes, weak interactions can collectively dictate the details of supramolecular geometry and they may even determine the directional preferences of strong hydrogen bonds.

\begin{center}
\includegraphics[width=0.5\textwidth]{figure.png}
\end{center}

Extensive studies on conventional or strong O-H...O and N-H...O hydrogen bonds have led to the formulation of empirical rules concerning their preferential binding patterns for various functional groups.\textsuperscript{2,4} For example, aromatic carboxylic acids (e.g., benzoic or cinnamic acids) crystallise as centrosymmetric O-H...O mediated dimers, but a 1:1 mixed crystal if obtained
from a pair of acids, say A and B, with substituents of different electronegativities, contains only carboxy heterodimers AB.\textsuperscript{4a,5} Such heterodimers are stable because of the variation in the proton donating and accepting capabilities of the two acids, which leads to the two hydrogen bonds in the ring being of unequal strengths. Such a structural motif is supposed to be robust and not perturbed by other interactions since it is formed in accordance with the principle that the strongest proton donor hydrogen bonds with the strongest proton acceptor followed by a matching of the next strongest proton donor and acceptor.\textsuperscript{4–6}

Do all aromatic carboxylic acids form centrosymmetric dimers and do all such donor-acceptor acid complexes form heterodimers? In a study of several nitro and amino-substituted benzoic acids, 1a-1d, and cinnamic acids, 2a-2f, and their corresponding 1:1 complexes, 1-10, it was noted that two anomalous structures were formed. These are respectively 3,5-dinitrocinnamic acid, 2b, which forms a twofold axis related carboxyl dimer instead of the usual centrosymmetric dimer and the 1:1 complex, 9 (3,5-dinitrobenzoic acid, 1b : 4-N,N-dimethylaminobenzoic acid, 1c), where the structure is made up exclusively of homodimers AA and BB instead of AB heterodimers. Interestingly, a closely related complex of 9, that is complex 21, of 3,5-dinitrobenzoic acid, 1b and 4-aminobenzoic acid, 1d, forms a heterodimer and crystallises in a non-centrosymmetric space group.\textsuperscript{5} These observations suggest that a consummate understanding of all crystal packing
effects is required in the prediction of even strongly hydrogen bonded structures. In fact it was found that weak intermolecular interactions have to be considered in order to rationalise these unusual occurrences. The \( \pi...\pi \) and C-H...O\(^8\) interactions are the possible weak interactions that can perturb the strong hydrogen bonds in these two instances. Indeed, the three types of interactions, O-H...O, C-H...O and \( \pi...\pi \) require special attention in the area of molecular recognition because of their omnipresence in most organic and biological structures. Traditionally, these interactions have been studied independently and there are no collective studies of these interactions, in other words on how these three type of interactions co-adjust or coexist.\(^9\) The main objective in this chapter is to study the interplay between O-H...O, C-H...O and \( \pi...\pi \) interactions.

### 3.2 Results and Discussion

#### 3.2.1 Crystal Structure of Acid 2b: A Carboxyl Dimer with a Twofold Axis

Acid 2b crystallises as an O-H...O dimer wherein the hydrogen-bonded molecules are related not by the more common inversion center but by a twofold axis.\(^2\) A close look at the crystal structure of acid 2b reveals that this curious phenomenon occurs because of abundant C-H...O interactions which discriminate between energetically similar yet geometrically dissimilar O-H...O hydrogen bond patterns. The energy of the C-H...O interaction is just in the range where it can compete with conformational process in small molecules and with forces responsible for the tertiary structure in macromolecules.\(^10\)

The eight membered carboxyl dimer ring of 2b is reasonably planar, but because of the twofold symmetry, the 28° intramolecular twist between carboxy and aromatic groups leads to an inclination of 56° between the two
aromatic rings in the dimer. Figure 1 provides a rationale for this observation. There is an extensive C-H...O bond network, (C...O, C-H...O, 3.19Å, 123°; 3.45Å, 152°; 3.40Å, 143°; 3.58Å, 151°; 3.64Å, 126°; 3.69Å, 160°) confirmed by the ordered carboxy group (C-O, 1.308(6), 1.226(6)). Acid 2b is particularly well suited for the formation of these C-H...O bonds, because the alkenic H atoms of 2b are acidic when compared to aliphatic H atoms. Further the electron-withdrawing nature of the NO2 group and cooperative effects may respectively enhance the acidity of the C-H group and basicity of the NO2 group. So, C-H...O bonds dominate the structure and their directional requirements appear to be incompatible with an O-H...O inversion dimer. Simple calculations (MOPAC) show that there is an energy difference of ca. 0.55 Kcal/mol between the all-planar conformation (which might have led to an inversion dimer) and a more energetic twisted conformation observed here. The total energy of the C-H...O bonds should be at least equal to this difference. The planarity and conformational flexibility of 2b increases its C-H...O bond-forming ability in the crystal since rotations of the substituent groups to optimise C-H...O hydrogen bonds are facile.

