CRYSTALLOGRAPHIC STUDIES RELATED TO THE USE OF MANDELIC ACID AND CAMPHOR-10-SULPHONIC ACID AS RESOLVING AGENTS

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All things were made by him, and without him was not anything made that was made.

John 1.3

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Lectures, Courses and Meetings Attended

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Multipulse NMR Spectroscopy, I Sadler, post-graduate lecture course, University of Edinburgh, 1986 and 1988

Drug Development, ICI Pharmaceuticals and Beechams Pharmaceuticals, Post-graduate lecture course, at University of Edinburgh, 1986

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Scribe, local implementation of the "Unilogic" text processor, Scribe, R Hare, Edinburgh, 1986 (1 week)

Mass Spectrometry, K. Jennings (Warwick) post-graduate lecture course, at University of Edinburgh, 1986

BCA Winter School in X-ray Crystal Structure Determination, Aston University, Birmingham 1987

Perspectives in Cell Biology, J.Phillips, (Biochemistry, Edinburgh) Post-graduate lecture course, University of Edinburgh, 1987

Solving and Refining Crystal Structures, R. Gould and A. Blake, Post-graduate lecture course, University of Edinburgh, 1987

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Medicinal Chemistry, P. Samms, S.K & F, Post-graduate lecture course at University of Edinburgh, 1987

Inorganic Materials, R. Gould, Chemistry 4 undergraduate lecture course, University of Edinburgh, 1988

Management, S. Coke, et al, (Business Studies, Edinburgh) Post-graduate lecture course, Edinburgh, 1988

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One Year of Inorganic Weekly Meetings, University of Edinburgh

ABSTRACT

This work describes and compares the crystal structures of diastereomeric pairs of compounds which could result from resolutions of neutral amino acids by both mandelic acid (MAN) and camphor-10-sulphonic acid (CSA).

Chapter 2 details experimental methods used. Tables list the outcome of NMR and mp analysis of crystals to suggest whether or not they were the desired products. Section 2.13 describes the conventions employed for the labelling of atoms.

Chapter 3 describes the determination of crystal structures of six MAN-amino acid complexes, and experimental data which suggested whether a 1:1 compound had been made in these and other attempts. Crystallographic data and tables listing atomic coordinates and thermal parameters are included in each of the six sections describing structures.

Chapter 4 details evidence that MAN molecules were undissociated. The molecular conformations are compared with those of other known structures, and the molecular packing arrangements; hydrophobic interactions; and hydrogen bonding schemes are given. Only 2 pairs of diastereomeric complexes were obtained. Tables listing bond lengths, angles and torsion angles are given at the end of the chapter.

Chapter 5 adopts the same format as chapter 3 and describes 5 simple salts and 4 amino acid salts of CSA. Progress towards the unsuccessful preparation and structure determination of other amino acid-CSA salts is described in section 5.10. The absolute configuration of (+)-CSA was verified as described in section 5.1.

Chapter 6, like chapter 4, is about molecular conformations, molecular packing arrangements and hydrogen bonds. A single pair of diastereomeric salts was prepared successfully to allow comparison of their crystal structures (MET/CSA) The structure of one other salt, PHG/CSA, was particularly important, since the molecular recognition that takes place is quite clear cut and results in the absolute preference for one diastereomer, R-PHG-1S-4R-CSA, over the other, and indeed makes CSA a particularly good resolving agent for PHG. The source of conformational comparisons between CSA molecules was the simple salts prepared in this work. Tables listing bond lengths, angles and torsion angles are to be found at the end of the chapter. Packing diagrams are included at the end of section 6.3 and part packing diagrams showing only the hydrophilic parts of the structures in section 6.4.

Chapter 7 analyses some resolution attempts, in which powder diffraction was the major tool. Photocopies of powder photographs are included. The results of resolutions were examined in the light of an understanding of the numbers of hydrogen bonds and the packing arrangements determined in the single crystal work.

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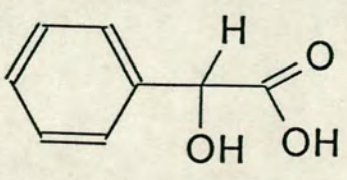
CHAPTER 1

INTRODUCTION

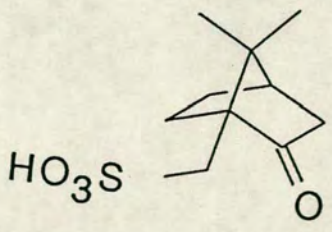
1.1 Scope of the work:

"Molecular recognition" is the name given to the process by which biomolecules sense the size, shape, and chemical functionality of a specific reagent. Normally molecules interacting in this way are chiral, and a pair of enantiomers (non-superimposable mirror image molecules) will interact differently with another chiral molecule. Resolution of racemic mixtures of acid (or base) by the addition of an optically active base (or acid to deposit the fastest forming insoluble diastereomeric salt is the classical method adopted by Pasteur[1]. Since the specific interactions in the two cases are the same, the study of the crystal structures of salts involved in optical resolutions can provide an insight into biomolecular recognition.

The present work is concerned with interactions between amino acids and the commonly used acidic resolving agents, mandelic acid **MAN** and camphor-10-sulphonic acid **CSA**[2]. Molecular formulae of these are given below:



MAN



CSA

There have been recent investigations of this sort in the optical resolution of amino acids by naturally occurring chiral alkaloid bases, such as strychnine or brucine[3,4]. In this work, chiral organic acids are used in place of the bases.

Amino acids, the building blocks of proteins, in general have two keys to their resolution by salt formation:- use of the acid end and use of the amino end. In the former method, the amino end is protected by reaction with a carboxylic acid to form an amide. The free acid end is thus much more strongly acid, and is able to form a salt with the basic alkaloid. To regenerate the resolved amino acid, the amide link must be hydrolysed to remove the protecting group, and this final step normally proceeds without re-racemisation of the amino acid[2]. Fischer[5] used this method to resolve RS-alanine in the form of N-benzoylalanine when the resolving agents were strychnine and brucine.

The latter method normally involves protection of the acid function of the amino acid by ester formation, enhancing the basicity of the amino end. After resolution, hydrolysis of the ester is necessary to regenerate the free amino acid, but this does tend to result in re-racemisation of the amino acid[2]. Japanese patents revealed that attempts had been made to resolve amino acids using optically active **MAN** which were successful, apparently, without recourse to protection by esterification[6,7,8,9,10]. **MAN** is a slim and polar molecule, and we found that it is prone to crystallising in bilayers with the neutral amino acids, it was decided to investigate a larger, more globular chiral organic acid, in the resolution of amino acids. **CSA** was selected because, like **MAN** it is polar, having hydrophilic and hyrdrophobic ends. Unlike **MAN**, it does not have phenyl rings, and should thus favour a different molecular

packing arrangement. It was decided to restrict the study to the neutral amino acids used with **MAN**, and, since so little structural work had been done on its salts, to investigate a few simple salts of **CSA** to see what packing motifs might emerge. The literature revealed that **CSA** and phenylglycine are particularly good mutual resolving agents[11,12,13].

1.2 Physical Properties of MAN and CSA[14]

1.2.1 Mandelic acid:

Mandelic acid, $C_6H_5CH(OH)COOH$, M=152.15.

R-(-)-Mandelic acid, m.p. 131-133°, $[\alpha]_D^{20}$ = -150° (c=2.5, H_2O) {Beilstein[15] **10**, 194; NMR[16] **2**(2) 140C}

S-(+)-Mandelic acid, m.p. 131-134°, $[\alpha]_D^{20}$ = +154°, (c=2.8, H_2O) {Beilstein **10**, 192}

(±)-Mandelic acid, m.p. 120-122°, {Beilstein **10**, 192; Merck Index[17] **10**,5539}

1.2.2 Camphor-10-sulphonic acid:

Camphor-10-sulphonic acid, $C_{10}H_{16}O_4S$, M = 232.30.

(1S,4R)-(+)-Camphor-10-sulphonic acid, m.p. 194° (d), $[\alpha]_D^{20}$ = +19.9° (c=2, H_2O) {Beilstein **11**, 314; NMR **2**(2) 788B, Merck Index **10**, 1712}

(±)-Camphor-10-sulphonic acid, m.p. 199° (d).

1.3 Acid-base Properties of Compounds Used.

The equilibria for the dissociation of acids in aqueous solution may generally be expressed:

$$HA \;=\!=\!=\!=\!=\; H^+ + A^- \qquad K_a = [H^+][A^-]/[HA]$$

where HA and A^- are a conjugate acid-base pair. The value of such an equilibrium constant is usually expressed in terms of its negative logarithm, called pK by analogy with pH. For the equilibrium above,

$$pK_a = pH - \log([A^-]/[HA])$$

when an interaction takes place between compounds of different acid strengths, pK_a values may be used to predict the position of the equilibrium, and hence the probable position of protons in any solid which is deposited. This may be a salt or a molecular complex. Values[18] for pK_a at 298K for various compounds studied in this work are given in the table below:

compound AH	pK_a for $AH_2^+ == AH + H^+$	pK_a for $AH == A^- + H^+$
glycine (GLYH)	2.35	9.87
alanine (ALAH)	2.34	9.87
phenylalanine (PHEH)	2.21	9.18
methionine (METH)	2.22	9.27
valine (VALH)	2.29	9.72
phenylglycine (PHGH)	1.83	4.39
mandelic acid (MANH)	----	3.85
camphor-10-sulphonic acid (CSAH)	----	<1.0

Taking the interaction of alanine with mandelic acid as a typical example, the interaction:

$$MANH + ALAH == MAN^- + ALAH_2^+$$

is the sum of $MANH === MAN^- + H^+$, $\log K = -3.85$

and $ALAH + H^+ === ALAH_2^+$ $\log K = +2.34$

Hence, log$K$ for the interaction is -1.51, indicating that ΔG has a positive sign, and salt formation is energeti-

cally unfavourable. Thus, a cocrystal of alanine and mandelic acid and alanine would expected to be a molecular complex rather than a salt, and consist of undissociated mandelic acid and zwitterionic alanine. Thus **MAN** will show unequal C=O and C-OH bond lengths in the carboxyl group, while **ALA** will show two approximately equal C-O bond lengths.

In contrast, camphor-10-sulphonic acid is essentially a strong acid, so for the interaction

$$CSAH + ALAH == CSA^- + ALAH_2^+$$

log$K$ will be positive, with salt formation favoured. The **CSA** moiety would be expected to be an anion with three equal S-O bond lengths, while the amino acid is in the cationic form, with three equal N-H bonds, but with unequal C=O and C-OH bonds in the carboxyl group.

CHAPTER 2

EXPERIMENTAL TECHNIQUES AND STRUCTURE DETERMINATION

2.1. Preparation of diastereomeric derivatives

Cocrystallisations of a single hand of amino acid with each hand in turn of either mandelic acid or camphor-10-sulphonic acid were attempted, in order to prepare both of the simple diastereomeric combinations possible in each case. It is not necessary to repeat this with the amino acid of the opposite hand since this would only produce diastereomeric derivatives which are enantiomers of the first set.

These were not resolutions because optically pure components were used and the molecular recognition taking place in the solution had no dimension of selection of molecules on the basis of handedness as a distinguishing feature.

2.1.1. Attempted crystallisations of amino acids with mandelic acid:

Where the amino acids are among those found in proteins, the naturally occurring configuration was used. Thus, L- or S-amino acids were usually used. (The configuration of L-cysteine is R-.) Glycine is a naturally occurring, achiral amino acid. α-Aminobutyric acid and phenylglycine are not among the amino acids found in

proteins. The configurations used in the preparation of diastereomeric derivatives were L-(S-)α-aminobutyric acid, and D-(R-)phenylglycine.

The amino acids used are listed below and classified according to side chain. Three letter abbreviations are given also.

neutral, non polar

alanine, **ALA**, a-aminobutyric acid, **ABA**, glycine, **GLY**, isoleucine, **ILE**, leucine, **LEU**, methionine, **MET**, phenylalanine, **PHE**, phenylglycine, **PHG**, proline, **PRO**, valine, **VAL**.

polar

cysteine, **CYS**, serine, **SER**, threonine, **THR**.

basic

arginine, **ARG**, histidine, **HIS**, lysine (as hydrochloride), **LYS**.

These were selected, in the first instance, on the basis of attempts given in the literature to accomplish optical resolution of mandelic acid by neutral amino acids or of neutral amino acids by mandelic acid[6,7,8,9,10]. **ABA**, **ALA**, **CYS**, **MET** and **PHE** came in this category. Secondly, neutral amino acids with side chains bearing some resemblance to these were selected. These were **LEU**, **ILE**, **PHG**, **PRO** and **VAL**. Other criteria were the expectation that a basic compound might crystallise as a salt with the acidic mandelic acid and also that increased hydrogen bonding possibility might increase the likelihood of crystallisation. The remainder of the amino acids used fell into these categories. With regard to

this last factor, acidic amino acids could have been tried, but two acids would not be expected to crystallise together. Mandelic acid itself crystallises not only as salts, for example with metal cations[19], but also with no counterion[20,21]. In this case the acid is undissociated. Also, amino acids with amide groups in them (glutamine and asparagine) might satisfy the latter criterion of increased possibility of hydrogen bonding. Achiral glycine was included for completeness, with its lack of chirality, of course, not necessarily precluding crystallisation with optically active or racemic mandelic acid.

2.1.2. Attempted crystallisations of camphor-10-sulphonic acid with amino acids:

Phenylglycine is a documented mutual resolving agent for camphor-10-sulphonic acid[11,12,13]. Attempts were made to cocrystallise neutral amino acids with a variety of side chains, which were not too dissimilar to phenylglycine, with (+) and (-)-camphor-10-sulphonic acid. (**ALA, GLY, MET, LEU, ILE, PHE, VAL**) Amino acids with charged and polar side chains were not employed although they might have proven successful, since it was hoped to focus on the amino acids with neutral side chains.

2.1.3 Method of preparation of cocrystallisation products:

Mandelic acid and camphor-10-sulphonic acid are soluble in both water and alcohol. The amino acids are less soluble overall, but do dissolve in water to varying degrees. Amino acid solubility was a limiting factor in the setting up of crystallisations.

1:1 molar mixtures of optically active mandelic acid or camphor-10-sulphonic acid and optically active amino acid were ground together in a mortar or mixed thoroughly. The bulk samples contained approximately 1, 0.5 or 0.3g mandelic or camphor-10-sulphonic acid and the equivalent weight of amino acid. Varying quantities of these mixtures were dissolved in hot or boiling solvent to give solutions of varying concentrations ranging downwards from saturated. Saturated solutions are most likely to result in crystallisation (though not necessarily of crystals of a quality suitable for structure determination by single crystal X-ray diffraction), whereas more dilute ones tend to improve crystal quality by encouraging slow crystallisation. Weighed samples, or numbers of microspatulatipfuls whose corresponding weights were estimated to the nearest 0.05g, were added to solvent in small 2ml vials or larger 10ml vials. The usual solvent volumes were in the range 0.25 to 1ml. The solutions were left to cool either stoppered or open to permit some evaporation of solvent. A variety of techniques were employed to induce crystallisation. They are listed in the key to the tables describing cocrystallisation attempts. It was intended that there should be cocrystallisation of the two components as a single compound identical to one of the potential crystalline deposits in the resolution of racemic amino acid by optically active mandelic acid or camphor-10-sulphonic acid, and vice versa. The details of individual crystallisations will be found in the tables in section 2.14.

Following an initial inspection under a microscope, crystals were collected either simply by lifting out of the solution with a spatula, or by filtering and washing to remove mother liquor. When they were not separated from mother liquor there was a tendency for solvent to evaporate with further rapid crystallisation of tiny thin

plates which might stick to the important crystals. This would make them behave on the diffractometer or on a camera as twinned or multiple crystals, giving rise to multiple spots or spot patterns overlaid and bearing an indeterminate relationship to one another dependent on the relative orientations of the crystallites.

They were placed on a microscope slide for examination and were usually covered in glycerol to keep them from flying all over the place at the slightest touch or from drying out and losing any solvent of crystallisation. Where appropriate, samples were left to dry for nmr and mp.

Firstly, if the morphology of a crop of crystals was uniform then they were assumed to contain the same material. The best use of melting point was to distinguish recrystallised starting material on the one hand from molecular complexes, salts or mixtures on the other. Proton nmr served to make the same distinction but with the added advantage of information on the relative amounts of components. These techniques are described in section 2.4 and 2.5 and melting behaviour and nmr results are contained in the relevant tables.

2.2. Resolutions of racemic mixtures

Separation of optically active compounds from solutions of their racemic mixtures is known as resolution of racemic mixtures. The method under consideration involved the addition of another optically active compound which extracts one of the enantiomeric components of the racemic mixture, selecting it in preference to the other and taking it out of solution by crystallisation. This is a molecular recognition process. The intermolecular forces

which hold the molecules together in crystalline arrays consist of hydrogen bonds and van der Waals interactions. Electrostatic forces also play a role because of charges on the molecules. Some of the present cocrystallisation products are salts between molecular ions of amino acid and camphor-10-sulphonate. Others are neutral complexes containing zwitterionic amino acid and undissociated mandelic acid.

The product of a resolution is the least soluble material which can come out of the mixture in solution. It is less soluble than any other possible combination of molecules, including pure, uncombined compounds. For two chiral compounds, each containing one chiral centre, there are three different resolution experiments possible. If the compounds are known as A and B, the mixtures possible are: optically active A and racemic B; racemic A and optically active B; and both A and B racemic.

In the first, the range of possible products consists of pure, optically active A; pure racemic B, as racemic crystals, or as a conglomerate of enantiomeric crystals, which is racemic overall; pure, optically active B; a compound of optically active A and racemic B; and a compound of optically active A and the other enantiomer of B. The second will have an analogous range. The third will have the possibility of additional racemic-racemic compounds. If there is to be compound formation then the most relevant possibililities are 1:1 A:B compounds of three sorts. These consist of the optically active compound with one enantiomer of each of A and B; the diastereomeric combination where one of A or B is of the opposite conformation; and the racemic compound containing both enantiomers of A and B together in the same crystals.

Resolutions were carried out in a manner similar to the crystallisation of the pure, diastereomeric compounds. 1:1 molar mixtures of reagents were prepared by grinding together components. In some cases, racemic compounds were available commercially and in others it was necessary to mix half quantities of both hands of a compound to make the equivalent of one part of the racemic compound. Small quantites of approximately 0.1 to 1g were dissolved in water or water-alcohol mixtures, with heating and stirring, and left to cool and crystallise. A sample of the first crop of crystals was collected by filtration or simply by scooping some out, and allowed to dry on a microscope slide.

Unusually, crystals suitable for single crystal X-ray diffraction were obtainable from resolutions without further recrystallisation. Section 2.8 explains criteria for single crystals. Determination of the unit cell and space group will distinguish products. Oscillation and Weissenberg photographs were used for this purpose as described in section 2.9. This, however, determines only the nature of the particular crystal selected and depends on suitable crystals having been formed. Also, having crystal morphology in common gives only an indication that all crystals in any one crop may be of the same structure.

Normally, the product was microcrystalline, having been deposited rapidly. Powder diffraction methods are able to distinguish products, and were used in a few cases. Comparison of powder photographs of the products of resolution experiments with a range of standards reveals which product has been formed and indeed whether or not there is a mixture of products. Products with large, or non-single crystals were ground for powder diffraction to verify that the bulk sample had the same structure as any crystals selected for single crystal

diffraction, and as an alternative to making oscillation and Weissenberg photographs. The results of resolution experiments were obtained simply by comparison of photographs. A list of cases in which the product of resolutions were studied is given below and results given in chapter 7.

MAN/ALA resolutions, 1:1 ratio, powder and single crystal diffraction methods.
MAN/PHE resolutions, 1:1 ratio, powder.
MAN/MET resolutions, 1:1 ratio, powder.
CSA spontaneous resolution, powder.

2.3. Preparation of simple salts of CSA.

2.3.1. General methods of preparation of salts from free acid:

Two general methods were used:-(i) reaction of an acid with an alkali; and (ii) reaction of an acid with a carbonate. Detailed descriptions of individual preparations and crystallisations of salts will be found in section 2.15. General equations will be given in which M represents the metal and A, camphor-10-sulphonic acid.

Method(ia)

The first variant of the first type entailed the reaction of camphor-10-sulphonic acid with the metal hydroxide. The metals were Na, K and Li. The details of the methods varied. While water was the best solvent for the reactants, there was a probability that the product salt would be too soluble. (The Merck Index[17] indicated that the simple salts were water soluble.) Evaporation did yield solid product from aqueous solutions, but not

always with ease. To ensure the rapid precipitation of the product the preferred solvent was either ethanol or an ethanol-water mixture. Water, of course is produced in acid-base neutralisations, and further dilutes the product. There was also the possibility that the salts might be deliquescent like camphor-10-sulphonic acid itself and might never crystallise except in a dried out form and possibly as tiny, rapidly formed microcrystals. Certainly, concentrated amino acid/camphor-10-sulphonic acid solutions tended to form gels rather than crystals.

The equation for the monobasic hydroxides is :-

$$MOH + AH \longrightarrow MA + H_2O$$

Fairly concentrated, equimolar solutions of the reagents were mixed; or solid metal hydroxide was added to a solution of camphor-10-sulphonic acid, or solid camphor-10-sulphonic acid was added to the hydroxide, commonly partially dissolved, the reaction between them gradually solublising the metal hydroxide. In order to compensate for water and carbonate impurities in the hydroxide pellets, a slight excess in the weighed quantities of these was used. At first, for CSK1 to CSK4, one pellet of hydroxide was used in each reaction, each of different weights which were a little over the required weight for 1:1 reaction with camphor-10-sulphonic acid. Preparing a stock solution of hydroxide would make trial reactions and recrystallisations more comparable, and would also be more efficient. The aim previously had been for solutions of molarity corresponding to 0.3g, 1.3×10^{-3}moles, of camphor-10-sulphonic acid in 1ml, but with a slight excess to allow for impurities and because units of whole pellets were used. Subsequently, the corresponding weights of potassium and sodium hydroxides for 5ml of solvent were used. The material was incompletely soluble in EtOH, but dissolved on the addition of 1.5g camphor-

10-sulphonic acid, which is five times the previous amount used. This method was applied to subsequent potasssium salts and to sodium salts.

Method(ib)

The second variant of the first type of reaction was the reaction of ammonia with camphor-10-sulphonic acid. Concentrated ammonia solution was added dropwise to a solution of camphor-10-sulphonic acid until the pH was alkaline and there was a smell of excess ammonia.

The equation for the reaction is:-

$$NH_3 + AH \text{ ----> } NH_4A$$

There were similar considerations as to solubility as for the preparation of metal salts.

Method(ii)

The second method involved the reaction of camphor-10-sulphonic acid with metal carbonate.The two equations are:-

$$MCO_3 + 2AH \text{ ----> } MA_2 + CO_2 + H_2O$$

$$M_2CO_3 + 2AH \text{ ----> } 2MA + CO_2 + H_2O$$

Carbonate and camphor-10-sulphonic acid were allowed to react in a 1:2 ratio. The solvents used were H_2O, EtOH or mixtures of these, chosen to try to compromise the need to dissolve the reactants and to induce the precipitation of the product salt, bearing in mind the H_2O by-product. The product salt would be more likely to precipitate from an EtOH-rich solution than from H_2O, but the

carbonates were expected to be of moderate to low solubility in H_2O and sparingly soluble in EtOH, forming suspensions rather than solutions. Camphor-10-sulphonic acid is completely soluble. When the carbonate dissolved to some extent, the strongly acidic camphor-10-sulphonic acid tended to dissolve it further by reacting with it. There was effervescence as CO_2 was released.

2.3.2. List of salts prepared:

Free acid ("hydronium salt"):

The Merck handbook[17] suggested successful crystallisation from ethyl acetate. The crystal structure showed that the actual form of this strong acid could be described as a 'hydronium salt'.

Simple salts:

K^+, Na^+, NH_4^+, Li^+, Ca^{2+}, and Cu^{2+} were the metal ions tried. K^+, Na^+ and NH_4^+ were mentioned in the Merck handbook with details of solvent suitable for crystallisation. Li^+ was prepared as one more in the series of singly charged small ions. Ca^{2+} was prepared to compare the effect of a doubly charged ion on the structure. Cu^{2+} was prepared to show the effect of a transition metal on the packing arrangement.

2.4. Melting point

Deposits were collected by scooping out of solution or by filtration and allowed to dry. A few crystals were placed inside a melting point tube, sometimes after being crushed. The sample was observed in a melting point apparatus with an electronic display and its behaviour recorded as the temperature was slowly raised to beyond

the point where the sample melted or decomposed. Wide melting ranges were consistent with mixtures or molecular complexes rather than ionic molecular salts. Amino acids tended to decompose at high temperatures, frequently >270°. R- or S-Mandelic acid melted sharply at around 133° producing a clear, colourless liquid which decomposed at around 150°, turning brown. Camphor-10-sulphonic acid melted at around 193-195°. The melting behaviour of some of the materials deposited in the crystallisation attempts descibed in section 2.14, will be found in the tables in section 2.17. See chapter 1, for melting points of **CSA** and **MAN** in the literature. The observed values corresponded well with the literature values.

2.5. Nuclear magnetic resonance spectroscopy (NMR)

Aproximately 10mmolar solutions were prepared in D_2O. D_2O was the preferred NMR solvent since the two acids and the amino acids were appreciably soluble in it as well as the cocrystallisation products. The solubility of phenylglycine was very low, but just sufficient for nmr. The disadvantage was the HOD, deuterated water peak at δ= 4.8ppm, occurring in the middle of each spectrum. Serendipitously, it did not obscure any sample resonances and indeed was helpful in scaling and fixing the origin on spectra where the computer outputted list of chemical shift values etc. was not available, or missed out relevant peaks because they were so tiny in comparison with others.

NMR showed whether or not both components were present in a crop of crystals and indeed their molar ratio. If the NMR spectrum contained peaks due to both molecules one or more distinctive NMR peaks were selected for each of the components. Bearing in mind the number of protons contributing to each peak, the ratio of compon-

ents was calculated from the drawn integrals or the printed values, or, if necessary, the peak heights. The results of the determination of molar ratios wil be found in the table in section 2.16.

2.6. Infrared spectroscopy (IR)

Infra-red analysis was investigated as a possible tool in the characterisation of the products of the attempted cocrystallisations. It was not a success.

The products of cocrystallisations of amino acid and mandelic acid were collected by scooping out of mother liquor of by filtration and washing, and allowed to dry on a microscope slide. Nujol mulls and KBr discs were both made with the samples and also with amino acid and mandelic acid standards. The resonances of interest were the hydroxyl, acid OH and ammonium resonances in the region 4000 - 2500cm^{-1} and the carbonyl resonances in the region 1850 - 1650cm^{-1}. The intention was to see if resonances of both molecules could be observed in IR spectra of a known 1:1 complex, in a manner similar to the NMR characterisation of the products. There was the possibility of ascertaining a very approximate molar ratio, that is that whether there were nearly equal amounts of both molecules, or whether one was vastly more in evidence than the other. Both mandelic acid and the amino acids contain carbonyl groups. It was envisaged that carbonyl resonances, which would be expected to be strong and sharp and might be differentiable, would be compared for this purpose. It was necessary to bear in mind that it was possible for complexation to have altered the IR resonances because of differences in the way the interesting functional groups were hydrogen bonded in a crystalline 1:1 complex and pure mandelic acid or amino acid. The spectrum of a 1:1 complex will probably not be the sum of the spectra of the two

components.

Three types of sample were prepared: pure single component mandelic acid or amino acid; product from a cocrystallisation attempt, which was known to have been successful; and a 1:1 mixture of mandelic acid and amino acid ground together, for comparison. The last of these was intended to provide a standard of what would be observed barring any complication due to complexation. But, grinding together the components, however, might be expected to allow some formation of the 1:1 complex, in which case the IR spectrum would again be different from the sum of that of the pure components.

The use of IR was investigated using primarily alanine as the amino acid and also phenylalanine. The peaks were rather broad beacause of the effect of hydrogen bonding on the IR absorption, which is to lower and broaden the frequency. The presence of water in the crystals, either because drying had been incomplete, or because there were water molecules in the crystal lattice, as in the case of the product of crystallisation of S-ALA/R-MAN, affected the absorption in the region 4000-2850cm^{-1}. The other peaks in this region were obscured by the broad water peak, appearing as shoulders on it. The peaks in the spectrum of a single pure component in this region were difficult to distinguish because there were several functional groups in each molecule having absorptions in this region and they tended to be broad. The C-H stretching vibration also occurred here. When both molecules were present the spectrum was very confused.

The carbonyl absorptions were not sufficiently resolved to show those of both molecules. Hydrogen bonding also lowered and broadened these.

2.7. Powder diffraction[22]

A Hägg-Guinier camera was used to make powder photographs. A small amount of the resolution product was collected by filtration or scooped out of the vial and allowed to dry in air. A portion was ground in a small mica mortar to ensure that there were no large crystal pieces. A sample of approximately a few tens of mg was then placed in the central hole of the sample holder, which is a 2cm metal disk with a central hole of diameter approximately 0.5cm. Special, non-diffracting sticky tape is stuck to the underside of the disk to whichthe sample adheres. A layer of powder is spread evenly over the hole and pressed down gently to even it. The random arrangement of the tiny crystals making up the powder ensures that there are always some crystals in the reflecting positions for a variety of planes. Slow rotation of the sample around the beam direction allows more planes to pass through the position for which the Bragg condition is fulfilled. Each crystal produces diffraction spots for each reflection which occur on cones of reflection with semi-vertical angle, 2θ, twice the Bragg angle for that reflection. The random orientation and the rotation of the tiny crystals cause complete cones of diffracted radiation which appear as slightly curved lines where they impinge on strips of X-ray film arranged on a circular cassette. Diffraction lines in particular positions along the unrolled strip,and of particular intensities, are thus produced. The pattern is unique to the crystal structure. Line position is determined by the unit cell and intensity by the unit cell contents, which is analogous to single crystal diffraction. Lines farther along the film correspond to reflections with a high 2θ-value, that is, reflections with a higher Bragg angle. The Hägg-Guinier camera uses focussed monochromatic radiation and the time required to obtain photographs is quite short. Exposures of approximately half an hour were

used in each case for uniformity. As for single crystal photographs, the lines farther out also correspond to finer and finer detail of the crystal structure. The atomic scattering power decreases at greater values of sinq causing a fall off in intensity of lines at higher 2θ values. This is the simplest of a range of factors which affect line intensity.

2.8. Selection and mounting of crystals for single crystal diffraction

Deposits were studied under a microscope to determine whether or not they were crystalline and of a suitable size for X-ray structure determination. Anisotropic crystalline materials are generally bright against a dark field when viewed through crossed polars. However, single crystals become entirely dark at certain points 90° apart, as the crystal is rotated. This is known as extinction and is a phenomenon exhibited because of anisotropy in refractive index of crystals. The orientation of a crystal relative to the directions of the crossed polars when it extinguishes, is known as the extinction direction. In a single crystal, extinction should be sharp and occur at the same instant over the entire crystal as it is rotated. If there are definite regions within the crystal which extinguish at given instants then the crystal is twinned or multiple. If the extinction moves over the crystal gradually then the structure varies gradually throughout the crystal. In neither case is the crystal suitable for data collection. Although the optimum range for crystal dimensions is 0.1 to 0.5 mm, it was not necessary for this to be adhered to strictly. Limiting factors included the collimator size; the crystal should be bathed in the X-ray beam and thus smaller that the collimator diameter, usually 1mm. Also, the larger the crystal the more it is subject to absorption, but the smaller the crystal the less the degree of

diffraction and the weaker the data.

Crystals were mounted in two ways for photography and data collection:- on a glass fibre or in a Lindemann tube. For photography and data collection on the STADI-2 two circle diffractometer, it was necessary to align the crystals such that the mounting, (rotation), axis was a real crystallographic axis with, by definition, the two other reciprocal axes lying perpendicular to this. Unit cell, crystallographic, axes tend to lie parallel to crystal edges or along diagonals. They also tend to lie in extinction directions, which in turn tend to correspond to two-fold symmetry axes. On the occasions when crystals were not first photographed on a Weissenberg camera, but placed directly on the AED-2 four circle diffractometer, alignment was of no importance. Occasionally the four circle diffractometer was the only option for crystals so badly misaligned that normal photographic methods of alignment were impossible. This was especially true for fragments, or crystals cut from larger pieces, when the natural crystal edges were not distinguishable and there was difficulty in being sure of mounting the fragment along an extinction direction because of movement and difficulty in sticking the crystal to the fibre. Frequently the crystals mounted in tubes were readily aligned because they were long and tended to lie along the length of the tube. The long axis often corresponded to an extinction direction and a unit cell axis. However, there is the obvious problem that control of the crystal orientation may not be possible in unfavourable cases. Just successfully to place an unfragmented crystal in a tube and to fix it with araldite was not always an easy process.

The aim was to attach the crystal to the end of a glass fibre or to the side of a Lindemann tube such that the fibre or the tube would be parallel, or nearly so, to

an extinction direction. When the fibre or tube was fitted on to a goniometer head, the extinction axis and the crystallographic axis would be, subject to some adjustment, in line with the rotation axis of the goniometer.

The crystals were fixed using araldite as an adhesive, or on occasion, nail varnish. A Lindemann tube was used when there was a possibility that the crystal would decay by loss or gain of solvent. The ends of the tube were sealed with beeswax to give a microenvironment which might protect the crystal. In one case the crystal was sealed with nail varnish, with which it was also stuck to the glass fibre because it was proving difficult to successfully manipulate copper(II) camphor-10-sulphonate crystals into Lindemann tubes without fragmentation.

2.9. Determination of unit cell and space group from photographs[23]

Space group and unit cell dimensions were determined from the symmetry, absences and spot separations on, primarily, oscillation and Weissenberg photographs made on a Stoë Weissenberg camera and also from precession photographs made on a Stoë Lattice Explorer precession camera. The Weissenberg camera used Cu radiation and the Lattice Explorer, Mo. An improved unit cell and information on absences in the mounting axis were obtained from the diffractometer after indexing reflections.

Below, a description of the identification of the space groups encountered in the present work will be given. Only holoaxial space groups are possible for these arrays of chiral molecules. The crystal system was determined from the symmetry in position and intensity of reflections about axes of the reciprocal lattice. Axes were themselves selected to have symmetry, where there is any, or to be as near to 90° apart as possible.

A search was made for any systematic absences in the entire reciprocal lattice, over all hkl, to establish any lattice repeat due to a centred unit cell. If there were, then the zero and first layer Weissenberg photographs intermeshed when overlaid, with spots on one layer being absent on the other. The absence condition for C-centred cells is that over all hkl, h+k=2n+1 are absent and for I centred cells, that over all hkl, h+k+l=2n+1 are absent.

No glide absences are possible since they involve reflection and, along with the inversion centre, would not be symmetry elements in a holoaxial space group. Screw axis absences would occur along rows of reflections on the zero layer photograph. Alternative spots are absent along the row which corresponds to the axis to which a 2_1 screw is parallel. The absence condition for a two-fold screw parallel to b is that for all 0k0, k=2n+1 are absent. Centring, 2_1 screws, two-fold rotations were the only symmetry elements encountered, apart from unit cell translations. Rotation axes are not indicated by any absences.

The space groups encountered were:- P1, $P2_1$, C2(I2), $P2_12_12_1$, $C222_1$.

P1: No symmetry or absences occur on photographs, except the 180° repeat on zero layer films because of the centric nature of the diffraction pattern itself.

$P2_1$ b-mounted: There is mirror symmetry on the oscillation photograph, but none about axes on Weissenberg films. Axes are selected for which b* is near and less than 90°. A 180° repeat along Weissenberg films is again observed. In the row 0k0, reflections are absent when k=2n+1. This indicates a 2_1 screw axis parallel to the b-axis of the unit cell. There are no absences of reflec-

tions on the two Weissenberg films, which represent h0l and h1l reflections. The 2_1 screw axis absences may be noted in the data collection output, or its presence confirmed by successful structure solution. On the STADI-2 diffractometer the mounting axis reflections, 0k0, will not be collected because they have $2\theta'$ of too low a value, that is, less than 5°.

$P2_1$ a-mounted: No mirror symmetry is exhibited on oscillation photographs. The 180° repeat occurs again along the zero level Weissenberg film. Axes are precisely 90° apart and have mirror symmetry. Mirror symmetry occurs on only one axis on upper layer Weissenberg films. The Weissenberg films represent 0kl and 1kl reflections. The 2_1 screw absences are observed on the zero layer film on one of the rows, 0k0.

C2 (b-mounted): There is mirror symmetry on the oscillation photograph, but none about the axes on the Weissenberg films. This indicates that the space group belongs to the monoclinic system, with the unique axis being b. The first upper layer and the zero layer Weissenberg photographs intermesh indicating that the cell is centred. Reflections are absent if h+k=2n+1, indicating C-centring. The fact that there is 2_1 screw axis parallel to b is obscured by the C-centring condition. The two-fold rotation and screw axes are parallel. One is a consequence of the other when there is C-centring.

