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ARTICLE

Relationships between the racemic structures of substituted mandelic acids containing 8- and 10-membered hydrogen bonded dimer rings.

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The structures of 27 monosubstituted mandelic acids, including several of their polymorphs, plus unsubstituted mandelic acid itself (two polymorphs) are investigated for structural similarity. The results, presented pictorially as a structural relationship plot, show that rather more structures are built up from the carboxyl-chain hydroxyl hydrogen bonded dimer than from the conventional carboxylic acid dimer. The results show how all the structures are related and, based on the two types of dimer, the degree of similarity that they possess. Some structures with $Z' > 1$ contain both sorts of dimers and there are many examples of isostructural sets within the structures so far determined. We also present an example where analysing similarity in related families of structures highlights a structure that should be present and which has indeed then proceeded to be synthesised and determined.

Introduction

For several years we have been making detailed comparisons of the crystal structures of large sets of related compounds, in an attempt to understand the factors determining the adoption of particular packing motifs^{1,2}. In all these projects, the XPac program³ was used to identify structural similarity in 0, 1, 2 and 3 dimensions as a preliminary to the detailed pairwise comparison of the structures so identified.

This paper presents some results that form part of a larger project intended to explore quasiracemate formation frequency and structure, diastereoisomer resolvability and structure and the relationship between racemate and enantiomer structure. As a first stage we have obtained the crystal structures of 19 previously undetermined monosubstituted racemic mandelic acids and additionally several polymorphs and some enantiomeric mandelic acids, but only the racemic acids and their polymorphs are discussed here. Furthermore the few structures not built up from hydrogen-bonded dimers have been excluded. The substituents chosen were fluoro, chloro, bromo, iodo, trifluoromethyl, methoxyl and methyl and these have been located in the ortho, meta and para positions. These substituents have been used in previous crystal structure comparisons^{4,5} of structures from large sets of related molecules and are chosen to probe structural similarity for a number of reasons. Firstly, they lack strong hydrogen bond donating features, so avoiding interference with the patterns dominated by the hydroxyl and carboxyl groups of mandelic acids, which would complicate or obscure comparison and interpretation. Secondly, they are sterically undemanding, which further minimizes complications in analyzing resulting packing arrangements. For this reason also, the attention of the study has been restricted to

monosubstitution in order to avoid expanding the number and complexity of comparisons unduly.

Of the 21 possible monosubstituted racemic mandelic acids outlined above, two methoxyl structures have proved elusive, five (excluding polymorphs) are already described in the literature (vide infra) and one has only formed a conglomerate to date and hence is not relevant to the subject of this paper (vide infra). We have succeeded in determining the structures of the remaining examples and in addition, several polymorphs. Larsen and Marthi⁶ described the structures of both the racemic and the enantiomeric fluoro-substituted mandelic acids, and hinted at the existence of polymorphs which they were not able to crystallise in a form suitable for crystal structure analysis. 2-chloromandelic acid has been the subject of much recent process and crystallisation research^{7,8} due to its role as an intermediate in clopidogrel synthesis. Consequently its crystal forms and their relationships have also been much investigated⁹. The structures of 2 polymorphic forms of the racemic and one structure of the enantiomer have been determined^{7,8,9}. Depending on the crystallisation conditions, it is possible to obtain racemic 2-chloromandelic acid as either a conglomerate or a racemic compound. The relationship between the two forms has been extensively investigated^{8,9}, because this might determine the ease of resolution. Polymorphism has also been noted for both the racemate and enantiomer of 3-chloromandelic acid¹⁰. In attempting to repeat the work of Larsen and Marti we observed several polymorphic forms and succeeded in obtaining the crystal structure of a polymorph of their racemic 4-fluoromandelic acid. We have also obtained the crystal structures of the methyl- and trifluoromethyl-mandelic acids which have not been reported previously and include in our comparisons the few structures of

substituted mandelic acids, and Polymorphs 1¹¹ and 2¹² of mandelic acid itself, that are already in the literature^{6,8}.

For the sake of clarity, the present paper is confined to those structures derived from 8 and 10 membered ring dimers i.e. with graph set descriptors of R₂²(8) and R₂²(10) respectively. These constitute the majority of structures so far encountered and so form a relatively homogenous group linked by numerous 0, 1, 2 and 3-dimensional relationships revealed by the XPac program⁴ for structural similarity. It is also confined to the polymorphs so far encountered during the attempts to obtain suitable crystals for single crystal diffraction experiments.