In contrast to acid 2b, 2,4-dinitrocinamic acid, 2c, crystallises as a normal inversion-symmetry O-H...O dimer. The 2-NO2 group and the styryl moiety make an angle of 25° and 40° with the aromatic ring respectively. Here, the 2-NO2 group does not participate effectively in C-H...O hydrogen bonding. Perhaps the conformational inflexibility caused by steric hindrance of the -CH=CHCO2H group results in such an inability to form C-H...O hydrogen bonds. However, the overall C-H...O interactions in this acid are equally good as in acid 2b (3.26Å, 121°; 3.32Å, 129°; 3.43Å, 148°; 3.47Å, 136°; 3.47Å, 120°; 3.62Å, 158°; 3.62Å, 142°). These interactions suggest that the inherent intramolecular twist in acid 2c may be conducive to making good C-H...O interactions leading to centrosymmetric carboxy dimers in
**Figure 1.** Crystal Structure of acid 2b showing O-H...O and C-H...O hydrogen bonds. The reference molecule is shaded and is linked to its twofold axis related neighbours by O-H...O bonds and to its c-glide, inversion and other twofold related neighbours by C-H...O bonds.
its crystal structure (Figure 2). The molecular skeleton of acid 2c is rigid and any intramolecular rotation requires high energy. So it is beyond the scope of C-H...O hydrogen bonds to cause any further twist in the intramolecular geometry of acid 2c.

A more general CSD\textsuperscript{14} search has also been carried out to examine the frequency of occurrence of a twofold axis in neutral carboxylic acid crystal structures. It was found that of a total of 2057 carboxylic acids in the CSD, 54 acids crystallise as carboxyl dimers in the space group C2/c. The majority of these acids contain a molecular twofold axis and/or dicarboxylic functionality. Acid dimers are usually related either by inversion centres or by psuedo-inversion centres. Five acids (DASDIK, DTBUBZ, DUGKEV, FICJAC and FIPXIL) which crystallise in C2/c were identified as having a twofold axis bisecting the carboxylic dimer ring with a significant twist between carboxyl dimer and the molecular skeleton (as in the compound under study in this work). Interestingly, all these acids have either no possibility or little possibility of having C-H...O hydrogen bonds in their crystal structures. It appears that steric reasons are associated with these geom-
Figure 2. Stereoview of the crystal structure of acid 2c showing C-H...O bonds.
etries. All these results indicate that C-H...O hydrogen bonds may be the main cause for a twofold axis observed in the crystal structure of acid 2b.

As mentioned earlier, one of the NO₂ groups of the acid 2b is also involved in a C-H...O self-recognition motif in its acid complexes (see Chapter 2, Figure 4b). To further investigate the C-H...O bond forming ability of the 3,5-dinitrocinnamoyl skeleton, the crystal structure of the corresponding methyl ester, 22 has been determined. The crystal structure of 22 contains an inversion dimer that is stabilised by two types of bifurcated-acceptor C-H...O bonds, Figure 3; the carbonyl O atom interacts with two alkene H atoms (C...O, 3.28Å, 3.70Å, C-H...O 168°, 148°) while the NO₂ O atom, interacts with two CH₃ H atoms albeit weakly (C...O 3.25Å, C-H...O 117°, 96°). These dimer units in turn form C-H...O bonds with surrounding dimers through other lateral C-H...O interactions leading to a planar structure along [100]. The crystal structure of 22 is, in effect, two-dimensional compared to that of the parent acid 2b which is three-dimensional. The strength of the C-H...O bonded inversion dimer was approximated using AM1 molecular orbital calculations and found to be -8.20 Kcal/mole.