I2 (b-mounted): This space group is an alternative setting of C2. If the axes of the I2 cell are a_1, b_1, and c_1 and those of the C2 cell are a_2, b_2, c_2, the following relationships describe a possible tansformation from an I2 cell with b close to and greater than 90° to a C2 cell also with a obtuse value of b.

$$a_2=a_1 \quad ; \quad b_2=b_1 \quad ; \quad c_2=c_1-a_1$$

The mounting axis and the a axis are the same in both cases. The photographs have the same features as for C2 except that the absences occur when h+k+l=2n+1 for all hkl. The two cells occupy the same volume and have the same cell contents.

$P2_12_12_1$ (a-mounted): Since there are two-fold axes parallel to each of the three unit cell axes, there is mirror symmetry about each of the axes on the oscillation and Weissenberg photographs. This indicates that the space group is orthorhombic. That the cell is primitive is indicated by the direct matching of spots in the zero and upper layer Weissenberg, photographs when they are overlaid. The zero layer Weissenberg photograph shows the absence of alternate spots on both row lines. This would also be the case with crystals mounted about other axes. The data collection output shows similar absences on the mounting axis row line, where this row line was collected. STADI-2 data collection excludes the mounting axis row line because these reflections have too low a value of 2θ', i.e. less than 5°. The absence conditions are :-

for all h00, h=2n+1 are absent
for all 0k0. k=2n+1 are absent
for all 001, l=2n+1 are absent

$C222_1$ (a mounted): As for $P2_12_12_1$, there is mirror symmetry about the row lines on the oscillation and Weissenberg photographs. This indicates that there are three mutually perpendicular two-fold symmetry elements and that the space group belongs to the orthorhombic system. The spots on the two Weissenberg films intermesh, showing the lattice centring absences for C-centring, h+k=2n+1 are absent for all hkl. There is only one of the three axes to have additional 2_1 screw absences, the c-axis. For 001, l=2n+1 are absent.

2.10. Data collection

Three diffractometers were used to collect diffraction data. They were primarily a STADI-2 two-circle diffractometer and an AED-2 four-circle diffractometer, (STADI-4) and also a CAD-4 four-circle diffractometer. The radiation used was graphite monochromated copper, or molybdenum, K_α.

Prior to data collection it was necessary for the diffractometer to be able to predict the angles to which to turn each of the diffractometer circles, for every spot to be collected. To this end, some reflections were located, assigned indices, and the angles in each of the circles corresponding to the spot centres determined. From the positions of these centred reflections an accurate unit cell was calulated.

2.10.1. STADI-2:

Crystals aligned such that a real crystallographic axis was parallel to the mounting axis were required. This was commonly the b-axis and usually the shortest. Oscillation photographs had been used previously to align the crystal on a camera of the same geometry. The crystal was visually centred, that is, placed at the centre of the diffractometer circles. A spot on the zero layer was located and alignment completed by adjustment of the arcs on the goniometer head so that the reflection remained of the same, maximum, intensity, regardless of the orientation around the mounting axis. This axis is the centre of the ω circle.

Zero layer Weissenberg photographs were used to help find and index reflections on the diffractometer.

Commonly, the crystals were monoclinic and b-mounted and the following is a description of the manual search, centring and indexing of such crystals. The details differ for other crystal systems and mounting axes and can be found with the details specific to each structure. The space group, as far as possible, and approximate cell dimensions were known from the photographs.

Making use of the zero layer film, an attempt was made to locate manually some of the reflections on the zero layer and to assign them indices. Step scans in ω were made through several reflections on the h00 and 001 row lines to check the assignment of axes and to allow the centre of the spot to be estimated by interpolation. Similar step scans were carried out through a variety of general zero layer spots, particularly those at high angle, all the time verifying the intensity pattern. The values of w corresponding to the spot centres were again estimated by interpolation. In all, 10 to 15 reflections were used in the centring process. Step scans in $2\theta'$, with the w angle changed to the improved value, were recorded and the spot centre in $2\theta'$ estimated.

A systematic search for medium to strong reflections was made, until 10 to 15 were collected. Indices were assigned and an automatic centring routine carried out, using the suite of programs, EDISTAD[24].

The lengths of the two axes apart from the mounting axis, and the angle between them, were refined by several cycles of least squares using the program REFINE, in EDISTAD. The refinement was based on the list of reflections with accurately determined w and 2θ angles. The length of the mounting axis was determined by finding the centres of some 0k0 spots, adjusting the μ circle to find the position of maximum intensity of the reflection. This gives the best value of μ, the inclination angle,

for the kth layer. The Bragg equation was adapted to enable the length of the mounting axis, in this case b, to be calculated. The usual form is $n\lambda=2d\sin\theta$. For the reflection 0k0, k=n, d=b and $\theta=\mu$. Thus $k\lambda=2b\sin\mu$. The detector position, n, and the inclination angle, w, were adjusted to the approximate value, calculated on the basis of the length of the mounting axis, which was determined from an oscillation photograph. For ω at four positions, 90° apart, the value of μ for maximum intensity was obtained by observing the position of a pointer on a scale, while slowly varying μ by hand to scan through the reflection. The average of averages of pairs 180° apart and 90° away from these was determined and the new b-value calculated from the formula. These refined values of the cell dimensions were used in data collection.

2.10.2. AED-2:

Normally, 25 to 30 strong reflections, of a variety of 2θ-values, were collected in a systematic scan of the space in which diffracted radiation might be found. The diffractometer program assigned them indices, and determined the crystal system and Laue group. An automatic centring routine was applied, and then an accurate unit cell refined. A matrix was refined to relate the crystal orientation to the origin used by the diffractometer.

An alternative method was employed on occasions on which a systematic reflection search might be expected to take a long time. This might be when there is a small organic crystal and copper radiation, where the diffracted radiation would be weak and widely spread in space. The length of time the photographic method takes would be up to an hour overall and it was often done in conjunction with the automatic search. For such crystals a systematic search might take the same, or a much longer,

time to find sufficient, strong spots. The AED-2 diffractometer was set up to take an oscillation photograph using a cassette with an intensifying screen. Marker spots and a pencil mark on one corner recorded the film orientation. A 20 to 30 minute photograph was recorded and (x,y) coordinates of the spots in millimetres measured with a ruler, or film measuring device. These coordinates served as an input to the diffractometer software to calculate the corresponding angular positions of the reflections. The centring and indexing etc. procedure continued as for the automatic reflection search.

2.10.3. CAD-4:

An automated reflection search, indexing and centring procedure was carried out in a manner similar to that for the AED-2 diffractometer.

2.10.4. Data collection:

Reflections with the value of 2θ, the Bragg angle, out to approximately 50° or 120°, respectively, for Mo and Cu radiation. were collected. After this value of 2θ they tended to die away because of the limits of resolution. The reflecting planes become too close together for there to be diffraction of x-rays.

It was unnecessary to collect all reflections, hkl, of the diffraction pattern because some reflections are equivalent by symmetry. For the triclinic space group P1, data in half of the volume of space was collected, that is data with one index positive only, and with the other two positive and negative. For the monoclinic space groups, a quarter was collected, that is with two indices positive only and the other positive and negative. In the case of the orthorhombic space groups, an eighth was required, that is with all indices positive. The excep-

tion to this was when data were collected for the determination of the absolute configuration of (+)-camphor-10-sulphonic acid.

Data were collected on the automatic four-circle diffractometers with little operator intervention. On the STADI-2 diffractometer the data were collected in successive layers each having the same mounting axis index, usually k for monoclinic crystals and h for orthorhombic. It was necessary to adjust the inclination angle, μ, to the required value for each layer. The shortest unit cell axis was frequently the long axis of the crystal, that is the fastest growing direction, and was often the mounting axis. This conveniently allowed for the fewest number of manual layer changes. Intensities were measured using ω-scans, with backgrounds on either side.

The intensity of two or three reflections measured repeatedly several times during data collection served as a check that the crystal remained intact and did not decay in any way. These intensity standards normally remained quite constant throughout.

2.10.5. Data reduction:

Reduction of AED-2 data was done on the attached PDP11, using the manufacturer's software, before transfer to the mainframe. Data collected on the STADI-2 and the CAD-4 were first transferred to the mainframe for reduction. The data reduction programs were STOEABS[25] and CADABS[26] respectively. STOEABS and CADABS included statisical tests for symmetry within sections of the data, in particular, whether or not sections of the data are centrosymmetric. Even when the structure is non-centrosymmetric, zones will be centrosymmetric if there is a two-fold rotation or screw axis perpendicular to the

zone. The presence of an inversion centre or a mirror or glide plane in the zone is ruled out in the present structures on the grounds of chirality.

2.11. Structure solution and refinement

2.11.1 Structure solution:

Both direct methods and Patterson methods of structure solution were employed as appropriate. The programs used were:- SHELX84[27] and 86[28] for direct methods, SHELX76[29] for Patterson, and DIRDIF[30] for phase refinement after Patterson determination of one atom position and for the placing of known, structurally conserved fragments, correctly oriented, in the unit cell, followed by phase refinement and the location of remaining atoms. In the latter method involving DIRDIF, the subprograms employed were ORIENT and TRADIR. Thus the entire or partial structures, apart from hydrogen atoms, were located in the unit cell once phases were determined for the reflections.

Where there were isomorphous structures it was possible to by-pass the normal structure solution methods. A Fourier calculation using the program SHELX76, to which the coordinates of the known non-hydrogen atoms were given, was carried out, adjusting the atomic scattering factors and atom types as appropriate.

In direct methods, an attempt is made to extract structural information from the amplitudes of the structure factors on a statistical basis. Normalised structure factor amplitudes, E, are employed to take account of the decay of individual scattering factor amplitudes as 2θ increases. A true assessment of the strength of reflections is required since only strong reflections are

employed. They represent crystal planes for which the electron density produces an efficient diffraction grating.

In a simple case, phases, ϕ, are assigned to up to four strong reflections to fix the origin and sometimes the enantiomorph. These suggest the probable phase of other reflections using the relationship

$$\phi_1 \approx -\phi_2 - \phi_3$$

when the sums of the values of h, k, and l are zero. The three reflections are known as a triple product. Only when this relationship is met can the three sets of planes all diffract efficiently. It is therefore a key relationship.

The method for centrosymmetric space groups is simplified in that there are only two possibilities for the phase angle, 0 or 180°, referred to as two signs, + or −, of the structure factors. This is because the terms used to calculate an electron density map include $|F|\cos\alpha$ and $|F|\sin\alpha$, which in this case take values $\pm|F|$ and zero respectively. In non-centrosymmteric stuctures the phase angle may take any value between 0 and 360°.

In the centrosymmetric case, the signs, S, of the strong reflections of the triple product are related in the following way:-

$$S_1 \approx S_2 S_3$$

where ≈ represents 'is probably equal to'.

Starting phases must be assigned arbitrarily to the first three reflections used to build up the phase set. In more complicated structures a larger starting set of phases is needed and letter symbols are given to other phases initially, in the hope that the phases may be

fixed subsequently as the set is built up. This is known as symbolic addition. Alternatively, many phase sets, or solutions, may be refined where some phases are given arbitrary starting values. The best may be selected on the basis of some figure of merit, commonly the consistency of the phase predictions. An electron density map, based on the set of relections with large E-values, for which phases have been assigned, is then plotted and represents the proposed electron density over the unit cell. If structurally identifiable fragments can be joined together and they make chemical sense, then the structure has been successfully solved and refinement may proceed.

Direct methods is most successful for equal atom, small molecule crystal structures. In this sense it is complementary to the Patterson method described below. It requires the building up of a possible solution from an arbitrary phase assignment and the repetition of this process many times. Many incorrect 'solutions' are also be generated. This is practicable with the high speed computational methods available, such as in SHELX86[28]

In the Patterson method of structure solution, a Patterson map is plotted with points u,v,w in a cell of the same size and shape as that of the crystal unit cell. The points represent vectors from each atom in the unit cell to itself and to every other. The intensity of each point on the map u,v,w is proportional to the product of the atomic numbers of the atoms at both ends of the vector (u,v,w). The Patterson function depends on the squares of the amplitudes of the structure factors and the indices of the reflections according the the formula

$$P(u,v,w) = V_c^{-1}\Sigma\Sigma\Sigma|F|2\cos 2\pi(hu + lv + kw)$$

where the summation is over all hkl.

Peaks in the Patterson function occur at the points u,v,w. The Patterson function may be thought of as the convolution of the electron density at all points x,y,z in the unit cell with the electron density at points x+u,y+v,z+w. This is equivalent to considering the Patterson function to be the total appearance of the structure viewed from each atom in turn. It is as if the sum had been taken, for all values of x,y,z, of the product of the electron density at a point x,y,z with that at the point x+u,y+v,z+w.

There is only one Patterson map for any structure and its interpretation depends on the peak heights and the symmetry operators relating asymmetric units. Large peaks result both from vectors between atoms heavier than others in the structure and from the overlap of similar interatomic vectors. It is necessary to calculate the vectors expected between symmetry related heavy atoms in the structure in terms of x,y and z, and look for Patterson peaks of the same form from amongst the more intense peaks. Trial positions for heavy atoms may thus be obtained. While it is easy to obtain trial positions for structures with a very small number of heavy atoms, structures with several heavy atoms; a molecule with the same structural unit repeated within the asymmetric unit; or a structure containing only atoms of similar atomic number, are more difficult because the Patterson map is confused and there are more strong peaks.

Patterson search techniques were employed to place a known camphor-10-sulphonate molecule in an amino acid-CSA salt structure. From fractional coordinates particular to one unit cell, orthogonalised coordinates were calculated in a general orthogonal cell of cell dimension 10Å. Intramolecular interatomic vectors were calculable from these. Patterson maps were calculated for both the new

stucture and the fragment and compared in the region around the origin at various relative orientations until the best fit of peaks was obtained. Such a rotation search was carried out using ORIENT, a subprogram of DIRDIF[30], to determine the optimum orientation of the known, rigid molecule in the unit cell of the new structure. This was followed by a translation search using the subprogram TRADIR, in which the Patterson map was searched by the program for vectors between the atoms of the known molecule in symmetry related positions in a manner related to the location of heavy atoms discussed previously. The location of the known molecule obtained in this way formed part of a trial structure, the remainder being located in a difference Fourier map on the basis of phases assigned by the positioning of the known molecule.

2.11.2 Structure refinement:

Remaining atoms were located in difference Fourier maps during the structure refinement process. Occasionally it was possible to locate the position of hydrogen atoms, but, for the most part, hydrogen atoms bonded to carbon atoms, about which there could be no ambiguity in position, were placed in ideal, calculated positions with isotropic thermal parametes fixed at a value of 0.05Å^2 and allowed to ride on their attached carbon atom. The ideal C-H bond length was 1.08Å. These were restraints on the proton positions and did not undergo refinement. Starting positions for the hydrogen atoms in methyl groups were assigned similarly but the group then allowed freedom to rotate about the bond made between the carbon atom and its neighbour in the molecule, as a rigid group, in order to bring it to conform to the electron density of the Fourier map and to best represent the actual structure. A rotational parameter about each of the crystallographic axes was refined for the carbon atom and

these frequently had values of shift/esd much larger than others in the same cycles of refinement. Hydrogen atoms in hydroxyl, carboxyl and ammonium groups and those in water molecules, were often found in difference maps and frequently constrained to lie particular distances away from nearby atoms in order to hold them in reasonable positions. Occasionally, a position for one of these hydrogen atoms was initially calculated, either to be between two atoms which are clearly hydrogen bonded or, in the case of ammonium hydrogen atoms, to be part of a tetrahedral functional group. The refinement proceeded with the atom constrained as described before.

The progress of the refinement towards convergence was coarsely assessed by the crystallographic R-factor, the shifts in atomic parameters in each cycle and the smoothness of the difference map calculated after every few cycles of refinement. The R-factor was calculated as the ratio of $\Sigma|F_o-|F_c||$ to ΣF_o, and was often quoted as a percentage. (Here, F_o and F_c represent the magnitudes of the observed and calculated structure factors for each reflection.) When the observed structure factors were best matched by the structure factors calculated from the electron density through space of the model structure, the R-factor took on a low percentage value, typically less than 10% and often below 5%.; the shifts in the atomic parameters divided by their esd's were low, commonly less than 0.01 in the final stages; and there were only small peaks on the difference Fourier map. These were considered to be no more than noise, created because of the summation of Fourier series which approximates to the actual, observed structure factors and real distribution of electron density over the structure. Peaks indicated that electron density at a particular point was greater in the observed structure than in the model and were used to pinpoint the location of atoms during structure solution and refinement. When the various cri-

teria were attained as describe above, the structure was said to have converged, which meant that all the atoms were refined to be in positions as accurate as possible and that the atomic positions and thermal parameters best represented the actual electron density distribution.

Normally, SHELX[28] assigned coordinates to regions of electron density, and plotted them as two-dimensional maps of the structure within the limits of a previously defined portion of the unit cell, to avoid unnecessary repeats, and viewed as a projection in a least squares plane determined by the program to best show the molecules. It was convenient, however, to print the full three dimensional difference map of the defined portion of the unit cell in layers perpendicular to one of the unit cell axes for part of the refinement of the structure of S-Methionine-R-Mandelic Acid. This was in order to locate atoms in two disordered MET side chains. The difference in electron density per cubic angstrom was plotted at points in a grid and attempts made to join up regions of electron density into two series of bonded atoms. Atomic coordinates were found by interpolation and refined with atoms in the same chain having the same site occupancy factor.

Once a structure had converged on the actual structure, a weighting scheme for reflections was determined by least squares refinement over a number of cycles, of a weighting factor, W, keeping the atomic parameters fixed. The weighting scheme then applied to the data was of the form $W=n/(\sigma^2(F) + wF^2)$. n depended on the value of w, which was kept fixed in subsequent structure refinements. Before the weighting scheme was calculated there was variation in the values of the variance of the square root of F/F_{max} over sections of the data. An acceptable weighting scheme levelled out the variances.

2.12. Determination of absolute configuration

A measurable amount of anomalous scattering takes place in non- centrosymmetric space groups when there are certain atoms present and with certain X-ray wavelengths. The X-ray wavelength used must be near the absorption edge of a particular atom in the structure[31]. Sulphur is a weak anomalous scatterer when the radiation is that of copper. Friedel pairs which would otherwise be of identical intensity because of the centricity of the diffraction pattern are non identical. The two enantiomorphs of the molecules would give different intensity patterns in the diffracted radiation.

To collect data for the determination of the absolute configuration it is necessary to collect two portions of the data which would otherwise be equivalent, here disobeying Friedel's Law. The inequivalent Friedel pairs must not be merged automatically by the structure solution program because in this non-centrosymmetric space group, although the amplitudes of the F's may be negligibly different, the amplitudes will be different. Friedel's law does not hold for non-centrosymmetric space groups. The amplitudes of the structure factors for hkl and -h-k-l will be negligibly different when there is little anomalous scattering but may be significantly different when anomalous scattering is an important feature of the diffraction.

The residuals in a structure refinement calculation will be smaller if the correct enantiomorph is used in the model than if the opposite were employed, since calculated structure factors will be closer to observed ones. Comparison of R-factors from both at the same stage of structure solution will indicate which hand is the actual hand of the compound under study.

2.13. Determination of molecular geometry, molecular packing arrangements and hydrogen bonding scheme

2.13.1 General:

The raw results of x-ray diffraction were translated into unit cell, space group, x,y,z positional coordinates and either one isotropic or six anisotropic thermal parameters of the asymmetric unit, which together define the crystal structure of the compound. These resulting parameters constituted the results of the crystal structure determination, and will be found in Chapters 3 and 5. These results were used to determine molecular geometry parameters such as bond lengths, angles and torsion angles which are to be found in the relevant tables in Chapters 4 and 6. The computer program used was called CALC[32]. CALC was also useful in indicating which atoms were involved in hydrogen bonding and the geometry of the hydrogen bonds, and to show any other atoms which were unusually close, such as atoms of oxygen near to carbon and hydrogen atoms at the rim of phenyl rings. Such close atoms are either involved in van der Waals interactions or are close by coincidence, because neighbouring atoms were involved in hydrogen bonds and drew their neighbours into close proximity with the atoms to which they were hydrogen bonded.

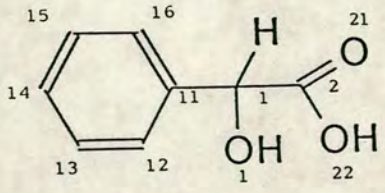
Diagrams of the individual molecules were obtained using ORTEP[33] in order to show the degree of anisotropy of the atomic thermal parameters. Diagrams of the crystal structures were obtained using PLUTO[34]. Views down reciprocal axes towards the origin were useful in determining the packing arrangements and for observing the hydrogen bonding schemes.

Photographs were made of mandelic acid molecules and their close environments in crystal structure on an

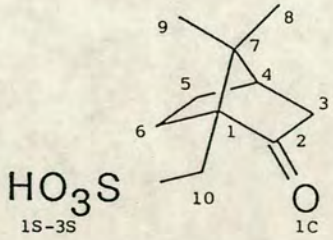
Evans and Sutherland Picture Systems Molecular Graphics computer. In combination with the information from CALC about actual separations between particular atoms, the pictorial informtion, both two dimensional plots and stereographic pairs of photographs led to an understanding of the environments of mandelic acid molecules and the similarities and differences between structures.

2.13.2. Molecular labelling schemes:

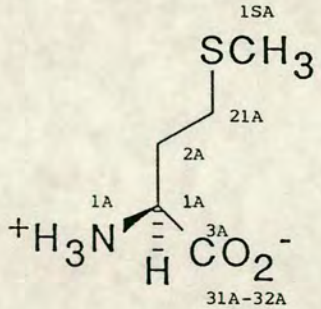
The labelling scheme is standardised for consistency and takes account of the position of the atom within the molecule and the molecule to which the atom belongs. Mandelic acid and camphor-10-sulphonate molecules have labels with the atom symbol followed by a number to indicate the position within the molecule. Where there is a second mandelic acid or camphor-10-sulphonate in the asymmetric unit, a dash is added after the symbol to distinguish the two. Amino acid molecules are labelled in a somewhat similar manner to mandelic acid molecules, but with the suffix A, and B where there is a second one. Water molecules are suffixed W. See the examples for the pattern to the labelling.



MAN



CSA



amino acids

The convention was laid down that for carboxylic acid groups, the carboxyl oxygen would have the lower number in its label, O(21), and the carboxylic acid the

higher, O(22). The hydrogen atom, if located, would be H(20). The hydrogen atom on the hydroxyl group. if located, would be H(10).

Some functional groups contain atoms that are not chemically distinguishable. The short table below describes the conventions laid down on the basis of the following observations about torsion angles. When there is a chiral atom as an atom in the central bond, the torsion angles for one enantiomer are, ideally, the negative of those for the opposite enantiomer. It was observed that the torsion angles of the two ortho-carbon atoms of phenyl rings to the carboxylate carbon atom, three bonds removed tend to be not far from 90°. The value of this torsion angle represents the angle between the central bond of the torsion angle and the plane of the phenyl ring. The other groups of atoms which would otherwise have an arbitrary labelling scheme are the oxygen atoms of carboxylate groups in the amino acids. It was observed that one oxygen atom tends in every case to nearly eclipse the ammonium nitrogen atom.

molecule	torsion	ideal angle	range to be allowed
R-MAN	C(2)-C(1)-C(11)-C(12)	-90°	0 to -180°
S-MAN	C(2)-C(1)-C(11)-C(12)	+90°	0 to +180°
S-PHE	C(1A)-C(2A)-C(21A)-C(22A)	+90°	0 to +180°
amino acids	N(1A)-C(1A)-C(3A)-O(31A)	0°	-90° to +90°

These conventions standardised the molecular labelling in order to facilitate comparisons among structures. No standardisation was attempted with aliphatic hydrogen atoms, for which it is not required, nor for the ammonium hydrogen atoms, because the non-hydrogen atoms involved defined the hydrogen bond. The labels of the two methyl groups in camphor-10-sulphonate have also not been standardised. Also, since only a single structure invol-

ving phenylglycine was attempted, no rule is given for the numbering of the phenyl ring.

2.13.3. Bond lengths, angles and torsion angles:

Bond lengths, angles and torsion angles are listed in the tables in Chapters 4 and 6. It was often possible to locate hydrogen atoms attached to carbon atoms in difference maps, but to reduce the ratio of number of parameters to number of data, they were usually placed in calculated positions. Such hydrogen atoms which were placed in ideal positions, using the AFIX instructions in SHELX76[29] and remained in a fixed relationship to the carbon atoms to which they were bonded and to the other atoms bonded to the carbon atom. The length of such C-H bonds was 1.08Å, the angle made with other bonds to the same carbon atom was, as near as possible, the ideal value of 109.4° for tetrahedral arrangements and 120° for trigonal arrangements. Except in the case of the alanine structures, the hydrogen atoms of methyl groups, were first placed in calculated positions using the AFIX33 instruction and then allowed to rotate around the C-C bond until they fitted the electron density map best, using the AFIX6 instruction. This was required because the positions calculated using the AFIX33 instruction did not necessarily reflect the true positions. Two or three known atoms within bonding distance were required to define the positions available to the new hydrogen atoms. The use of this 'rigid rotation'for hydrogen atoms reduced the total number of parameters for all of the hydrogen atoms on each methyl group from nine to three, when three rotational parameters replaced three coordinates for each atom. In the alanine cases, there were no refining parameters for methyl hydrogens. The rigid rotation facility was not used for these two structures.

Esd's are dependent on the esd's of the fractional coordinates and on the thermal parameters. Cell esd's were not included in the calculation. Esd's on geometrical parameters should therefore be slightly larger than they were calculated, but the difference was not considered to be large enough to make any important difference.

The only bond lengths of particular interest are the C-O separations in the carboxylic acid groups to determine which were dissociated. Differences between the lengths greater than three times the sum of the esd's on the two lengths were considered significantly different. Where the pair of bond lengths were not significantly different, they formed a carboxylate ion, the dissociated form of the carboxylic acid. Where there was a long and short C-O separation that carboxylic acid was undissociated and should have a hydrogen atom bonded to the oxygen atom which is at the longer distance from the carbon atom of the carboxylic acid group. This hydrogen atom was not always able to be found in electron density maps because of its extremely low scattering power and perhaps because it had a great deal of thermal vibration or was disordered.

Bond angles are listed in the tables at the end of this chapter. They were mostly as expected. Angles at carbon atoms made by the two oxygen atoms of carboxylate and carboxylic acid groups were often wider than the expected 120°.

Torsion angles between bonds were studied in order to compare molecular conformations. They are listed for the six crystal structures, in the appropriate tables at the end of this chapter. Comparisons were drawn with mandelic acid and amino acid molecules found in the Cambridge Database[35].

A torsion angle is labelled X-A-B-Y and relates to the three bonds between any four adjacent atoms in a molecule. It must be imagined that one looks along the central bond and sees the other two bonds at an angle to one another. There is a convention for the sign of such a dihedral angle in that, keeping within the range -180° to +180°, one of the front bonds is imagined to be rotated to eclipse one of the rear bonds. If it moves clockwise, then the torsion angle is positive and if it moves anticlockwise it is negative. It is immaterial in which direction, A to B or B to A, one 'views' the central bond. If A or B is a chiral centre, then for opposite configurations about the central bond, the torsion angles have opposite signs. When labelling atoms in molecules, which may be otherwise identical, an arbitrary convention was made about the sign or range of certain torsion angles. This is to prevent, for example, the problem that in phenyl rings, there may be a difference of 180° in torsion angles if rings are numbered in opposite directions. Such conventions are given at the start of chapter 3.

When both carbon atoms of the central bond are tetrahedral, the expected, ideal conformation would have bonds staggered, with the minimum number of bonds to non-hydrogen atoms in a gauche arrangement, having torsion angle + or - 60°, and the maximum in a trans arrangement, having torsion angle 180°. When viewed along the central bond, the three atoms attached to one of the central atoms will be 120° apart.

When one of the carbon atoms involved in the central bond is tetrahedral and the other trigonal, then the two atoms attached to the trigonal atom will be coplanar with both central atoms and the angle between this plane and the bonds second removed will be represented by the

torsion angles of the atoms bonded to the trigonal central atom and atoms bonded to the tetrahedral central atom. No favoured conformation will be predictable when the tetrahedral atom is bonded to three non-hydrogen atoms. The exception is when two of the atoms bonded to the tetrahedral atom are hydrogen atoms, in which case, the torsion angles to the non-hydrogen might be expected to be 90° and that to the hydrogen atoms, 30°. Examples of trigonal carbon atoms are the central carbon atom of a carboxylic acid or a carboxylate ion and the carbon atom by which a phenyl ring is attached to a molecule.

In Chapters 4 and 6, for each structure, molecular conformations are described and compared. A list is included of some of the important torsion angles, but reference should be made to the tables at the end of those chapters for torsion angles for each structure. Other things being equal, two enantiomeric molecules will have equal and opposite torsion angles, and can be compared with one another simply by changing all the signs of the torsion angles of one of them. In addition to this, however, differences in hydrogen bonds and other packing forces will normally alter the torsion angles significantly from ideal values.

Key to tables of experimental conditions and results

Comments

DR	dissolved readily
DD	dissolved with difficulty
PD	partly dissolved
I	insoluble

Treatment

a	left stoppered as cooled to room temperature to reduce evaporation.
b	left unstoppered as cooled to room temperature to allow evaporation.
c	left stoppered to prevent evaporation.
d	left unstoppered to allow evaporation.
e	heated to evaporate some solvent: ep on hotplate, eb in heating block.
f	left loosely stoppered to allow some evaporation.
g	placed in vacuum desiccator to encourage evaporation of solvent.
h	heated to dissolve material or redissolve precipitate.
i	heating block used to cool slowly to room temperature.
j	cooled in fridge to encourage precipitation.
k	addition of seed crystals, the result of a specified crystallisation.
l	addition of a given volume of a given solvent.
m	scraped with a glass rod to induce crystallisation.
n	isothermal distillation: solution placed

unstoppered in vacuum desiccator with container of EtOH at reduced pressure. EtOH gradually mixes with original solvent, increasing the EtOH/H_2O ratio.

o isothermal distillation: As n, but at ambient pressure.

Results

C crystals

NC no crystals

2.14 Experimental conditions and results

TABLE

code	mixture; solubility	treatment	result:	comments; appearance; analysis
		ALA/R-MAN		
1	0.15g/1.1ml hot H_2O; D	a	NC	left for 5 days
		d	C	after a few hours, small crystals around waterline and one thick, colourless rectangular plate, 8x2mm. no extinction. piece broken and crushed for seeds. after 2 days small crystals grown slightly, became trapezium-shaped plates. large plate split into two lengthways. the larger piece with the surface etched. dried precipitate on sides of vial by evaporation. mp.
2	0.25g/1.6ml hot H_2O; D	a	NC	
		k ex1,c	C	after a few minutes, small, thin, diamond-shaped plates. too small and thin for data collection. mp. nmr.
	recrystallisation of product ex2			
3	0.2g/1ml warm H_2O; DR]	a	NC	
		k ex2,c	NC	seed dissolved overnight
		d	C	solvent largely evaporated. large plates on sides of vial, just above waterline. one is a cruciform, twinned crystal.
4	0.15g/1ml hot EtOH; I			
	+0.5ml hot H_2O; I	I,h		(partly dissolved)
	+0.5ml hot H_2O; D	I,h	C	overnight, small crystals on base.
		d		solvent evaporated. many crystals. small and narrow. also, larger, elongated rectangular plates with good faces, one set of which are parallel, with interfacial angles not 90^{o}. crystal structure determined.
		ALA/S-MAN		
1	0.1g/0.7ml hot H_2O; D	a,c	NC	left for 5 days.
		d	C	after a week small amount of thin crystals on sides of vial by evaporation. used as seeds.
		k self,d	NC	seeds dissolved.
		d	NC	for a few days.
		c	C	after a month from the start, two long, fat needles. not single crystals because a bright spot remains in each when the rest is extinguished. used as seeds.
2	0.25g/1ml hot H_2O; D	a	C	after 15 minutes small, white needles. mp. nmr.
	recrystallisation of some of product of 2, more dilute.			
3	0.1g/1ml hot H_2O; D	a,k ex2,d	NC	left overnight.
		k ex2,d	NC	left overnight
		k ex2,d	NC	left overnight
		d	C	after two weeks, solvent evaporated, white needles.
	+0.5ml hot H_2O	I,h,a,d	NC	
4	0.05g/1ml hot EtOH; I			
	+1ml hot H_2O; D	I,h,a,c	NC	
5	0.1g/0.5ml hot H_2O; DR	a,k ex1,c	C	overnight, several thick, slightly etched, elongated, lamellar plates. cut one into three and mounted a piece. x-ray photography indicated twinned.
6	0.05g/0.5ml hot H_2O; DR	a,k ex1,c	NC	seeds dissolved.

		k ex1,c	NC	seeds dissolved
		d	C	after 2 days small amount of crystallisation on sides of vial by evaporation. used as seeds.
		k ex5&6,c	NC	left for 3 weeks
		d	C	after a few days, small amount of crystallisation as before.
		k ex6,c	NC	
7	0.1g/0.6ml hot 5%EtOH; DR	a,d	NC	left overnight
		k ex5,c	C	within an hour, thin elongated plates, 1-2mm long. sharp extinction. crystal structure determination.
8	0.2g/0.6ml hot 5%EtOH; DR	a,k ex5,c	C	thin elongated plates 1-2mm long.

ABA/R-MAN

1	0.795g stock mixture			
2	0.25g/1ml hot H_2O; DR	b	NC	for a few hours
	+0.1g; DR	h,b	NC	for a few hours
		e_p,b	C	after a few hours, larged, etched, elongated, rectangular plates. extinguished ppl. sharply along and perpendicular to needle axis. one mounted 0.65x0.25x0.15mm. mp. structure determination. slight decomposition after several months.
3	0.05g/1ml hot 75%EtOH; D	b	C	small plates and hairs on sides of vial.
		k self,d	C	after a few days, seeds dissolved. small amount of crystallisation on sides of vial. poorly formed plates. sharp extinction.
		k self,d		crystals remained. now observed to be lamellar.
4	0.15g/0.5ml hot H_2O; DR	b	C	tiny amount of crystalline material on sides of vial
	+0.15g; DR	h,b	NC	for a few days
	+0.05g; DR	h,b	NC	for 3 days
	+0.05g; DR	h,e_p,b	C	after a few days, dried up precipitation on sides of vial and elongated, rectangular blocks in solution and protruding. collected crystals by filtration.

ABA/S-MAN

1	0.1g/0.5ml warm H_2O; DR	b	C	after several days, solvent evaporated leaving mainly long fibres and some tiny crystals. decompostion after several weeks. mp. 2 narrow, elongated, rectangular plates mounted 0.4x0.06 and 0.6x0.05mm. x-ray photographs.
2	0.25g/1ml hot H_2O;DR	b	C	overnight some crystals on sides of vial by evaporation.
		k self	NC	for a few hours
	+0.1g; DR	h,b	NC	for an hour
	evap to 0.25ml	e_p,b	c	after evaporation some tiny specks floating in solution. after a day, some fine hairs and crystalson sides of vial. collected some for mp.
		k self	C	much crystallisation. tiny needles and rectangular plates. also, larger narrow, elongated, rectangular plates and tiny parallelogram and rhombus-shaped plates. collected crystals by filtration and washing with H_2O. gave a small amount of large plates, 1mm across. mp.
3	0.05g/0.5ml boiling EtOH; I			
	+0.2ml hot H_2O; D	I,b	C	after a few days, narrow hairs on sides of vial by evaporation.tiny quantity. unable to scrape into solution as seeds.
		k ex2,b,d		needles and plates ex2 as seeds dissolved. after a few days, many hair-like crystals on sides of vial and a few in solution.
		c	C	grown thicker into needles located on base.
4	0.20g/0.25ml warm H_2O; DR	b,d	C	overnight needles appeared (which were then kept stoppered) radiating out to the edges of the vial from the centre. They were elongated, flattened needles, whose cross-section was a flattened hexagon. They were very thin and did extinguish. 3, 1mm in length, were mounted on fibres. photographs of one showed it was actually a bundle of parallel crystallites, misoriented about the mounting axis. mp.

GLY/R-MAN

1	0.2g/0.5ml hot H_2O; DR	b	NC	
2	0.1g/0.5ml hot 50%EtOH; DR	b	NC	
3	0.35g/1ml hot H_2O;DR	b	C	after a week, one large, white,trapezium-shaped crystal with a small crystal stuck on it. collected by filtration and washing with H_2O. long edge, 9mm, short, 5mm, width, 5mm. lamellar. extinction gradual and patchy over plate. mp.