Experimental

The mandelic acids were synthesized from benzaldehydes either via the cyanohydrin¹³ route or the Merz two-phase dichlorocarbene route¹⁴. We were unable to obtain anything other than benzoic acids by Compere's one-phase dichlorocarbene route¹⁵, although others appear to have done so^{16,17}. The yields were incredibly variable, for example 6% for 2-bromomandelic acid and 60% for 3-iodomandelic acid, but sufficient material was obtained in all cases for the present purpose of obtaining a crystal structure. Larger quantities will be needed for the chiral separations, so several sets of Design of Experiment¹⁸ runs were undertaken on 4-chloro-, 4-bromo- and 4-methyl-mandelic acid preparations to try to optimize the yields. The yields were erratic and the results inconclusive for both routes: lithium ions, the key to Compere's synthesis, appeared ineffective in improving the yields by the Merz route. A modification of Jenkins' procedure¹⁹ for the cyanohydrin route without sodium bisulfate but with phase transfer catalyst was generally the most successful.

GENERAL DESCRIPTION OF THE DICHLOROCARBENE ROUTE, AS USED FOR 2-METHYL: A mixture of chloroform (8ml), 2-methylbenzaldehyde (5.8ml = 1/20mol) and benzyltriethylammonium chloride (1.14g) was stirred vigorously with a magnetic stirrer and heated to 60°. Sodium hydroxide (10g in 10ml water) was added dropwise over 2.5hrs. Maintenance of the temperature below 60°C is critical. Distilled water (30 ml) was added to the orange-brown solution to dissolve any solids, and the solution was extracted with 2x30 ml ether. The aqueous layer was acidified with concentrated HCl, and extracted 2x30 ml ether. The orange extract was dried over sodium sulfate and the resulting oil crystallised from toluene. Yield 5.15g = 62%. 3-methyl-, 3-trifluoromethyl-, 4-bromo- and 4-chloromandelic acid were prepared according to this approach.

GENERAL DESCRIPTION OF THE CYANOHYDRIN ROUTE, AS USED FOR 3-BROMO: Sodium cyanide (1.5g), and 3-bromobenzaldehyde (4.6g = 1/40mol) and benzyltrimethylammonium chloride (10mg) were stirred and cooled in ice-water. A homogeneous mixture of concentrated HCl (5ml) and ether (4ml) was added dropwise over 1hr so as to maintain the temperature always below 10°C. The mixture darkened to deep orange during the addition, but eventually became pale yellow. 20 ml concentrated HCl was added and stood overnight, then heated to 70°C for 1 hr. The mixture was extracted 2x10ml ether. The ether layer was basified and extracted 2x10ml ether. The aqueous layer was acidified and extracted 3x10 ml ether. The ether extracts were dried with sodium sulfate, filtered and evaporated to dryness to give 12.3g of product, mostly inorganic salts. This was recrystallized from

dichloromethane to give 2.0g 3-bromomandelic acid (35% yield). 2-, 3- and 4-fluoro, 2-, 3- and 4-chloro, 2- and 4-bromo, 2-,3- and 4-methyl, 2- and 3-trifluoromethyl, 2-, 3- and 4-methoxy and 3-iodomandelic acid were all prepared in a similar fashion.

Commercial samples of 2-chloro-, 3-chloro-, 4-methoxy- and 4-trifluoromethylmandelic acid were also used, while 2-iodo and 4-iodo-, 3-chloro, 3-bromo- and 3-methylmandelic acid were a gift from Jan von Langermann of the Max Planck Institute, Magdeburg.

The mandelic acids do not crystallise so well as, for example, substituted sulphonamides^{1,2} or acetanilides²⁰. Hydroxylic solvents, especially ethanol, generally so useful for growing large crystals, are particularly poor in the case of all the mandelic acids tried in providing material for single crystal studies. Ether, dichloromethane, chloroform, acetonitrile, toluene and nitromethane were amongst the most successful solvents.