3.2.2 Crystal Structure of Complex 9: A Homodimer

The crystal structures of acid complexes 1-10, and 21, consist of acid dimers which are themselves stacked so as to optimise π...π donor-acceptor interactions (Figure 4). Therefore, two stacked heterodimers are related by an inversion centre (except in complex 21 which is non-centrosymmetric) while two stacked homodimers (complex 9) are not crystallographically related, the inversion centres being located at the middle of each homodimer. It is to be mentioned here that the crystal structure of complex 3 has not been solved and that complex 10 (a heterodimer) forms twinned crystals for
Figure 3. Crystal structure of ester 22 along [100] to show the planar structure.
Figure 4. Schematic diagram of carboxy hetero (left) and homo (right) dimers in the donor-acceptor complexes 1-8, 21 and 9 showing the directional nature of the three interactions types (O-H...O, C-H...O and π...π) which are important in these complexes. Each donor monomer is represented by a blank rectangle while each acceptor monomer is represented by a shaded rectangle.
Effects of C-H...O Hydrogen Bonding on O-H...O

which only an approximate structure is available.

Inspection of the carboxy dimer motif in these ten structures (1-10 and 21) shows that except complex 9, all the others contain the 'expected' heterodimer. The crystal stucture of 9, however, contains dinitrobenzoic and dimethylaminobenzoic homodimers (Figure 5). This is an unusual hydrogen bond pattern and the absence of such homodimers in other systems was verified with the CSD. A total of 32 acid mixed crystals was obtained from the CSD, but none contain homodimers. AM1 calculations performed by Dannenberg show that the heterodimers AB for any given (aromatic) acid pair A and B are stabler than the either of the homodimers AA or BB by around 1.0 Kcal/mol. These calculations were repeated on the acid pairs found in complexes 1-10 and very similar results were obtained. Even in complex 9, the AM1 heterodimer energy obtained was -7.02 Kcal/mol while the two homodimer energies were -6.27 Kcal/mol (dinitro) and -6.15 Kcal/mol (dimethylamino). Though AM1 methods do not consider electronic correlation effects and underestimate the hydrogen bond energy, their use in hydrogen bonded systems is well-documented and it is believed that the calculations permit a relative comparison of hydrogen bond energies. Therefore it may be concluded that the calculations of relative O-H...O bond energies are all reasonably accurate. Accordingly, the formation of homodimers in complex 9 is exceptional; the stabilisation of heterodimer over homodimer to the extent of ca. 1.0 Kcal/mol must be compensated by other (weaker) interactions in the crystal if the homodimer is even to be obtained.

Complex 9 is a good example of molecular recognition because from a mixture of heterodimers, homodimers and monomers in solution, the heterodimer:homodimer ratio being approximately 3:1 (assuming an energy difference of 0.8 Kcal/mole between hetero and homo dimers) only the minor component (homodimer) is obtained in the crystal. It is clear from the calculations and from structures 1-10 and 21 that the isolated heterodimer
Figure 5 O-H...O dimers in donor-acceptor complexes 1-9 and 21. Note that only complex 9 has homodimers 1b - 1b, 1c - 1c in the crystal structure, but that all the others form the more common hetero dimer. O-H...O bonds are shown as dashed line.
is stabler than the isolated homodimers. The occurrence of only homodimers in the crystal of \textit{9}, obtained by either recrystallisation or grinding is therefore indicative of the importance of other factors.

Three weaker forces, van der Waals, C-H...O and \pi...\pi interactions, were identified as possible perturbing factors which cause the tilt towards homodimer formation in \textit{9}. It has been held by Hunter and Sanders\textsuperscript{7a} that van der Waals or isotropic forces cannot in themselves determine the crystal packing of donor-acceptor complexes.\textsuperscript{19} This is so because these forces are proportional to the extent of overlap between two stacked molecules. These ideas have already been detailed in Chapter 1. If these forces were structure-determining, the overlap between stacked molecules would be maximised. This is never so, because \pi...\pi repulsions dominate at large overlaps. Thus, van der Waals forces are important only within the framework of the more electrostatic \pi...\pi interactions. Therefore attention was shifted to C-H...O and \pi...\pi interactions in complexes 1-10. The C-H...O bonds in complexes 1-8 have been mentioned earlier in Sections 2.2.1 and 2.2.2. Complex 21 was found not to contain any characteristic C-H...O bonds because the NO\textsubscript{2} group of 1\textit{b} is involved, not surprisingly, in strong N-H...O hydrogen bonds with NH\textsubscript{2} group of 1\textit{d}. The C-H...O bonds in complex \textit{9} are discussed here in some detail.