ILE/R-MAN

1	0.10g/0.5ml hot H_2O; DD	a,c	C	crystallisation began after 10 minutes, while still warm. increased over another 30 minutes. many fine needles.
2	0.05g/0.5ml hot H_2O; DD	a	C	after 3 days, a few long, thin crystals : needles and a narrow elongated rectangular plate.
		d		after a month, dried up.
3	0.35g/1ml hot H_2O; DD	b,c	C	after ca. 20 minutes, crystals. collected by filtration and washing with H_2O. very thin, elongated, rectangular plates. ca. 0.5x0.05mm. essentially needles. occasionally some wider. some in fanlike clusters. mp. nmr.

ILE/S-MAN

1	0.1g/0.5ml hot H_2O; DD	a	C	overnight, small amount of crystals. probably recrystallised starting material.
		h 90°,f		
	+0.25ml H_2O	l,f	C	stirred to mix solvent. after a month, crystals on surface of solution. interpenetrating spikes.
2	0.05g/0.5ml hot H_2O: DD	a,d	C	after 3 days, one small, thin plate on surface. crystallisation on sides of vial by evaporation.
		k self,c	C	overnight, small crystals in solution. tiny needles and some rounded, non crystalline material, probably starting material.
3	0.1g/0.5ml hot H_2O; DD	c,i 60°	C	within a few hours, crystallisation of plates on sides of vial by evaporation.
		k self,a,d		floating short, thin, colourless, elongated, rectangular plates. sharp extinction.
4	0.35g/1ml hot H_2O; S	b,c	C	after 20 minutes. small amount of crystals. collected by filtration and washing with H_2O, tiny, very thin, elongated, rectangular plates 0.05x0.01mm. mp. nmr.

LEU/R-MAN

1	0.1g/0.5ml hot H_2O; S	a	C	within a few minutes, while still warm, many thin flakes. shiny when dry. mp. nmr.
2	0.05g/0.5ml hot H_2O; S	a	C	crystallisation began after a few minutes. after 30 minutes, many, tiny, thin flakes. volume reduced.
	+0.25 ml H_2Ol	l,h,i 40°	NC	
		c	NC	
		k ex1, d	C	crystallisation on sides of vial by evaporation.
		h		incompletely dissolved. crystallised as soon as removed from heat. small rectangular plates, patchy extinction.
3	0.05g/0.5ml hot H_2O	DR	a	NC
		k ex2,d	C	crystallisation on sides by evporation
		k self,c	NC	
4	0.05g/0.5ml hot H_2O; S	c,i 60°	NC	
		a	C	overnight, some crystallisation on sides by evaporation.

		k self, c	NC	
5	0.10g/1ml hot 5%EtOH; DD	a	NC	
		d	C	overnight, some crystallisation on sides of vial by evaporation.
		k self,c	NC	
		repeat	NC	
6	0.02g/1ml hot 50%EtOH; D	a	NC	
		d	C	overnight, some crystallisatiion on sides of vial by evaporation and some thin, floating plates.
		c	C	after 1 day, more crystals. thin and irregular flakes whose shapes are basically rectangles. extinction gradual along length of crystals.
7	0.10g/1ml 10%MeOH; DD	a	NC	
		d	C	after a few hours, small amount of crystallisation on sides of vial.
		k self, d	C	tiny amount of crystallisation on sides of vial and some floating plates and specks. increased in size and number overnight. plates in two shapes: elongated hexagon and trapezium. plates up to ca. 6mm long. often curved. not so thin as to show interference colours. extinction of ppl gradual over crystals. corresponds to bends in crystals.
8	0.1g/1ml hot H_2O; DD			
	+0.25ml EtOH	l,a	NC	(added to warm solution, no stirring to mix solvents)
		c		overnight, no change
	+0.25ml EtOH	l,c	C	no stirring. repeated twice more. after 3 hours, tiny elongated, hexagonal plates.
		c	C	overnight, increased in size and number. wide, elongated hexagonal and trapezoidal plates and some smaller crystals. interference colours, although plates do not look thin. many plates twinned, with plates growing through plates. sample collected by filtration and washing with EtOH. shiny, colourless flakes when dry. nmr. mp.
9	0.1g/1ml hot H_2O; DD			
	+0.25ml BuOH	l,b,c	NC	added while warm. 2 immiscible layers, butanol upper. aim : nucleation at interface. shaking only leads to a cloudy emulsion. layers separate within a few minutes.
10	0.1g/1ml hot H_2O; D			
	+0.25ml pet-eth	l,f	NC	added while warm. 2 immiscible layers. pet-ether upper. after 1 hour, top layer entirely evaporated.
	+0.25ml pet-eth	l,f	NC	layers separated rapidly after shaking. top layer evaporated
11	0.05g/1ml EtOAc	l		
12	0.1g/0.5mlhot H_2O; DD	a		
	+0.5mlEtOH	l,c	C	2 immiscible layers. EtOH upper. after 45 minutes, small number of spacks and flakes at interface, in EtOH layer. shaking did not immediately lead to further crystallisation. over a number of days, a little more crystallisation. thin, elongated hexagonal plates and irregular shaped specks.
13	0.1g/1ml hot H_2O; D	a		
	+0.5ml EtOAc	l,c	NC	after shaking, layers separated immediately. shaking repeated twice. layers separated more slowly.
14	0.05g/0.5ml hot H_2O; DD	a		slight cooling
	+1.5ml EtOH	l,c	C	left solvents to mix by diffusion. after a few hours ,crystallisation in lower third of the mixture and on surface. irregular flakes, broadly hexagonal. thin, interference colours seen under ppl. extinction is patchy. sample collected by filtration and washing with EtOH. shiny, colourless-white flakes. mp.
15	0.25g/1ml hot H_2O; DD			
	+0.2ml H_2O	l,b	C	within 5 minutes, crystals. tiny flakes, trapezoidal and triangular plates and some irregular flakes. nmr. mp.

1	0.1g/0.5ml hot H_2O; DD	a	C	many crystals in less than 10 minutes. many thin plates. some extinguish sharply. nmr. mp.
2	0.05g/0.5ml hot H_2O; D	a	C	crystallisation began after 5 minutes. tiny irregular plates and needles. fragile and thin. show interference colours.
		h,i 40°,f	C	after 2 hours, very thin and fragile elongated rectangular plates. extinction of ppl not sharp over entire crystal.
		h,i 50°, f	C	after 30 minutes, fragile rectangular plates and resulting irregular broken plates. sometimes, small plates stuck on a larger one.
3	0.05g/0.5ml hot H_2O; D	i 40°,f	NC	seed added while warm.
		a	NC	for a week
		k ex1,d	NC	after 2 days
		k ex1,d	NC	after a week, solvent mostly evaporated. some narrow elongated rectangular in solution, transferred to 4. remainder of product is moist, granular precipitate.
		h 90°,d		tended to sit on surface of water rather than to dissolve.
4	ex3+ H_2O			placed in a little water. did not dissolve initially. colourless. flexible, ragged, elongated plates. sharp extinction parallel to long axis. interference colours seen. 2.5x0.25mm. too flexible for structure determination.
		c		dissolved over time.
5	0.1g/1ml hot 50% EtOH: D	a,d	NC	
6	0.05g/1ml hot 50% EtOH: D	a,d	NC	after several days, clusters of tiny, elongated rectangular plates on sides of vial by evaporation
		k self,d	NC	
7	0.05g/1ml hot 10%MeOH; D	a	NC	
		d	C	after several days, tiny, elongated rectangular plates on sides of vial by evaporation
		k self, d	NC	
8	0.1g/1ml hot H_2O; D	a	NC	
	+0.5ml EtOH	l,c	NC	no shaking to mix. overnight.
	+0.75ml EtOH	l,c	C	no shaking to mix. after a few hours, elongated rectangular plates in lower half of solution. extinction gradual along length of crystals. thin and bent into a curve.
9	0.1g/1ml hot H_2O; D	a	NC	
	+0.25ml BuOH	l,c	NC	butanol immiscible upper layer.
		shaking	NC	slow separation of layers. repeated.
10	0.1g/1ml hot H_2O; D	a	NC	
	+0.25ml pet-eth	l,c	NC	pet-ether immiscible upper layer.
		shaking	C	rapid layer separation. tiny amount of crystals at interface.
		shaking	NC	slow separation of layers. no increase in crystallisation.
11	0.2g/1ml hot H_2O; D	a	NC	
	+0.25ml EtOH	l,c	C	EtOH immiscible upper layer.
		shaking,c	NC	slow separation of layers. small amount of crystals at interface.
		shaking,c	NC	slow separation of layers. no further crystal growth.
12	0.05g/1ml hot H_2O; D	a	NC	
	+1.5ml EtOH	l,c	C	no shaking to mix solvents. after several hours, long, wide trapezoidal flakes in the solution and on the surface. more elongated in solution. extinction gradual along crystal.
13	0.25g/1ml hot H_2O; DD	b,c	C	after 15 minutes small amount of crystals. grew in size and number for 15 minutes. collected by filtration and washing with EtOH and H_2O. elongated rectangular plates. tiny needles on faces.

	filtrate	d	C	collected sample by filtration and washing with EtOAc.

MET/R-MAN

1	0.7g/1ml boiling H_2O;D	b	C	within a few minutes much crystallisation. elongated rectangular plates ca.0.75x0.05mm. sample scooped out. sharp extinction. tiny rectangular plates on surface of plates by evaporation. sample collected by filtration for mp and nmr.
	recrystallisation of remaining product. aim: slower crsytallisation.			
	0.65g/0.5ml hot H_2O; D	l,h,k ex1,b	C	crystallisation began as cooled. long needles.
	+0.25ml cool H_2O	l	C	needles were elongated, triangular prisms. up to 20x2mm. probably not single crystals. striations along prisms through crossed polars.
	+0.25ml hot H_2O; D	l,h,a	C	after 30 minutes, needles as before.
	+0.25ml hot H_2O	l,h,a	C	after 30 minutes, large needles, actually bundles of elongated, rectangular plates. fragments mounted on glass fibre. structure determination. sample collected by filtration and washing with H_2O for powder diffraction.
2	0.3g/1ml hot H_2O; DR	b	C	after a few hours, very long (1cm) and thick, elongated, rectangular blocks. surfaces etched. extinction not sharp.
		h ,f,i0°,f,	C	thick rectangular blocks as before. no further work. structure determined using 1.
3	0.02g/0.6ml hot EtOH; l			
	+0.4ml H_2O; D	l,h,b	C	after a few hours, very thin, narrow, elongated, rectangular plates. frequently irregularly shaped, reflecting fragility. extinction not sharp.
		h,e_p,b	C	tiny amount of thin plates.
	+0.5ml H_2O	l,h,k ex2,b	NC	
4	recrystallisation of 1 after being covered with glycerol.			
	0.05g/0.5ml warm H_2O; DR	b,k ex2,d	C	after ca. 2 months, long elongated, rectangular plates.

MET/S-MAN

1	0.7g/1ml hot H_2O; DR	a	C	after a few minutes tiny crystals and rounded agglomerations of sample scooped out for mp and nmr. must have come intocontactwith glycerol before nmr.
	0.65g/1ml hot H_2O; DR	l,h,a	C	after a few minutes, tiny crystals. some product scooped out for recrystallisation in 4-8 below.
	0.32g/1ml hot H_2O	h,iRT,a,	C	large vial resting on top of heating block, not inside. rapid crystallisation. rounded precipitate and crystals.
	+0.25ml hot H_2O	l,h50°,k ex4,f	C	after a few minutes, crystallisation as before.
		i35°,RT,a	C	elongated, rectangular plates, ca. 0.45x0.12x0.05mm, mostly with tiny fragments adhering to them. others etched. interference colours observed because thin. some mounted on glass fibres.
	+0.5ml warm H_2O; DR	l,h,i RT,a	C	narrow, elongated, rectangular plates in double-fan clusters.
	+0.5ml warm H_2O; DR	l,h RT,a	NC	
		k ex2,	C	small, elongated, rectangular plates.
		h,a,k ex2	C	bundles of flat needles making up rectangular plates.
	readdition of product examined under microscope, left covered in glycerol to prevent drying out.			
		h,i RT,f	C	one small crystal, probably fallen from rim where there had been precipitation by evaporation.
		k ex3,d	C	elongated rectangular platesup to ca. 0.75x0.1mm. extinction sharp. 2 mounted.
		h,i RT,a	C	after 5 days, tiny elongated, rectangular plates. extinction gradual.
	+0.2ml warm H_2O; DR	l,h,iRT,a	C	overnight, tiny crystals.
	+0.2ml H_2O; DR	l,h,i 40°,d	C	tiny crystals.

2	0.3/1ml hot H_2O; DR	a	C	after a few hours, many small needles. mp
	+0.3ml warm H_2O; DR	l,h,b,d	C	after a few days, tiny needles on sides of vial by evaporation.
		h,a,d	C	after several days, all dried up. bundles of needles.
3	0.02g/0.6ml hot EtOH; I			
	+0.4ml hot H_2O; D		C	after a few hours, long, thin and very narrow needles and plates. fragile. some irregularly shaped crystals on account of fragility.
	recrystallisation of some of moist product of 1			
4	0.02g/0.5ml hot MeOH; I			
	+0.5ml H_2O, heating;D	l,b,k ex3,d	NC	
	+0.02g, hot; D	h,b,d	C	after two weeks, dry. tiny needles.
5	0.05g/1.5ml hot 33%EtOH; DR	b,k ex3,d	NC	
	+0.05g, boiling; D	h,b,d	C	after 2 weeks, precipitate on sides of vial by evaporation. subsequently, very narrow and some wider rectangular plates. extinction gradual along crystals.
6	0.05g/1.5ml 33%MeOH; D	b	NC	
	0.05g, warm; D	b,d	C	after 2 weeks, some of solvent evaporated, dry precipitate on sides of vial.
7	0.1g/1ml hot H_2O; DR	f,i 80°	NC	
		f,i 55°,k ex2	NC	
		repeated	NC	
		f,iRT	NC	overall, 1 day to reach RT
		k ex1,d	C	after a few days, solvent evaporated. dry needles in fan clusters.
	recrystallisation of 7			
	+1ml H_2O,97°;DR	l,h,a,iRT	NC	
		d	NC	for 5 days.
		k ex1,d	NC	
8	0.05g/1ml hot H_2O; DR	f,i 97-80°	NC	
		f,i 55°,k ex2	NC	(repeated seeding)
		f,i RT,k ex1	NC	
9	1.01g stock mixture			
10	0.2g/1ml hot H_2O; DR	b		within 30 minutes tiny elongated rectangular plates. in clumps closely packed together. some crystals kept back as seeds. sample for powder photography.
	+0.1ml H_2O; DR	l,h,f,i 50°	NC	during 2 hours.
		f,k self,i 35°	C	
		a,i 25,RT		to let cool. elongated rectangular plates, larger than in 11. extinction patchy.
11	0.2g/1ml hot H_2O;DR			
	+0.1ml EtOH	l,b		within 30 minutes, tiny elongated rectangular plates suspended throughout the solution. extinction patchy.
	+0.1ml H_2O; DR	l,h,f,k ex10	C	after 15 minutes, crystallisation at the surface.
		iRT,a	C	stepwise cooling. more crystals. small, elongated, rectangular plates. extinction not sharp. actually needle crystalites forming a plate. ends of plates ragged.

PHE/R-MAN

1	0.05g/1ml hot H_2O; DD	a	C	after 1 hour, tiny needles. after 1 day, clusters of thin, elongated trapezium-shaped plates. sharp extinction. mp. nmr. crystal structure determination.
2	0.05g/1.5ml hot H_2O; DD	a,k ex1,c	C	after 2 weeks, large elongated plates.

PHE/S-MAN

1	0.05g/1ml hot H_2O; DD	a	C	after 1 hour, short, thick needles which grew in size and number to give two types of crystals. Thin plates, which extinguished and thicker lamellar plates which did not extinguish because they consisted of plates stacked on plates in slightly different orientations. nmr.
2	0.05g/1ml hot H_2O; DD	a	C	one large parallelopiped 7x3x2mm and one smaller.
		c		increased in number. large crystals.
3	0.05g/2ml 50%EtOH; DD	l,h	NC	
4	0.05g/1ml hot H_2O; DD			
	+0.2ml EtOH	l,a	C	after 30 minutes, large, thick, lamellar, rectangular plates as in 1. faces became etched over time.
5	0.05g/1ml hot H_2O; DD			
	+0.5ml EtOH	l,a	NC	
		k ex4,c	NC	
6	0.05g/1.5ml hot H_2O; DD			
	+0.3mlEtOH	l,a	C	overnight, a few big crystals. grew larger over time. too large for structure determination.
7	0.05g/1ml hot H_2O; DD			
	+0.35mlEtOH	l,a,k ex4	C	seeded while still warm. immediate crystallisation. lamellar plates. unsuitable for structure determination.
8	0.05g/1ml hot H_2O;	DD		
	+0.2mlEtOH	l,a	NC	
		k ex7,c	C	overnight, many lamellar plates. rectangular and wedge-shaped. no extinction.
9	0.05g/1ml hot H_2O; DD	a,k ex9	C	two crystals on side above waterline. pushed into solution after 45 minutes many tiny plates also. grew to suitable size over a few hours. xray photographs showed diffraction only out to a low θ-value.
10	0.05g/1ml hot H_2O; DD	k ex8,a	C	after 15 minutes small rectangular plates. no extinction.
11	0.05g/1ml hot H_2O; DD			
	+0.3ml EtOH	l,a	C	overnight many plates in a clump. faces etched. no sharp extinction.
12	0.05g/1ml hot H_2O; DD			
	+0.3ml EtOH	l,k ex8,a	C	large etched rectangular plates in a clump. no sharp extinction of ppl.
13	0.02g/1ml hot H_2O; DD	a	C	long, chunky spikes.
14	0.02g/1ml hot H_2O; DD			
	+0.3ml EtOH	l,a	NC	
15	0.02g/1ml hot H_2O; DD	a	NC	
		k ex7	C	after a few hours tiny crystals. became elongated rectangular plates. many long and narrow. medium sized rectangular plate, wider than many others. crystal structure determination.
16	0.02g/1ml hot H_2O; DD			
	+0.3ml EtOH	l,a	NC	
		k ex7	C	long spikes, narrower than in 15.

PHG/R-MAN

1	0.6g/30ml hot H_2O; DD	b	C	removed some undissolved PHG. after a few minutes, crystallisation as needles in clusters. sample collected by filtration and washing with H_2O. final appearance, slippery, shiny, white flakes. sparingly soluble in H_2O. mp.

PHG/S-MAN

1	0.6g/30 ml hot H_2O; DD	b	C	removed some undissolved PHG. after a few minutes, crystallisation as needles in clusters. sample collected by filtration and washing with H_2O. final appearancs, slippery, shiny, white flakes. sparingly soluble in H_2O. mp.

PRO/R-MAN

1	0.25g/0.7ml hot H_2O; DR	a	NC	solution yellow-brown in colour, probable decomposition
		d	NC	
2	0.15g/warm H_2O; DR	d	NC	solution light brown in colour, probable decomposition.
		d	NC	
3	0.9g/3ml hot H_2O;DR	s	NC	
		d	NC	
		e_p,d	NC	
		e_p,d	NC	
		m,d	NC	
		g	NC	
4	0.9g/0.3ml hot H_2O; DR	b	NC	viscous solution
		m,j	NC	

PRO/S-MAN

1	0.25g/0.7ml hot H_2O; DR	a	NC	solution yellow-brown in colour, probable decomposition.
		d	NC	
2	0.15g/warm H_2O; DR	a	NC	solution light-brown in colour, probable decomposition.
		d	NC	
3	0.90g/3ml hot H_2O; DR	a	NC	
		d	NC	
		e_p,d	NC	
		m,d	NC	
		g	NC	
4	0.85g/0.5ml hot H_2O	b	NC	viscous solution
		m,d	NC	
		j	NC	

VAL/R-MAN

1	0.25g/0.7g hot H_2O; DR	a	C	crystallisation began after 30 minutes. mass of fine needles
		f,h 90°		
		i 60°	NC	
		i 40°	C	needles
		h		
		i 70°	C	needles
	make up to 1ml	l,h		
		k ex2,c	C	narrow elongated rectangular plates. 1cm long. extingiushed as twins joined along needle axis. nmr.
2	0.1g/0.5ml hot H_2O; DR	a	NC	

		d	C	small amount on sides of vial by evaporation. self seed.
		k self, c	C	after 3 months, narrow elongated, rectangular plates. 1cm long. some tiny needles.
3	0.15g/0.5ml hot H_2O; D	a	NC	
		d	C	after a week, tiny crystals on sides of vial. self seed.
		k self,c	C	after two days, irregularly-shaped plates.
		h,i,d,i,d	NC	
		i,d	C	tiny crystals on sides of vial by evaporation. self seed. narrow, elongated, rectangular plates in clusters.
4	0.15g/0.5ml hot 5% EtOH; DD	a	NC	
		k ex1,c	NC	
		d	C	after a week solvent evaporated to leave mass of fine needles. also much precipitation sides of vial. removed to leave ca. half original quantity.
	ca. 0.1g/0.5ml hot 5% EtOH; D	l,a	NC	for several hours
		f	C	after a week, one crystal on side of vial by evaporation.
		k self,f	NC	
		d	NC	
		e_b,i RT,b	NC	
		d	C	after 3 days, mass of fine needles. mp.
5	0.35g/1ml hot H_2O; D	i RT,a	NC	for 1 week
		k ex3,f	C	after 1 week, needles on sides of vial by evaporation self seed.
		k self,f	NC	overnight
		k self,f	C	overnight, small amount long, fine needles.
6	0.1g/1ml hot H_2O; D	i RT,b	C	many needles in the solution. mp.
7	0.1g/0.5ml hot H_2O; D	d	NC	let cool slightly
	+0.75ml EtOH	l,a	C	no stirring to mix. after a few minutes, elongated rectangular plates. 0.5x0.1mm. extinction crystals growing out of one another.
8	0.1g/0.5ml hot H_2O; D	d	NC	let cool slightly.
	+0.5ml EtOH	l,a		no stirring to mix. after a few minutes narrow elongated rectangular plates up to 1.5x0.13mm in size. many tiny similarly shaped plates by evaporation when vial opened. nmr. data collection. shown to be L-VAL.
9	0.1g/0.5ml hot H_2O; D	a	NC	let cool slightly
	+0.25ml EtOH	l,a,	C	after a few minute elongated rectangular plates in clusters. length up to ca. 1mm. width frequently wider than in 8.
10	0.15g/0.5ml hot EtOH; DR	a	C	a few elongated rectangular plates
	+0.25ml EtOH	l,c	C	immediately, tiny crystals at interface. (liquids not mixed yet). shaken, many tiny rectangular plates throughout. over time, settled thickly on base. smaller and larger narrow, elongated, rectangular plates. nmr. recrystallised in 12 and 13.
11	0.1g/0.5ml 50%EtOH; DR	a	NC	
	+0.5ml EtOH	l,c		when cool, EtOH added. liquids did not mix fully immediately. EtOH as layer on top. immediately needles at interface. one long, others smaller. increased in size and number to give elongated rectangular plates.,ca. 1x0.05mm. extinction gradual over plates. mp.
12	recrystallisation of some of 10 after filtration and washing with EtOH to give shiny, white flakes.			
	0.02g/0.5ml hot H_2O; DR	c	NC	let cool slightly
	+0.25ml EtOH	l,b	NC	
	+0.2ml EtOH	l,k ex10,d	C	small amount of crystals on sides of vial by evaporation.
		k self,j	NC	
13	recrystallisation of some of product of 10. crystals scooped out of vial. no filtration.			

	0.05g/1ml H_2O; DR	d	NC	
14	0.25g/1ml hot 5%EtOH; D	a	NC	
+0.5ml EtOH		shake,c	C	immediate appearance of tiny specks and flakes. over a few minutes, increased in size and number. overnight, great deal of crystallisation. most of product collected by filtration. elongated rectangular plates, 0.1-0.15mm wide. extinction patchy along crystals. cut a plate to get a piece of single crystal, 0.75x0.1mm. oscillation photograph. mp.
15	0.25g/1ml hot H_2O; DR	a,i RT	NC	reduced temperature gradually over 4 hours.
		e_p,i 55°	NC	left for several hours.
		e_p,i 80°	C	after two hours, some crystallisation by evaporation. used as seeds.
		k self,i RT,a	C	overnight, needles and elongated rectangular plates, ca. 0.05mm wide. collected by filtration and washing with EtOH.

L-VAL/S-MAN

1	0.25/0.7ml hot H_2O; D	a,c	C	overnight, mass of fine needles, ca. 0.2cm long. some extinction. nmr.
2	0.1g/0.5ml hot H_2O; D	a,c	C	after three days, narrow,elongated, rectangular plates, ca. 3mm long. thin, show interference colours. also some shorter needles in a mass.
3	0.15g/0.5ml hot H_2O; D	a,k ex1,c	NC	left overnight.
		k ex1,d	C	after a week, small amount of crystallisation on sides of vial by evaporation.
		h	C	small amount of crystallisation on sides of vial by evaporation.
		k self,d	C	after a few hours. elongated rectangular plates, 1x0.05mm. some extinction. too small to be useful.
	+0.2ml H_2O	l,h,a,d	NC	left for two days.
		d	C	crystallisation on sides of vial by evaporation.
		k self,d	NC	left for three days.
		h,i 90°,f	NC	some decomposition to a brown solution.
		i 60°,f	C	over a few minutes, crystallisation began. narrow, elongated, colourless, thin, rectangular plates.
4	0.15g/0.5ml hot 5% EtOH; DD	a,k ex1,c	NC	left overnight.
		k ex1,d	C	after a week, small amount of crystallisation on sides of vial by evaporation.
		h	C	small amount of crystallisation on sides of vial by evaporation.
		k self,d	C	after a few hours. elongated rectangular plates, 1x0.1x0.01mm. extinction in ¢waves¢ along crystals. mp.
5	0.1g/0.5ml hot H_2O; D over several hours.	a,i 60°	NC	gradual cooling
		d	C	after two weeks, crystallisation on sides of vial by evaporation. some thin plates in solution, which show interference colours. equilateral triangles and trapezia. many are cracked so extinction patchy in these. others, sharp extinction. lamellar. mounted triangular plate parallel to one edge. no photographs nor data collection, because mp similar to L-VAL/R-MAN and it proved to be L-VAL. mp.

ARG/R-MAN

1	1.1g/2ml hot H_2O; DR	b,d	NC	overnight
		e-(p),b d	NC	left for a week
		k ex3,g	C	(product of 3 later taken to be ARG) within a few minutes, much cream-coloured precipitate. probably ARG, which is cream in colour.
2	1.1g/1ml hot H_2O; DR	b,d	NC	left for 4 days.

		m,d		left for 4 days.
		k ex3,g	C	within a feew minutes, small amount of crystals.
		c	C	overnight. fair amount of cream-coloured crystals in a gel. probably ARG.
3	1.1g/0.5ml hot H_2O; DR	b,d	NC	viscous solution.
		m,j	C	fine needles in a gel.needles very soluble in H_2O, sparingly soluble in EtOH. tried to collect sample by filtration and washing with EtOH, but needles inseparable from gel. evaporation in a warm oven did not help. no nmr etc done therefore. did use as seeds, crystals and gel scooped out directly. later decided product probably ARG.
	recrystallisation of 3			
	+0.5ml H_2O; DR	l,b,d		after a week, many cream-coloured needles. presumably ARG.
4	0.65g/0.5ml warm 5%EtOH; DR	g	NC	

ARG/S-MAN

1	1.1g/2ml warm H_2O; DR	b,d		left overnight.
		e_p,d	NC	left for a week.
		g	NC	
2	1.1g/1ml hot H_2O; DR	b,d	NC	left for 2 days.
		m,d	NC	left for 4 days.
		g	NC	
3	1.1g/0.5ml hot H_2O; DR	b,d	NC	viscous solution.
		m,j	NC	
4	0.65g/0.5ml warm 5%EtOH; DR	g	NC	

CYS/R-MAN

1	0.10g/0.5ml hot H_2O; DR	a	NC	for 5 days
		d	NC	for two days
		k ex2,d	NC	for 5 days
2	0.15g/0.7ml hot H_2O; DR	a	C	white needles on sides of vial by evaporation. increased in size and number. 2xmp.
		k ex2, d		after several days, dry. small, fine needles and long thick needles as long as the vial was wide. 2xmp. after one month, decompostion.
3	0.2g/1ml hot H_2O;DR	a	C	after 30 minutes, thin rectangular plates. too thin for structure determination. mp.
4	recrystallisation of some of product of 3, more dilute.			
	0.05g/0.5ml hot H_2O; DR	a	NC	
		k ex3, c	NC	seeds dissolved. (repeated seeding. NC)
5	0.15g/1ml hot H_2O; DR	a	NC	overnight
		k ex3, d	C	overnight, cluster of elongated rectangular plates. some quite wide.
6	0.20g/1ml warm H_2O; DR	b,d	C	after two days, some irregular, elongated, rectangular plates on sides of vial by evaporation.
		k self,d	NC	after three weeks, no further crystallisation. decomposed to give a brown solution.
7	0.35g/1ml hot H_2O; DR	b,d	C	after two days some solvent had evaporated and there were many long, cream coloured crystals in bundles. they were elongated rectangular plates of various widths, thin, showing interference colours. sharp extinction. in a sample scooped out on to a slide evaporation of solvent produced tiny needles rapidly.

		c	NC	after three weeks, no further crystallisation. decomposed to give a brown solution. nmr.

CYS/S-MAN

1	0.10g/0.4ml H_2O; DR	a	NC	after 5 days
		k ex2,d	C	after aweek, tiny crystals.
		c		after a month, brown solution, cream-coloured precipitate.
2	0.15g/0.7ml hot H_2O; DR	a	C	white fat needles. unsuitable for structure determination because some crystals grow out of others. mp. after a month, decomposition.
	recrystallisation of some of product of 2			
3	0.05g/0.3ml hot H_2O; DR	a	NC	
		k ex2, c	NC	overnight seeds dissolved.
		k ex4, d	NC	overnight seeds dissolved
		k ex4,d	C	after a week most of solvent evaporated. small, thin needles.
		c		after three weeks, cream-coloured precipitate, slight decomposition.
4	0.15g/min hot H_2O; DD	a	NC	
		k ex2, c	C	immediately a small amount of tiny, thin, elongated rectangular plates .after a few minutes, many crystals. all thin plates. some elongated rectangular, some irregular. 3xmp
	recrystallisation of some of product of 4. aim: slower crystallisation from slightly more dilute solution			
5	0.1g			
	+min warm H_2O; DD	a	NC	
		k ex4,c	C	rapidly, elongated needles floating on surface. after a few hours, also a few needles on the base.
		c		after a few hours, no change
		d		overnight, thickened into needles. some are clearly hexagonal about the needle axis. needles and thin plates on sides of vial.
		c		overnight increased in number. pushed into solution. after 3 weeks, solution yellow. decomposition. cluster of fat needles in the solution with encrustation on the surface.
	recrystallisation of some of product of 4			
6	0.1g			
	sm. amt hot EtOH; l			
	+H_2O to ca. 50%EtOH	l,a	NC	H_2O added until mixture soluble.
		k ex4, a	NC	still warm. seeds dissolved.
		k ex4, a	NC	seeds dissolved.
		k ex4, c	NC	seeds dissolved.
		j	NC	
7	0.3ml soln ex6			
	+0.3ml EtOH	l,drpwse,c	NC	
		k ex4,c	NC	after a few hours
		j	NC	overnight seeds dissolved
		k ex4,j	NC	no change
8	0.2ml soln ex6			
	+0.7ml EtOH	l drpwse	NC	
		k ex4,j	NC	after a few hours
		j	NC	overnight, seeds dissolved
		k ex4,j	NC	overnight, no change

		d	NC	
		k ex4, d		after 3 weeks solvent evaporated. dry material on vial. (not crystals).
9	0.1g/1ml hot 5%EtOH; DR	a	NC	initially no change. after 3 weeks, brown solution. granular precipitate. decomposition.
10	0.1g/1ml hot 90%EtOH; I	b	C	solvent evaporated to leave dry starting material.
11	0.1g/1ml hot 85%EtOH; I	b	C	after 5 days, solvent evaporated to leave dry starting material
	+1ml hot 50%EtOH; I	b		after 3 weeks, undissolved material turned yellow.
	recrystallisation of some of product of 4			
12	0.1g/1ml hot H_2O; D	f,i,30°		almost all dissolved after 30 minutes, no further dissolution. no deposition of crystals.
		d	C	after 3 weeks, dried, yellow precipitate. decomposition.
13				recrystallisation of some product from 4
	0.05g/0.5ml dil NaOH; D	l,f,i,30°	NC	pH rose from 2.61 to 4.44.
		k ex4,d	NC	repeated
		d	C	dried to a brown precipitate, some solution remaining. decomposition.
14	0.15g/1ml hot H_2O; DR	a	C	within 30 minutes, many crystals on base and at surface. thin elongated rectangular plates. probably too thin for crystal structure determination. mp.
15	0.02g/0.4ml hot H_2O; DR	a	NC	
		k ex14,d	NC	seeds dissolved. repeated several times. same result.
16	0.2g/1ml warm H_2O; DR	b	C	after an hour, a few small elongated rectangular plates floating on the surface.
		c		after two days, increased in size and number. crytals on base were elongated rectangular plates ca. 2.25x0.3mm loosely stacked in bundles. easily separable into platesm which are thin and show interference colours. sharp extinction. nmr. mp. crystals on surface were more variable in size than those on base, some had ragged narrow edges and some were etched. size ca. 1x0.15mm.
		c	NC	after three weeks, no further crystallisation. decomposed to give a brown solution.
18	0.15g/0.5ml hot H_2O; DR	b,d	C	after two days, some large colourless plates, stuck together face to face, floating on the surface. rhombus shaped, some 4.5mm along the edge and some half this size. as soon as a sample was removed from solution it turned white on the surface with evaporation to form tiny plates. in solution also, tiny plates appeared because of evaporation. a plate was cleaned as far as possible by wahing in glycerol. a sample of each of plates and tiny crystals was kept for nmr and mp.

HIS/R-MAN

1	1g/3ml hot H_2O; DR	a	NC	left until cool
		d	NC	left overnight
		e_p,b,d	NC	left for 3 days
		m,d	NC	
		j	NC	
2	1g/1.1ml hot H_2O; D	a		within 2 days, viscous solution.
		m,j	C	tiny amount of dry powder on sides of vial by evaporation.
		k self,j	C	after 4 days, long needles in gel. needles water soluble, insoluble in EtOH. unable to separate from gel for further analysis. probably histidine.
3	0.6g/0.6ml hot 5%EtOH; DD	b	NC	(a few undissolved particles)
		g	C	small amount of crystallisation. long rectangular plates and clumps of tiny needles. solution viscous, but less so than 2. crystals soluble in H_2O, insoluble in EtOH and $CHCl_3$. crystals inseparable from the viscous solution, which would not wash away with EtOH or $CHCl_3$.

HIS/S-MAN

1	1.g/3ml hot H_2O; DR	a	NC	left until cool
		d	NC	left overnight
		e_p,b,d	NC	left for 3 days
		m,p	NC	left for 4 days
		g	NC	
2	1g/1.1ml boiling H_2O; DD	b	NC	within 2 days viscous solution.
		m,j	NC	
3	0.6g/0.6ml hot 5%EtOH; DD	b	NC	a few undissolved particles
		g	NC	

LYS.HCl/R-MAN

1	1.1g/2ml warm H_2O; DR	b,d	NC	left overnight
		e_p,b,d	NC	left for 2 days
		k ex3,d	C	after a few minutes, thin approximately rectangular flakes ca. 3mm in length. extinction of ppl. probably too thin for structure determination. sample collected by filtration and washing with H_2O. nmr.
2	1.2g/1ml warm H_2O; DR	b,d	NC	left overnight.
		k ex3,d	C	within a few minutes, thin flakes. collected entire product by filtration.
	recrystallisation of wet product from a more dilute solution.			
	0.2g/1ml warm H_2O; DR	b,k ex1,d	NC	left for a day.
		f	C	after a month, solvent all evaporated. a dry white-colourless rhombus-shaped plate 0.5mm thick, with diagonals 2.5 and 3.5mm. extinction along diagonals. single crystal. nmr. mp. also, dry white powder, consisting of elongated plates with a pair of faces parallel with fragments adhering. extinction parallel and perpendicular to the pair of edges. single crystals.
3	1.1g/0.5ml hot H_2O; DR	b		as cooled. gel with small dry crystals on top. scoops of powder and gel used to seed 1 and 2.
4	0.65g/1.5ml hot EtOH; I			
	+0.5ml hot H_2O; D	l,h,b,d	C	after a week, much crystallisation. tiny plates.

LYS.HCl/S-MAN

1	1.1g/2ml hot H_2O; DR	b,d	C	overnight, some crystallisation. thin parallelogram-shaped plates with rounded corners and thin triangular plates. interference colours shown because thin. patchy extinction, sample scooped out for nmr and mp.
	recrystallisation of some of product of 1			
2	0.05g/1ml warm H_2O; DR	e_p,b,d	C	dried material at rim.
	k self			rapid crystallisation.
3	0.65g/1.5ml boiling EtOH; I			
	+0.6ml H_2O; D	l,h,b,d	C	after 2 days, one large opaque triangular prism in the solution. extinction in definite regions. there is a rhombus shaped prism and two triangular prisms making up the complete crystal.
		d	C	much crystallisation of tiny crystals all through the solution.