Single crystal experiments have been routinely performed according to previously published procedures²¹ with details of data collection and refinement parameters for all structures summarised in the Electronic Supporting Information. It is not the aim of this paper to discuss the individual structures and therefore experimental details in the form of a summary table of data collection and refinement parameters is provided for reference (Table S1). All structures compared in this study are presented in Table S1, however only pertinent crystal data (such as unit cell dimensions and space group) are given for those previously reported. CIF files are available as Electronic Supporting Information and have also been deposited with the Cambridge Crystallographic Data Centre (CCDC1007650 - CCDC1007667 inclusive and CCDC1008570).

Discussion

The monosubstituted racemic mandelic acids with fluoro, chloro, bromo, iodo, trifluoromethyl, methyl and methoxyl substituents at the ortho, meta and para positions, as shown in Figure 1, are presented (note we have not managed to determine the structures of 2- and 3-methoxyl). Only seven structures are already described in the literature (we do not include binary or higher component systems such as salts, solvates or co-crystals), which comprise 2, 3, and 4-fluoromandelic acids⁶, two polymorphs of 2-chloromandelic acid²² and two polymorphs of 3-chloromandelic acid²³. However, the substituted mandelic acids are polymorphically prolific, thus adding more comparable structures and with the further inclusion of unsubstituted mandelic acid (2 polymorphs), 27 structures have been compared.

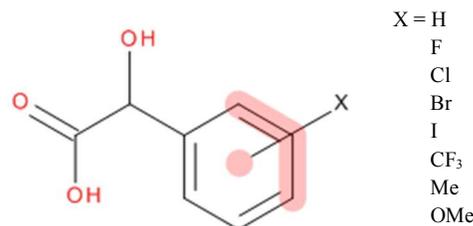


Figure 1. The mandelic acid substitution pattern employed in this study

The nomenclature system used in this study is one of RX-n, where R is the substitution position, X is the substituent and n can denote a polymorphic form.

The XPac program³ allows the level of similarity between different crystal structures to be evaluated. Sets of vectors between the component atoms of an arbitrary 'seed' molecule and the equivalent atoms of the neighbouring molecules within each structure are generated and compared across different structures. The comparison identifies common packing motifs or supramolecular constructs between the structures. These supramolecular constructs are characterised as 0-dimensional, 0D i.e. discrete molecular arrangements such as dimers, trimers, etc; 1D chains or stacks; 2D sheets or planes; 3D frameworks and fully isostructural systems. Figure 2 summarises the supramolecular constructs and relationships arising from a pairwise comparison between all the crystal structures studied in this investigation.

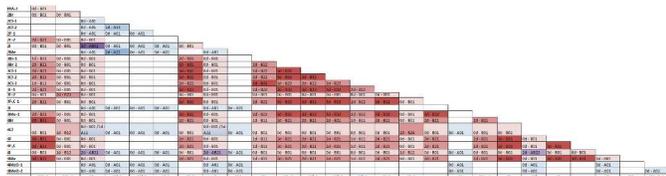


Figure 2. Common supramolecular constructs exhibited by the structures in this study.

All relationships can be considered as having the lowest common dimensionality of either 0D 8- or 0D 10- membered hydrogen bonded dimer rings and these have been denoted A- and B-type respectively (Figure 3).

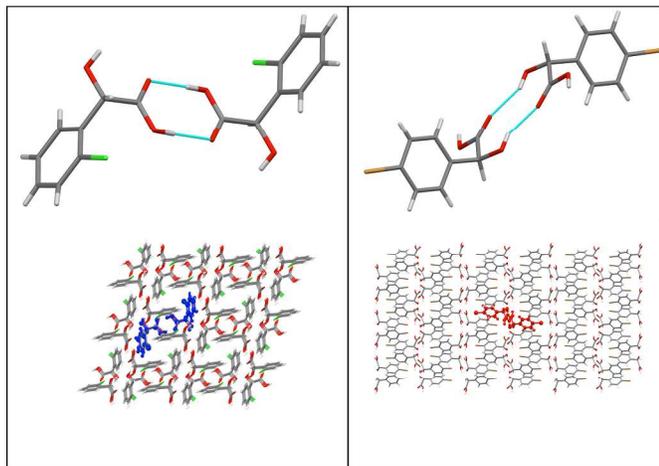


Figure 3. A-type and B-type hydrogen-bonded dimers considered as the 0D supramolecular constructs with the top diagram illustrating the construct and the lower one an example of that construct as exhibited in the 2Cl-1 and 4Br structures respectively (both viewed down the b axis).