\subsection*{3.2.2.1 C-H...O Hydrogen Bonds in Complex 9}

Unlike complexes 1-8 which display rich and distinctive C-H...O patterns, complex 9 contains only a few C-H...O bonds and that too of marginal significance. Figure 6 is a plot of C-H...O angle versus the H...O distance for all C-H...O bonds in structures 1-9 and 21. In these plots, normalised H atom positions are used with the C-H distance taken to be 1.08Å. C-H...O bonds in complex 9 are shown as darkened circles. It is very clear from the plot that the C-H...O bonds in 9 are neither the shortest nor the most linear
Figure 6. Scatter plot of H...O distance (normalised to 1.08Å) versus C-H...O angle for all C-H...O bonds in complexes 1-9 and 21. Bonds in complex 9 are shown as dashed circles. It is clear from the figure that C-H...O bonds in complex 9 are weak either with our prescription (solid line) or with Saenger's\textsuperscript{9t} (broken line). Note that excepting 9, all other complexes have contributors in the strong bonds region.
in the group. The solid line in the plot appears to be a natural separation between regions containing strong and weak C-H...O bonds. The dashed line is drawn according to the prescription of Steiner and Saenger and makes allowance for elliptically-shaped H atoms. Whatever the type of demarcation, C-H...O contacts in complex 9 are feeble and unlike in 1-8, probably do not play a key role in the stabilisation of the structure. Could this observation correlate with the presence of homodimers in 9 and heterodimers in 1-8?

Inspection of the molecular formulae of 1b and 1c suggests further probable reasons for the lack of C-H...O bonds in 9. While 1b has three acidic C-H protons, they are sterically inaccessible to O atoms. The only C-H...O pattern possible is the NO2-N(CH3)2 recognition motif (Chapter 2, Figure 4a) which makes weak bonds of 3.59, 3.41, 3.71 and 3.68Å. Therefore H4 of acid 1b which is the most acidic H atom in the system is blocked. Atoms H2 and H6 of acid 1b are also blocked by the flanking substituents. Most critically, the absence of styryl H atoms which are invariably involved in C-H...O bonding in a large number of α,β-unsaturated carbonyl and nitro compounds (Chapter 2, Figures 4b, 4c), means that there is just not enough C-H...O bond forming propensity here. In turn, it may be stated that the presence of such styryl H atoms as in acids 2a-2f leads to distinctively favourable C-H...O bonding which causes layering or sheet-formation of molecules. This is depicted schematically in Figure 4. The structures of complexes 1-8 (especially cinnamic acid-containing complexes 4-8) may be understood as being formed by a stacking of layers which are themselves composed of C-H...O networked O-H...O heterodimers. Conversely, complex 9, which has only weak C-H...O bonds, has no layer structure. Figure 7 shows columns of stacked molecules which are inclined to one another at an angle of 23° to optimise a few weak C-H...O bonds and close-packing aromatic...aromatic herringbone interactions. Thus, it is believed that it is
Figure 7. Stereoview of the crystal structure of complex 9. It can be seen that the adjacent stacked columns of 1b and 1c make an angle of 23° indicating the stabilisation of stacks by herringbone interactions.
the lack of C-H...O bond forming ability in complex 9 which causes it to adopt the anomalous homodimer structure. This absence of C-H...O bonds compels one to consider the third variety of weak interactions in these structures, namely π...π stacking.

3.2.2.2 II...II Stacking in Complex 9 and Elsewhere

Now let us consider the π...π stacking interactions in the donor-acceptor complexes 1-9 and 21 and their possible role in stabilising the homodimer structure in 9 is considered. Hunter and Sanders have shown that the nature of these interactions is dependent on the intermolecular contacts between the relevant atoms rather than on the overall redox properties of the molecules. An attempt is made here to analyse the π...π interactions according to this concept.