SER/R-MAN

1	0.2g/1ml hot H_2O; DR	b,d	C	after a few hours, 2 large agglomerations of rectangular plates stacked with plate faces parallel and oriented some in one direction and some at right angles. separated individual plates from one group. rapid appearance of rhombus-shaped plates 0.1mm across. filtered to collect product. most dissolved on washing with H_2O. obtained only one large, thin rectangular plate with a tiny rhombus-shaped plate stuck to it. mp.
2	0.15g/1ml v hot H-(2)O; DR	b	NC	
	addition of more of stock mixture			
	+0.1g; DR	h,b,d	C	after a week, one tiny crystal.
		d		solvent evaporated to leave needles and one large plate. dry precipitate around rim.
3	0.2g/1ml hot 5%EtOH; DR	b,d	C	after week, a few thin plates.
4	0.05g/1ml boiling 50%MeOH; D	b,d	NC	left for a week.
5	0.1g/1ml hot 50%EtOH; D	b,d	C	a tiny quantity of crystallisation on sides of vial by evaporation.
6	0.05g/1ml hot 50%iPrOH/H-(2)O; D	b,d	NC	left for a week.
7	1.25g/0.65ml hot H_2O; D	b	C	H_2O added gradually to just dissolve solid. much precipitation throughout entire solution of tiny crystals.
	+0.075ml H_2O; DR	l,h,a	C	overnight, precipitation as before.
	+0.15ml H_2O; DR	l,h,a	C	overnight small amount of similar crystals. over a few days, more crystals.
	+0.15ml H_2O; DR	l,h,a	C	after an hour, very narrow, elongated plates, up to 0.5mm in length. small amount removed for examination under a microscope under glycerol. tiny plates were also observed. hard to separate the two sorts.
	+0.5ml H_2O; DR	l,h,a	NC	left for an hour and 10 minutes.
		d	C	after 15 minutes, because of evaporation at the surface, tiny rhombus shaped plates began to form, up to 1mm in length.
		d	C	after 10 days, crystals had grown in size and number. a sample was collected by filtration and washing with H_2O. They were colourless, fragile fragments of trapezia and parallelograms up to 3-4mm across. sharp extinction. thin: a few showed interference colours. mp.

SER/S-MAN

1	0.2g/1ml hot H_2O; DR	b,d		after a few hours, fairly large parallelogram-shaped plates, adhering to one another. plates were single crystals.
		d	C	within a few hours, also thin, rhombus-shaped plates. collected by filtration. mp.
2	0.15g/1ml very hot H_2O; DR	b	NC	
	addition of more of stock mixture			
	+0.1g; DR	b,d	C	after a week, thin elongated, hexagonal plates. dry precipitate on rim.
3	0.2g/1ml hot 5%EtOH; D	b,d	NC	left for a week.
4	0.05g/1ml hot 50%MeOH; D	b,d	NC	left for a week.
5	0.1g/1ml hot 50%EtOH; D	b, d	NC	left for a week.
6	0.05g/1ml hot 50%iPrOH; D	b,d	NC	left for a week.
7	1.25g/0.65ml hot H_2O; D	b	C	H_2O added gradually to just dissolve solid. much precipitation throughout entire solution of tiny crystals.
	+0.075ml H_2O; DR	l,h,a	C	overnight, precipitation as before.
	+0.15ml H_2O; DR	l,h,a	C	overnight small amount of similar crystals. over a few days, more crystals.
	+0.15ml H_2O; DR	l,h,a	C	after an hour, very narrow, elongated plates, up to 2mm in length. small amount removed for examination under a microscope under glycerol. tiny rhombic plates were also

				observed. hard to separate the two sorts.
	+0.3ml H_2O; DR	l,h,a	NC	left for an hour.
		d	C	after 15 minutes, because of evaporation at the surface, tiny rhombus shaped plates began to form, up to 2mm in length. mp.
		d	C	shook gently before left still for five minutes. crystals grew slightly.
		c	C	crystals grew in size and number over 10 days. sample collected by filtration and washing with H_2O. They were colourless, fragile fragments of trapezia and parallelograms up to 2-3mm across, smaller fragments than in SER/R-MAN7. sharp extinction. thin: a few showed interference colours.

THR/R-MAN

1	0.4g/1ml hot H_2O; DR	a,i RT	C	within a few hours, tiny elongated, hexagonal, lamellar plates.
		c	C	overnight, grew in size and number. collected sample by filtration and washing with H_2O. crystals now larger with some wide as well as elongated. all are a little irregular, suggesting they are fragile. sharp extinction. mp. nmr.
2	0.4g/0.5ml hot H_2O; DR	b,d	C	dry powdery precipitate collected on rim of vial, and dry needles and plates at the base. some solution had spilled and the remainder evaporated. nmr. mp.
3	0.05g/1ml hot 50%EtOH; DR	b,d	NC	
4	0.20g/1ml warm H_2O; DR	b	NC	over two days.
		d	C	over two weeks, solvent evaporated to leave large, elongated, rectangular plates. precipitate on the rim was removed and the vial stoppered to preserve the crystals.
5	0.45g/1ml hot H_2O; D	b	C	solvent was added gradually to just dissolve the solid. crystals, needles, appeared on the surface after 15 minutes.
		c	C	over an hour, more and larger crystals, narrow rectangular plates, up to 2mm in length. a sample was collected by filtration and washing with H_2O contained needles and rectangular plates. Plates were either irregular hexagonal or triangular flakes. they were fragile, with many fragments. needles and plates were thin and up to 1.5mm in length. plates and needles were separated by hand for nmr and mp.

THR/S-MAN

1	0.45g/1ml boiling H-(2)O; DR	a,i RT	C	within a few hours, tiny elongated hexagonal lamellar plates.
		c		overnight, increased in size and number. sample collected by filtration and washing with H_2O. sharp extinction. mixture of chunky needles and elongated rhombic prisms and rhombic and triangular plates. mp. nmr.
2	0.4g/0.5ml hot H_2O; DR	b,d		dry, powdery, precipitate around rim and large needles and plates in the solution, some of which had been spilled. mp.
3	0.05g/0.5ml hot 50%EtOH; DR	b,d	NC	
4	0.20g/1ml warm H_2O; DR	b	NC	over two days.
		d	C	over two weeks, solvent evaporated to leave large, elongated plates on the base and dry precipitate on the sides which was removed and the vial stoppered to preserve the crystals. crystals were wide elongated rectangular plates up to 3mm in length, often fragmented and with extinction which was not sharp. one trapezium shaped plate with sharp extinction and of dimensions 0.8x0.35mm. 2xmp of this plate.
5	0.45g/1ml hot H_2O; D	b	C	solvent was added gradually to just dissolve the solid. crystals, needles, appeared on the surface after 15 minutes.
		c	C	over an hour, more and larger crystals, narrow rectangular plates, up to 2mm in length and wider than in THR/R-MAN5. a sample was collected by filtration and washing with H_2O contained needles and plates. Plates were either irregular hexagonal or trapezium-shaped flakes. they were fragile, with many fragments, and less well formed as THR/R-MAN5. needles and plates were thin and up to 1.5mm in length. plates and needles were separated by hand, with some

difficulty. mp of each ad nmr of plates. similar in morphology to the products THR/R-MAN5, which indicates that the result wasthe same in both cases.

TYR/R-MAN

1	0.05g/2ml hot H_2O; PD	a	C	as cooled, tiny, fine needles recrystallised. probably mandelic acid. (TYR the less soluble part of the mixture.)
2	0.005g/2ml boiling H_2O; PD	a	C	after 3 days, medium legnth fine needles. again probably mandelic acid. (TYR less soluble than MAN)

L-ALA/(-)-CSA

1	stock mixture			
2	0.1g/1ml hot H_2O; DR	g,b,d	NC	gel
3	0.15g/0.5ml hot H_2O; DR	g,b,d	NC	gel
4	0.1g/0.5ml hot EtOH; D	g,b,d	NC	gel
5	0.05g/0.5ml hot acetone; PD			
	+0.1ml H_2O; D	l,h,b,d	NC	gel

L-ALA/(+)-CSA

1	stock mixture			
2	0.1g/1ml hot H_2O; DR	g,b,d	C	after a month, a few thin fragments of rectangular plates in a gel.
		c		no change.
3	0.15g/0.5ml hot H_2O; DR	g,b,d	C	after a month, a few thin fragments of rectangular plates in gel.
		c		no change.
4	0.1g/0.5ml hot H_2O; DR			
	+0.5ml hot EtOH	l,g,b,d	C	after a month, a few thin fragments of rectangular plates with etched faces in a gel.
		c		no change
5	0.05g/0.5ml hot acetone; PD			
	+0.1ml H_2O; D	l,h,g,b,d	C	after a month a few thin fragments of rectangular plates arranged in a feathery pattern in a gel.

GLY/(+)-CSA

1	stock mixture			
2	0.35g/0.5ml hot H_2O; DR	b,d	NC	left for a week
		n	NC	left for a week
		d	C	after two days, gel with crystallisation on sides of vial as moist, thin, irregular film and thin, irregular plates on surface of gel. mp. of film.
3	0.15g/1ml hot H_2O; DR	n,b,d	NC	left for a month
		k ex2, d	NC	(seeded with a scoop of gel and tiny crystals). left for four days.
		k ex2, d	C	left for seven weeks, thick white irregular shaped crystals. extinction not sharp. not single.
4	0.1g/0.5ml hot H_2O; DR	n,b,d	NC	left for four days.
		k ex2, d	NC	(seeded with a scoop of gel and tiny crystals). left for four days.
		k ex2, d	C	after seven weeks, small amount of crystallisation.

		j		
5	0.05g/1ml hot 50%acet.; DD	n,b,d	NC	after four days, gel with feathery crystals around tiny granules.
		d		dry, small, feathery needles.

L-ILE/(-)-CSA

1	stock mixture			
2	0.1g/1ml hot H_2O; DR	g,b,d	NC	gel
3	0.1g/0.5ml hot H_2O; DR	g,b,d	C	after a month, a few long, thin, elongated, rectangular plates in a gel.

L-ILE/(+)-CSA

1	stock mixture			
2	0.1g/1ml hot H_2O; DR	g,b,d	C	after a month, white gel consisting of tiny crystals in fan-shaped arrangements in a gel.
3	0.10g/0.5ml hot H_2O; DR	g,b,d	NC	gel

L-LEU/(-)-CSA

1	stock mixture			
2	0.1g/1ml hot H_2O; DR	g,b,d	C	after a month, clear colourless gel and, on sides of vial, small amount of gel with tiny crystals, which appears white.
3	0.10g/0.5ml hot H_2O; DR	g,b,d	C	after a month, colourless gel and, on sides of vial, small crystals, which appears white.

L-LEU/(+)-CSA

1	stock mixture			
2	0.1g/1ml hot H_2O; DR	g,b,d	C	after a month, white powder on surface of a gel with thin plates in the gel.
		c		no change
3	0.10g/0.5ml hot H_2O; DR	g,b,d	C	after a month, small, elongated, narrow, rectangular plates arranged in fans in a gel.

L-MET/(-)-CSA

1	stock mixture			
2	0.7g/1ml hot H_2O; D	b,d	NC	left for 3 days.
		g	C	after 3 weeks, gel with long, thick, elongated, rectangular plates, and some thinner ones.
3	0.7g/1ml hot 5%EtOH/H_2O; D	b,d	NC	left for 3 days.
		g	c	after 3 weeks, long, thick, elongated plates, not quite rectangular, wider than in (2), in gel. crystals have rounded edges, are and surfaces are white. after checking that crystals are not rapidly soluble in H_2O, collected entire product by filtration and washing with H_2O. nmr. mp.
4	0.25g/1ml hot 50%EtOH; D	b,d	NC	left for 3 days.
		g	NC	after 3 weeks, gel.

L-MET/(+)-CSA

1	0.25g/0.2ml hot H_2O;D	b,d	NC	overnight, formation of a gel.
		m,d	NC	left overnight.
	0.1ml	l,d	NC	left overnight.
	0.1ml	l,g	NC	within 3 weeks, formation of a gel.
		g	C	after 3 weeks, fan shaped arrangement of elongated crystals.
2	0.7g/1ml boiling H_2O; D	b,d	NC	left overnight.
		m,d	NC	after two days, no change.
		g	C	rectangular blocks in gel. collected by filtration and washing with H_2O. some dissolved, some used as seed in (3). sharp extinction. cut a chunk to a better size for structure determination. mp.
		k,self,m,d	C	overnight, formation of tiny plates throughout gel.
3	0.7g/1ml boiling 5%EtOH/H_2O	b,d	NC	left overnight.
		m,d	NC	left for two days, no change.
		g		after 3 weeks, gel.
		k ex2,m	C	overnight, formation of tiny plates in an area of the gel.

L-PHE/(-)-CSA

1	0.45g/4ml hot H_2O; DR	a,c	NC	left for 5 days.
		d	NC	left for 6 days.
		c	NC	left for 3 weeks.
		e_p,b,d	NC	left for 6 days.
		g	NC	after 4 days, gel.
		m,d	NC	
	+0.05ml EtOH	l,m,c	NC	
2	0.45g/4ml warm 5%EtOH; DR	a,c	NC	left for 5 days.
		d	NC	left for 6 days.
		c	NC	left for 3 weeks.
		e_p,b,d	NC	left for 8 days.
		g	NC	within 4 days, gel.
		m,d	NC	
	+0.05ml EtOH	l,m,c	NC	

L-PHE/(+)-CSA

1	0.45g/4ml warm H_2O; DR	a,c	NC	left for 5 days.
		d	NC	let for 6 days.
		c	NC	left for 3 weeks.
		e_p,b,d	NC	left for 8 days.
		g	NC	within 4 days, gel.
		m	C	clear gel became white where scraped and stirred.
	+0.05ml EtOH	l,m,c	C	white material, presumably crystals, throughout gel. 3 months later, collected sample by filtration and washing with H_2O. product quite soluble in H_2O. mp.
2	0.45g/4ml warm 5%EtOH/H_2O; DR	a,c	NC	left for 5 days.
		d	NC	left for 6 days.

		c	NC	left for 3 weeks.
		e_p,b,d	NC	left for 8 days.
		g	NC	within 4 days, gel.
		m	C	clear gel became white where scraped and stirred.
	+0.05ml EtOH	l,m,c	C	white material, presumably crystals, throughout gel.
3	0.45g/1ml hot H_2O; DR	b,d	NC	left for several days.
		c	C	tiny, white plates on surface of solution and tiny crystals on base. surface plates extinguished.
		j	NC	after a few minutes, viscous solution. filtered to collect. mp.
4	0.05g/0.3ml hot H_2O; DR	g, b	NC	
		g,k ex2,d	NC	
5	0.05g/0.25ml hot acet.; PD			
	+0.4ml H_2O	l		
		g,b	NC	
		g,k ex2, d	NC	

D-PHG/(-)-CSA

1	0.45g/4ml hot H_2O; DD	a		as cooled small amount of crystallisation.
		c		needles up to 5mm in clusters. sample collected by filtration poorly soluble in H_2O, just like PHG. nmr.
2	0.45g/4ml hot 5%EtOH/H_2O; DD	a	NC	some undissolved PHG removed.
		c		after 3 days, many long needles, up to 20mm in length radiating from a central point in a cluster. samples collected by filtration nmr. mp. sample ground for powder diffraction.

D-PHG/(+)-CSA

1	0.45g/4ml hot H_2O; DD	a	C	within a few minutes, as cooled, small needles.
		c	C	further crystallisation over 3 days as equant, rhombic prisms, 1 to 3mm across, patchy extinction of ppl. sample collected by filtration for nmr. one crystal cut into pieces which extinguished sharply. kite-shaped flake, 0.6x0.35mm along diagonals for structure determination. also some small needles up to 3mm in length. nmr of equant crystals. needles insoluble in D_2O.
2	0.45g/4ml hot 5%EtOH; DD	a	C	within a few minutes, as cooled, small needles.
		c	C	further crystallisation over 3 days as equant, rhombic prisms, 1 to 3mm across, patchy extinction. samples collected by filtration. nmr. powder diffraction. also some small needles up to 3mm in length, more than in 1.

L-VAL/(-)-CSA

1	0.25g/1.5ml boiling H_2O; DR	f,iRT,f	NC	temperature stepped down to RT. left overnight.
		e_p sl.,b,d	C	after 5 days, elongated plates on surface of a gel arranged in fan clusters. sharp extinction.
		f		left for a few days to grow. through crossed polars, striations parallel to plate. shaped mostly irregular, but elongated. soluble in glycerol. one crystal, plate basically rectangular but with one slant short edge 0.85x0.3x0.05mm. structure determination.
2	0.4g/1ml hot H_2O; DR	b,d	NC	left overnight.
		g	C	after 3 weeks tiny plates in a gel.
		g		after 2 months, elongated plates arranged in lines radiating from a central point. not single crystals, gradual extinction.

	+0.5ml H_2O; DR	l,h,d,i RT,d	NC	left for 5 days.
		g	NC	
3	0.15g/1ml hot 50%EtOH; DR	b,d	NC	left overnight.
		g	C	after 3 weeks, narrow, elongated, rectangular plates in fan-shaped clusters in a gel.
4	0.05g/1ml hot EtOH; PD			
	+0.5ml H_2O, hot; D	l,h,b,d	NC	
		g	C	after 3 weeks.long, narrow, elongated, rectangular plates in fan-shaped clusters in a gel.
5	0.05g/1ml hot 33%IPA; DR	b, d	NC	left overnight.
		g	C	after 3 weeks, small volume of gel and a precipitate of tiny crystals.
6	0.05g/0.25ml warm H_2O; DR	g,b,d	C	after a few days, tiny, thin narrow elongated rectangular plates in fan shaped cluster.
7	0.05g/0.25ml hot acetone; PD			
	+0.25ml H_2O	l,g,b,d	C	after a few days, thin, narrow, elongated rectangular plates, longer than in 6, in a fan-shaped cluster.
8	0.4g/1ml boiling H-(2)O;DR	f,d,iRT,f	NC	
		e_p(sl.),b,d	C	after 5 days, elongated, rectangular plates on surface of gel. sharp extinction indicated single crystals.
		f		left to let grow.

L-VAL/(+)-CSA

1	0.25g/1ml boiling H@-(2)O; DR	f,iRT,f	NC	immediately, viscous solution. temperature stepped down to RT. left overnight.
		e_p(warm),a,j	NC	after several days, gel.
		j	C	after two months,gel cloudy and thin plates , irregular in shape on surface of gel.
2	0.15g/1ml boiling H_2O; DR	b,d	NC	left for 2 days.
		g	C	after 3 weeks, gel with thick, etched plates, irregular in shape. collected by filtration and washing with H_2O. nmr. mp. crystals misplaced before structure determination attempted.
3	0.15g/1ml boiling 50%EtOH; DR	b, d	NC	left for 2 days.
		g	NC	after 3 weeks, gel.
		g	C	after two months, tiny fibrous crystals in gel. volume reduced by evaporation over time.
	addition of more stock mixture and solvent.			
	+0.05g/0.5ml H_2O; D	l,h,d,iRT,d	NC	
4	0.05g/1ml hot EtOH; PD			
	+0.5ml hot H_2O; D	l,h,b,d	NC	left for 2 days.
		g	NC	left for 3 weeks, much solvent evaporated.
		d	C	after 2 months, tiny crystals in gel and very thin plates on sides of vial.
		j	NC	
	addition of more stock mixture and solvent			
	0.2g/0.5ml H_2O; DR	l,h,d,i RT	NC	made up to 1ml. stepwise reduction of temperature.
		d	NC	left for a week.
		g	NC	

2.15 Experimental conditions and results
CSA simple salts

TABLE

mixture; solubility	treatment	result	comments; appearance; analysis
CSA1 recrystallisation			
0.40g/2ml hot EtOAc; DR	b	C	within 15 minutes, long, elongated, triangular prisms, some in dense clusters with crystals packed parallel to needle axis, dimensions, ca. 2.3x0.1x0.1mm, extinction parallel to needle axis, but in some patchy, in others, sharp, all are coloured when viewed through crossed polars, because they are thin, crystals cut to reduce them to a suitable size, one fragment mounted along needle axis on a glass fibre, tiny crystals adhering to it were scraped off as far as possible, disappeared within a week because of deliquesence, a second search for crystals failed because too many tiny fragments were adhering, nmr in D_2O.
CSA2 recrystallisation			
0.04g/1ml hot EtOAc; DR	b	C	within 5 mins, this significantly more dilute solution deposited long, narrow, triangular prisms.
0.25ml EtOAc	l,h,b,d	C	after a few days, large, dry, elongated, triangular prisms, extinction, a crystal, 0.65x0.1x0.1mm was mounted in a Lindemann tube, determination of structure and absolute configuration.
CSK1 preparation			
0.10g KOH was insoluble or sparingly soluble in 1ml EtOH. 0.30g CSA were added which dissolved. An insoluble, white material was observed, probably some of the desired product. The pellet of KOH remained incompletely dissolved at first, but did dissolve overnight. A white precipitate was formed overnight and was presumed to be the required potassium salt. 0.60g of moist product were collected by filtration and washing with EtOH and stored in a fridge.			
recrystallisation			
CSK1(i)			
0.13g/1ml EtOH; DD	b	C	within a few minutes, mass of tiny needles throughout the solution.
0.2ml 50% EtOH H_2O; D	l,h,b	C	within a few minutes, long needles.
0.1ml warm H_2O; DR	l,h,b,d	C	overnight, a few needles sides of vessel, by evaporation of solvent, pushed into solution as seeds.
	n	NC	left for a few hours.
	c	NC	overnight, no change.
	n	C	overnight, small crystals.
	c	C	after 3 days, long needles in the solution and dry precipitate above solvent level.
CSK1(ii)			
0.30g/1ml hot H_2O; DR	n	C	after several hours, many long needles, evaporated to dryness
CSK2 preparation			
Approximately equimolar, aqueous solutions of potassium hydroxide and camphor-10-sulphonic acid were mixed, generating heat on reaction. Reacting quantities were 0.09g in 1ml and 0.31g in 1ml respectively. There was no precipitation of the potassium salt initially from 2ml solution.			
Action to induce precipitation. (Expected yield is 0.38g.) e_D gently,	b,d	NC	left overnight.
	n	NC	left for several hours.
	c	NC	left overnight.
	n	NC	left overnight.
	o	C	after 3 days, dry precipitate of needles around sides of vial, wider,

			longer needles, elliptical in cross section, on base and at lower part of sides. extinction. crystal mounted in Lindemann tube. oscillation photograph indicated twinned crystal.
	c		crushed needles used as seeds in CSK5

CSK3
preparation

Approximately equimolar solutions of potassium hydroxide in water and camphor-10-sulphonate in EtOH were mixed, generating heat on reaction. Quantities were 0.08g in 1ml H_2O and 0.31g in 1ml EtOH respectively. There was no initial precipitation of the salt from 2ml 1:1 EtOH/H_2O.

action to induce crystallisation.

e_p gently for 10 minutes	b,d	NC	left overnight.
	n	NC	left for several hours.
	c	NC	left overnight.
	n	NC	left overnight.
	o	C	after 3 days, evaporated to dryness, leaving needles in feather-like clusters.

CSK4
preparation

Approximately equimolar solutions of potassium hydroxide in EtOH and camphor-10-sulphonic acid in H_2O were mixed, generating heat on reaction. Quantities were 0.10g in 1ml EtOH and 0.32g in 1ml H_2O respectively. There was no initial precipitation of the salt from 2ml 1:1 EtOH/H_2O.

action to induce crystallisation.

	d	NC	left overnight.
	n	NC	left for several hours.
	c	NC	left overnight.
	n	C	overnight, many tiny needles throughout solution. crystals soluble in glycerol, insoluble in nujol.

CSK5
preparation

0.46g KOH was added to 5ml EtOH in which it remained mostly undissolved and transferred with washings into a 10ml beaker containing 1.51g camphor-10-sulphonic acid (slight excess of base.)

recrystallisation of product from 5

CSK5(i) 0.32g/1ml 90% hot EtOH; D	n,b,d	C	after 2 to 3 hours, long needles.
CSK5(ii) 0.30g/1ml hot EtOH and 0.2ml H_2O; D	b	NC	
	k from 5(i),d	NC	seeds dissolved.
	k from 5(i),n	C	overnight, needles on sides of vial by evaporation
	k from self, shaking,d		NC
CSK5(iii) 0.30g/1ml hot EtOH and 0.15ml H_2O; DR		b	NC
k from 5(i),	c	C	needles. (more than just undissolved seeds.) marginally wider than in 5(i)

CSK5(iv)

0.29g/2ml warm H_2O; DR	n,b,d	NC	this aqueous solution is similar to, but slightly more dilute than in CSK2 which yielded crystals of the right size, but not single, for structure determination. In this case slower crystallisation is expected. after 20 hours, no crystallisation
	o	C	after 3 days, evaporated to dryness.
1ml H_2O; DR	l,h,n,b,d	C	after 7 days, evaporated to dryness. dried needles.
1.2ml H_2O; DR	l,h,n,b,d	C	after 6 days, evaporated to dryness. dried needles in clusters
1ml H_2O; DR	l,h,o	NC	left for 2 days.
	k from 2,o		after 2 days, elongated needles in solution. sharp extinction.

	c		after 3 days, mounted an elongated crystal, semi-elliptical in cross section, in a 0.5mm Lindemann tube. dimensions, 0.95x0.2x0.15mm. structure determination. Thus finally, successful crystallisation from a solution just under twice as concentrated as CSK2, with seeding.

CSNa1

0.31g sodium hydroxide partially dissolved in 5ml EtOH were transferred with washings into a 10ml beaker containing 1.52g camphor-10-sulphonic acid. the acid dissolved immediately but the hydroxide remained incompletely dissolved over a period of 2 to 3 hours at room temperature. Upon boiling, the hydroxide dissolved. There had been no early precipitation of sodium camphor-10-sulphonate unlike the potassium case, so a iittle solvent was allowed to evaporate in order to increase the concentration of the solution and thereby induce crystallisation. After leaving to cool uncovered for 2 to 3 hours, the only precipitate was some encrustation around the sides of the beaker above the solvent level. This was scraped into the solution to seed it and after some minutes precipitation began. in the solution. A gelatinous white precipitate resulted and the value of the pH was 10 (tested with litmus paper.) The excess hydroxide created an alkaline environment which perhaps contibuted, along with the fact that the solvent was now an alcohol/water mixture as a result of the reaction of the acid with the base, to the difficulty in precipitating the product.

The product was collected by filtration and washing with EtOH to remove excess hydroxide solution. It was dried in a vacuum desiccator and the dry weight was 0.33g which corresponds to only a 20% yield relative to the camphor-10-sulphonic acid added. Solubility of the sodium salt caused this. mp determined.

CSNa1(i) 0.33g/1ml H_2O; DR	n,b,d	NC	after a few hours released vacuum.
	o	NC	left for 3 days.
	n	NC	left overnight. volume reduced. viscous solution.
	n	C	poorly formed crystals in viscous solution.
1ml hot H_2O; DR	l,h,n,b,d	C	after 6 days, solvent all evaporated. powder and some rectangular plates.
1ml/H_2O; DR	l,n	C	after a week, dried needles.
1ml/H_2O; DR	l,o	NC	left for 4 days.
	n	C	after 3 days, dried precipitate.

recrystallisation of product of CSNa1(i)

CSNa1(ii)			
0.05g/8ml warm EtOAc; l			filtered to collect the undissolved material for recrystallisation.
1ml H_2O; DR	n	NC	left for several hours.
	n,f	NC	left for a week.
	n	NC	left overnight.
	m,n	C	after a few days, dried precipitate.
CSNa1(iii) 0.30g/1.5ml H_2O; DR			
0.25ml EtOH	l,n		after a number of days, dried precipitate.

Failure to produce crystals suitable for data collection.

$CSNH_4$
preparation

To 1.58g dissolved in 5ml EtOH, concentrated ammonia was added dropwise until the solution was alkaline and a slight excess had been added. Initially the pH was 2. After addition of 11 drops the pH had risen to 9, there was a thick white precipitate, but there was no strong smell of ammonia to indicate that excess had been added. After addition of a further 6 drops, ammonia could be smelled. The pH was between 9 and 10.

The product was collected by filtration and washing with EtOH until the smell of ammonia could no longer be detected. After drying in a vacuum desiccator the weight of product, a compact powder, was 1.00g. This corresponded to a 59.4% yield relative to the weight of camphor-10-sulphonate used. As with all these camphor-10-sulphonate - containing materials, this was stored in the fridge until required.

recrystallisation.

$CSNH_4$1(i)			
0.30g/1ml warm H_2O; DR	n,b,d		left for a few hours.
	o	C	after 3 days, some precipitate on sides of vial by evaporation.
	n	C	overnight, colourless crystals in solution and a lot of white, dried precipitate on sides of vial. crystals are long and relatively wide, elongated, triangular prisms. One was cut in two, slightly skew, across the long axis, such that the dimensions of one piece were 0.65mm along the longest edge of the base, 0.5mm along the top,

0.3mm was the width of the base and 0.2mm was the height. mounted in a Lindemann tube. extinction and x-ray photographs showed this to be a single crystal. The other piece was probably not single, its structure having been affected by cutting, and not now showing a single set of extinction positions. structure determination.

CSLi1
preparation

To 0.10g Lithium carbonate partially dissolved in 2ml H_2O, 0.60g camphor-10-sulphonic acid were added. There was initial effervescence followed by a slower reaction during which most of the carbonate was consumed. The solution was filtered from undissolved carbonate and placed in a 10ml vial for crystallisation.

crystallisation

CSLi1(i)

n	NC	left overnight.
n,f	NC	left for a week.
o	NC	left overnight.
m,o		after a number of days, evaporation to dryness. thin covering of precipitate on sides and base of vial.

Failure to produce crystals suitable for data collection.

CSCA1
preparation

0.50g camphor-10-sulphonic acid was dissolved in 1.5ml H_2O and 0.13g calcium carbonate added. At first, in the cold, there was apparently no reaction, but upon warming effervescence began to be observed. Product precipitated on the surface of the solution initially and soon more collected. There was no undissolved carbonate. The product was collected by filtration and washing with EtOH. After leaving to dry in air, the weight of product was 0.50g, which corresponds to a yield of approximately 76%, excluding any water molecules bound in the crystal lattice.

CSCa2
preparation

0.59g camphor-10-sulphonic acid dissolved readily in a tiny amount of H_2O, ca. 0.25ml. 0.13g calcium carbonate were added, with immediate effervescence upon reaction with the acid without warming. After a few minutes the mixture was warmed to try to complete the reaction. The calcium camphor-10-sulphonic acid salt was soluble in H_2O and the solution was separated from any undissolved calcium carbonate by filtration. The beaker was washed with ca.0.2ml H_2O and this was added. The filtrate was set aside in a 10ml vial to crystallise.

crystallisation

d	NC	left overnight.
n	C	after 2 days, crystallisation began.
c		after 3 days, slow growth to large etched rhombic plates which extinguish cleanly on the directions of the corner to corner diagonals. mounted one. structure determination.

CSSr1
preparation

0.20g strontium carbonate was swirled in 2ml H_2O, in which it did not dissolve. 0.60g camphor-10-sulphonic acid was added. causing immediate effervescence as CO_2 escaped. A further 0.06g was added to try to dissolve some of the remaining strontium carbonate. The solution was separated from carbonate, which did remain undissolved, by filtration, the beaker being washed with ca. 0.2ml H_2O and these washings being added. Equal volumes(ca. 1.5ml of filtrate were placed in two different 10ml vials for crystallisation.

crystallisation

CSSr1(i)

1.5ml filtrate	e_p,n.b.d	C	after 8 days, evaporation to dryness had occurred. dry precipitate, no good crystals.
0.5ml H_2O; DR	i,h.n.b.d	NC	overnight.
	n,f	NC	left for a week.
	n,f,k from (ii)	NC	left overnight.
	c,k (CSSr2)	NC	

CSSr1(ii)

1.5ml filtrate/2ml EtOH	i,e_p,n.b.d	C	after 8 days, evaporation to dryness had occurred. no good crystals.
0.5ml 50%EtOH/H_2O; DR occurred.	i,h,n.b.d	C	overnight evaporation to dryness

CSSr2
preparation

0.20g strontium carbonate and 0.62g camphor-10-sulphonic acid were added to 2ml EtOH. The carbonate did not dissolve. There was no reaction until a few drops of H_2O were added, when there was immediate effervesence. The mixture was heated and H_2O was added slowly until most of the carbonate was dissolved and reacted. The solution was transferred into a 10ml vial along with EtOH washings, being filtered to separate the product from any unreacted carbonate and efforts made to crystallise the camphor-10-sulphonate.

crystallisation

	n	C	after 8 days, evaporation to dryness had occurred.
0.25ml 60% EtOH	l,h,n,b,d	NC	left for 2 days.
	n,f	NC	left for a week.
	n,k from (ii)	C	overnight, precipitation of tiny crystals.
	n,c		after a few days, crystals grown into long, elongated, triangular prisms, extinction somewhat patchy in most crystals, found one probably single, dimensions, 0.75x0.15x0.15mm, mounted in Lindemann tube, cell? single? isomorphous with CSCa.?

CSCu1
preparation

0.18g dull, light, green copper (II) carbonate and 0.56g camphor-10-sulphonic acid were added to 2ml H_2O. The acid dissolved readily and the carbonate dissolved in part. The result was a greenish blue suspension. Gravity filtration from unreacted, green carbonate yielded a bright, light blue solution, the colour of $Cu(II)(H_2O)_6$, hydrated copper(II).

crystallisation of 1

CSCu1(i)

	a_p,f,k from 2	NC	no change within a few hours.
	k from 2,d	C	within a few days, crystallisation, not suitable for structure determination.

recrystallisation of CSCu1(i)

CSCu1(ii)
0.10g/1ml warm H_2O; DR

	b,d	NC	left for a few days.

CSCu1(iii)
0.10g/0.5ml warm H_2O; DR

0.5ml EtOH	l,b,d	NC	left for a few days.

CSCu2
preparation

0.18g copper(II) carbonate were added to 2ml EtOH in which it formed a pale green suspension. There was no reaction obvious immediately. 1ml H_2O was added gradually in order to partially dissolve the carbonate. The mixture turned blue as in 1, but with a significant amount of carbonate remaining unreacted or undissolved suspended in it. Camphor-10-sulphonic acid was added, about 0.1g, which dissolved most of the remainder, giving a clear blue solution with a few lumps of carbonate. 2ml of this solution, (i), were collected by gravity filtration as in 1. Droplets of solution left behind in the reaction flask evaporated to pale blue flakes, roughly trapezium-shaped, which were used as seeds in 1 and 2. The remaining solution, (ii), ca. 1ml, was filtered into a separate vial.

CSCu2(i)

2ml	k from 2,f	C	within a few minutes, small amount of tiny crystals on base of vial.
	f	C	overnight, became small feathery clusters, and one large, elongated, hexagonal plate, pale blue in colour.
	f		left for 6 weeks.
	h,b	C	chunky needles as cooled.

CSCu2(ii)

1ml		C	as filtered, crystallisation in filter paper, in funnel and also in filtrate, because of evaporation and self seeding.
	d		left open for several days. In the pale blue solution, large, clear, pale blue, irregular, hexagonal plates and long, narow hexagonal plates on sides of tube, crystals in funnel and paper became dry, insoluble in glycerol, under which they were manipulated, dimensions variable,some thin, showing interference colours, up to 8x6x1mm, positions of sharp extinction 90° apart, through midpoints of one pair of opposite edges and at right angles to this, several crystals or cut fragments mounted on glass fibre, securing with araldite, data collection, but with crystal decay, fragments cut from the large crystal 8x6x1mm were attempted to be mounted in Lindemann tubes. Either not single or crystals broke up on manipulation, also, possible solvent loss from this exposed crop of crystals.

CSCu3
preparation

0.16g copper(II) carbonate and 0.60g camphor-10-sulphonic acid were mixed. 2ml EtOH were added to give a green suspension. On addition of 1ml H_2O, some carbonate dissolved. The mixture was heated to aid the reaction and a further 1ml portion of $_2O$ added. Gradually the green suspension became a turquoise green solution with some green, undissolved carbonate and finally a blue solution. There still remained some unreacted carbonate. ca 0.1g camphor-10-sulphonic acid was added to the hot solution and the lumps of carbonate fizzed and dissolved. The warm solution was filtered by gravity into a 10ml vial. No crystals were deposited during filtration, nor on the moist paper as it dried.

crystallisation.

3ml	RT	NC	
	e_n,b,d	C	fragment mounted and sealed on a glass fibre with nail varnish. too large to attempt to put into a 0.7mm Lindemann tube. structure determination.