In Figure 2, A-type supramolecular constructs are shaded in blue, whilst B-type are coloured red and the darkening of the shade of these colours represents an increase in dimensionality of similarity. Empty cells in the grid indicate there is no similarity found between a pair of structures and the purple cells indicate a combination of A- and B-type dimers being simultaneously present. Whilst figure 2 gives a good idea of the number and distribution of supramolecular constructs, it is difficult to establish the relationship between them for sets of

structures and therefore a structural relationship plot representation is given below.

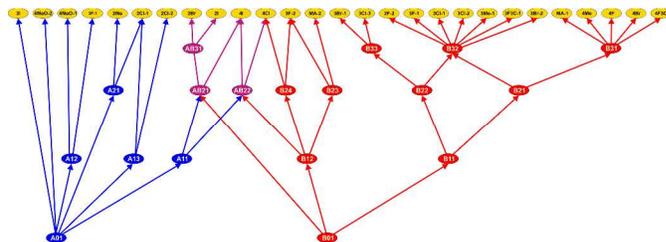


Figure 4. Structural relationship plot showing relationship between supramolecular constructs exhibited by our family of structures.

As one moves up from the bottom of the structural relationship plot in Figure 4 from the 'root' A- and B-type dimers, the degree of dimensionality increases at each level. Beginning with the 0D dimers, denoted A/B01, one moves up, through 1D and 2D to 3D, where the common supramolecular constructs are denoted A/B1*, A/B2* and A/B3* respectively. From the figure it can be seen that there are five 1D constructs, seven 2D constructs and four 3D constructs. 3D constructs are indicative of isostructurality and in this study the following isostructural groups are observed: AB31 = 2-bromo & 2-iodo; B31 = Mandelic acid (polymorph 1), 4-methyl, 4-fluoro, 4-bromo & 4-trifluoromethyl; B32 = 2-fluoro (polymorph 2), 3-fluoro (polymorph 1), 3-chloro (polymorph 1); 3-chloro (polymorph 2), 3-methyl & 3-trifluoromethyl; B33 = 3-bromo & 3-chloro (polymorph 3). Additionally, of particular note, are three sets of relationships that are labelled AB constructs where a combination of A- and B-type assemblies are observed.

A-type constructs based on 8-membered H-bonded rings

The structural relationship plot indicates that in our family of structures there are three relationships that are 1D constructs and a single 2D construct that are solely based on the A-type dimer and these are depicted in Figures 5 and 6 respectively. There are however two structures, 3-iodo and 4-methoxyl, that do not have any higher dimensional relationships and are based purely on the dimer arrangement.

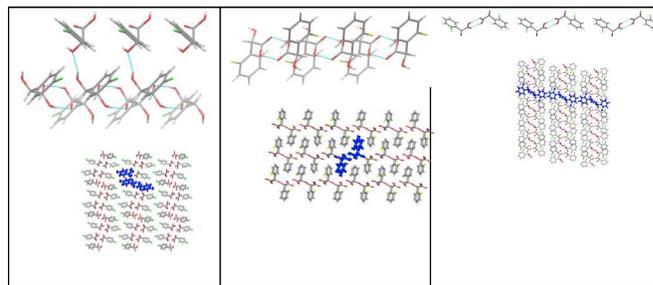


Figure 5. A-type 1D supramolecular constructs (A11, A12 & A13 respectively). The top diagrams illustrate the construct and the lower ones an example of that construct as exhibited in the 4Cl, 2F-1 and 2Cl-2 structures respectively (viewed down the a, b and b axes respectively).

It can be seen from Figure 5 that the A11 and A12 supramolecular constructs are two different kinds of stacks of the dimer motif, whilst A13 is a 'head-to-tail' chain arrangement. A11 is exhibited by 4 structures and is an

interesting case in that it is combined with B-type dimers to generate the hybrid 2D and 3D AB-type motifs and these cases will be discussed later (vide infra). A12 is exhibited by a second polymorph of 4-methoxy and has the same 1D arrangement as the 2-fluoro structure. A13 is a supramolecular construct of particular note in that it is particular to the 2-chloro structures but the 1D chain packs in two distinctly different ways to form two polymorphs and this feature is shown in the constructs highlighted in the two structures shown in Figure 6 (it should be noted that these are not the only occurrences of this construct in these structures, but the highlighted ones are the occurrences with matching orientations).