The electronic properties of atoms in carboxy homo- and heterodimers in complexes 1-9 and 21 are conveniently differentiated because the substituents on the aromatic rings are either powerful electron donors or acceptors. Let us consider complex 9. The atoms in the aromatic ring and carboxyl group in the isolated 1b molecule possess a partial (+) charge and correspondingly in 1c, a partial (-) charge, because of the presence of -NO₂.
and -N(CH₃)₂ groups respectively. If acids 1b and 1c were to form a heterodimer, there would be a flow of charge from 1c to 1b through the dimer ring as shown in Scheme I via resonance assisted hydrogen bonding.²² As a result, the (+) and (-) charges in the aromatic rings of 1b and 1c will be diminished in the heterodimer as compared to the isolated monomers.

If, however, 1b and 1c were to form homodimers instead, as observed in reality, the (+) and (-) charges on the rings are enhanced. In other words, homodimer formation leads to a greater polarisation or charge separation in 1b and 1c molecules when compared to the isolated monomers. The AM1 charges obtained for homo- and heterodimers of 1b and 1c corroborate this statement but the magnitudes of all the charges are very small and the differences in charges for corresponding atoms between homo and heterodimers is less than 0.02 e. However, the direction of change in charge is always so as to support the hypothesis above. More satisfactory evidence for this hypothesis is obtained from the O-H...O bond lengths in homodimers and heterodimers of some of the acids in the study (Table 1). The crystal structure of the pure acid is a model for the homodimer to compare their carboxyl O...O distances with the corresponding heterodimers, when no homodimers are obtained in the acid complexes. Except acids 1b and 1c, all other acids form heterodimers. Table 1 shows that both the O...O distances in a heterodimer are always less than the O...O distance in either of the two corresponding homodimers. These figures argue convincingly for a net flow of charge across the hydrogen-bonded ring in heterodimers and conversely, for an accentuation of charge in a homodimer.
Table 1

O...O distances (Å) in the hydrogen-bonded rings in some of the pure acids and complexes in this study.

<table>
<thead>
<tr>
<th>Compound</th>
<th>Pure</th>
<th>Complex&lt;sup&gt;a&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>1a</td>
<td>2.660</td>
<td>2.632 (1)</td>
</tr>
<tr>
<td>1b</td>
<td>2.636</td>
<td>2.655 (9)&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>1c</td>
<td>2.627</td>
<td>2.625 (9)&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>1d</td>
<td>2.642</td>
<td>2.616 (21)</td>
</tr>
<tr>
<td>2b</td>
<td>2.661</td>
<td>2.628 (4)</td>
</tr>
<tr>
<td>2c</td>
<td>2.657</td>
<td>2.632 (7)</td>
</tr>
<tr>
<td>2f</td>
<td>2.632</td>
<td>2.619 (7)</td>
</tr>
</tbody>
</table>

<sup>a</sup>Except 9 all the complexes are heterodimers and have O...O distances less than those found in pure acids. <sup>b</sup> Homodimers.

According to this argument, the polarisation of C and O atoms in the 1b...1b and 1c...1c homodimers will be greater than in the 1b...1c heterodimer. So, if one considers stacking interactions, these should be more favourable for homodimers than for heterodimers (Figure 8). It is possible to verify the approximate strengths of these π...π interactions in complexes 1-9 and 21 by examining the donor-acceptor aryl...aryl stacking distances.

Scheme II

There are many possible modes of aryl...aryl stacking (See, Sections 1.2.1 and 1.2.3). For example, the two aryl rings can interact each other with var-
Figure 8. Stereoview of stacked homodimers of 1b and 1c in complex 9. For clarity, homodimer 1c is shaded. Interestingly these homodimers stack with the shortest aryl-aryl and carboxy-carboxy distances among all the complexes in this study.
ious offsets and perpendicular interplanar distances and simultaneously may have different orientation angles ranging from 0 to 30° (Scheme II). Indeed, it is not possible to represent stacking interactions of aryl-aryl rings based on interplanar distance alone because aromatic rings with a short interplanar distance may well be separated with large offsets, in which case the overlapping between the rings would be almost negligible (Scheme II, c). In other cases, when the phenyl rings are non-parallel it is not possible to define the interplanar distance uniquely (Scheme II, b). Further, as the interplanar angle increases, the stacking interaction would be reduced and edge-face or herringbone interactions start operating. So in order to evaluate stacking interactions properly, one should consider all these possibilities. Probably the most complete way of representing stacking interactions is to consider both centroid-to-centroid \( (X_1...X_2) \) and mean-interplanar stacking distance, that is \( (d_1+d_2)/2 \). So an ideal stacking interaction (or overlapping) will have small centroid-to-centroid and mean-interplanar distances and any deviation from such an ideal position may be indicative of poorer stacking interactions.