2.16 NMR results

During attempts to prepare the distereomeric compounds from pure components, nmr spectra were made to verify that a 1:1 product had been obtained. The trials are listed below, together with a code number referring to section 2.14 or 2.15. Unless otherwise stated, averages were taken of sets of ratios of peak integrals for unambiguously assignable proton peaks, and these were used to give the ratio of amino acid to camphor-10-sulphonic acid or mandelic acid to amino acid. When the EM360 spectrometer was used, integrals were not measured, and component ratios are based on peak heights.

The diastereomeric compounds prepared successfully are listed separately in section 2.2.3. NMR was also used in some cases to supplement the identification of the products of resolution, as a 1:1 compound can easily be distinguished from crystals of one or other component.

R- or S-Mandelic Acid

1:1 mixture of	code no	percent present MAN	AA	Spect	comments
		Amino Acids with Nonpolar Side Chains			
S-ALA/R-MAN	2	51	49	EM360	Suggests 1:1 cmpd.
S-ALA/S-MAN	2	52	48	EM360	Suggests 1:1 cmpd.
S-ILE/R-MAN	3	12	88	WP200	ILE plus some MAN
S-ILE/S-MAN	4	2	98	WP200	ILE plus tr. MAN
S-LEU/R-MAN	1	40	60	WP80	LEU and MAN
S-LEU/R-MAN	8	0	100	WP80	LEU only
S-LEU/R-MAN	15	6	94	WP200	LEU plus tr. MAN
S-LEU/S-MAN	1	24	76	WP80	LEU plus some MAN
S-MET/R-MAN	1	49	51	WP80	Suggests 1:1 cmpd.
S-MET/S-MAN	1	50	50	WP80	Suggests 1:1 cmpd.
S-PHE/R-MAN	1	~50	~50	EM360	[Low signal:noise]
S-PHE/S-MAN	1	~50	~50	EM360	[Low signal:noise]
S-VAL/R-MAN	1	45	55	WP80	VAL plus MAN
S-VAL/R-MAN	8	21	79	WP80	VAL plus some MAN
S-VAL/R-MAN	14	0	100	EM360	VAL only
S-VAL/R-MAN	16	23	77	EM360	VAL plus some MAN
S-VAL/S-MAN	1	26	74	WP80	VAL plus some MAN
		Amino Acids with Acidic Side Chains			
R-CYS/R-MAN	7	53	47	WP80	Suggests 1:1 cmpd.
R-CYS/S-MAN	16	47	53	WP80	Suggests 1:1 cmpd.
R-CYS/S-MAN	17T	51	49	WP80	Suggests 1:1 cmpd.
R-CYS/S-MAN	17P	100	0	WP80	MAN only

	Amino Acids with Basic Side Chains				
R-LYS.HCl/R-MAN	1	95	5	WP80	MAN plus tr. LYS
R-LYS.HCl/R-MAN	2	100	0	WP80	MAN only
R-LYS.HCl/S-MAN	1	90	10	WP80	MAN plus tr. LYS
	Amino Acids with Polar Side Chains				
S-SER/S-MAN	7	50	50	WP80	Suggests 1:1 cmpd.
S-THR/R-MAN	1	62	38	WP80	inconclusive
S-THR/R-MAN	2	45	55	WP80	Suggests 1:1 cmpd.
S-THR/R-MAN	5N	6	94	WP80	THR plus tr. MAN
S-THR/R-MAN	5P	78	22	WP80	MAN plus some THR
S-THR/S-MAN	1	49	51	WP80	Suggests 1:1 cmpd.

RS- or SR-Camphor-10-Sulphonic Acid

1:1 mixture of	code no	percent CSA	present AA	Spect	comments
S-MET/RS-CSA	3	56	44	WP80	Suggests 1:1 cmpd.
R-PHG/RS-CSA	1	0	100	WP80	PHG only
R-PHG/RS-CSA	2	0	100	WP80	PHG only
R-PHG/SR-CSA	1	48	52	WP80	Suggests 1:1 cmpd.
S-VAL/SR-CSA	2	53	47	WP80	Suggests 1:1 cmpd.

2.17 MELTING POINT DETAILS

PRODUCTS OF TRIAL CRYSTALLISATIONS WITH MANDELIC ACID

ALA/R-MAN

1, piece of large plate. not crushed. 155.5°, tube cloudy near crystal. 157-159°, appreciably darker in colour. 167.8-17°, melted to a clear droplet.

2a, 140°, soften slightly. 154.9°, tube cloudy. 165.6-167.6°, melt to soft blobs. 168.2°, became brown liquid.

2b, 133.1°, clear crystals became opaque. 157.7°, slightly cloudy. 158°, softens. 161.5°, more cloudy. 162.5°, first liquid at edges of crystal, near to tube. 165.9-166.6° melted. became a brownish, clear blob.

2c, 160.3°, tube slightly cloudy near crystal. 166.3°, cloudiness had increased.166.4-167.2°, melted to give a clear blob ca.170°, became brown. the above samples were little crystals, not powder. more efficient melting might have taken place if properly prepared powder.

ALA/S-MAN

2, dried and crushed sample. 143.8°, some cloudiness on tube near crystals. 151.6°, turns brown and very soft. 157.2°, formation of a brown blob at centre of tube. became softer, more liquid, and by 158.5°, had moved on to the sides. blobs gradually became droplets and there were bubbles. 165°, droplets ran together, some collecting in the tube and some moving up the tube.

ABA/R-MAN

2, crystal fragments 127.7°, tube cloudy near crystals. 130°, ends of crystals on sides of tube soften. 141°, becomes blobs on sides of tube. 150°, slight brown tinge. by 176°, blobs more liquid in character. 181°, more obviously brown in colour, liquid drops with a few bubbles. 185°, liquid begins to collect. it bubbles.

ABA/S-MAN 1:1 mixture. 106.5°, some tiny spots of liquid. 110°, becomes

a colourless blob in the middle, of the tube, away from sides. 119.2°, colourless liquid begins to collect, blob remains. 169.4°, blob remains. a few bubbles in clear, colourless liquid and blob. 172.9°, liquid moves up tube, bubbling and evaporates. few colourless blobs remain. 190°, blobs melt giving a colourless liquid. 216°, bubbles in liquid. 220°, faint brown colour observed.

ABA/S-MAN

1, 143°, a few tiny spots of liquid at edges, where touch sides. 153°, increased. 167°, faint, pale, yellow colouration. 184°, liquid begins to collect. 189°, pale, yellow, separate liquid drops.

2a, early product. fine hair and ppt on sides. 109.2°, a few tiny spots of liquid at edges, where sample contacts the sides of the tube. 110°, sample softens and becomes located in the middle, away from the sides. cloudy on sides near crystals. 112°, becomes white blob on side. 116.7°, colourless liquid collects. 150°, tiny bubbles in liquid. 181°, faintly brown liquid moves up tube with some evaporation. until 200°, pale brown liquid with occasional bubbles.

2b, later growth. plates, 125°, a few spots of liquid on plates. 128°, becomes a colourless blob on side of tube. 130°, becomes a drop of liquid and a blob. 135°, cloudy condensation on sides above level of liquid. 159°, yellow-brown colouration.

4, 124.5°, first tiny liquid drops and some condensation around the material. 134°, softens. 140°, liquid drops. 141°, becomes a blob on side of tube. 147°, tinge of brown colour. 159°, blob becomes liquid blob on the side, pale brown in colour. 164°, bubbles in the brown blobby liquid.

a colourless liquid.

GLY/R-MAN

3, crushed, dried plate. 126°, condensation on sides of tube near sample. 130-133°, melts to a colourless liquid.

GLY/S-MAN

3, dried fragments. 128°, condensation on sides of tube near sample. by 133.4°, fully melted to a colourless liquid.

ILE/R-MAN

3, 170°, condensation on sides of tube near sample. 189°, yellow tinge. 207°, some brown liquid drops on sides of tube. 219°, central mass of sample more brown. 248°, more has turned liquid. 252 smaller in volume. 253°, some brown liquid collects at bottom of tube. 259°, bubbles froth up. very dark brown. some has boiled and collected farther up tube as cream coloured spots.

ILE/S-MAN

4, 190°, turns slightly yellow. 207°, softer. 245°, a few brown, liquid drops on sides of tube. by 260°, softer, more brown liquid on sides. 261°, very dark brown. 273°, smaller in volume, 274°, some liquid froths up. continues to reduce until the blob froths up and moves up tube. some has evaporated and recondensed as cream coloured spots farther up tube.

LEU/R-MAN

1, dried, shiny flakes. 148.8°, tiny drops of liquid where sample touches sides of tubes. 150°, condensation on sides. 157.5°, sample blobby, 165.8°, yellowing, 171.8°, more liquid at sides. 178.2°, browning. 180°, brown. 180.9-193.8°, gradually more liquid appears, becoming a blob in centre with orange-brown liquid in bottom of tube. 198.6°, some more liquid collected in bottom. 207°, blobby on sides with liquid in bottom. 208.3°, blob bubbles. 209°, colour red-brown. 210.5°, blob becomes brown liquid on side.

8, shiny, white flakes, 240-250°, white solid sublimes or decomposes,

gradually disappearing.

14, shiny, white flakes, 240-255°, white solid sublimes or decomposes, gradually disappearing.

15, 169°, condensation on sides of tube. 259-262°, softens and sublimes, turning brown at 261 and collecting farther up tube as a cream coloured deposit.

LEU/S-MAN

1, 145.8°, tiny liquid drops where sample touches sides of tube. 157.5°, sample has become a blob. 165.8°, yellowing. 173.8°, more liquid where touches sides. 177.3°, condensation on sides near blob. 180°, has become brown gradually. 193.7°, some orange-brown liquid collects in bottom of tube. 204.9°, blob, still in middle of tube, becomes vey soft. 209°, blob and liquid red brown in colour. 209.8°, blob rests on side of tube. 211.1°, blob bubbles. 212.3°, blob on side has mostly become liquid. 212.7°, some liquid drops down into bottom, some stays on side. 213.2°, entirely red liquid.

MET/R-MAN

1, 148°, softens. 160°, on side of tube. 176°, blob on side. 186°, brown tinge. 160-186 condensation appears on sides of tube near sample. 190°, bubbles in blob.

MET/S-MAN

1, 127°, softens. up to 158.1°, becomes a soft blob on side of tube. at 158.1°, bubbles in this colourless blob. 160.7°, colourless liquid begins to collect. 165.8°, tinge of brown. big bubble within blob.

2, 155°, slight softening. 181°, soft material starts to go brown. by 185°, bubbles in brown liquid.

PHE/R-MAN

1, 147.9°, condensation on sides of tube near sample. 154.6°, softens. 157.9°, liquid drops appear on sides. 160.9°, starts to turn brown. 161.7°,

softens further. 162.4°, brown blobs, some in middle of tube, some on side. 165.1°, blobs entirely on side of tube. 170.2°, begins to run together as a liquid with blobs in it. bubbles.

PHE/S-MAN N/A

PHG/R-MAN

1, crushed needles. 264-276.9°, decomposed, turning brown and disappearing.

PHG/S-MAN

1, crushed needles. 282.6°, decomposed, turning brown and disappearing.

VAL/R-MAN

4, 150°, condensation on sides of tube near sample. 152°, tiny liquid drops where sample meets sides of tube. 158.3°, softens and yellows. 175.3°, quantity of liquid has increased on sides. 175.8°, colour becomes orange-brown. 177.8°, becomes blob on side of tube. 181.6°, blob turns more liquid and bubbles. 187.2°, some liquid drops down to bottom. 203°, fully liquid at bottom.

6, 108.3°, softens, liquid drops where sample touches sides and sample withdraws from sides into the middle. 125°, blob very soft, moves to side. 136.3°, blobby liquid on side. 171.7°, clear liquid starts collecting in bottom. 174.5°, frothy on sides. 183.3°, frothy at bottom, liqiud higher up round side. 186°, yellow tinge to liquid. by 197°, brown liquid.

11, 144.5°, tiny liquid drops where sample touches side of tube. 150°, condensation on sides near sample. 163°, slightly more liquid observed. 167°, larger liquid drops where touches sides. 177.4°, softens. 188.7°, more liquid drops. 246.5°, liquid drops turn brown. 255.4°, gradually darker brown, evaporates to leave a few spots of liquid.

13, 153.8°, tiny liquid drops where sample touches side. 176°, these drops become larger. 204.4°, softens, 225°, sample evaporating.

14 1:1 MIXTURE. 116°, turns blobby. 129°, some liquid collects in base,

some blobs remain. 190-200°, blobs shoot up tube together. 240°, liquid in bottom turns brown from the top. 249.8°, brown part of liquid shoots up tube.

VAL/S-MAN

5, 121°, tiny liquid drops where sample touches sides of tube.

137.8°, large liquid drops on sides and solid in middle. 145.3°, drain down into bottom. by 181°, brown. 187°, red-brown. 190°, softer sharply. 199.6°, decomposes to a dry red material on sides.

CYS/R-MAN

1a, 121.7°, tiny drops of liqiud where sample touches side of tube. 124-127.7°, softens and becomes colourless. 137.5°, becomes runnier. 151°, yellow.

1b, 105°, softens slightly. 115°, softer, 121.9°, tiny drops of liquid where sample touches sides of tube. 122.9°, become a blob in the middle and a drop of colourless liquid. 141.5°, yellow blobby liquid.

2a, 123.3°, needle bends and sticks to side of tube. up to 123.8°, crystal spreads out further.

2b, 120.9°, sample of the encrustation produces condensation on sides of tube near it. 121.2°, become blobby. 122.5°, liquid begins on sides. 142°, yellow.

3, 118.8-129.9°, crushed dried crystals produce liquid drops where touch sides of tube. 134°, condensation od sides near sample. 139°, turns to yellow blobs. 146-155°, gradually blobs move together more and beome more yellow-brown. beyond 155°, yellow brown blobs close together. some bubbles.

CYS/S-MAN

2, 146.5°, softens. 149°, condensation on sides near sample. 150-153°, melts to a pale yellow liquid. 169°, brown liquid.

4a, 125.7°, slight softening. 140.5°, condensation on sides. 146.2°, liquid drops appear. by 151.2°, fully melted to a yellow blob.

4b, 127.5°, slight softening. 138.8°, further softening. 144.2°, first liquid

drops. 146.5°, becomes a colourless blob in the middle with liquid drops at edges. by 148.8°, blob has become more liqiud. 149.2°, turns yellow. by 155.4°, brownish-yellow blobby liquid.

4c, 142.3 condensation on sides. 144°, edges of crystal melt where touch side of tube to yelow blobs. 150.8°, blob more liquid. 153.8-155.2°, crystal in middle melts to a yellow-brown blobby liquid on sides of tube.

14, 2-3mm of crushed dried crystals, 134°, condensation on sides. 139°, dark specks on sides of tube. 144.9°, bulk of sample becomes blobby. from 149°, progressively more yellow. 149°, fairly liquid blobs. 151.1-153.4°, blobs move together ans move to sides of tube. 155.5°, yellow-brown blobby liquid. 157.4°, frothy, bubbles.

16, crushed sample, 108.5°, tiny liquid drops where sample touches side if tube. 114°, these drops larger. 123.5°, bulk of sample begins to melt. 136°, thr drops are larger. 153°, bulk of sample moves from middle to sode and becomes a blob. 155°, entirely a lumpy blob. 157°, starts to turn yellow-brown.

17a, large plates, crushed partly, sample moist because kept under glycerol. <100°, softens. 127.5°, dissolves or melts to a colourless liquid. 157°, starts to turn yellow-brown.

17b, tiny crystals, dried. °,108.5 tiny liquid drops where sample touches sides. 114°, these drops are larger. 139.5°, bulk of sample begins to melt. 142°, condensation on sides near sample. 157°, starts to turn yellow-brown. 160°, entirly a lumpy blob in middle of tube.

LYSHCI/R-MAN

2, 114°, softens. 120.6-123.8°, melts to colourless liquid drop on side.

LYSHCI/S-MAN

1, 118°, softens. 120.6-126°, melts to colourless liquid drop on side. 127.2°, liquid collcted at bottom of tube.

SER/R-MAN

1, 127°, softens. 133.6–133.9°, melts sharply to a colourless liquid.

7, 122°, softens to a white blob. by 126.7°, melted to a brown liquid with a few bubbles. 131°, more bubbles.

SER/S–MAN

1, 127°, softens. 130–132.8°, melts to a colourless liquid. 154.9°, brown tinge. bubbles.

7, 122°, softens to a white blob. by 124°, melted to a colourless liquid. 126.7°, turns brown and bubbles.

THR/R–MAN

1, 105°, softens slightly. 120°, condensation on sides of tube near sample. 125.8–127.3°, melts to a colourless, blobby liquid. 152°, bubbles in liquid. 156°, brown tinge. 2, 133.8°, condensation on sides near sample. 136.9°, slight softening. 153°, brown tinge. tiny liquid drops where sample touches sides of tube. soft crystals in middle. 179.2°, larger brown liquid drops. >179°, more condensation.

5N, needles. 133.5°, condensation on sides near sample. 137°, slight softening. 144.9°, tiny brown liquid drops where sample touches sides. 159.5–178°, size of liquid drops increase and sample becomes entirely brown. by 207°, some solid still remains along with liquid.

5P, plates. 125.5°, tiny liquid drops where sample touches side. 126.8°, condensation on side. 128°, liquid drops larger. 130°, sample liquid with tiny blobs in. 150°, bubbles rise up through sample. 154.5°, slight yellow colouration. 169°, yellow–brown. after a bubble ises, liquid drops doen to bottom. by 173.5°, brown in colour. by 185°, red–brown.

THR/S–MAN

1, 125.8–127.3°, melts to a colourless, blobby liquid.

2, 127.9–128°, melts sharply to a colourless, blobby liquid. 150°, yellow tinge. >150°, bubbles rise up through liquid. progressively browner, although

some clear drops remain.

4a, crushed piece of large plate. 124°, condensation on sides near sample. 131.4–133.9°, melts to a colourless liquid.

4b, uncrushed fragmenta of large plate. 124°, surface looks sweaty. 131°, a tiny frament melts. 134.5–138°, sample moves to side of tube, progressively more rounded edes. 146°, side of crystal nearest side of tube melts to a yellowish liquid. 173°, some liquid, some sample with edges still defined. sample brownish. 188°, a few bubbles rise from liquid. some crystals remains. 202.4°, condensation on sides of tube near sample. by 214°, red–brown in colour. >230°, dark red–brown, crystal gradually becoming red–brown liquid.

5N, needles. 133.5°, condensation on sides near sample. 137°, slight softening. 144.9°, tiny brown liquid drops where sample

touches sides. 159.5–178°, size of liquid drops increase and sample becomes entirely brown. by 207°, some solid still remains along with liquid.

5P, plates. 125.9°, tiny liquid drops where sample touches side. 128.7°, liquid drops larger. 129°, liquid collects at bottom. 130.2°, sample has become liquid with tiny blobs in, colourless. 160°, starts to turn yellow, bubbles.

PRODUCTS OF TRIAL CRYSTALLISATIONS WITH CAMPHOR–10–SULPHONIC ACID

L–MET/(–)–CSA

3, dried, crushed, clear crystals. 135–138°, melts to a colourless liquid.

L–MET/(+–CSA]

2, block, cut from a chunk, not crushed, sticky. 121.9°, becomes a blob on side of tube. by 126.9°, becomes liquid drop on side. 193°, condensation on sides of tube near sample. 201°,tiny bubbles in drop. 230–240°, turns brown.

L–PHE/(+)–CSA

1, 180°, darkens. 194°, becomes a brown blob.

3, 129°, softens. 129–139°, gradual softening. 139°, condensation on sides

of tube near sample. 195.8°, brown tinge. more condensation. rapidly becomes soft brown pieces.

D-PHG/(-)CSA

2, 237°, brown tinge. 247°, condensation on sides of tube, volume reduces. 252°, remaining crystals turn black-brown. 254°, sample evaporated to leave a faint brown film on sides of tube.

L-VAL/(+)-CSA

2, crushed, tacky crystal. 135-137.5°, melts to a colourless liquid.

CHAPTER 3

THE DETERMINATION OF THE STRUCTURES OF MANDELIC ACID COMPLEXES

The method of structure determination for each of the six structures is described. Details of the progress made towards the unsuccessful structure determination of several other complexes are also given.

3.1 S-Alanine/R-Mandelic Acid

3.1.1 Crystal Data:

$2C_3H_7NO_2.2C_8H_8O_3.H_2O$, M_r =500.45, triclinic, P1, a =6.000(12), b =8.196(5), c =12.538(6)Å, α = 82.45(4), β =86.40(14), γ =89.61(14)°, V = 610.0Å^3, Z =1, D_c =1.362 gcm^{-3}, Mo K_α, λ= 0.71069Å, μ =1.03cm^{-1}, F(000) = 266, T = 293 K, final R,R_w =0.060, 0.076 for 1966 observed reflections F>4σ(F), final maximum shift/esd =0.253, final difference Fourier: max = 0.38, min = -0.42.

3.1.2 Structure solution and refinement:

Details of the crystal preparation are given in the table in section 2.14 under ALA/R-MAN4. Information about the method of structure determination may be found in chapter 2. The deposited crystals were all of similar

morphology, indicating that there was a single product. Nmr and mp indicated that both components were present in the precipitated crystals. Refer to sections 2.16 and 2.17 for details. A plate whose maximum dimension was less than 1mm was selected for data collection. It was mounted on a glass fibre parallel to a direction of optical extinction, which was found to correspond to the a-axis. The space group was P1, determined using oscillation and Weissenberg photographs. A refined unit cell was obtained on an Enraf-Nonius CAD-4 four circle diffractometer during an automated search for reflections prior to data collection.

2311 data, with $2\theta_{max} = 50°$, were collected using the method of ω, 2θ-scans. The ranges of the indices were $-7 \leq h \leq 7$, $-9 \leq k \leq 9$ and $0 \leq l \leq 14$. 2126 data remained after merging equivalent reflections, when the merging R-factor was 0.048. The structure was determined and refined using 1966 reflections with $F > 4\sigma(F)$. This takes account of the single reflection, -1 1 1, omitted because of the significant deviation of F_{obs} from F_{calc}. The structure was solved using the direct methods program, SHELX84[27], which found all non-hydrogen atoms of two each of mandelic acid and alanine and including an unexpected and relatively heavy atom not bonded to anything. This last peak was attributed to the oxygen atom of a molecule of water. It was the structure solution which revealed the presence of the water molecule.

All of these atoms were passed into the least squares refinement program, SHELX76[29]. Before any refinement, the R-factor was 0.201, which was quite satisfactory at this early stage. With the x,y and z coordinates of the chiral carbon of one of the mandelic acid molecules held fixed, in order to provide a reference point for all of the other coordinates; there being no symmetry to provide this, the structure was refined. All non-hydrogen atoms

were refined anisotropically and all hydrogen atoms bonded to carbon atoms were placed in calculated positions, with C-H = 1.08Å. Hydrogen atoms which were located in difference maps included both carboxyl hydrogen atoms on the undissociated mandelic acid molecules, three ammonium hydrogen atoms on each of the zwitterionic alanine molecules and one water hydrogen atom. A second was included during refinement, but after calculations had been done to determine bond lengths etc, and the hydrogen bonding scheme, it was decided to discard it, because the geometry around it was improbable. The lengths of the N-H bonds were constrained to be 1.0Å, using the DFIX instruction in SHELX76. Only separations between bonded atoms were constrained. The observed N-H separations remained a little short of 1.0Å. The asymmetric unit was divided into two blocks, refined alternately, to reduce the number of parameters refined in any cycle. Mandelic acid molecules were in one block and alanine and water in the other. The weighting scheme applied was $W^{-1} = \sigma^2(F) + 0.0045\ F^2$.

3.1.3: Results of Structure Determination:

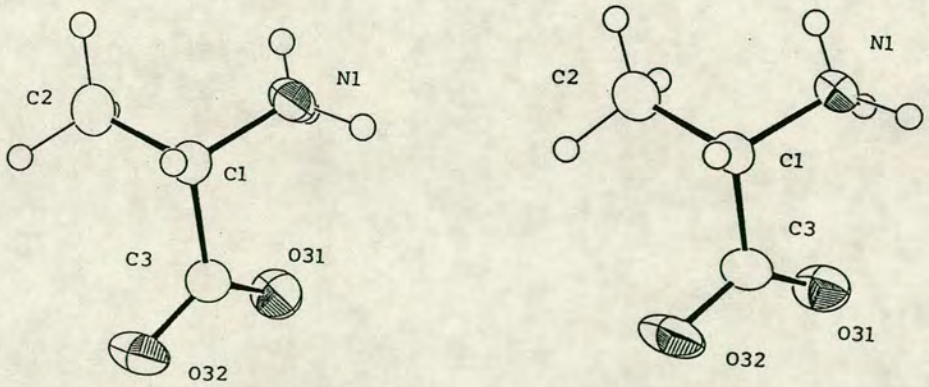
Fractional coordinates of non-hydrogen atoms, six anisotropic thermal parameters for each and fractional coordinates of hydrogen atoms are listed in the following tables. Isotropic thermal parameters for all hydrogen atoms were fixed at $0.05Å^2$. The asymmetric unit consists of two mandelic acid molecules, two alanine molecules and one molecule of water, which is the entire unit cell in this structure with space group P1. Points of interest include that it was possible to locate in difference maps all hydrogen atoms apart from one in the water molecule. To reduce the ratio of refining parameters to x-ray diffraction data, hydrogen atoms bonded to carbon atoms were placed in ideal, calculated positions. Esd's on fractional coordinates ranged from 0.00025 to 0.0012.

The range of the values of principal anisotropic thermal parameters was 0.0223(17) to 0.094(4)Å². Principal thermal parameters on remote carbon atoms in the mandelic acid phenyl rings ranged from 0.0297(19) to 0.088(4)Å², approximately. This was larger than most others, apart, mainly, from the water oxygen atom. The esd's were slightly larger on atoms with relatively large thermal parameters. These facts suggest that there was some small freedom in the positions of these atoms.

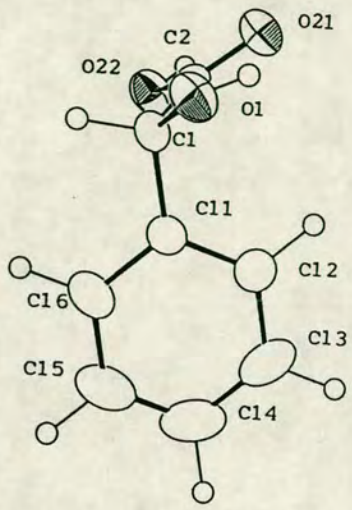
Lengths of C-O bonds in the carboxylic acid parts of the molecules and the fact that three hydrogen atoms, making a suitable tetrahedral arrangement, were located in the vicinity of the nitrogen atom of the alanine molecule, revealed that the mandelic acid was an undissociated acid and that the amino acid was a zwitterion. The cocrystallisation product was therefore not a salt, but a molecular complex, with no charged electrostatic interactions causing them to combine. See section 4.1 for details.

Figure 3.1 S-Alanine R-Mandelic Acid

alanine, molecule A *alanine, molecule B*



mandelic acid, molecule 1



mandelic acid, molecule 2

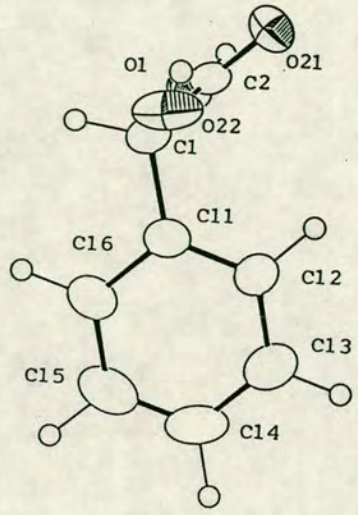


Table 3.1.1 Fractional coordinates with isotropic thermal parameters in Å² (U_{iso} for H fixed at 0.05Å²)

	x	y	z	U_{iso}
C(1)	0.2852	0.8144	0.1825	0.0328(18)
O(1)	0.1555(6)	0.8689(4)	0.2692(3)	0.0436(16)
C(2)	0.3197(6)	0.6298(5)	0.2044(3)	0.0312(18)
O(21)	0.2073(6)	0.5469(4)	0.2766(3)	0.0428(16)
O(22)	0.4697(5)	0.5738(4)	0.1405(3)	0.0446(17)
C(11)	0.1813(7)	0.8558(5)	0.0759(3)	0.0330(19)
C(12)	-0.0268(8)	0.7920(6)	0.0612(4)	0.0451(23)
C(13)	-0.1227(10)	0.8292(8)	-0.0353(5)	0.066(3)
C(14)	-0.0133(12)	0.9339(8)	-0.1176(5)	0.069(4)
C(15)	0.1913(11)	0.9991(7)	-0.1037(4)	0.063(3)
C(16)	0.2887(8)	0.9597(5)	-0.0073(4)	0.0449(23)
C(1')	0.1809(7)	0.4303(5)	0.5794(4)	0.0374(20)
O(1')	0.3130(8)	0.5262(5)	0.4964(3)	0.0556(20)
C(2')	0.1615(6)	0.2556(5)	0.5515(3)	0.0325(18)
O(21')	0.2667(6)	0.2102(4)	0.4763(3)	0.0462(17)
O(22')	0.0206(5)	0.1644(4)	0.6174(3)	0.0442(16)
C(11')	0.2929(7)	0.4344(5)	0.6831(3)	0.0358(20)
C(12')	0.4963(7)	0.3596(6)	0.6991(4)	0.0443(23)
C(13')	0.5979(9)	0.3672(7)	0.7921(4)	0.058(3)
C(14')	0.4981(10)	0.4516(7)	0.8712(4)	0.064(3)
C(15')	0.2992(10)	0.5289(7)	0.8559(4)	0.058(3)
C(16')	0.1945(8)	0.5184(6)	0.7630(4)	0.0461(23)
C(1A)	0.8732(6)	0.2863(4)	0.1966(3)	0.0284(16)
N(1A)	1.0330(6)	0.2076(4)	0.2719(3)	0.0354(18)
C(3A)	0.6487(6)	0.1974(4)	0.2250(3)	0.0292(17)
O(31A)	0.6460(5)	0.0608(3)	0.27707(25)	0.0433(16)
O(32A)	0.4825(4)	0.2699(4)	0.1841(3)	0.0431(15)
C(2A)	0.9535(8)	0.2780(7)	0.0816(4)	0.052(3)
C(1B)	0.6161(5)	0.9169(4)	0.5301(3)	0.0292(17)
N(1B)	0.4485(5)	0.8664(4)	0.4595(3)	0.0316(16)
C(3B)	0.8392(6)	0.8370(4)	0.5015(3)	0.0332(19)
O(31B)	0.8455(5)	0.7277(4)	0.4434(3)	0.0457(16)
O(32B)	1.0034(5)	0.8919(4)	0.5433(3)	0.0526(18)
C(2B)	0.5400(7)	0.8674(7)	0.6466(4)	0.055(3)
O(1W)	0.7542(8)	0.3838(5)	0.4223(4)	0.0626(23)

	x	y	z
H(1)	0.4433	0.8782	0.1768
H(1O)	0.070(10)	0.799(7)	0.302(5)
H(2O)	0.460(8)	0.458(7)	0.157(5)
H(12)	−0.1133	0.7128	0.1261
H(13)	−0.2828	0.7772	−0.0472
H(14)	−0.0899	0.9645	−0.1933
H(15)	0.2753	1.0809	−0.1682
H(16)	0.4502	1.0102	0.0037
H(1')	0.0136	0.4783	0.5879
H(1O')	0.312(12)	0.509(8)	0.455(5)
H(2O')	0.017(9)	0.063(7)	0.592(5)
H(12')	0.5755	0.2946	0.6374
H(13')	0.7569	0.3074	0.8044
H(14')	0.5786	0.4559	0.9455
H(15')	0.2243	0.5981	0.9164
H(16')	0.0338	0.5761	0.7518
H(1A)	0.8559	0.4155	0.2043
H(1NA)	0.996(9)	0.210(6)	0.348(5)
H(2NA)	1.031(9)	0.094(8)	0.273(4)
H(3NA)	1.146(10)	0.217(7)	0.250(5)
H(21A)	0.8330	0.3366	0.0286
H(22A)	0.9732	0.1509	0.0687
H(23A)	1.1120	0.3407	0.0648
H(1B)	0.6363	1.0490	0.5181
H(1NB)	0.471(9)	0.890(6)	0.383(5)
H(2NB)	0.455(8)	0.757(8)	0.448(4)
H(3NB)	0.320(10)	0.867(6)	0.497(5)
H(21B)	0.6769	0.8805	0.6968
H(22B)	0.4850	0.7408	0.6579
H(23B)	0.4035	0.9455	0.6686
H(2W)	0.657(10)	0.396(7)	0.473(5)

Table 3.1.2 Anisotropic thermal parameters in Å²

	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
C(1)	0.0357(18)	0.0327(18)	0.0292(18)	−0.0035(14)	0.0014(14)	−0.0082(14)
O(1)	0.0556(18)	0.0370(15)	0.0371(16)	−0.0080(12)	0.0068(13)	−0.0041(13)
C(2)	0.0288(17)	0.0416(19)	0.0223(17)	−0.0011(14)	−0.0062(14)	−0.0042(14)
O(21)	0.0524(17)	0.0366(14)	0.0377(15)	−0.0040(12)	0.0073(12)	−0.0026(12)
O(22)	0.0450(16)	0.0367(15)	0.0496(18)	0.0014(13)	0.0076(13)	0.0034(12)
C(11)	0.0355(18)	0.0330(18)	0.0297(19)	−0.0045(14)	0.0007(14)	0.0000(14)
C(12)	0.0415(22)	0.0468(23)	0.0455(23)	−0.0001(18)	−0.0073(18)	−0.0032(17)
C(13)	0.056(3)	0.075(4)	0.068(4)	−0.013(3)	−0.031(3)	0.008(3)
C(14)	0.088(4)	0.080(4)	0.040(3)	−0.0078(25)	−0.025(3)	0.013(3)
C(15)	0.084(4)	0.070(3)	0.0324(25)	0.0056(22)	0.0042(24)	0.006(3)
C(16)	0.056(3)	0.0427(21)	0.0342(21)	−0.0021(17)	0.0092(18)	−0.0027(18)
C(1')	0.0382(20)	0.0385(19)	0.0354(20)	−0.0048(15)	−0.0109(16)	−0.0007(15)
O(1')	0.0843(25)	0.0440(17)	0.0377(18)	0.0039(15)	−0.0227(19)	−0.0219(16)
C(2')	0.0346(18)	0.0375(18)	0.0249(18)	−0.0024(14)	−0.0076(14)	−0.0020(14)
O(21')	0.0554(18)	0.0428(15)	0.0393(16)	−0.0082(13)	0.0059(14)	0.0009(13)
O(22')	0.0443(16)	0.0453(16)	0.0428(16)	−0.0121(13)	0.0012(13)	−0.0067(13)
C(11')	0.0407(20)	0.0323(17)	0.0335(20)	−0.0028(14)	−0.0038(15)	−0.0091(15)
C(12')	0.0395(22)	0.0528(24)	0.0400(22)	−0.0075(18)	−0.0080(17)	0.0026(18)
C(13')	0.054(3)	0.066(3)	0.051(3)	−0.0037(23)	−0.0151(21)	−0.0029(23)
C(14')	0.078(4)	0.072(3)	0.041(3)	−0.0085(23)	−0.0219(24)	−0.011(3)
C(15')	0.082(4)	0.060(3)	0.0307(21)	−0.0096(20)	0.0078(22)	−0.007(3)
C(16')	0.0476(23)	0.0518(24)	0.0383(22)	−0.0127(18)	0.0051(18)	−0.0045(19)
C(1A)	0.0277(16)	0.0269(15)	0.0292(17)	0.0029(12)	−0.0029(13)	0.0001(12)
N(1A)	0.0280(15)	0.0366(17)	0.0405(19)	0.0020(14)	−0.0109(13)	−0.0037(13)
C(3A)	0.0282(16)	0.0300(17)	0.0296(17)	−0.0089(13)	−0.0021(13)	−0.0025(13)
O(31A)	0.0415(15)	0.0339(14)	0.0522(17)	0.0067(12)	−0.0059(12)	−0.0105(11)
O(32A)	0.0252(13)	0.0380(13)	0.0649(18)	−0.0030(12)	−0.0078(11)	−0.0006(10)
C(2A)	0.0408(22)	0.077(3)	0.0352(22)	0.0096(20)	−0.0045(17)	0.0017(20)
C(1B)	0.0243(15)	0.0339(16)	0.0296(17)	−0.0081(13)	−0.0038(13)	−0.0041(12)
N(1B)	0.0246(15)	0.0380(16)	0.0320(17)	−0.0053(12)	−0.0063(12)	−0.0011(12)
C(3B)	0.0272(17)	0.0290(16)	0.0423(21)	−0.0036(14)	−0.0003(14)	−0.0020(13)
O(31B)	0.0364(14)	0.0401(15)	0.0610(19)	−0.0191(13)	−0.0004(12)	0.0013(11)
O(32B)	0.0241(13)	0.0511(16)	0.0837(23)	−0.0256(16)	−0.0066(13)	−0.0045(11)
C(2B)	0.0347(20)	0.094(4)	0.0353(22)	−0.0130(22)	−0.0026(16)	−0.0075(21)
O(1W)	0.0697(25)	0.0659(21)	0.0519(22)	−0.0198(18)	0.0076(19)	0.0103(18)

3.2 S-Alanine/S-Mandelic Acid

3.2.1 Crystal data:

$C_3H_7NO_2.C_8H_8O_3$, M_r = 241.22, monoclinic, C2, a =17.784(8),b =5.334(2), c =12.418(5)Å, β = 100.682(10)°, V = 1569.3Å^3, Z = 4, D_c =1.343gcm^{-3}, MoK_α, λ = 0.71069Å, μ =1.03cm^{-1}, F(000) =512, T =293K, final R,R_w =0.067, 0.071 for 732 observed reflections with F>4σ(F), final max shift/esd =-0.962, final difference Fourier : max =0.22, min =-0.24.