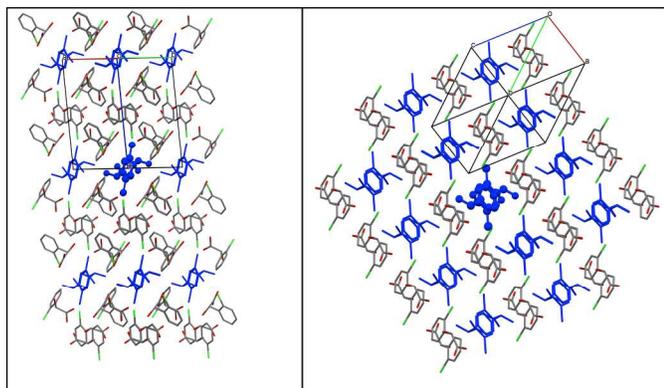


Figure 6. The two different packing environments for the 1D motif exhibited in the 2-chloro structures in the A13 construct.

In addition to the A13 chains, the 2-chloro Polymorph 1 structure also exhibits the A21 construct (Figure 7) and this 2D motif is also exhibited by the 2-methyl structure.

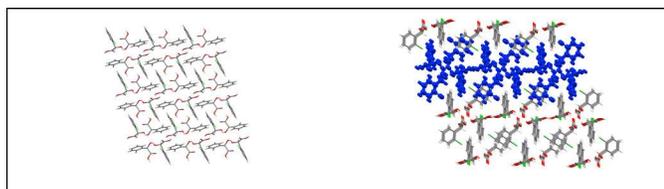


Figure 7. The A21 supramolecular construct. The left diagram illustrates the construct and the right one an example of that construct as exhibited in the 2Cl-1 structure viewed down the b axis.

B-type constructs based on 10-membered H-bonded rings

The B-type dimer construct is more prevalent than the A-type, which might be considered as contrary to the observation that the carboxylic acid dimer is probably the most common synthon in supramolecular chemistry²⁴ however this could be attributed to a greater degree of flexibility in the 10-membered ring, which enables the structure to make a strong structure directing contact and also simultaneously accommodate and/or optimise other packing requirements. There are two 1D relationships (B11 & B12) which each form the basis for further 2D relationships - B21 & B22 for the former and B23 & B24, and including some additional 2D similarities of a hybrid AB nature, for the latter.

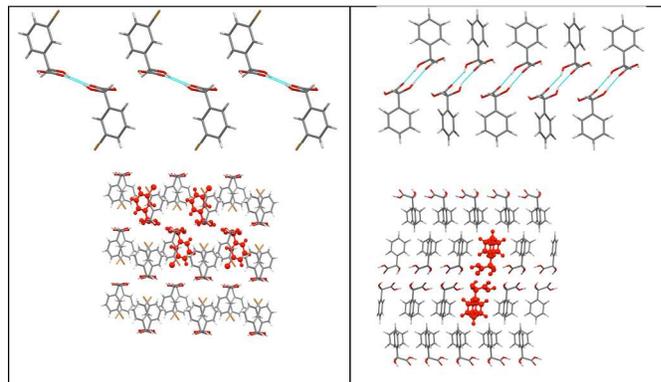


Figure 8. The B-type 1D supramolecular constructs (B11 & B12 respectively). The top diagrams illustrate the construct and the lower ones an example of that construct as exhibited in the 3Br-1 and MA-2 structures respectively (viewed down the b and a/c axes respectively).

The two 1D relationships, B11 and B12, are shown in Figure 8. B11 and B12 are composed of stacks of the dimer unit whereby aromatic rings lie orthogonal to the plane of the H-bonded 10-membered ring. The difference between these relationships arises from the spacing of the component molecules, B12 comprises close-packed constituents, whereas the component molecules in B11 are spaced so that other instances of the B11 stack partially interleaf in the structures in which it is present. The 2D relationships based on the B-type dimer can be divided into two groups – those arising from the B11 and the B12 1D constructs. Figure 9 illustrates B21 and B22 which are both sheets derived from the B11 motif. B21 is formed from B11 stacks hydrogen-bonding to oppositely aligned neighbouring B11 stacks giving rise to a bilayer structure with the aromatic rings in each layer forming a herring bone arrangement. The B22 sheet is formed via the π - π interactions of parallel aromatic rings of similarly aligned neighbouring B11 stacks.