Figure 9 is a scatterplot of centroid-to-centroid versus average perpendicular interplanar distances for the stacked aromatic rings in these complexes. It is clear from this figure that complex 9 is a striking outlier. The short interplanar and centroid-to-centroid distances in complex 9 (C...O, 3.38, 3.22, 3.41Å; C...C 3.38, 3.35, 3.40, 3.41, 3.42Å) are not found in any of the heterodimer structures 1-8 and 21 and show that the overlap of aromatic rings in 9 is very effective. Further, there is a significant overlap of the carboxyl hydrogen bonded rings (Figure 8), a structural feature which is absent in all the heterodimer structures studied here and one which argues convincingly in favour of enhanced atomic charges throughout the homodimer framework. So it may be assumed that the combined aromatic and carboxyl \( \pi...\pi \) /electrostatic interactions obtained via overlap, are a critical
**Figure 9.** A graph between donor-acceptor aryl-aryl interplanar distances versus centroid-to-centroid distances. Complex 9 which forms homodimers is an outlier with a short interplanar distance. Note that complexes 4 and 21 with moderately short stacking distances do not have a good overlap between carboxy hetero dimers.
source of stabilisation of the homodimer structure in complex 9 and that they are more than sufficient to compensate for the lack of O-H...O heterodimer stabilisation (ca. 0.80 Kcal/mol) and for the unsatisfactory C-H...O situation.

3.2.2.3 A Possible Sequence for Crystallisation of Complex 9

In MeOH solution, component acid molecules are likely to exist as hydrogen bonded solvated monomers, heterodimers and homodimers. If it is assumed that in all cases the energy difference between heterodimers and homodimers in solution is around 0.80 Kcal/mol, it means that the heterodimer : homodimer ratio in solution is around 3:1. Indeed the energy difference between homodimer and heterodimer may be more than 0.8 Kcal in solution, as this energy difference more appropriately corresponds to gas phase carboxyl dimers. In solution, polarisation by the solvent may further enhance the energy gap between homodimers and heterodimers. Either type of dimer can form crystal nuclei by aggregation with other dimers laterally or along a stack. It is suggested that in the majority of cases 1-8, crystal nuclei develop by a lateral organisation of O-H...O dimers via C-H...O bonding, the interaction of next importance (Figure 4). These lateral interactions are equally easy for hetero- and homodimers because of the presence of favourable features in the molecular structures of the monomers (styrenic H atoms). Accordingly, the more abundant heterodimers form crystal nuclei easier. These nuclei must also involve stacked molecules but the exact nature of this stacking is probably not critical, the growing nuclei already having obtained adequate stability from the O-H...O (hetero) and C-H...O interactions.

In the case of complex 9, however, neither homodimers nor heterodimers can nucleate properly via lateral C-H...O bonds. Therefore both these types of dimers aggregate primarily via stacking interactions. In this event, the
homodimers are distinctly favoured as detailed above. Growing homodimer stacks are formed in spite of an unfavourable heterodimer : homodimer ratio in solution and they aggregate via weak van der Waals forces to achieve close packing (Figure 7). The exclusive formation of the homodimer structure of 9 indicates that the stabilisation gained from $\pi...\pi$ interactions more than offsets the loss in O-H...O stability in avoiding the heterodimer alternative.

As crystallisation progresses, the heterodimer $\rightleftharpoons$ homodimer equilibrium in solution shifts towards homodimer. It is remarkable that very slight energetic preferences dictate an almost completely unequivocal crystallisation pathway. This, in general, has been observed by others and augurs well for future experiments in molecular recognition and crystal engineering.