3.2.2 Structure solution and refinement:

Details of crystal preparation are given in the table in 2.14, under ALA/S-MAN7, and descriptions of the methods of structure determination, etc., are given in Chapter 2. NMR and mp were consistent with a 1:1 compound (see sections 2.16 and 2.17). A plate 0.5x0.4x0.1mm was selected and mounted parallel to an optical extinction direction which was found to correspond to the crystallographic b-axis. From oscillation and Weissenberg photographs, the space group was determined to be C2. 1134 data were collected on the STADI-2 diffractometer, with $2\theta_{max}$= 50° and 0<h<21, 0<k<6, -15<l<15, leaving 1062 reflections after merging, for which R_m = 0.006. Of these, 732 with F>4σ(F) were used for structure determination and refinement.

The structure was solved by SHELX84[27] direct methods. All non-hydrogen atoms, except the five carbon atoms of the phenyl ring of the mandelic acid, which are remote from the chiral centre, were located. These twelve atoms were refined isotropically for three cycles to give R = 0.23, and the remaining five non-hydrogen atoms were then located in a difference electron density map. All non-hydrogen atoms were refined anisotropically. Hydrogen

atoms bonded to carbon were included in calculated positions, with C-H = 1.08Å, and all hydrogen atoms bonded to nitrogen and oxygen were found in subsequent difference maps. A weighting scheme of the form $W^{-1} = \sigma^2(F) + 0.000747F^2$ was applied.

3.2.3 Results of Structure Determination:

Fractional coordinates of non-hydrogen atoms, six anisotropic thermal parameters for each and fractional coordinates of hydrogen atoms are listed in tables at the end of this section.

Isotropic thermal parameters for all hydrogen atoms were fixed at 0.05Å². The asymmetric unit consists of one mandelic acid molecule and one alanine molecule. There are four asymmetric units in the entire unit cell.

Three hydrogen atoms, making a suitable ammonium group on the alanine molecule and the hydroxyl hydrogen atom of the mandelic acid were located in difference maps and fractional coordinates refined. The acid hydrogen atom of the mandelic acid, however, was not found in difference maps, but the lengths of the C-O bonds in the mandelic acid showed to which oxygen atom it must be bound.

The esd's on the fractional coordinates were larger than those in S-alanine-R-mandelic acid, in the range 0.0003 to 0.005. Anisotropic thermal parameters were, mostly, of a similar order to those for S-alanine-R-mandelic acid, in the range 0.014(4) to 0.284(22)Å². Principal anisotropic thermal parameters of carbon atoms of the phenyl ring in the mandelic acid molecule were two to ten times those of many other atoms in the structure, in the range 0.039(7) to 0.284(22)Å², with esd's frequently double, in the range 0.0006 to 0.0012. There

was a far greater difference in the thermal parameters between phenyl ring remote carbon atoms and other atoms, in this diastereomer than in S-alanine-R-mandelic acid. This suggests a far greater freedom of 'movement' of the phenyl ring.

Figure 3.2 S-Alanine S-Mandelic Acid

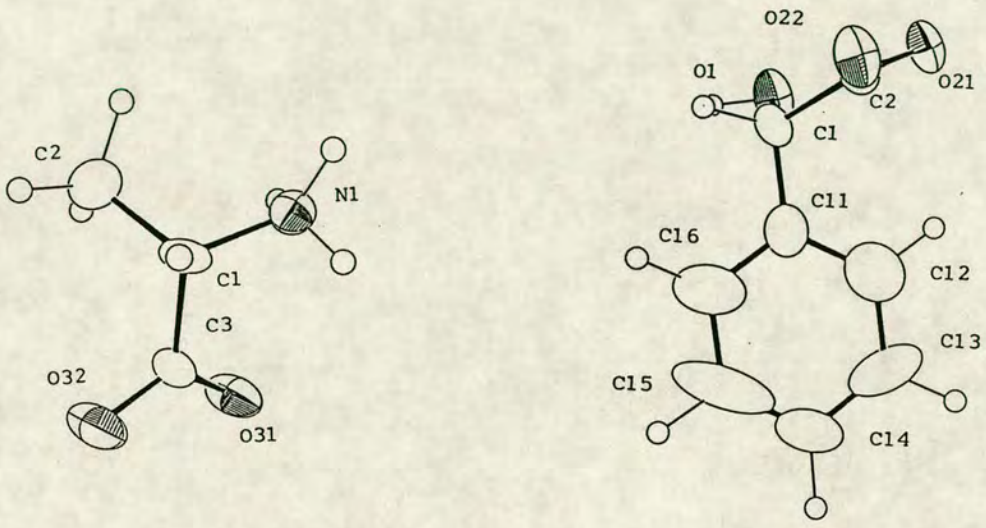


Table 3.2.1 Fractional coordinates with isotropic thermal parameters in Å² (U_{iso} for H fixed at 0.05Å²)

	x	y	z	U_{iso}
C(1)	0.3542(4)	-0.1330(19)	0.7932(6)	0.032(4)
O(1)	0.2827(3)	-0.2357(17)	0.8097(5)	0.045(4)
C(2)	0.3581(4)	0.1333(20)	0.8367(6)	0.032(5)
O(21)	0.3000(4)	0.2487(18)	0.8420(4)	0.042(3)
O(22)	0.4249(3)	0.2274(19)	0.8655(4)	0.045(3)
C(11)	0.3594(4)	-0.1308(21)	0.6748(7)	0.043(5)
C(12)	0.3204(9)	0.045(3)	0.6038(10)	0.108(11)
C(13)	0.3250(11)	0.044(4)	0.4937(11)	0.152(15)
C(14)	0.3647(10)	-0.137(4)	0.4502(10)	0.108(11)
C(15)	0.4038(7)	-0.301(5)	0.5233(12)	0.137(14)
C(16)	0.3987(6)	-0.309(4)	0.6316(8)	0.090(9)
C(1A)	0.6006(5)	0.3533	0.8793(6)	0.032(5)
N(1A)	0.6741(4)	0.4648(21)	0.9324(6)	0.033(5)
C(3A)	0.6027(5)	0.0773(18)	0.8969(6)	0.029(5)
O(31A)	0.6642(4)	-0.0277(17)	0.9252(5)	0.045(4)
O(32A)	0.5385(3)	-0.0340(17)	0.8784(5)	0.050(4)
C(2A)	0.5835(4)	0.4186(21)	0.7570(6)	0.046(5)
H(1)	0.4010	-0.2460	0.8350	
H(1O)	0.295(5)	-0.403(19)	0.815(7)	
H(12)	0.2852	0.183	0.6348	
H(13)	0.2984	0.192	0.4406	
H(14)	0.3675	-0.146	0.3641	
H(15)	0.4371	-0.447	0.4938	
H(16)	0.4267	-0.454	0.6850	
H(1A)	0.5553	0.4283	0.9168	
H(1NA)	0.682(4)	0.407(19)	1.003(7)	
H(2NA)	0.695(5)	0.436(21)	0.892(7)	
H(3NA)	0.691(5)	0.630(22)	0.949(6)	
H(21A)	0.5227	0.4144	0.7257	
H(22A)	0.6118	0.2834	0.7134	
H(23A)	0.6054	0.6038	0.7457	

Table 3.2.2 Anisotropic thermal parameters in Å²

	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
C(1)	0.028(4)	0.026(4)	0.040(5)	-0.007(4)	0.009(3)	-0.001(3)
O(1)	0.029(3)	0.027(3)	0.078(4)	0.001(3)	0.019(3)	-0.007(3)
C(2)	0.024(5)	0.032(4)	0.041(5)	-0.001(3)	0.013(4)	-0.002(4)
O(21)	0.034(4)	0.030(3)	0.060(4)	-0.005(3)	0.016(3)	0.003(3)
O(22)	0.031(3)	0.032(3)	0.070(4)	-0.007(4)	0.0069(23)	-0.008(3)
C(11)	0.037(4)	0.034(4)	0.058(6)	0.003(5)	0.012(4)	-0.005(4)
C(12)	0.164(13)	0.071(9)	0.090(10)	0.002(8)	0.054(9)	0.017(10)
C(13)	0.284(22)	0.127(14)	0.039(7)	0.026(8)	0.025(10)	0.042(17)
C(14)	0.169(14)	0.098(9)	0.059(8)	-0.006(9)	0.057(9)	0.028(10)
C(15)	0.093(9)	0.243(24)	0.077(10)	-0.065(15)	0.034(7)	0.028(14)
C(16)	0.075(7)	0.141(12)	0.051(7)	-0.015(8)	0.007(5)	0.029(10)
C(1A)	0.031(5)	0.014(4)	0.050(5)	0.003(4)	0.009(4)	0.002(3)
N(1A)	0.037(5)	0.027(4)	0.033(5)	-0.002(4)	0.007(3)	0.006(4)
C(3A)	0.030(5)	0.022(4)	0.033(5)	-0.005(3)	0.007(4)	-0.005(4)
O(31A)	0.025(4)	0.026(3)	0.081(4)	0.007(3)	0.005(3)	0.003(3)
O(32A)	0.042(3)	0.031(3)	0.075(4)	0.003(3)	0.011(3)	-0.008(3)
C(2A)	0.049(5)	0.043(5)	0.045(5)	0.005(4)	0.007(4)	0.005(4)

3.3 S-Phenylalanine/R-Mandelic Acid

3.3.1 Crystal Data:

$C_9H_{11}NO_2.C_8H_8O_3$, M_r = 317.32, monoclinic, C2, a = 19.906(16), b = 5.546(6), c =17.110(13)Å, β = 123.82(2)°, V = 1569.3Å^3, Z = 4, D_c =1.343gcm^{-3}, MoK_α, λ = 0.71069Å, μ = 0.93cm^{-1}, $F(000)$ = 672, T = 293K, final R, R_w =0.044, 0.043 for 1199 observed reflections F>4σ(F), final max shift/esd =-0.109, final difference Fourier : max =0.17, min =-0.19 eÅ^{-3}.

3.3.2 Structure solution and refinement

The crystal selected for data collection was an elongated trapezoidal plate of dimensions 0.42 x 0.18 x 0.08mm. Detail of its method of preparation are given in section 2.14 under PHE/R-MAN1. The deposited crystals were all of similar morphology, suggesting that there was a single product. Nmr and mp indicated that both components were present in the precipitated crystals, probably as a molecular complex. Refer to section 2.16 and 2.17 for details.

The crystal was mounted on a glass fibre parallel to an extinction direction, which corresponded to the crystallographic b-axis. Oscillation and Weissenberg photographs revealed that the space group was C2. 1637 data were collected on a Stadi-2 diffractometer by ω-scans, with $2\theta_{max} = 50°$, and with $0 \leq h \leq 24$, $0 \leq k \leq 6$ and $-20 \leq l \leq 20$. 1528 data remained after merging, when the merging R-factor was 0.044 and 1199 data with $F > 4\sigma(F)$ were used for structure determination. The structure was solved using SHELX84[27] direct methods. All non-hydrogen atoms were located and were passed to the least-squares refinement program, SHELX76[29]. Non-hydrogen atoms were refined anisotropically, hydrogen atoms bonded to carbon atoms were placed in ideal positions, and all hydrogen atoms attached to nitrogen and oxygen atoms were located in difference maps and refined with a fixed isotropic thermal parameter. The two molecules were divided into two blocks to be refined separately in turn. The weighting scheme applied was $W^{-1} = \sigma^2(F) + 0.00039\ F^2$.

3.3.3 Results of structure determination:

Fractional coordinates of non-hydrogen atoms, six anisotropic thermal parameters for each and fractional coordinates of hydrogen atoms are listed in the following tables. Isotropic thermal parameters for all hydrogen atoms were fixed at $0.05Å^2$. The asymmetric unit consists of one mandelic acid molecule and one phenylalanine molecule. There are four asymmetric units in the entire unit cell.

Three hydrogen atoms, making a suitable ammonium group on the phenylalanine molecule, the carboxylic acid hydrogen atom and the hydroxyl hydrogen atom of the mandelic acid were located in difference maps and fractional coordinates refined. The remainder of the hydrogen atoms, while many were able to be located in differ-

ence maps, were placed in ideal positions, to reduce the parameters to data ratio and because their positions were not of any special interest.

Coordinates had far smaller esd's than in the alanine structures, in the range 0.00013 to 0.0012 and many were reported accurately to five decimal places. Exceptions were the mandelic acid phenyl ring carbon atoms along one edge and the four more remote carbon atoms of the phenylalanine phenyl ring, which were quoted to four decimal places and with esd's of, usually, 0.0003 or 0.0004. There was little distinction in the sizes of the anistropic thermal parameters, which ranged from 0.0254(16) to 0.113(3)Å². They were in a similar range to the alanine structures. The few distinctions occurred in the mandelic acid hydroxyl oxygen U_{22} value and some of numbers for the remote carbon atoms of the phenyl ring in the phenylalanine molecule, which varied from 0.039(7) to 0.284(10)Å². This suggests that molecules in this structure exhibited little variation in their thermal vibrations and no single part was any more free to move than any other.

Figure 3.3 S-Phenylalanine R-Mandelic Acid

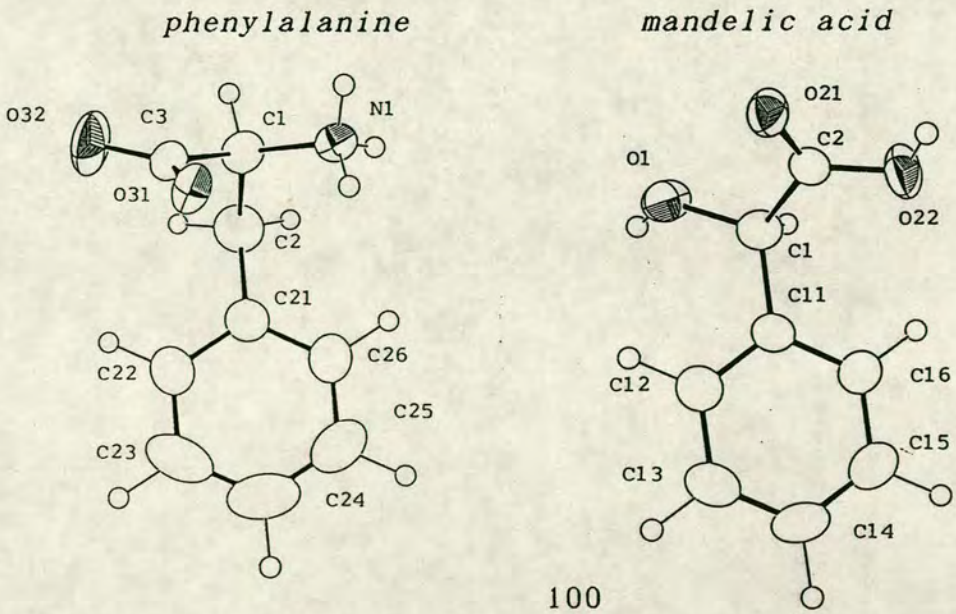


Table 3.3.1 Fractional coordinates with isotropic thermal parameters in Å² (U_{iso} for H fixed at 0.05Å²)

	x	y	z	U_{iso}
C(1)	0.19941(18)	0.2551(8)	0.14390(23)	0.048(3)
O(1)	0.20981(14)	0.0482(7)	0.10422(19)	0.0753(23)
C(2)	0.11757(19)	0.2236(8)	0.12898(23)	0.040(3)
O(21)	0.08074(13)	0.0373(5)	0.10409(16)	0.0522(19)
O(22)	0.09083(15)	0.4222(5)	0.14456(20)	0.0676(23)
C(11)	0.26605(18)	0.2910(7)	0.24795(23)	0.0393(24)
C(12)	0.32384(20)	0.1186(8)	0.29820(25)	0.052(3)
C(13)	0.38457(22)	0.1561(10)	0.39270(25)	0.060(3)
C(14)	0.38688(23)	0.3648(9)	0.4367(3)	0.059(3)
C(15)	0.32972(22)	0.5390(9)	0.3861(3)	0.065(3)
C(16)	0.26928(22)	0.5051(8)	0.29193(24)	0.054(3)
C(1A)	0.38826(19)	0.5379(7)	0.11711(24)	0.045(3)
N(1A)	0.42463(19)	0.4107(6)	0.07236(22)	0.0390(21)
C(3A)	0.38992(20)	0.8116(7)	0.10463(24)	0.041(3)
O(31A)	0.43945(13)	0.8957(5)	0.08883(17)	0.0475(18)
O(32A)	0.34266(15)	0.9331(6)	0.11367(22)	0.085(3)
C(2A)	0.42992(20)	0.4695(8)	0.22086(23)	0.059(3)
C(21A)	0.51593(21)	0.5569(7)	0.28505(22)	0.0442(25)
C(22A)	0.5335(3)	0.7698(8)	0.3342(3)	0.060(3)
C(23A)	0.6126(3)	0.8501(9)	0.3924(3)	0.077(4)
C(24A)	0.6751(3)	0.7185(12)	0.4023(3)	0.079(4)
C(25A)	0.6590(3)	0.5093(12)	0.3541(3)	0.078(4)
C(26A)	0.57982(23)	0.4250(9)	0.29577(25)	0.061(3)
H(1)	0.20293	0.4157	0.11065	
H(1O)	0.2491(20)	0.046(8)	0.1066(23)	
H(2O)	0.0478(21)	0.391(8)	0.1336(23)	
H(12)	0.32235	-0.0477	0.26441	
H(13)	0.43012	0.0196	0.43145	
H(14)	0.43310	0.3921	0.5103	
H(15)	0.33187	0.7054	0.4201	
H(16)	0.22491	0.6444	0.25301	
H(1A)	0.32607	0.4807	0.08209	
H(1NA)	0.3943(19)	0.439(7)	0.0037(24)	
H(2NA)	0.4735(22)	0.476(7)	0.0899(23)	
H(3NA)	0.4325(22)	0.268(8)	0.086(3)	
H(20A)	0.43023	0.2752	0.22551	
H(21A)	0.39494	0.5444	0.24566	
H(22A)	0.4850	0.8757	0.3274	
H(23A)	0.6250	1.0178	0.4301	
H(24A)	0.7366	0.7810	0.4481	
H(25A)	0.7080	0.4064	0.3609	
H(26A)	0.56819	0.2563	0.25878	

Table 3.3.2 Anisotropic thermal parameters in Å²

	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
C(1)	0.0294(17)	0.063(3)	0.0397(20)	-0.0095(20)	0.0229(17)	-0.0061(19)
O(1)	0.0288(13)	0.113(3)	0.0635(17)	-0.0452(19)	0.0261(13)	-0.0032(18)
C(2)	0.0254(16)	0.0463(24)	0.0346(19)	-0.0053(18)	0.0162(15)	0.0000(19)
O(21)	0.0383(13)	0.0411(15)	0.0585(16)	-0.0111(14)	0.0306(12)	-0.0038(14)
O(22)	0.0363(14)	0.0415(16)	0.0979(22)	-0.0199(16)	0.0410(16)	-0.0032(14)
C(11)	0.0254(16)	0.0443(20)	0.0359(19)	-0.0019(18)	0.0188(15)	-0.0053(16)
C(12)	0.0369(19)	0.0496(24)	0.0498(23)	-0.0039(20)	0.0237(18)	-0.0023(19)
C(13)	0.0400(21)	0.068(3)	0.0470(25)	0.0053(25)	0.0164(20)	0.0049(23)
C(14)	0.0452(22)	0.068(3)	0.0383(20)	-0.0107(23)	0.0157(18)	-0.0146(23)
C(15)	0.0566(24)	0.059(3)	0.0526(25)	-0.0182(25)	0.0277(22)	-0.008(3)
C(16)	0.0419(20)	0.0497(24)	0.0467(22)	-0.0103(21)	0.0218(18)	-0.0023(19)
C(1A)	0.0304(18)	0.0424(20)	0.0483(21)	-0.0002(20)	0.0261(17)	-0.0052(19)
N(1A)	0.0312(15)	0.0280(15)	0.0399(17)	0.0036(16)	0.0174(14)	-0.0046(16)
C(3A)	0.0283(18)	0.0374(20)	0.0413(21)	-0.0019(17)	0.0172(17)	0.0036(17)
O(31A)	0.0358(13)	0.0288(13)	0.0602(16)	0.0063(13)	0.0314(13)	0.0023(12)
O(32A)	0.0556(16)	0.0612(20)	0.1127(23)	-0.0105(19)	0.0610(18)	0.0090(16)
C(2A)	0.0558(22)	0.054(3)	0.0491(22)	0.0065(20)	0.0367(20)	-0.0072(20)
C(21A)	0.0472(19)	0.0372(19)	0.0322(18)	0.0092(18)	0.0245(17)	-0.0007(20)
C(22A)	0.065(3)	0.0467(25)	0.0417(22)	0.0028(21)	0.0262(22)	0.0078(23)
C(23A)	0.094(4)	0.059(3)	0.0359(23)	0.0003(23)	0.019(3)	-0.022(3)
C(24A)	0.054(3)	0.107(5)	0.045(3)	0.015(3)	0.0176(23)	-0.012(3)
C(25A)	0.054(3)	0.108(5)	0.049(3)	0.018(3)	0.0275(23)	0.025(3)
C(26A)	0.0601(24)	0.0549(25)	0.0431(21)	0.0060(22)	0.0266(20)	0.0160(25)

3.4 S-Phenylalanine/S-Mandelic Acid

3.4.1 Crystal Data

$C_9H_{11}NO_2.C_8H_8O_3$, M_r = 317.32, monoclinic, C2, a =19.296(12), b =5.7109(4), c =15.672(15)Å, β = 115.29(1)°, V = 1561.49Å^3, Z = 4, D_c =1.350gcm^{-3}, MoK_α, λ = 0.71069Å, μ =0 .93cm^{-1}, $F(000)$ = 672, T =293 K, final R, R_w = 0.084, 0.080 for 906 observed reflections , final max shift/esd =0.048, final difference Fourier :- max =0.41, min =-0.38 eÅ^{-3}.

3.4.2 Structure solution and refinement:

Details of the preparation of this crystal are given in section 2.14 under PHE/S-MAN15. The crystal morphology was uniform, which suggested that there was a single product. Nmr and mp indicated that both components were present in the crystals deposited (see sections 2.16 and 2.17). The trapezium-shaped plate selected was of dimensions 0.4 x 0.16 x 0.08mm. It was mounted on a glass fibre, along an extinction axis, which was found to run parallel to the crystallographic b-axis. The space group, C2, was obtained from oscillation and Weissenberg photographs. 1542 data were collected on the Stadi-2 diffractometer in ω-scans, with $2\theta_{max}$ = 50° and $-22 \leq h \leq 22$, $0 \leq k \leq 6$, $0 \leq l \leq 18$. 1509 data remained after merging, when the R-factor was 0.012. 906 data with $F > 3\sigma(F)$ were used for structure determination.

The structure was solved using SHELX84[27] direct methods, and all non-hydrogen atoms were located apart from one carbon atom in the phenyl ring of the phenylalanine molecule. These atomic positions were read into the structure refinement program SHELX76[29] and the remaining atom found in a subsequent difference map. After the first structure factor calculation the R-factor

was 0.26, which was quite satisfactory. All hydrogen atoms attached to carbon atoms were placed in ideal positions. The ratio of number of reflections to number of refining parameters was approximately 4.5:1, which is quite low, so the asymmetric unit was divided into two blocks each containing one of the molecules, to be refined alternately. This increased the data to parameters ratio to approximately 9:1 in each cycle. All non-hydrogen atoms were allowed to refine with six anisotropic thermal parameters. One of the ammonium hydrogen atoms of the phenylalanine molecule was located in difference maps, the remaining two were placed in ideal, calculated positions and the atomic arrangement in this functional group was constrained during refinement to keep N-H distances 1.03Å and the angles tetrahedral. The hydroxyl hydrogen atom of the mandelic acid was located, but not the expected acid hydrogen atom. Bond lengths indicated to which oxygen atom the latter atom would be bonded, but there was insufficient information about the orientation relative to the carboxylate carbon atom and the torsion angle it would make with the chiral carbon atom, to calculate its position. The weighting scheme which was applied was $W^{-1} = \sigma^2(F) + 0.00094F^2$.

3.4.3 Results of structure determination:

Fractional coordinates of non-hydrogen atoms, six anisotropic thermal parameters for each and fractional coordinates of hydrogen atoms are listed in tables at the end of this section.

Isotropic thermal parameters for all hydrogen atoms were fixed at $0.05Å^2$. The asymmetric unit consists of one mandelic acid molecule and one phenylalanine molecule. There are four asymmetric units in the entire unit cell. Phenyl ring and tetrahedral carbon atoms were placed in ideal positions. One hydrogen atom bonded to the nitrogen

atom in the amino acid molecule was located in the difference map. It was assumed that this structure would be like the others in having a charged ammonium group on the amino acid because the pKa values predicted that this would be the case. Three hydrogen atoms were placed at coordinates to make a tetrahedral arrangement, based on the coordinates of the nitrogen atom, the α-carbon atom and the single hydrogen atom located in difference maps. The mandelic acid hydroxyl hydrogen atom was located in the electron density maps and remained satisfactory. No acid hydogen atom was located, despite the fact that from C-O bond lengths, the mandelic acid was clearly undissociated and the phenylalanine carboxylic acid functional group clearly ionised. The only peak in the difference map within bonding distance of any of these oxygen atoms occurred close to the doubly bonded oxygen atom of the mandelic acid. It was therefore attributable either to a lone pair of electrons on this atom or simply to noise.

The esd's on the fractional coordinates were similar to those in the structure of S-alanine-R-mandelic acid, being found in the range, 0.0003 to 0.0012. The pattern to the values of the anisotropic thermal parameters was similar to the other structures, except the esd's were broadly larger. Principal thermal parameters ranged from 0.021(6) to 0.151(1)Å^2. The remote carbon atoms in the phenyl rings had principal anisotropic thermal parameters which ranged from 0.028(7) to 0.151(17)Å^2. The values for the remote carbon atoms of the phenyl rings were larger than for S-phenylalanine-R-mandelic acid, but smaller than for S-alanine-S-mandelic acid. This suggests that the structure of S-phenylalanine-S-mandelic acid has more freedom, particularly in the phenyl rings, than its diastereomer; much less freedom than in S-alanine-R-mandelic acid and a little less freedom than in S-alanine-S-mandelic acid.

Figure 3.4 S-Phenylalanine S-Mandelic Acid

phenylalanine *mandelic acid*

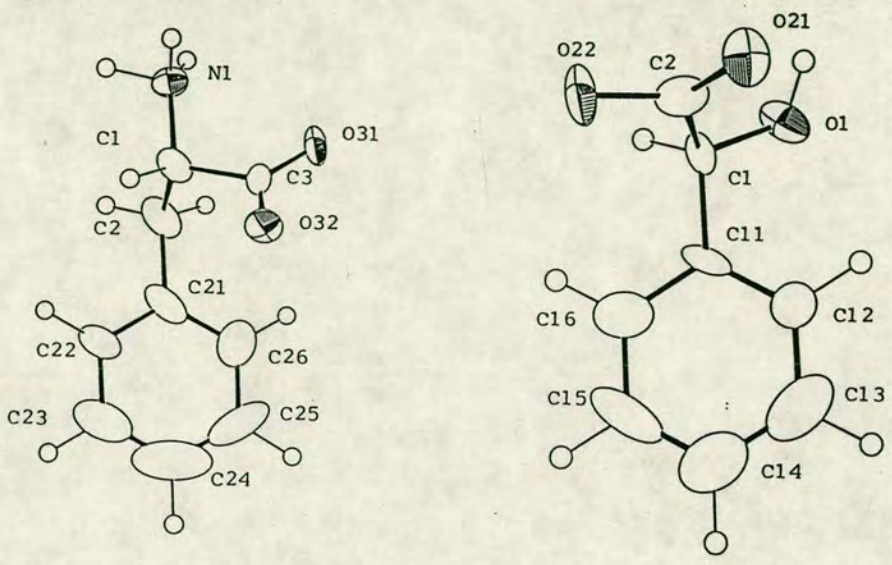


Table 3.4.1 Fractional coordinates with isotropic thermal parameters in Å² (U_{iso} for H fixed at 0.05Å²)

	x	y	z	U_{iso}
C(1)	0.2291(5)	-0.279(3)	0.1242(7)	0.035(7)
O(1)	0.2581(4)	-0.140(3)	0.0732(5)	0.046(6)
C(2)	0.1518(6)	-0.181(4)	0.1141(8)	0.035(8)
O(21)	0.1324(4)	0.016(3)	0.0989(6)	0.046(6)
O(22)	0.1101(4)	-0.354(3)	0.1283(6)	0.051(6)
C(12)	0.3314(6)	-0.097(3)	0.2664(8)	0.043(9)
C(13)	0.3825(7)	-0.099(4)	0.3631(10)	0.075(13)
C(14)	0.3843(8)	-0.293(5)	0.4172(11)	0.077(13)
C(15)	0.3378(9)	-0.479(4)	0.3758(10)	0.077(13)
C(16)	0.2878(7)	-0.475(3)	0.2803(8)	0.056(10)
C(1A)	0.4647(6)	0.6249	0.1248(8)	0.034(8)
N(1A)	0.4036(5)	0.795(3)	0.0662(7)	0.034(7)
C(3A)	0.4314(7)	0.379(3)	0.1082(7)	0.034(9)
O(31A)	0.3643(4)	0.356(3)	0.0959(5)	0.042(6)
O(32A)	0.4750(4)	0.217(3)	0.1087(5)	0.038(6)
C(2A)	0.4907(6)	0.705(3)	0.2280(7)	0.047(9)
C(21A)	0.5536(6)	0.539(3)	0.2952(7)	0.040(9)
C(22A)	0.6285(6)	0.574(3)	0.3114(7)	0.053(10)
C(23A)	0.6840(8)	0.426(4)	0.3694(9)	0.070(13)
C(24A)	0.6668(11)	0.240(5)	0.4075(10)	0.094(16)
C(25A)	0.5934(12)	0.199(4)	0.3940(9)	0.088(14)
C(26A)	0.5337(8)	0.351(3)	0.3371(9)	0.060(10)
H(11)	0.2210	-0.455	0.0964	
H(1O)	0.228(6)	-0.074(22)	0.019(7)	
H(12)	0.3296	0.053	0.2238	
H(13)	0.4197	0.049	0.3945	
H(14)	0.4224	-0.296	0.4916	
H(15)	0.3398	-0.631	0.4177	
H(16)	0.2515	-0.624	0.2486	
H(1A)	0.5129	0.6206	0.1069	
H(1NA)	0.386(5)	0.773(21)	-0.003(7)	
H(2NA)	0.366(6)	0.861(23)	0.072(7)	
H(3NA)	0.431(6)	0.970(23)	0.064(7)	
H(20A)	0.4423	0.702	0.2455	
H(21A)	0.5134	0.880	0.2358	
H(22A)	0.6433	0.718	0.2778	
H(23A)	0.7432	0.462	0.3849	
H(24A)	0.7116	0.119	0.4493	
H(25A)	0.5808	0.049	0.4275	
H(26A)	0.4752	0.322	0.3264	

Table 3.4.2 Anisotropic thermal parameters in Å²

	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
C(1)	0.026(6)	0.037(7)	0.039(7)	0.016(7)	0.021(5)	-0.004(6)
O(1)	0.034(4)	0.056(7)	0.042(5)	0.022(5)	0.023(4)	0.015(5)
C(2)	0.022(6)	0.045(9)	0.032(7)	-0.004(7)	0.012(5)	0.013(7)
O(21)	0.042(5)	0.031(6)	0.060(6)	-0.001(5)	0.032(5)	0.008(4)
O(22)	0.048(5)	0.022(5)	0.073(6)	0.011(5)	0.034(5)	-0.002(4)
C(12)	0.031(6)	0.041(8)	0.048(8)	0.002(8)	0.014(6)	0.002(7)
C(13)	0.039(8)	0.093(14)	0.083(12)	-0.039(12)	0.034(9)	-0.013(10)
C(14)	0.060(10)	0.089(14)	0.068(11)	-0.027(13)	0.029(9)	-0.002(11)
C(15)	0.086(11)	0.081(12)	0.055(10)	0.041(10)	0.045(9)	0.052(11)
C(16)	0.044(8)	0.074(11)	0.042(8)	-0.001(9)	0.019(7)	0.009(8)
C(1A)	0.023(6)	0.041(8)	0.032(7)	-0.008(6)	0.011(6)	0.001(6)
N(1A)	0.032(6)	0.030(7)	0.032(5)	0.005(5)	0.012(5)	0.009(5)
C(3A)	0.038(8)	0.030(9)	0.021(6)	0.003(6)	0.000(5)	-0.019(8)
O(31A)	0.029(4)	0.032(5)	0.053(5)	-0.003(5)	0.013(4)	-0.016(4)
O(32A)	0.029(4)	0.021(5)	0.052(6)	0.000(5)	0.012(4)	0.011(4)
C(2A)	0.032(6)	0.046(8)	0.051(8)	-0.023(8)	0.011(6)	-0.002(7)
C(21A)	0.025(7)	0.062(10)	0.026(7)	-0.027(8)	0.008(5)	-0.002(7)
C(22A)	0.028(7)	0.094(13)	0.028(7)	0.013(8)	0.006(6)	-0.002(7)
C(23A)	0.050(9)	0.114(16)	0.031(9)	-0.011(10)	0.003(7)	0.008(12)
C(24A)	0.104(15)	0.113(18)	0.043(10)	-0.004(12)	0.021(10)	0.066(15)
C(25A)	0.151(17)	0.050(11)	0.037(9)	0.019(9)	0.029(11)	0.014(13)
C(26A)	0.075(10)	0.038(9)	0.052(8)	-0.013(8)	0.028(8)	-0.013(9)

3.5 S-α-Aminobutyric Acid/R-Mandelic Acid

3.5.1 Crystal data:

$2C_4H_9NO_2.2C_8H_8O_3.H_2O$, M_r = 528.50, monoclinic, $P2_1$, a = 5.970(5), b = 8.441(6), c =26.784(22)Å, β = 86.40(14)°, V = 1345.2Å³, Z = 2, D_c = 1.305gcm⁻³, Mo K_α, λ = 0.71069Å, μ = 0.97cm⁻¹, $F(000)$ = 564, T =293 K, final R, R_w =0.046, 0.047 for 1917 observed reflections F>4σ(F), final max shift/esd =0.49, final difference Fourier : max =0.24, min =-0.24 eÅ⁻³.

3.5.2 Structure solution and refinement:

Details of the preparation of these crystals are given in the table in section 2.14, under ABA/R-MAN2. Although the mp determination (sections 2.16 and 2.17) indicated impure mandelic acid, subsequent structure determination showed that a 1:1 complex had indeed formed. The crystal selected, of dimensions

1.2x0.25x0.1mm, was mounted along the needle axis, which was parallel to an extinction direction and which was later found to correspond to the crystallographic a-axis. The space group was shown to be $P2_1$ from precession and Weissenberg photographs, which also showed that the crystal was a good diffractor. The data collection set up procedure made use of automatic relection search, indexing and 2-dimensional least squares refinement routines. The refinement program, STFIT[36], normally refines the two reciprocal cell edges perpendicular to the mounting axis and the angle between them. If the crystal is monoclinic and *b*-mounted (or of higher symmetry) then the real and reciprocal mounting axes are coincident and the values of *a*, *c* and β may be determined directly from these. In this case, the value of *b* was determined directly from $b=1/b^*$ and the real value of the *c* cell dimension was obtained using the relationship $c=\sin\beta/c^*$. Thus, the apparent value of *c* that the program produced was corrected by multiplying by sinβ. It was also necessary to correct, by the same factor, the apparent value of a, the mounting axis, which had been calculated from the accurate determination of the best value of the μ-angle as described in section 2.10. The β angle was refined by comparing how well centred some reflections were using various values of β. The final, refined values are listed in the crystal data section.