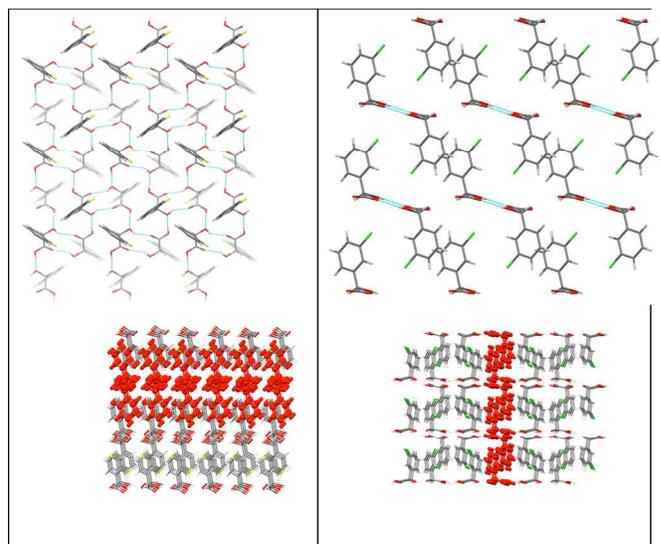


Figure 9. The 2D B21 and B22 constructs arising from the B11 construct. The top diagrams illustrate the construct and the lower ones an example of that construct as exhibited in the 3Br-1 and MA-2 structures respectively (viewed down the b and a/c axes respectively).

lower ones an example of that construct as exhibited in the 2F-2 and 3Cl-1 structures respectively (viewed down the b axes).

The B21 and B22 sheets share a common vector (B11) and combine to form the B32 3D packing arrangement exhibited by the largest group of structures in this study. Additionally each of these sheets gives rise to another 3D construct namely B31 and B33 respectively and comprise further isostructural sets, which together with B32, form the well-populated isostructural sets. These sets predominantly contain 4- and 3-substituted structures respectively.

Figure 10 shows the B23 sheet arrangement consisting of neighbouring hydrogen-bonded B12 stacks ($R_4^4(12)$) which form a 2D bilayer. Also shown is the B24 sheet which comprises an arrangement of double B12 stacks extending through their edge-to-edge, close-packed substituted aromatic rings to form a bilayer.

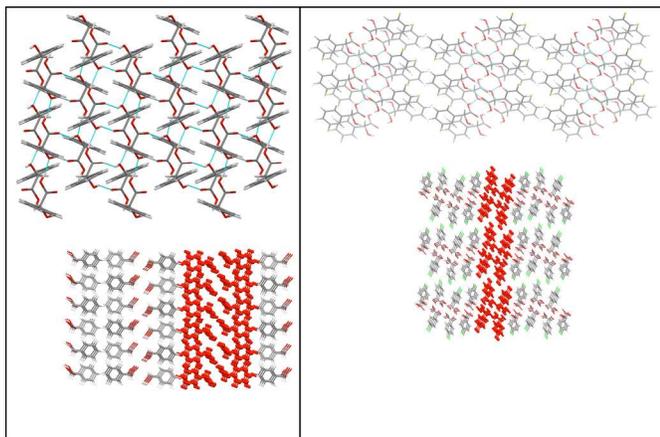


Figure 10. The 2D B23 and B24 constructs arising from the B12 construct. The top diagrams illustrate the construct and the lower ones an example of that construct as exhibited in the MA-2 and 4-Cl structures respectively (viewed down the a axes).

Whilst B23 is analogous to B21 described above, this is not the case for B24 and B22 layers where the aromatic rings of the respective 1D constructs (B11 and B12) close-pack edge-to-edge in the former and interleaf in the latter. However, similarly to B21 and B22, B23 and B24 combine with a common vector to give the 3D structure of polymorph 2 of 3-fluoro.

Hybrid AB constructs comprised of 8- and 10-membered H-bonded rings

The structural relationship plot includes a number of AB labelled constructs coloured in purple. The 2D hybrid constructs are AB21 and AB22 and are shown in Figures 11 and 12 respectively.