3.3 Conclusions

C-H...O hydrogen bonds are the reason underlying the two anomalous crystal structures discussed in this Chapter. The presence of a carboxyl dimer bisected by the uncommon twofold axis in the crystal structure of acid 2b is a result of a surfeit C-H...O hydrogen bonds, whilst the unusual carboxyl homodimers obtained in the crystal structure of complex 9 are a result of poor C-H...O hydrogen bonding. These examples indicate that weak C-H...O hydrogen bonds can dictate molecular geometry in certain favourable circumstances. More interestingly, a homodimer complex 9 is a good case study to examine stacking interactions \textit{vis-a-vis} weak and strong hydrogen bonding. These interactions which are sometimes in competition and sometimes in consonance are of great importance in biological molecules where the nature of the stacking may dictate the type of hydrogen bonding (Watson-Crick and Hoogsteen). The interplay between these two types of interactions has also been studied in the binding of Kemp’s acid derivations with adenines.\textsuperscript{23} However, these studies are involved with changes in the exposed surface area between stacked molecules whereas the present example
considers mainly changes in the atomic charges in stacked molecules brought about by different kinds of hydrogen bonding. The assumption of charge transfer through hydrogen bonding involves a new perception in studies of hydrogen bonding and π...π interactions.

The analysis of complexes 1-10 in this study addresses the following three points which are of current interest: (i) Weak C-H...O hydrogen bonds can control the crystal packing even in strongly hydrogen bonded compounds. (ii) O-H...O hydrogen bonds can act as channels for charge transfer and alter the polarisation of atoms. (iii) Hydrogen bonding interactions influence the nature of stacking interaction and vice versa.

The anomalous structures of acid 2b and complex 9 shows that a strong interaction alone need not always dictate the crystal geometry if other weaker interactions are of special significance. These results caution one to keep track of weak interactions while designing novel structures of new materials and suggests that without a proper appreciation of both strong and weak interactions, the prediction and design of crystal structures may often turn out to be an elusive objective.
3.4 Experimental Section

3.4.1 Synthesis

The preparation of acids 1b and 1c has been described in Section 2.4.1, while *trans*-3,5-dinitromethylcinnamate, 22 (m.p. 160°C) was prepared by reacting 3,5-dinitrocinamic acid with diazomethane in dry ether at 0°C. 

NMR, (CDCl₃), δ 9.1 (m, 1H), δ 8.7 (m, 2H), δ 7.8 (d, 1H), δ 6.7 (d, 1H), δ 3.8 (s, 3H). Crystallisation of all the acid complexes has been discussed in Chapter 2. Complex 21 has been described elsewhere.

3.4.2 X-Ray Crystallographic Studies

Crystal data for acids 1b and 1c was collected by Prof. W.T. Robinson, University of Canterbury, New Zealand and the structure was determined using SHELXTL. Crystal data for ester 22 was collected by Dr. T. Pilati, University of Milano, Italy. The crystal structure solution of 22 was carried out in this study with the program SHELX86 and the refinements were carried out with the program SHELXL93. All non-H atoms were refined anisotropically and the final R-factors and other crystallographic information of acids 1b, 1c and ester 22 are presented in Appendix B-1. Tables of coordinates and thermal vibrational parameters are given in Appendix B-2.

3.4.3 CSD Study

All the carboxylic acids were retrieved from the CSD (Version 5.07) using the 3D graphics option. Screens -28, -55, 153 and 85 were set to eliminate metal containing and charged organic compounds, structures without coordinates or unmatched chemical and crystallographic connectivities. A distance of 3.20Å was specified for O...O atoms between carboxyl groups for obtaining hydrogen bonded carboxylic dimers. Further, acids crystallising the space group C2/c were retrieved and closely inspected.
References
   (b) M.C. Etter and D.A. Adsmond, *J.Chem.Soc., Chem.Commun.*, 1990,
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589.


9. Strong hydrogen bonding and stacking have previously been considered jointly (reference 23) but it is believed that the present work is the first where both strong and weak hydrogen bonds are considered along with stacking interactions. In any case these previous studies dealt with phenomena in solution.


19. However, van der Waals forces can distort N-H...O hydrogen bond pattern in other cases as is seen in the unusual crystal structure of adipamide., A.T. Hagler, L. Leiserowitz, J.Am.Chem.Soc., 1978, 100, 5879.
20. Further evidence for the weakness of the C-H...O bonds in complex 9 is provided by the disordered carboxyl group in acid 1b. Complexes 1-8 however contain ordered carboxyl groups.