2499 data were collected on the STADI-2 diffractometer using the method of ω-scans. The maximum value of 2θ was 50°, with $0\leq h\leq 5$, $0\leq k\leq 10$, $-32\leq l\leq 32$. Merging equivalent reflections left 2481 unique data and the merging R-factor was 0.021. Of these 1917 data with $F>4\sigma(F)$ were employed for structure solution and refinement. The structure was solved using SHELX86[28] direct methods, when the positions of all non-hydrogen atoms in the structure were found. It was at this stage that the inclusion of one water molecule to every two ABA and MAN molecules was

discovered. Before refinement the R-factor was 17.1% and a difference Fourier map revealed no new atom peaks.

Hydrogen atoms were placed in ideal calculated positions and allowed to ride on the attached atom as it refined. Terminal methyl groups were later allowed to refine as rigid groups rotating around the bond joining the group to the rest of the molecule. One of the mandelic acid acid hydroxyl hydrogen atoms was located as well as two acid hydrogen atoms. Three hydrogens on each of the ammonium and methyl groups on the amino acids were located. Of the three candidates for hydrogens on the water molecule, two were considered acceptable. A peak near one of the mandelic acid hydroxyl oxygen atoms was a poor because the bond angle at the oxygen atom would have been 60(1)° and thus far too small compared to the ideal tetrahedral angle of 109.4°. Nevertheless, this peak position was put in as a starting point for the hydrogen.

Prior to refinement with DFIX constraints, a structure factor calculation and difference map with the new hydrogen atoms in indicated that the new hydrogen atoms were largely quite acceptable. The crude DFIX constraints on the new hydrogen atoms were later altered so that the N-H and O-H separations were 1.00Å and C-H through space distances to constrain the hydrogen atoms more fully were included. The ideal tetrahedral angle was used throughout. Some low angle reflections with $Fo<Fc$ were omitted because they were considered to be affected by extinction. The weighting scheme applied was $W^{-1} = \sigma^2(F) + 0.00041\ F^2$. After the four final cycles of refinement the R-factor was 0.046 the weighted R-factor, R_w, was 0.047, the maximum in the diference map amounted to 0.24 $eÅ^{-3}$.

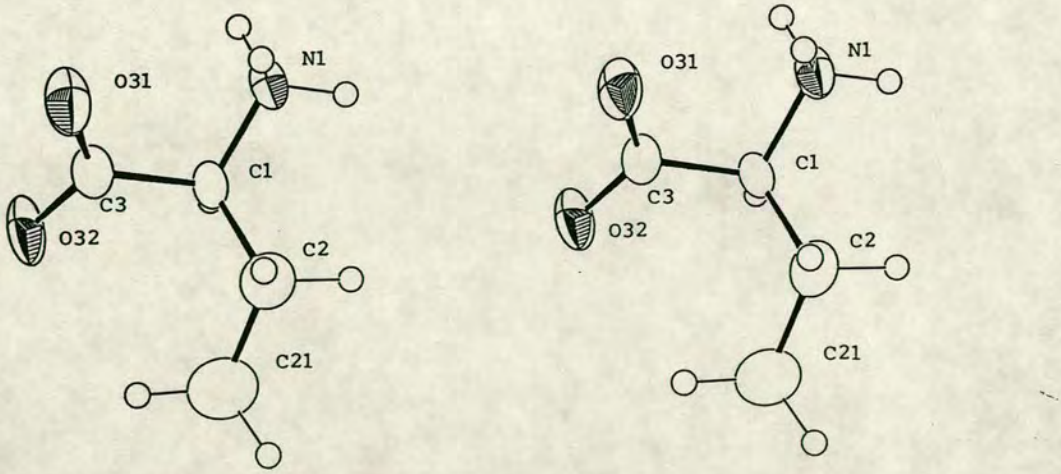
3.5.3 Results of structure determination.

Fractional coordinates of non-hydrogen atoms, six anisotropic thermal parameters for each and fractional coordinates of hydrogen atoms are listed in tables at the end of this chapter. Isotropic thermal parameters for all hydrogen atoms were fixed at 0.05Å^{-2}. The asymmetric unit consists of two mandelic acid molecules, two α-amino-butyric acid molecules and one molecule of water. There are two asymmetric units in the unit cell.

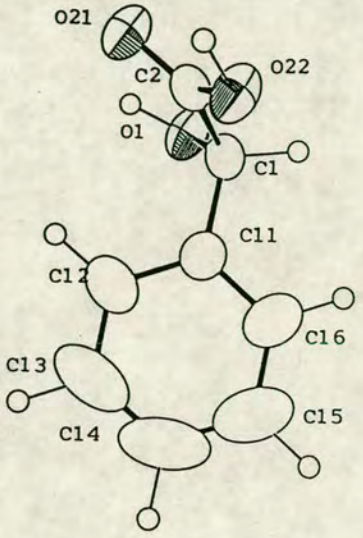
Esd's on fractional coordinates of non-hydrogen atoms vary from 0.00011 to 0.0017, so coordinates are known quite precisely. Principal anisotropic thermal parameters are in the range 0.0184(14) to 0.154(8)Å^2 and most are quite small. It is the remote carbon atoms of the phenyl rings and the amino acid side chains which tend to have the larget thermal parameters, because they are freer to move. ABA-R-MAN approaches ALA-R-MAN in precision of fractiopnal coordinates, but with thermal parameters more akin to PHE-S-MAN in size.

Figure 3.5 S-α-Aminobutyric Acid - R-Mandelic Acid

α-aminobutyric acid(A) *α-aminobutyric acid (B)*



mandelic acid, molecule 1



mandelic acid, molecule 2

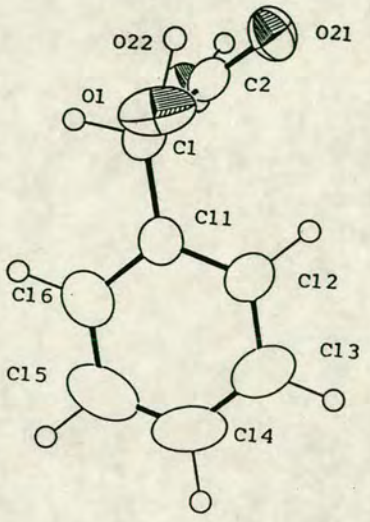


Table 3.5.1 Fractional coordinates with isotropic thermal parameters in Å² (U_{iso} for H fixed at 0.05Å²)

	x	y	z	U_{iso}
C(1)	-0.5424(7)	0.9976	0.16570(15)	0.041(3)
O(1)	-0.3930(5)	0.9267(7)	0.20282(11)	0.0491(19)
C(2)	-0.5655(7)	1.1717(8)	0.17674(17)	0.040(3)
O(21)	-0.4418(5)	1.2395(7)	0.20809(12)	0.0523(20)
O(22)	-0.7254(5)	1.2412(7)	0.14882(13)	0.0571(21)
C(11)	-0.4677(8)	0.9735(8)	0.11376(17)	0.0421(25)
C(12)	-0.2655(9)	1.0352(9)	0.10066(21)	0.062(3)
C(13)	-0.1965(13)	1.0066(11)	0.0536(3)	0.093(5)
C(14)	-0.3301(17)	0.9188(12)	0.01920(25)	0.104(6)
C(15)	-0.5241(14)	0.8572(11)	0.03197(23)	0.091(5)
C(16)	-0.5971(9)	0.8870(9)	0.07924(19)	0.063(3)
C(1')	0.5895(8)	0.3062(8)	0.35067(16)	0.046(3)
O(1')	0.4635(7)	0.2198(7)	0.31305(13)	0.0685(24)
C(2')	0.5989(7)	0.4796(8)	0.33580(17)	0.040(3)
O(21')	0.4816(6)	0.5340(7)	0.30166(12)	0.0543(20)
O(22')	0.7445(5)	0.5611(7)	0.36453(11)	0.0500(20)
C(11')	0.4814(7)	0.2837(8)	0.39969(16)	0.041(3)
C(12')	0.2776(7)	0.3533(8)	0.40640(17)	0.049(3)
C(13')	0.1741(10)	0.3258(9)	0.44974(21)	0.070(4)
C(14')	0.2746(12)	0.2314(10)	0.48702(21)	0.082(5)
C(15')	0.4769(13)	0.1642(10)	0.48036(21)	0.079(5)
C(16')	0.5823(9)	0.1905(9)	0.43692(19)	0.060(3)
C(1A)	-0.1234(6)	0.5299(8)	0.17012(13)	0.0298(21)
N(1A)	-0.2797(5)	0.5864(7)	0.20688(13)	0.0373(20)
C(3A)	0.1057(6)	0.6020(8)	0.18524(14)	0.0304(22)
O(31A)	0.1121(4)	0.7266(7)	0.20882(11)	0.0444(18)
O(32A)	0.2734(4)	0.5306(7)	0.17054(11)	0.0452(18)
C(2A)	-0.2118(7)	0.5799(9)	0.11743(15)	0.048(3)
C(21A)	-0.0791(9)	0.5151(9)	0.07631(17)	0.068(4)
C(1B)	0.1543(5)	0.8375(7)	0.32595(13)	0.0301(21)
N(1B)	0.3151(5)	0.8909(7)	0.29037(12)	0.0350(18)
C(3B)	-0.0749(6)	0.9089(8)	0.30992(15)	0.0339(23)
O(31B)	-0.0825(4)	1.0313(7)	0.28479(12)	0.0486(19)
O(32B)	-0.2405(4)	0.8355(7)	0.32402(12)	0.0535(20)
C(2B)	0.2380(7)	0.8913(9)	0.37886(15)	0.055(3)
C(21B)	0.1035(10)	0.8341(10)	0.41974(18)	0.074(4)
O(1W)	0.0046(7)	0.3759(8)	0.27388(14)	0.0660(23)

H(1)	−0.7040	0.9406	0.16665
H(1O)	−0.290(5)	1.0141(18)	0.2151(12)
H(2O)	−0.721(5)	1.3549(12)	0.1593(12)
H(12)	−0.1622	1.1054	0.12718
H(13)	−0.0376	1.0530	0.0435
H(14)	−0.2774	0.9003	−0.01800
H(15)	−0.6238	0.7842	0.00560
H(16)	−0.7573	0.8412	0.08871
H(1')	0.7605	0.2636	0.35524
H(1O')	0.493(6)	0.272(4)	0.2807(3)
H(2O')	0.754(6)	0.6661(20)	0.3475(9)
H(12')	0.1986	0.4291	0.37766
H(13')	0.0124	0.3788	0.45447
H(14')	0.1941	0.2115	0.52117
H(15')	0.5559	0.0890	0.50925
H(16')	0.7444	0.1379	0.43247
H(1A)	−0.1098	0.4023	0.17006
H(1NA)	−0.265(5)	0.710(3)	0.2072(11)
H(2NA)	−0.230(5)	0.549(4)	0.2402(6)
H(3NA)	−0.433(3)	0.561(4)	0.1959(11)
H(21A)	−0.2094	0.7077	0.11550
H(22A)	−0.3828	0.5383	0.11098
H(23A)	−0.154(3)	0.555(3)	0.0404(3)
H(24A)	−0.079(4)	0.3872(9)	0.0772(7)
H(25A)	0.0916(15)	0.558(3)	0.0813(7)
H(1B)	0.1402	0.7100	0.32603
H(1NB)	0.309(3)	1.0090(8)	0.2878(8)
H(2NB)	0.273(3)	0.843(3)	0.2567(3)
H(3NB)	0.4703(11)	0.857(3)	0.3025(6)
H(21B)	0.2377	1.0192	0.37950
H(22B)	0.4079	0.8486	0.38644
H(23B)	−0.0677(16)	0.876(3)	0.4138(7)
H(24B)	0.102(4)	0.7062(10)	0.4206(7)
H(25B)	0.174(3)	0.877(3)	0.4557(3)
H(1W)	0.147(8)	0.413(5)	0.2841(16)
H(2W)	−0.008(7)	0.264(6)	0.2726(16)

Table 3.5.2 Anisotropic thermal parameters in Å²

	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
C(1)	0.0354(23)	0.038(3)	0.048(3)	0.0016(22)	0.0039(20)	−0.0010(22)
O(1)	0.0538(20)	0.0328(18)	0.0592(20)	0.0043(15)	−0.0125(16)	−0.0019(16)
C(2)	0.0286(23)	0.043(3)	0.049(3)	0.0005(24)	0.0054(21)	0.0041(23)
O(21)	0.0518(19)	0.0402(21)	0.0629(20)	−0.0056(17)	−0.0147(17)	0.0022(17)
O(22)	0.0424(18)	0.0424(22)	0.0842(23)	−0.0134(19)	−0.0185(17)	0.0128(17)
C(11)	0.0442(24)	0.0313(24)	0.050(3)	0.0046(21)	−0.0027(21)	0.0084(21)
C(12)	0.058(3)	0.053(3)	0.077(4)	0.011(3)	0.020(3)	0.007(3)
C(13)	0.096(5)	0.088(5)	0.097(5)	0.035(5)	0.050(4)	0.031(5)
C(14)	0.154(8)	0.101(6)	0.059(4)	0.009(4)	0.031(5)	0.048(6)
C(15)	0.127(6)	0.087(5)	0.057(4)	−0.006(4)	−0.016(4)	0.029(5)
C(16)	0.071(3)	0.056(3)	0.060(3)	−0.003(3)	−0.015(3)	0.015(3)
C(1')	0.0383(24)	0.037(3)	0.063(3)	0.0003(24)	0.0127(22)	−0.0016(22)
O(1')	0.093(3)	0.0525(23)	0.0614(21)	−0.0177(19)	0.0301(20)	−0.0373(23)
C(2')	0.0304(23)	0.041(3)	0.048(3)	−0.0040(23)	0.0092(22)	−0.0041(22)
O(21')	0.0511(18)	0.0552(24)	0.0550(19)	0.0036(18)	−0.0100(17)	−0.0026(18)
O(22')	0.0475(18)	0.0383(21)	0.0628(20)	0.0069(16)	−0.0081(16)	−0.0114(16)
C(11')	0.0380(24)	0.035(3)	0.050(3)	−0.0033(22)	−0.0011(20)	−0.0063(22)
C(12')	0.046(3)	0.048(3)	0.054(3)	−0.007(3)	0.0093(22)	−0.004(3)
C(13')	0.066(3)	0.075(4)	0.070(4)	−0.014(3)	0.024(3)	−0.014(3)
C(14')	0.100(5)	0.088(5)	0.058(4)	−0.004(4)	0.029(4)	−0.028(5)
C(15')	0.104(5)	0.078(5)	0.054(3)	0.014(3)	−0.019(4)	−0.026(4)
C(16')	0.051(3)	0.054(3)	0.074(4)	0.009(3)	−0.009(3)	−0.011(3)

C(1A)	0.0200(18)	0.0320(23)	0.0375(21)	-0.0037(19)	0.0049(16)	0.0032(18)
N(1A)	0.0242(17)	0.0365(21)	0.0512(21)	-0.0048(19)	0.0051(15)	-0.0036(17)
C(3A)	0.0261(20)	0.0258(23)	0.0388(22)	0.0024(20)	-0.0003(17)	-0.0012(20)
O(31A)	0.0318(15)	0.0352(19)	0.0658(19)	-0.0156(17)	0.0033(14)	-0.0105(15)
O(32A)	0.0221(14)	0.0410(19)	0.0724(21)	-0.0101(16)	0.0059(13)	0.0051(15)
C(2A)	0.0388(24)	0.057(3)	0.046(3)	-0.0011(24)	-0.0052(20)	0.0050(25)
C(21A)	0.072(3)	0.079(4)	0.051(3)	-0.009(3)	0.002(3)	0.007(4)
C(1B)	0.0199(17)	0.0319(24)	0.0381(21)	0.0017(19)	0.0020(16)	0.0033(18)
N(1B)	0.0225(15)	0.0360(20)	0.0464(19)	0.0005(18)	0.0058(14)	-0.0012(17)
C(3B)	0.0257(20)	0.030(3)	0.0455(24)	0.0023(22)	0.0006(18)	-0.0026(20)
O(31B)	0.0286(15)	0.0396(20)	0.0771(22)	0.0173(17)	0.0020(14)	0.0019(15)
O(32B)	0.0184(14)	0.0494(23)	0.0923(23)	0.0219(19)	0.0041(14)	-0.0055(15)
C(2B)	0.049(3)	0.066(4)	0.048(3)	0.000(3)	-0.0002(22)	-0.010(3)
C(21B)	0.081(4)	0.081(5)	0.058(3)	0.001(3)	0.004(3)	-0.014(4)
O(1W)	0.0640(21)	0.0510(23)	0.0817(24)	0.0107(22)	-0.0074(18)	0.0046(23)

3.6 S-Methionine/R-Mandelic Acid

3.6.1 Crystal data:

$SC_5H_{11}NO_2.C_8H_8O_3$, M_r = 301.33, monoclinic, $P2_1$, a =9.014(5), b =5.831(3), c =14.832(6)Å, β = 99.686(17)°, V = 768.5Å^3, Z = 2, D_c =1.302gcm^{-3}, Mo K_α, λ = 0.71069Å, μ = 2.17cm^{-1}, $F(000)$ = 672, T = 293 K, final R, R_w = 0.097 for 1063 observed reflections with $F>6\sigma(F)$, final difference Fourier: max= 0.59, min= -0.40.

3.6.2 Structure solution and refinement:

Details of the preparation of this crystal are given in section 2.14 under MET/R-MAN1 and general descriptions of the methods of structure determination are given in chapter 2.

The product crystallised readily upon cooling to room temperature as bundles of elongated, rectangular plates. The uniform crystal morphology suggested that

there was a single product. Nmr and mp indicated that both components were present in the crystals deposited, in a 1:1 ratio. Refer to sections 2.16 and 2.17 for details. It was quite hard to get single crystals. An equant rectangular chunk with a tiny clip out of it in the middle of one face, 1.0x1.0x0.8mm in size was mounted on a glass fibre parallel to an extinction axis, which was found to correspond to the b-axis of this monoclinic structure. The space group was determined from oscillation and Weissenberg photographs in the manner described in section 2.8. It was possible only to narrow down the possibilities for space group to $P2_1$ or P2, since the 2-fold screw absences occur along the mounting axis and were therefore not observable on the photographs nor in the data collected on the Stadi-2 diffractometer. The former was more likely since it is a far more common space group than the latter amongst chiral organic compounds. Successful structure solution in $P2_1$ confirmed the assignment of the space group. 1529 data were collected on a Stadi-2 diffractometer with $2\theta < 50°$ and $-11 \leq h \leq 11$, $0 \leq k \leq 6$ and $0 \leq l \leq 18$. 1476 data remained after merging equivalent reflections and the merging R-factor was 0.009. Of these, 1063 reflections with $|F| < 6\sigma(F)$ were used for structure determination.

The solution of the structure was attempted using SHELX86[28] direct methods. The first E-map yielded only a few fragments of the molecules because peak list optimisation had been carried out, which made the assumption that it was an equal atom structure. However, the sulphur is significantly heavier than the other atoms. SHELX86 direct methods was repeated, inputting the best solution and calculating an E-map with no peak list optimisation. The result was a improved solution showing the hydrophilic end of the methionine molecule and most of the mandelic acid molecule, excluding the remote carbon atoms of the phenyl ring. A single, unattached atom, which had

been of low weight previously, was now of high enough weight to represent another real atom, the sulphur atom. It was lower in weight than might be expected from a sulphur atom, but this was explained later by the disorder in the methionine side chain. In all, fourteen atoms were located at this early stage. A structure factor calculation using the program SHELX76[29] gave the R-factor as 0.36, which was promising.

The top three peaks in the first difference map, each amounting to 1.5-2 electrons were identified as the remaining three carbon atoms of the mandelic acid phenyl ring. There was a large minimum in the difference map amounting to 6 electrons. The fourth peak gave an alternative location for the sulphur atom, with the sixth and seventh peaks also in the area. The fifth peak gave another location for the β-carbon atom and a lower peak an approximate position for the γ-carbon atom. Each of these peaks corresponded to about 1-1.5 electrons. It was not clear, at this stage, whether or not there were two distinct positions for the sulphur atoms or a smearing of its location, and similarly, therefore for the γ-carbon atoms and β-carbon atoms. The methyl carbon atoms bonded to the sulphur atoms might be in any orientation about the sulphur-γ-carbon bonds, and there was no clear information at this stage of where they lay. There appeared to be no doubt about the positions of the α-carbon atom and the other atoms of the amino acid.

The first line of attack was to refine the site occupancy of the electron density representing a sulphur atom. The three mandelic acid carbon atoms were added to the peak list, and no others. The isotropic thermal parameter of the original sulphur atom was fixed at 0.05Å^2 and the site occupancy factor allowed to refine for two cycles of least squares, in addition to the coordinates of all atoms and the isotropic thermal para-

meters of all the other atoms. The R-factor went from 0.33 to 0.22. The site occupancy factor of the sulphur atom refined to 0.54(2), that is about half occupancy.

The next step was to print a full Fourier map out in layers, with the sulphur atom excluded from the atom list. Coordinates for the disordered β, (C2); γ, (C21); and methyl carbon atoms, (C1S) had not yet been included anyway. The purpose was to find two amino acid side chains, each of approximately half occupancy. It was expected that they would appear as peaks of electron density in the Fourier map. Two cycles of least squares refinement were carried out the R-factor going from 0.30 to 0.28. The scale on the map was adjusted so that it was similar in all directions, to aid the visual identification of the shapes of peaks and their separations. A number of smears and peaks of electron density were observed. In order to show in which region to look for possible positions for the β-carbon atom, the two ideal positions of the β-carbon atom were calculated using the program CALC. One of these should correspond closely to the observed positions. The two different positions are simply those it would occupy in the two opposite hands of methionine and this was the easiest way to show in which region to look. One set of calculated coordinates had peaks in the region of it, which corresponded to the correct hand of the methionine molecule. There was a large, bumpy smear of electron density which was believed to contain two sulphur atoms and both methyl carbon atoms, one sulphur position being clearly more important than the other.

The structure of the disordered area slowly built up using full Fourier maps. With the site occupancies of the major and minor side chains fixed at 70% and 30%; isotropic thermal parameters for the atoms in the disordered chain fixed at 0.1Å^2, except for the sulphur atom

of the major chain, which was refined from a starting value of 0.1Å²; the bond lengths and angles within the disordered chain were loosely constrained, according to the average of several methionine structures compared by Torii and Iitaka[37]. Three methionine ammonium hydrogen atoms, one having been placed in a calculated position; and the mandelic acid hydroxl hydrogen atom were included.

The R-factor at the end of four cycles of least squares refinement was 0.13 and the deviations of observed bond lengths and angles from the constrained ones were small. The isotropic thermal parameter of the sulphur atom had refined to a value of 0.104(2).

The changes made to the above after updating the input file were to let the site occupancies of the two chains refine tied to sum to unity, beginning at 0.7 and 0.3 to let all of the isotropic thermal parameters of the disordered part refine begining at 0.01Å²; and to let the major sulphur atom refine anisotropically. The result was that the R-factor dropped from 0.13 to 0.097. The range of the isotropic thermal parameters was 0.116(8) to 0.21(3). The largest anisotropic thermal parameter on the sulphur atom was 0.146(6)Å. The observed separations between constrained atoms were close to the distances set. There were peaks amounting to about half an electron in the difference map in the disorded region. It was expected that once some of the atoms had anisotropic thermal parameters some of this would be taken account of. It was no longer the intention to include any hydrogen atoms in the disordered region because it had proved so difficult to refine the structure satisfactorily with them in previously and their electron density would be very low. The site occupancy of the major chain refined to 0.68.

The next step was to remove the hydroxyl hydrogen

atom and look for a better position for it in the difference maps. The ammonium group was constrained to have atoms in an ideal arrangement, including the angles between the hydrogen atoms and the α-carbon atom of the amino acid. The R-factor was 0.10 after four cycles and after having risen a few 1/100 percent. The range of the isotropic thermal parameters was 0.122(10) to 0.23(5). The largest anisotropic thermal parameter on the major sulphur atom was 0.149(7). The constraints on the constrained atoms were adhered to. No suitable location for the hydroxyl hydrogen atom was found, so it was returned to the former location, and DFIX constraints were applied to try to push it to a better position. The thermal parameters on the α-carbon of the methionine were large for U_{11} and U_{33}, which suggests that there is some freedom in the position of this atom as part of the disorder. In addition the lengths of the bonds between the α-carbon atom and the nitrogen and carboxylate carbon atom were 1.41 and 1.46Å. They are a little short, which would be a consequence of the large thermal vibration, or disorder, in the α-carbon atom. Also the length of the bond between the α-carbon atom and the β-carbon atom of the minor chain was 1.61Å, which is rather long. No suitable peak in the difference map was located which made a satisfactory position for a minor α-carbon atom, but attempts to refine a split atom based on the anisotropic thermal parameter did give a slight improvement in the molecular geometry.

With the weighting scheme $W^{-1} = \sigma^2(F) + 0.00057F^2$ applied and several reflections specifically omitted because they appeared to be affected by secondary extinction, three cycles of refinement were carried out. The position of the hydroxyl hydrogen atom was at first poor, but it appeared to improve as contraints took effect, as shown by the deviations from the constrained atom separations of the O-H bond and the through space separation of

the carbon atom to which the hydroxyl group was attached and the hydroxyl hydrogen atom. In determining the constraints, the ideal tetahedral angle, 109.4° was taken to be the angle made at the oxygen atom, although the expected angle might be nearer 105°. Subsequent calculation of the geometry in this region showed that the actual angle was rather far from ideal and the hydroxyl hydrogen atom was finally removed from the atom list altogether. At the end the R-factor was 0.097 and all atoms adhered quite well to their constraints, where appropriate. The thermal parameters on the two α-carbon atoms were similar in size and reasonably sized, at an average of 0.43Å². The shifts/esd's in the final of these cycles were almost entirely less than 0.4.

Atoms were relabelled and reordered as required to conform to the standard format used in all the mandelic acid/amino acid structures. Three final cycles of least squares refinement were carried out; the R-factor was 0.098 at the end, the shifts/esd's in the final cycle were largely below 0.05 and the difference map had a maximum of 0.59eÅ^{-3} and was a little noisy, but quite acceptable.

3.6.3 Results of structure determination:

Fractional coordinates of non-hydrogen atoms, six anisotropic thermal parameters for each and fractional coordinates of hydrogen atoms are listed in tables at the end of this section. Isotropic thermal parameters for all hydrogen atoms were fixed at 0.05Å². The asymmetric unit consists of mandelic acid molecule and one methionine molecule, with disorder in the methionine side chain from the α-carbon onwards, such that the two structures are in a 70-30% ratio. There are two asymmetric units in the unit cell. Esd's on fractional coordinates range from 0.0004 to 0.008, the larger ones

being for some coordinates of atoms in the phenyl ring, refined hydrogen atoms and atoms in the methionine side chains.

Principal anisotropic thermal parameters were in the range 0.025(4) to 0.21(3). Thermal parameters tend to be large on the atoms of the phenyl ring, oxygen atoms in some directions and on the atoms of the methionine side chains, particularly. The range for phenyl ring principal anisotropic thermal parameters is 0.059(7) to 0.21(3)Å² and in the two methionine side chans, 0.046(3) to 0.140(4)Å². This indicates more thermal vibration on these parts of the molecules than on others, which are more fixed in position by being in the middle of molecules.

The structure is most like S-alanine-S-mandelic acid in terms of the thermal vibration on atoms, that is that there is a relatively large degree of freedom in atomic positions.

Figure 3.6 S-Methionine R-Mandelic Acid

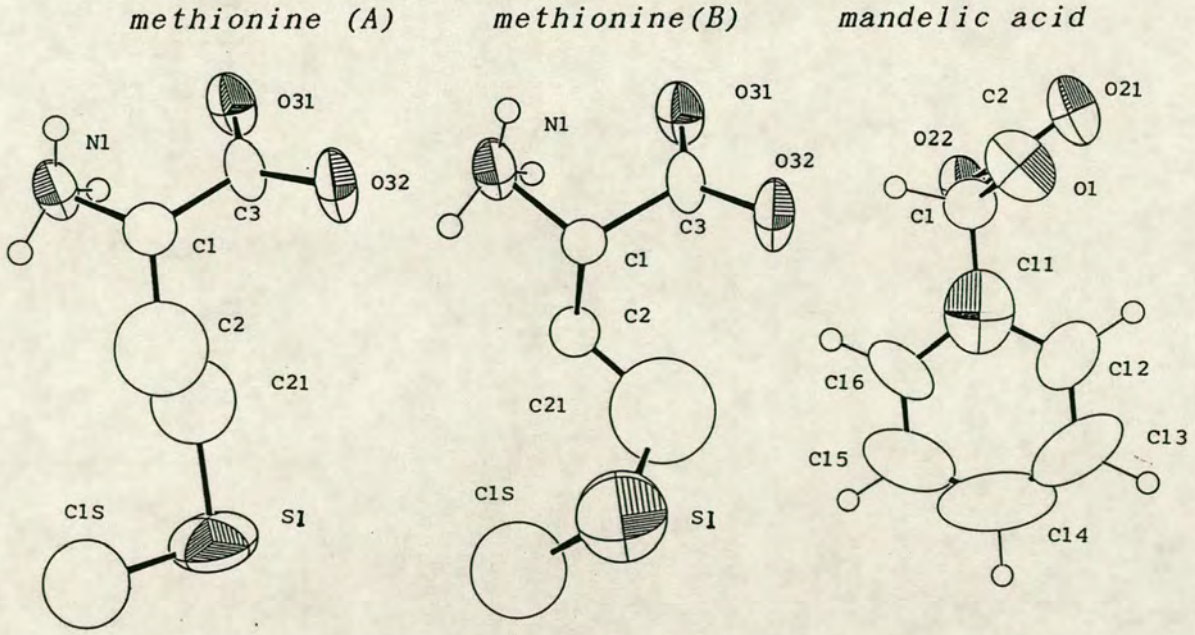


Table 3.6.1 Fractional coordinates with isotropic thermal parameters in Å² (U_{iso} for H fixed at 0.05Å²)

	x	y	z	U_{iso}
C(1)	0.3583(8)	0.6032(23)	0.6244(5)	0.051(5)
O(1)	0.2821(6)	0.7652	0.5621(5)	0.077(4)
C(2)	0.5207(9)	0.5760(23)	0.6085(6)	0.050(5)
O(21)	0.5744(7)	0.6965(20)	0.5570(5)	0.073(4)
O(22)	0.5923(6)	0.4135(19)	0.6574(4)	0.059(3)
C(11)	0.3570(9)	0.6713(25)	0.7237(7)	0.108(7)
C(12)	0.4110(14)	0.885(3)	0.7571(9)	0.085(8)
C(13)	0.4144(20)	0.948(4)	0.8458(12)	0.124(13)
C(14)	0.367(3)	0.792(6)	0.9035(11)	0.154(18)
C(15)	0.3109(22)	0.579(4)	0.8722(12)	0.131(15)
C(16)	0.3011(13)	0.528(3)	0.7847(7)	0.083(7)
N(1A)	0.9628(8)	-0.1635(20)	0.5953(5)	0.053(4)
C(3A)	0.9513(7)	0.2419(19)	0.6285(5)	0.042(4)
O(31A)	1.0662(5)	0.2577(19)	0.5925(4)	0.055(4)
O(32A)	0.8767(6)	0.4140(19)	0.6502(5)	0.063(4)
S(1A)	0.8897(7)	-0.0828(20)	0.9165(3)	0.111(4)
C(1A)	0.8789(13)	0.0119(21)	0.6362(6)	0.046(4)
C(1B)	0.9142(19)	0.0050(22)	0.6583(8)	0.033(7)
C(2A)	0.8382(15)	-0.045(3)	0.7272(6)	0.141(9)
C(21A)	0.9600(17)	-0.031(5)	0.8096(6)	0.128(8)
C(1SA)	0.806(3)	-0.360(3)	0.8921(15)	0.124(9)
C(2B)	0.9883(18)	-0.047(3)	0.7562(6)	0.044(6)
C(21B)	0.933(3)	0.120(4)	0.8230(13)	0.20(3)
S(1B)	0.7694(16)	-0.002(4)	0.8600(10)	0.132(6)
C(1SB)	0.853(5)	-0.245(8)	0.923(4)	0.156(24)
H(1)	0.2996	0.4417	0.6123	
H(12)	0.4513	1.004	0.7110	
H(13)	0.4536	1.115	0.8702	
H(14)	0.373	0.834	0.9750	
H(15)	0.2738	0.456	0.9182	
H(16)	0.2488	0.368	0.7596	
H(1NA)	0.916(4)	-0.275(3)	0.628(3)	
H(2NA)	1.0529(12)	-0.089(6)	0.624(3)	
H(3NA)	0.913(4)	-0.111(6)	0.5368(7)	

Table 3.6.2 Anisotropic thermal parameters in Å²

	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
C(1)	0.042(4)	0.057(5)	0.052(5)	0.000(5)	0.003(4)	0.006(4)
O(1)	0.047(3)	0.099(6)	0.083(4)	0.027(5)	0.008(3)	0.014(4)
C(2)	0.040(4)	0.046(5)	0.061(5)	0.002(5)	0.006(4)	-0.003(4)
O(21)	0.049(3)	0.068(5)	0.099(5)	0.030(4)	0.018(3)	0.006(3)
O(22)	0.040(3)	0.052(3)	0.085(4)	0.006(4)	0.023(3)	0.006(3)
C(11)	0.069(5)	0.093(7)	0.159(9)	0.004(7)	0.025(5)	0.021(5)
C(12)	0.092(8)	0.059(7)	0.099(8)	-0.013(7)	0.005(6)	0.014(6)
C(13)	0.163(15)	0.094(12)	0.103(11)	-0.040(10)	-0.025(10)	0.063(11)
C(14)	0.174(18)	0.21(3)	0.073(9)	-0.011(14)	0.003(10)	0.126(20)
C(15)	0.154(14)	0.148(18)	0.095(11)	0.038(12)	0.061(11)	0.058(15)
C(16)	0.088(7)	0.094(8)	0.070(7)	0.033(7)	0.039(6)	0.011(7)
N(1A)	0.054(4)	0.032(4)	0.071(5)	0.000(3)	0.016(4)	-0.002(3)
C(3A)	0.030(3)	0.025(4)	0.069(5)	0.001(4)	0.008(3)	0.005(3)
O(31A)	0.040(3)	0.040(3)	0.086(4)	0.000(3)	0.025(3)	-0.007(3)
O(32A)	0.054(3)	0.027(3)	0.108(5)	-0.008(3)	0.033(3)	0.001(3)
S(1A)	0.140(5)	0.142(6)	0.0470(25)	0.006(3)	0.0163(25)	-0.014(5)

3.7 Cocrystallisations not leading to Successful Structure Solution

3.7.1 α-Aminobutyric Acid/S-Mandelic Acid:

Narrow rectangular plates were readily obtainable when equimolar solutions of S-α-aminobutyric Acid and S-mandelic Acid were allowed to cool. Details of crystallisation attempts are given in section 2.14.1 under the heading ABA/S-MAN. Crystals obtained at any time were of uniform morphology, which suggested that one product crystallised. However, single crystals were unobtainable which were large enough for diffraction of X-rays that was sufficiently strong to allow structure determination. While crystals were long in many cases, they were never very wide nor thick. Also, crystals tended to form that consisted of bundles of plates orientated in different directions, parallel to the needle axis. Crystals were often themselves single, but not separable from the rest of the bundle.

The melting behaviour was compared with that of a 1:1 mixture of the two components as well as with the single components, but was inconclusive. All that could be said was that the product was neither of the pure, single components, but could be a mixture or a compound containing both. See section 2.17.

An oscillation and a zero level Weissenberg photograph were obtained for one crystal and a zero level Weissenberg photograph for a second, both from ABA/S-MAN4 in section 2.14. Later, crystals were obtained from attempt ABA/S-MAN1 and an oscillation photograph of one of these crystals made prior to collection of data. Alignment by eye was possible because of the shape of the crystal, as the direct, correct positioning of the first crystal showed. At first the first two crystals were

believed to be single, but they turned out to be made of bundles of parallel crystalites. The oscillation photograph had, apparently, single spots. That the spots, and therefore the crystal, were multiple, was revealed by the translational component of the Weissenberg photograph. The crystal was a moderate to poor diffractor, as shown in the low intensity of the diffraction spots on the films. That the spots were frequently horizontal lines on the Weissenberg photographs suggested that there was some disorder in the molecular arrangement. The spots on the oscillation photograph of the third crystal were of low intensity again because of the small size of the crystal, but they were a litle narrower than in the earlier oscillation photograph. Data were collected from this third, single crystal.

Oscillation and Weissenberg photographs showed that the spacegroup was orthorhombic. In the oscillation photograph there was mirroring about the zero line, which indicated that there was a two-fold axis parallel to the mounting axis. On the zero-level Weissenberg photograph an axis could be identified which had mirror symmetry about it. There was therefore a two-fold axis parallel to this axis also and hence the third axis should be 90° away in ω, also with mirror symmetry about it. It was possible to identify such an axis. The space group was thus orthorhombic and had three mutually perpendicular two-fold axes, which might be two-fold rotation or two-fold screw axes. It was not possible to see any pattern of absences on the row lines because of the myriad of diffraction spots.