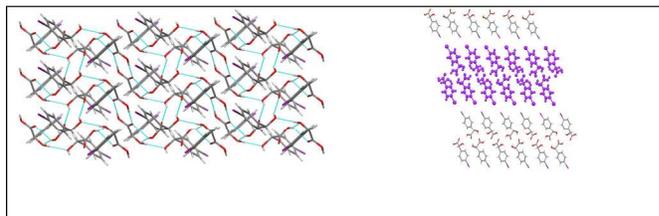


Figure 11. The AB21 hybrid construct. The left diagram illustrates the construct and the right one an example of that construct as exhibited in the 4I structure viewed down the a axis.

AB21 is comprised of stacks of the A11 motif which hydrogen bond via the available hydroxyl group to B01 dimers, with these dimers lining up as defined by the H-bonding to the A11 stack. The AB21 motif gives rise to the AB31 3D isostructural set, which comprises the 2-bromo and 2-iodo structures.

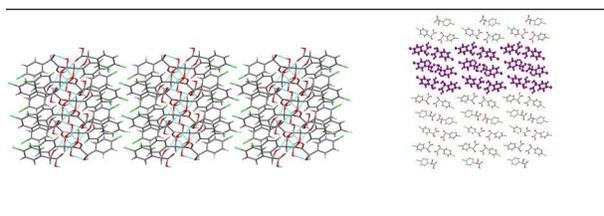


Figure 12. The AB22 hybrid construct. The left diagram illustrates the construct and the right one an example of that construct as exhibited in the 4Cl structure viewed down the a axis.

AB22 combines a single A11 stack of dimers with two antiparallel stacks of the B12 motif, where this three-strand arrangement results in a hydrogen-bonded bilayer. The hydrogen bonding all occurs between the two halves of the bilayer, leaving the surface with no H-bonding functionality. The bilayers align to form a 2D sheet. The AB22 motif combines with other motifs in the structures where it is observed – with AB21 in the case of 4-iodo and with B24 in the case of 4-chloro.

Further relationships between Mandelic acid structures

The structures presented herein are all racemic and it is the subject of further work to investigate similarity in the corresponding enantiomeric structures and also to compare these with their racemic counterparts. The structural relationship plot presented in Figure 4 uniquely demonstrates how the hierarchy of dimensionality is built up for a large set of structures via a series of common, but in some cases complex, 1D and 2D arrangements originating from just two predominant hydrogen-bonding dimer (0D) motifs. Analysing these common motifs and the sets of structures that exhibit them has the potential to provide many interesting insights and highlight areas for exploration and further experimentation.

Of general interest is the B01 group in which the dimer is formed between hydroxyl group adjacent to the aromatic ring and the carbonyl of the carboxyl group. The question arises as to why this particular grouping should be more frequent than the A01 grouping. Ten-membered rings are not generally thought to be more frequent than 8 membered rings. Furthermore no resonance stabilisation gain can be expected

from this combination. Also, making a broad observation, it appears that 2- substituted structures are generally based on A-type dimers whilst 3- and 4- substituted tend to be B-type.

Of the many intriguing structural inter-relationships that are apparent from examination of the structural relationship plot, the following are noted for immediate comment:

- Several polymorphs display close structural relationships with each other. Most notable are the two isostructural polymorphs of 3-chloromandelic acid, which have been discussed in detail in an earlier publication²³. The third polymorph of 3-chloromandelic acid also shares many structural features of the isostructural pair. The two polymorphs of mandelic acid are also very similar. By contrast, the two polymorphs of 2-fluoromandelic acid, the two polymorphs of 3-methylmandelic acid, the two polymorphs of 3-trifluoromethylmandelic acid and the two polymorphs of 4-methoxymandelic acid have no packing features in common. This point illustrates how little is understood about polymorphic structural relationships or, more generally, about the assembly of any crystal structure.

- One of the most useful features of the structural relationship plot is the clear way in which it highlights the absence of expected structures. For example, a missing 2-bromomandelic acid based on A21, a missing 3-methylmandelic acid based on B33 and a missing 4-bromomandelic acid based on AB22 are noted. A possible missing 2-chloromandelic acid of structure AB21 is most interesting because of the large amount of effort by numerous groups in the past that has gone into the crystallisation of 2-chloromandelic acid, particularly in connection with chiral resolution⁷⁻¹⁰. So it would be expected that any of the most readily accessible polymorphs of 2-chloromandelic acid would have already been encountered. These observations immediately suggest that the missing structures might be obtained by cross-seeding with a different member of the similarity group.

Based on this simple reasoning about the most probable cross-seeding approaches, we succeeded in making a new polymorph of 3-methylmandelic acid by seeding a solution in toluene with 3-chloromandelic acid and have incorporated it into this current study to illustrate this point. There are several other hints of the potential existence of further polymorphs from consideration of the structural relationship plot and these would have varying degrees of probability dependent on structural closeness and size. It is to be noted in this latter context that the B31 isostructural set accommodates a wide range of substituent size, mirroring previous observations in the sulfonamides⁵.

- An interesting structural relationship is that between 2-fluoro- and 3-fluoro- mandelic acids, two compounds that are isostructural within the B32 group. The molecular assembly of the two adjacent molecules which gives rise to this unexpected relationship is shown in Figure 13. A simple simultaneous swapping of the ortho and meta substituents leads to no overall change of the crystal structure. This immediately raises the question as to why isostructurality of ortho and meta substituted aromatics is not more common, or even of why it is not seen in 2- and 3- substituted heteroaromatics or more highly substituted aromatics and polycyclics. Since a 3-chloromandelic acid polymorph belongs to the same group it also suggests the possibility that there may be yet another 2-chloromandelic acid polymorph, again a surprising possibility.

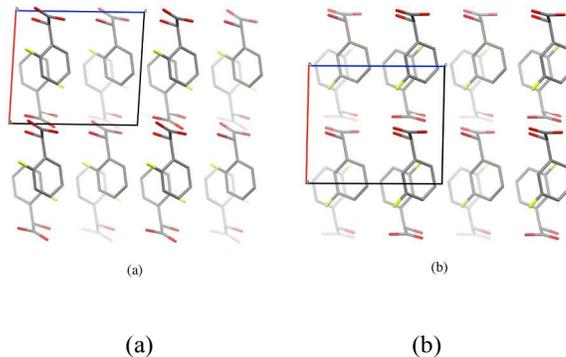


Fig. 13 Isostructural 2-fluoro (a) and 3-fluoro (b) mandelic acids viewed along the b-axis illustrating the equivalent packing of the structures despite the different positions of the fluoro substituent.

- A final comment concerns the frequency of the 10-membered ring dimers and the rarity of catemers. Carboxylic acids often self-associate²⁵ to form 8-membered hydrogen bonded ring dimers of which there are several examples in this study. The most common dimer is, however, the 10-membered ring formed by hydrogen bonding between the chain hydroxyl and the carbonyl of the carboxylic acid group (see Figure 3b). There is no clear reason why this dimer should be so favoured. It is possible that this is mere chance and that further structures identified within this mandelic acid set might alter the balance. So far crystallisation from acetic acid or in the presence of phenylacetic acid, which might have been expected to specifically favour the AO dimer structure, or from S-methyl mandelate expected to favour the BO structure, has not produced any novel polymorphs. Carboxylic acids also form catemer structures readily²⁶, although less commonly than dimers²⁸. So the infrequency of occurrence of catemers is even more interesting – as they have been identified only in 3-trifluoromethylmandelic acid amongst the racemates and in mandelic acid itself amongst the enantiomers.

Conclusions

An analysis of the extent of structural similarity in a large family of related substituted mandelic acid structures has been performed. This work shows that there are extensive relationships of a 1, 2 and 3-dimensional nature between all the members of the set and indicates that building blocks comprising arrangements of common motifs can be the basis of varying degrees of similarity. Accordingly, the substituted mandelic acids appear to be polymorphically prolific and other extensive polymorph screens and attempts to produce the ‘obviously missing’ structures are underway. Two dimensional relationships – that is sheets of molecules comprised of similar packing motifs, are shown to be the basis for a considerable amount of similarity. It is expected that further catemer based structures and more structures related to those suggested by a polymorph prediction study on 3-chloromandelic acid²⁸ or expected from consideration of the structural relationship plot can be obtained of which preliminary results are interesting and will be reported in a subsequent paper.

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Colin Seaton, then of the University of Limerick (now University of Bradford), from samples also originating in the Magdeburg laboratories. The authors would like to thank the Engineering and Physical Sciences Research Council for funding the UK National Crystallography Service, which provided the basis for most of the crystallographic experimental work.

Notes and references

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Electronic Supplementary Information (ESI) available: Full data collection and structure refinement details for all novel crystal structures determined. See DOI: 10.1039/b000000x/

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