There was a possibility that, instead of representing zero level spots exclusively, every second festoon contained first level spots from another crystalite, lying between zero-level spots, so that the cell was actually C-centred. The unit cell from the photographs

was approximately a = 26.18, b = 18.50, c = 5.36Å, with a volume of 2596Å^3, which corresponds to 144 non-hydrogen atoms with a volume per atom of 18Å^3. In one pair of ABA and MAN there are 18 non-hydrogen atoms, so there would be 8 pairs in the unit cell. This might correspond to an expected four asymmetric units, containing two each of ABA and MAN molecules, in the primitive, orthorhombic cell. The volume of the postulated centred cell would be a quarter of the primitive. This would allow for two pairs of ABA and MAN in the unit cell, which is inconsistent with the space group and chiral nature of the molecules. One would expect eight asymmetric units in a centred, orthorhombic cell. This calculation suggested that the cell was indeed primitive and the data collection confirmed this, see below. The structure was shown to have cell dimensions, a = 17.962(8), b = 26.771(9)Å, γ = 90.00(6)° by least squares refinement, after an automatic search routine on the STADI-2 diffractometer. The value of the c-axis, c = 5.094Å, was determined by manually refining the value of μ to give a maximum in the intensity of reflections on the row line, 001.

Data collection output revealed more information about the space group. The cell was not centred because there was no pattern of absences over all hkl, in which h+k=2n+1 were absent. In rows h00 and 0k0, reflections with h or k, respectively, odd were absent. There were therefore 2_1 screw axes parallel to the a and b- axes. Automatic measurement of the 00l spots to see if there was any pattern of absences here did not take place because of the geometry of the diffractometer and the fact that reflections with $2\theta' < 2°$ were not measured. It was assumed that there was a 2_1 screw axis parallel to the c-axis also, since space group $P2_12_12_1$ is very much more common than the alternative, $P2_12_12$.

That the unit cell differed from those either of

pure mandelic acid of a single hand or of pure amino acid of a single hand indicated that the deposited crystals were indeed those of a molecular complex. 2003 data were collected on a STADI-2 two circle diffractometer. Only one had an uneven background, but the data were very weak because the crystal was so thin. Out of 2003 reflections, only 109 had $6\sigma(F)<F$ and 1487 had $F<2\sigma(F)$. The data were too weak for successful structure solution in either space group. SHELX86[28] direct methods was the program used. Attempts to prepare this diastereomer were abandoned.

3.7.2 R-Cysteine/S- and R-Mandelic Acid:

Both diastereomers appeared to be formed when separate cocrystallisations of R-cysteine with S and R-mandelic acids were attempted. Nmr showed that both components were present in deposited crystals (section 2.16) and the uniform morphology of crystals formed suggested that one structure had been deposited. They were probably 1:1 molecular complexes. In a later crystallisation attempt, of L-CYS with S-MAN large rhombic plates, up to 4.5mm along their edge were obtained. Evaporation of the solvent from wet crystals produced tiny rhombic plates. Nmr showed that the large plates were mandelic acid whereas the small ones constituted either a 1:1 compound or a 1:1 mixture. In the case of L-CYS/R-MAN the same sorts of crystals were produced, but the large plates were smaller. It was assumed that there would be the same result as for the L-CYS/S-MAN case. It was probable that the left over 1:1 mixture used for the later cocrystallisation attempts contained an excess of mandelic acid, which caused its preferential crystallisation. Also, problems with decomposition discouraged continuing with this diastereomeric pair.

3.7.3 S-Methionine/S-Mandelic Acid:

Crystals formed readily when solutions of equimolar mixtures of S-Methionine and S-Mandelic Acid were allowed to cool to room temperature. The product was elongated narrow rectangular plates and the uniform morphology suggested that a single product was being formed. Section 2.14 gives full details of cocrystallisation attempts.

The results of the melting point determination were inconclusive. The deposited crystals could be a mixture of components of a compound of the components. Section 2.17 describes the melting behaviour.

The nmr spectrum showed that mandelic acid and methionine were present in equal proportions, suggesting either a 1:1 compound or a 1:1 mixture (section 2.16). Upon examination under a polarising microscope, the crystals always showed gradual extinction. The crystals were thus non-single, with the structure varying gradually over the crystal. Attempts to prepare single crystals of this diastereomer were eventually abandoned.

3.8 Attempts to Cocrystallise Neutral Amino Acid with Mandelic Acid which Failed

3.8.1 S-Valine, S-Leucine and SS-Isoleucine with Mandelic Acid:

When attempts were made to cocrystallise valine, leucine and isoleucine with the enantiomers of mandelic acid, as described in section 2.14, the crystalline products were shown by nmr to contain, principally, the amino acid (see section 2.16). Therefore these longer chain neutral amino acids do not cocrystallise with mandelic acid. Autocrystallisation with like molecules is

preferred by these single hands of amino acids. They form a series of similar hydrogen bonded layer structures[38,39,40,41,42]. There was little liklihood of success in resolution using these three amino acids and mandelic acid.

Further details for VAL/R-MAN, for which crystals were obtained are given in the next section. the other five attempts produced fine needles, and attempts were made to obtain better crystals by slowing down the rate of growth. However, dilute solutions tended to deposit fragments. Further attempts were abandoned, when nmr showed that only amino acid was being deposited.

3.8.2 S-Valine/R-Mandelic Acid:

Single crystals suitable for structure determination were obtained from equimolar mixtures of **S-VAL** and **R-MAN**. Typically,deposited crystals were long, fine needles (see section 2.14). Before an nmr spectrum was obtained a crystal, made according to VAL/R-MAN8, was mounted, oscillation and Weissenberg photographs taken and data collected on a Stadi-2 two circle diffractometer. The space group was $P2_1$, symmetry and absences being as described in section 2.9. Several reflections on the row 0k0 were measured manually in order to establish whether or not there was a two-fold screw or a two-fold rotation axis parallel to the mounting axis. These reflections were not included in the normal data collection output because the value of 2θ' was less than 2°. The unit cell determined on the diffractometer was a = 9.709, b = 5.318, c = 12.075Å, β = 89.24°.

Attempts to find **MAN** molecules in the structure failed before it was noticed that the unit cell and space group were identical to those of **S-VAL**. Subsequent nmr showed that the product of this crystallisation attempt

and of several others was indeed **S-VAL**. (See section 2.16). It must be case that the **MAN** remained in solution when the **VAL** crystallised. The structure was solved and proved to be **S-VAL**, and is not further reported here, since the structure is known[42].

3.8.3 Glycine/R-Mandelic Acid:

MAN did not cocrystallise with **GLY**. Mp showed that small amounts of **MAN** were deposited from equimolar solutions of **GLY** with a single hand of **MAN**. See sections 2.14 and 2.17.

3.8.4 R-Phenylglycine/ R- and S-Mandelic Acid:

PHG is insoluble in many solvents and scarcely soluble in water. 1:1 mixtures of **PHG** and **R-or S-MAN** were dissolved in hot water as far as possible and left to cool in the hope of crystals forming. Some undissolved PHG often had to be removed before cooling. Crystals (sparingly soluble in water) were always readily deposited. They decomposed just below 300°, and were, in fact recrystallised **PHG**[43].

3.8.5 S-Proline/R- and S-Mandelic Acid:

No crystals were deposited from solutions of equimolar mixtures of **PRO** and both **R- and S-MAN**. The solutions rapidly turned brown, suggesting that decompositon was taking place.

3.9 Attempts to Cocrystallise Polar Amino Acids with Mandelic Acid, which failed

3.9.1 S-Serine/R- and S-Mandelic Acid:

Attempts to cocrystallise **SER** with **MAN** are described in section 2.14. Dilute solutions failed to yield crystals, but there was more success with concentrated solutions, when the sample was dissolved in little more than the minimum volume of water. The solutions were gradually made more dilute until slow crystallisation took place. Crystals were thin, colourless plates, which were fragments of triangles, trapezia and parallelograms, up to approximately 3mm across. Such shapes can be considered to be fragments of one another, therefore the crystal were of uniform morphology. They extinguished, indicating that they were single. They looked like crystals of **R-MAN**. The first technique adopted to identify them was melting point. As section 2.17 shows, the melting points for both cases were consistent with the crystals' being mandelic acid. This was so clear, that nmr was not carried out, despite the possibility of a coincidence in the values of the melting points. The conclusion was that serine did not cocrystallise with mandelic acid.

3.9.2 SR-Threonine/R- and S-Mandelic Acid:

When it was attempted to cocrystallise each hand of **MAN** with **2-S-3-R-THR**, it was at first encouraging to find that crystals were obtained readily from equimolar solutions, upon cooling to room temperature. However, there were two type of crystal formed, needles and plates. It was possible to separate small quantities of each from both sets of crystallisations by hand. Nmr and mp showed that needles contained **THR** and plates **MAN**. See sections 2.16 and 2.17. Thus, for both diastereomeric possibilities, **MAN and THR** crystallised in similar quantities at the same time in separate crystals. There was likely to be no possibility of resolution of a racemic mixture of **MAN** by **THR** nor vice versa.

3.9.3 S-Tyrosine/R-Mandelic Acid:

It was difficult to dissolve enough **TYR** in water to prepare the 1:1 solutions. The deposited crystals were needles whose composition was not determined (see section 2.14) This work seemed unpromising, and no attempt was made to cocrystallise **TYR** with **S-MAN**.

3.10 Attempts to crystallise basic amino acids with mandelic acid.

3.10.1 S-Arginine/R- and S-Mandelic Acid:

Equimolar mixtures of **S-ARG** with both hands of **MAN** gave viscous solutions or gels. Crystals were obtained with **R-MAN**, but not with **S-**. They were creamy-white needles. It was difficult to separate them from the gel, and they appeared to be crystals of **ARG**. See ARG/R-MAN3 in section 2.14.

3.10.2 S-Histidine/R- and S-Mandelic Acid:

Separate 1:1 mixtures of **S-HIS** with**R-** and **S-MAN** also tended to form gels or viscous solutions. The only product obtained appeared to be **HIS**, and crystals could not be separated from the gel. See HIS/R-MAN2 and 3 in section 2.14.

3.10.3 S-Lysine Hydrochloride/R- and S-Mandelic Acid:

Crystals were readily obtained, as described in section 2.14. They were parallelogram-shaped plates, some of which appeared to be single crystals. Nmr and mp indicated that they were **MAN** with small amounts of **LYS** as an impurity. Refer to sections 2.16 and 2.17.

CHAPTER 4

MOLECULAR GEOMETRY, CRYSTAL PACKING ARRANGEMENT AND HYDROGEN BONDS IN MANDELIC ACID STRUCTURES

Bond lengths and torsion angles will be discussed, as there is nothing further to be added about bond angles. Reference may be made to the molecular geometry tables at the end of this chapter.

Delta (δ) is the difference, expressed in Ångström, between the lengths of C-O bonds in carboxylate or carboxylic acid groups. The esd (σ) on this difference is the square root of the sum of the squares of the esd's on the individual bond lengths. A measure of the significance of delta is given by the ratio $\delta/\sqrt{(\sigma_1^2+\sigma_2^2)}$. In general, if this is 3 or more, the lengths are considered to be significantly different; this will be interpreted loosely. Also taken into account were the actual δ, how δ compares with those for other structures, and how the sizes of the esd's compare with other structures. Amino acid carboxylate groups should have C-O bonds essentially the same, while those in mandelic acid carboxylic acid groups should differ significantly.

4.1 Bond lengths

4.1.1 S-Alanine-R-Mandelic Acid:

Most bond lengths were essentially as expected. The esd's ranged from 0.003 to 0.06, with the larger values for bonds to refined hydrogen atoms. The size of the

esd's was smaller than the corresponding diastereomer, because of the greater precision in fractional coordinates. As the short table below shows, the lengths of the C-O bonds in the **MAN** acid groups were clearly significantly different, which shows that the **MAN** is undissociated. Hydrogen atoms were found on these acid groups. The C-O bonds in the carboxylate groups of the **ALA** molecules were marginally significantly different. The anisotropic thermal parameters of each of these four oxygen atoms were broadly similar to each other and, in general, of moderate size, with U_{33} larger than the others. It was not the case therefore that librational shortening of the bond lengths reduced one more than the other in each case. No hydrogen atoms were found in electon density maps which could be part of an acid group, nor were any expected, since they would have to come from the ammonium groups or from the water molecule, neither of which are sufficiently acidic. It was concluded that these were ionised carboxylate groups with one C-O bond, of each, stretched because of hydrogen bonding (see section 4.5). Notably, in both cases there is a very short hydrogen bond donated from the **MAN** carboxylic acid oxygen atoms to the **ALA** carboxylate oxygen atoms, O32A and O32B, which have the stretched C-O bond lengths. Of the two short hydrogen bonds, the shorter one is between the oxygen atoms of **ALA** and **MAN** for which the difference in the difference in C-O bond lengths is smaller. The deltas for this ALA/MAN pair are similar to those for the other diastereomer.

Only one of the two hydrogen atoms of the water molecule was located precisely, so the structure was missing one overall.

C-O(1)	C-O(2)	δ	σ	δ/σ	difference
alanine					
1.260	1.219	0.041	0.007	5.9	marginal
1.257	1.226	0.031	0.007	4.2	marginal
mandelic acid					
1.290	1.226	0.064	0.007	9.1	significant
1.310	1.200	0.110	0.007	15.7	significant

4.1.2 S-Alanine-S-Mandelic Acid:

Bond lengths were mostly as expected. The esd's ranged from 0.010 to 0.10Å. The esd's were two to three times those in **S-ALA-R-MAN**, which is a function of the greater esd's in fractional coordinates, in turn due to there being a smaller number of significant X-ray data. Esd's were largest in the phenyl ring because of the freedom the structure exhibits here and in bonds to hydrogen atoms on nitrogen and oxygen atoms because the precision in the positions of such hydrogen atoms is low.

Comparing bond lengths in the carboxylic acid groups of the **ALA** and the **MAN** suggested that, as before, the **MAN** was undissociated and the ALA ionised. The bond lengths in the **ALA** case were marginally different, and the actual values, as in the diastereomeric structure, showed that one bond was noticeably longer than the other, perhaps for the same reason as in the opposite diastereomeric structure. Again, there was a strong, short hydrogen bond between the oxygen atoms in the 'long' C-O bond of the **ALA** carboxylate group and the acid oxygen of the **MAN**. See section 4.5 on hydrogen bonding for further details. The bonds cannot be really significantly different in the **MAN** because the esd's are so large. They were noticeably different and more so than in the **ALA**. No acid hydrogen was located, but pKa values

would indicate that the **MAN** should be undissociated and the **ALA** dissociated. (See chapter 1)

The sizes of the esd's on the C-O bond lengths were relatively large, which reduced the ratio, δ/σ. If the esd's in **ALA-S-MAN** were as in **ALA-R-MAN**, then the "ratios" would be similar for these pairs, thus it is the larger esd's that make **ALA-S-MAN** have only a marginally significant difference in C-O bond lengths in the acid group instead of the expected significant difference.

The actual differences in the C-O lengths in the two functional groups were at the upper and lower ends of the ranges observed for amino acid carboxylate and **MAN** carboxylic acid groups respectively. this is reflected in the short hydrogen bond, mentioned above being the shortest, and therefore the strongest, amongst the present structures, and hence the most likely to stretch the C-O bonds involved, as occurs here.

C-O(1)	C-O(2)	δ	σ	δ/σ	difference
alanine					
1.269	1.222	0.047	0.016	2.9	insignificant
mandelic acid					
1.278	1.215	0.063	0.016	3.9	marginal

4.1.3 S-Phenylalanine-R-Mandelic Acid:

Bond lengths were mostly as expected. Esd's took values between 0.005 and 0.05, the larger values being for bonds to refined hydrogen atoms. They were approximately a half to a third times the esd's for the diastereomeric structure, **S-PHE-S-MAN**. The lengths of the C-O bonds in the carboxylic acid groups were compared. Those in **PHE** were not significantly different, whereas those in **MAN** were. One carboxylate C-O bond was

slightly stretched compared to the other. It was this oxygen atom which, again, accepted the short hydrogen bond from the **MAN** carboxylic acid group. See section 4.5 hydrogen bonding schemes. This was consistent with the expected ionised nature of the **PHE** and the unionised nature of the **MAN**. The following short table summarises the values.

C-O(1)	C-O(2)	δ	σ	δ/σ	difference
phenylalanine					
1.249	1.235	0.004	0.007	0.6	insignificant
mandelic acid					
1.314	1.200	0.124	0.007	17.7	significant

4.1.4 S-Phenylalanine-S-Mandelic Acid:

Bond lengths were mostly as expected. the esd's were in the range 0.016 to 0.03Å, and were two to three times those in the the diastereomeric structure because of the lower degree of precision in the present structure. The larger esd's again occurred on bonds involving refined hydrogen atoms. Upon comparing the lengths of the C-O bonds in the carboxylic acid groups, it was found that those in **PHE** were not significantly different, whereas those in **MAN** were. The larger esd's on the bond lengths reduced the ratio δ/σ for the **MAN** carboxylic acid group to 7, in contrast to 18 in the other diastereomer, despite **PHE-S-MAN** having the largest delta between the C-O bonds in **MAN** of the six structures. Once again, the slightly stretched C-O bond in the amino acid carboxylate group accepted the shortest hydrogen bond from the **MAN** carboxylic acid function. See the section on hydrogen bonds for more details. The bond lengths were consistent with the expected dissociated nature of the **PHE** and the undissociated nature of the **MAN**. The hydrogen atom in the acid function was not located. The following

short table summarises the values.

C-O(1)	C-O(2)	δ	σ	δ/σ	difference
phenylalanine					
1.244	1.233	0.011	0.024	0.5	insignificant
mandelic acid					
1.350	1.182	0.186	0.027	6.9	significant

4.1.5 S-α-Aminobutyric acid-R-Mandelic Acid:

The bond lengths were largely as expected. The esd's were in the range 0.005 to 0.04Å which was similar to the range for the structures **S-PHE-R-MAN** and **S-ALA-R-MAN**. The larger esd's occurred in bonds containing refined hydrogen atoms. The lengths of the C-O bonds in the carboxylic acid groups show that in the **MAN** they are undissociated and in the **ABA** they are dissociated, which is, again, as expected. Both acid hydrogen atoms were located in difference maps. One C-O bond is slightly stretched in each of the **ABA** molecules, which is again due to the two, strong and short hydrogen bonds formed when the **MAN** carboxylic acid hydrogen atoms are donated to an oxygen atom of each of the carboxylate groups on the amino acid.

C-O(1)	C-O(2)	δ	σ	δ/σ	difference
S-α-aminobutyric acid					
1.250	1.232	0.018	0.008	2.2	insignificant
1.258	1.225	0.032	0.008	4.0	marginal
mandelic acid					
1.304	1.216	0.088	0.010	8.8	significant
1.309	1.198	0.111	0.010	11.0	significant

4.1.6 S-Methionine-R-Mandelic acid:

The bond lengths were mostly as expected. The esd's were in the range 0.012 to 0.05Å, the larger ones involving the refined hydrogen atoms, atoms in the phenyl ring of the **MAN** molecule and atoms in the disordered side chain of the **MET** molecule. The largest esd, by far, occurred on the bond between the sulphur atom and the methyl carbon atom in the minor side chain of the **MET**.

Bond lengths and angles in the **MET** side chains were compared to see if either of the **MET** conformations in the disordered structure were more like any of the **MET** molecules in the literature (S-methionine, S/R-methionine or dichloro-S/R-methionine palladium[37,44,45]). See also sections 4.2.8-13 for details of the comparison in torsion angles. In the present structure, these bond lengths and angles were constrained to reasonable values based on the average of each type found in the **MET**-containing structures in the literature. As expected, DFIXed bond lengths and angles were not significantly different in the two disordered forms of **MET** in the present structure; nor from the literature structures. The actual differences in corresponding bond lengths were almost entirely less than 0.03Å, with the larger differences tending to occur between the γ-carbon, δ-sulphur and ϵ-carbon. angles were more variable, even varying by more than 7°. Only a few of the angles were strictly significantly different. The differences in bond lengths and angles were the result of the 'wobble' in the **MET** side chains described by the large anisotropic thermal parameters.

A comparison of the C-O bond lengths in the carboxylic acid groups was made. The **MAN** molecules were undissociated and the **MET** carboxylate group, dissociated. One bond

length was marginally significantly different in the **MAN** carboxylic acid function. The actual difference was quite great, but the esd's were large, reducing the significance of the difference. One bond length was noticeably, but not significantly, longer than the other in the amino acid caboxylate group. As for the other structures, the slightly stetched C-O bond in the **MET** contained the oxygen atom which accepted the short hydrogen bond from the **MAN** carboxylic acid group. For more details see section 4.5. The following short table summarises the comparisons of C-O bond lengths. No acid hydrogen atom was located.

C-O(1)	C-O(2)	δ	σ	δ/σ	difference
methionine					
1.278	1.247	0.031	0.017	1.8	insignificant
mandelic acid					
1.297	1.199	0.098	0.019	5.1	significant

4.1.7 General Discussion:

The difference, δ, between the C-O bond lengths in carboxylic acid and carboxylate groups is always far greater in the mandelic acids than in the amino acids in all these structures, and it is always more significant in mandelic acid than in the amino acid in the same structure. In the amino acids, it is least significant in **PHE-R-MAN** and **PHE-S-MAN**, the ratio of δ/σ being 0.6 and 0.5 respectively. This ratio is between 2 and 6 in the other structures. it is interesting that in **PHE-R-MAN**, where δ in **PHE** is truly insignificant, the 'short' hydrogen bond is the longest out of the present structures. In contrast, in **ALA-S-MAN**, where both **ALA** and **MAN** C-O bonds are marginally different, the hydrogen bond is the shortest of all the structures. The general rule would appear to be that the shorter the 'short' hydrogen bond, the more significant the difference in C-O bond

lengths in amino acid acid groups because the 'long' C-O bond to the oxygen atom involved in the short hydrogen bond is stretched more by the shorter, stronger hydrogen bond. The exception is **PHE-S-MAN** where although the short hydrogen bond is on the short side, the difference in the amino acid C-O bond lengths is insignificant, suggesting that this C-O bond is not stretched by the hydrogen bonding, unlike the other structures. If the esd's in **PHE-S-MAN** were the same size as in **ALA-R-MAN**, where the short hydrogen bond between the first **MAN** molecule and the second amino acid molecule is of a similar length (that is 0.005 as opposed to 0.017Å) then the ratio δ/σ would be about 2 and the difference in lengths of marginal significance as in the other structures.

Studies of pure, neutral amino acids in the zwitterionic form have shown that when one oxygen atom in a carboxylate group accepts two hydrogen bonds and the other only one and all the hydrogen bonds are of similar length, then the bond from the carbon to the first oxygen has more double-bond character than that to the other. Examples of this effect are **RS-ALA**[46] and **RS-MET**[44].

This pattern is followed to some extent in the present structures containing zwitterionic amino acids. An exception lies in **S-ALA-S-MAN**, where the oxygen with one hydrogen bond has a longer C-O bond than the other. This is, however, the shortest hydrogen bond in all the structures. There are two further exceptions where the asymmetry of the carboxylate group is maintained, but the oxygen atoms are both involved in two hydrogen bonds, and the shorter hydrogen bond in each case is associated with the longer C-O bond. In any case, the strict marginality of the differences in C-O bond lengths should be borne in mind.

4.2 Torsion Angles

The principal torsion angles of interest in **MAN** are the orientation of the hydroxyl group to the carboxylate group (O1-C1-C2-O21 or O22) and of the hydroxyl group to the phenyl ring (O1-C1-C11-C12 or C16), In the amino acid molecules, the orientation of the ammonium group to the carboxylate group (N1-C1-C3-O31 or O32) is always given. In all cases the angle having the value nearest zero is used. In amino acids other than **ALA**, other torsion angles are also listed.

4.2.1 Alanine-R-Mandelic Acid:

	torsion angle	value/degrees
mandelic acid		
	O1-C1-C2-O21	13.6(4)
	O1'-C1'-C2'-O21'	7.6(6)
	O1-C1-C11-C12	-61.3(4)
	O1'-C1'-C11'-C12'	-67.4(5)
alanine		
	N1A-C1A-C3A-O31A	-19.5(4)
	N1B-C1B-C3B-O31B	-12.1(5)

In the **MAN** molecules, the bonds to the hydroxyl groups tend to eclipse the bond to carbonyl groups of the **MAN**. The planes of the phenyl rings tend to lie gauche to both the bonds to the hydroxyl groups and the carbon atoms of the carboxyl groups; but to eclipse the C-H bond quite closely.

In the **ALA** molecules, one of the carboxylate bonds tends, in each case, to eclipse the C-N bond. This is the 'short' C-O bond.

4.2.2 S-Alanine-S-Mandelic Acid:

	torsion angle	value/degrees
mandelic acid		
	O1-C1-C2-O21	-24.6(11)
	O1-C1-C11-C12	76.2(12)
alanine		
	N1A-C1A-C3A-O31A	-17.4(11)

In the **MAN** molecules, the bond to the hydroxyl group tends to eclipse the bond to carbonyl groups of the **MAN**, but not strongly, being far nearer to 30° than 0° away. The plane of the phenyl ring tends to lie gauche to both the bonds to the hydroxyl groups and the carbon atoms of the carboxyl groups; and to eclipse the C-H bond, but far less nearly than in the diastereomeric structure.

In the **ALA** molecule, one of the carboxylate bonds tends to eclipse the C-N bond. This is the 'short' C-O bond.

4.2.3 S-Phenylalanine-R-Mandelic Acid:

	torsion angle	value/degrees
mandelic acid		
	O1-C1-C2-O21	12.0(5)
	O1-C1-C11-C12	-7.5(5)
phenylalanine		
	N1A-C1A-C3A-O31A	-21.7(5)
	N1A-C1A-C2A-C21A	68.1(4)
	C3A-C1A-C2A-C21A	-55.5(5)
	C1A-C2A-C21A-C22A	94.8(5)

In the **MAN** molecule, the bond to the hydroxyl group tends to eclipse the bond to carbonyl group of the **MAN**. The plane of the phenyl ring tends to eclipse the bond to the hydroxyl group, C12 remaining between O1 and C2, the carbon atom of the carboxyl groups, when viewed along the central bond. This plane is gauche to the C-H bond.

In the **PHE** molecule, one of the carboxylate bonds tends to eclipse the C-N bond. This is the 'short' C-O bond. The bridgehead atom of the phenyl ring lies gauche to both the C-N bond and the C-C bond to the carbon atom of the carboxylate group, lying at approximately 90° to the C1A-C2A bond. The **PHE** molecule therefore curls round at this point. The plane of the phenyl ring is approximately at right angles to the bond to the chiral centre, C21A-C1A.

4.2.4 S-Phenylalanine-S-Mandelic Acid:

torsion angle	value/degrees
mandelic acid	
O1-C1-C2-O21	-26.7(20)
O1-C1-C11-C12	29.3(18)
phenylalanine	
N1A-C1A-C3A-O31A	-35.9(4)
N1A-C1A-C2A-C21A	-179.5(10)
C3A-C1A-C2A-C21A	60.6(13)
C1A-C2A-C21A-C22A	83.8(16)

In the **MAN** molecules, the bond to the hydroxyl group tends to eclipse the bond to carbonyl groups of the **MAN**, but not strongly, being far nearer to 30° than 0° away. The plane of the phenyl ring tends to lie nearly 30° from the bonds to the hydroxyl groups and the hydrgen atom, H1O; and at right angles to the carbon atom of the

carboxyl groups. The orientation of the ring is perhaps close to the most stable conformation possible, given that the ring does not eclipse any other bonds and is farthest from the carboxylate group, which is the bulkiest of the groups in the vicinity.

In the **PHE** molecule, one of the carboxylate bonds lies a little over 30° away from eclipsing the bond to the ammonium nitrogen atom, the plane of the carboxylate group being approximately at right angles to the bond C3A-C2A. This is somewhat similar to the diastereomeric structure, except that in the present structure the carboxylate C-O bond is turned away from the C2A-N1A bond. The bond C1A-N1A is trans to the bond C2A-C21A, so that the molecule is stretched out in this direction. The molecule curls round to join on the carboxylate group, the carbon atom of which being gauche to the bridgehead of the phenyl ring, atom C21A. The plane of the phenyl ring, as in the diastereomeric structure, is near 90° from the bond C2A-C1A, except that it is turned closer.

4.2.5 S-α-Aminobutyric acid-R-Mandelic Acid:

torsion angle	value/degrees
mandelic acid	
O1-C1-C2-O21	11.4(6)
O1'-C1'-C2'-O21'	12.2(7)
O1-C1-C11-C12	-62.5(6)
O1'-C1'-C11'-C12'	-70.9(6)
α-aminobutyric acid	
N1A-C1A-C3A-O31A	-26.0(6)
N1B-C1B-C3B-O31B	-24.2(6)
N1A-C1A-C2A-C21A	-174.2(4)
N1B-C1B-C2B-C21B	-174.9(4)
C3A-C1A-C2A-C21A	67.2(6)
C3A-C1A-C2A-C21A	65.9(6)

In the **MAN** molecules, the bonds to the hydroxyl groups tend to eclipse the bond to carbonyl groups of the **MAN'S**. The planes of the phenyl rings tend to lie gauche to both the bonds to the hydroxyl groups and the carbon atoms of the carboxyl groups; but to eclipse the C-H bond quite closely as a consequence.

In the **ABA** molecules, one of the carboxylate bonds, in each case, tends to eclipse the C-N bond, but nearly 30° away. This is the 'short' C-O bond. The C-C bonds in the amino acid side chains, C2A-C21A and C2B-C21B, are both trans to the bond to the ammoinum groups and gauche to the C-C bonds to the carboxylate groups. The molecules are thus curled from the carboxylate ends to the ethyl side chains, with the ammonium group sticking out on the outside curve.

4.2.6 S-Methionine-R-Mandelic acid:

torsion angle	value/degrees
mandelic acid	
O1-C1-C2-O21	7.4(14)
O1-C1-C11-C12	-55.2(14)
methionione	
N1A-C1A-C3A-O31A	-0.8((13)
N1A-C1B-C3A-O31A	-32.3(13)
N1A-C1A-C2A-C21A	76.0(15)
N1A-C1B-C2B-C21B	-177.2(13)
C3A-C1A-C2A-C21A	-54.8(16)
C3A-C1A-C2A-C21A	61.4(16)
C1A-C2A-C21A-S1A	175.4(10)
C1B-C2B-C21B-S1B	90.5(16)
C2A-C21A-S1A-C1SA	56.6(15)
C2B-C21B-S1B-C1SB	66.3(23)

In the **MAN** molecule, the bond to the hydroxyl group tends to eclipse the bond to the carbonyl group of the **MAN**. The plane of the phenyl ring tends to lie gauche to both the bonds to the hydroxyl groups and the carbon atoms of the carboxyl groups; and to eclipse the C-H bond as a result.

The two types of **MET** molecule differ in their conformation, creating disorder in the crystal structure. they differ first of all in the orientation of the carboxylate group. In the 'A' molecule, the bond to the ammonium group is eclipsed by the 'shorter' of the two C-O bonds, but in the 'B' molecule, the torsion angle is just over 30°, *i.e.* between eclipsed and gauche. The plane of the carboxylate in the 'B' molecule is far more nearly at right angles to the bond between the α-carbon atom and the β-carbon atom. The bond between the β-carbon atom and the γ-carbon atom of the side chain is trans to the C-N bond in the 'A' molecule but tends to be gauche in the 'B'. Both are gauche to the bond to the carboxylate carbon atom, C3A, but on opposite sides of it. In the 'A' molecule the sulphur atom is trans to the α-carbon atom, whereas the 'B' sulphur atom is at right angles to it. The terminal methyl groups in both cases adopt similar torsion angles to the β-carbon atoms, to which they are both gauche and from the same direction.

4.2.7 Comparison of conformations of amino acid molecules, introductory comments:

The suffix A as a general label for the atoms in amino acids and the unprimed labels for **MAN** atoms shall be used, unless the distinction is relevant. The conventional labels Cα, etc. are also used, where appropriate. For brevity torsion angles shall usually be described in terms of the atoms at the ends rather than the bonds to these atoms.

One torsion angle, the view about C3A-C1A, O21A-C3A-C1A-N1A defines the conformation in the hydrophilic group. Three torsion angles define the conformations of these amino acid side chains:

χ_1, the view about C2A-C1A, Cγ-Cβ-Cα-N;
χ_2, the view about C21A-C2A, Sδ-Cγ-Cβ-Cα or Cδ-Cγ-Cβ-Cα

(where the first refers to **MET**, and in the second, Cδ is an ortho carbon atom of the phenyl ring in **PHE** or the penultimate, methylene carbon atom of the longer chain in **NOR**, norleucine, one of the terminal methyl groups of **LEU**, or the methylene carbon atom of the ethyl group in **ILE**, which are included in the literature structures);

χ_3, the view about S1A-C21A or C22A-C21A, (Cε-Sδ-Cγ-Cβ or Cε-Cδ-Cγ-Cβ, in **MET** and **NOR** respectively.)

The ideal staggered conformations for side chains have labels and torsion angles as follows:

gauche+: 60°, trans: 180°, gauche-: -60°

The ideal conformation for χ_2 in **PHE** is ±90° because of the phenyl ring.

4.2.8 Comparison of O31A-C3A-C1A-N1A torsion angles in amino acids:

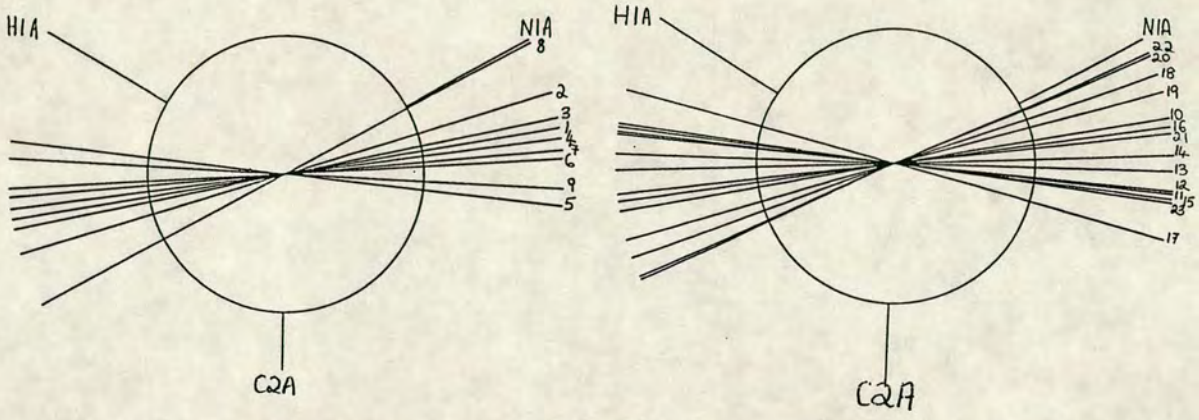
The conformations in the present structures (diagrams on left) were compared with those in a selection of amino acids for which torsion angles were readily available (diagrams on right). All molecules are represented by a number code (see key).

Key for amino-acid diagrams

diagram abbreviated ref. diagram abbreviated ref.

code	name			code	name		
1	**S-ALA-R-MAN**	**A**	*	13	**DL-MET**	**β**	44
2	**S-ALA-R-MAN**	**B**	*	14	**L-NOR**		37
3	**S-ALA-S-MAN**		*	15	**DL-NOR**		37
4	**S-PHE-R-MAN**		*	16	**L-VAL**	**A**	42
5	**S-PHE-S-MAN**		*	17	**L-VAL**	**B**	42
6	**S-ABA-R-MAN**	**A**	*	18	**L-VAL.HCl**		48
7	**S-ABA-R-MAN**	**B**	*	19	**L-VAL.HBr**		48
8	**S-MET-R-MAN**	**A**	*	20	**L-VAL.HCl.H2O**		48
9	**S-MET-R-MAN**	**B**	*	21	**DL-VAL**		49
10	**L-MET**	**A**	37	22	**L-CYS**	**A**	50
11	**L-MET**	**B**	37	23	**L-CYS**	**B**	50
12	**DL-MET**	**α**	44				

(* = this work)



The torsion angle, O31A-C3A-C1A-N1A, is without exception within the range 0 to just over -30°, putting the 'short' C-O bond between N1A and C2A, the β-carbon and towards eclipsing the C1A-N1A bond. The oxygen atom most nearly eclipses the nitrogen atom in the **S-MET-R-MAN-A** and is farthest away from it in **S-PHE-S-MAN**. Thus the nitrogen atom is usually rotated less than about 30° out of the plane of the carboxylate group, and the opposite carboxylate oxygen atom is gauche to both H1A and C2A. This conformation is maintained in the saml1 survey of amino acids as shown in the right-hand diagram above. Torii and Iitaka[37] found that the nitrogen atom deviates slightly from the plane of the Cα and carboxylate atoms. They state that this is usual.

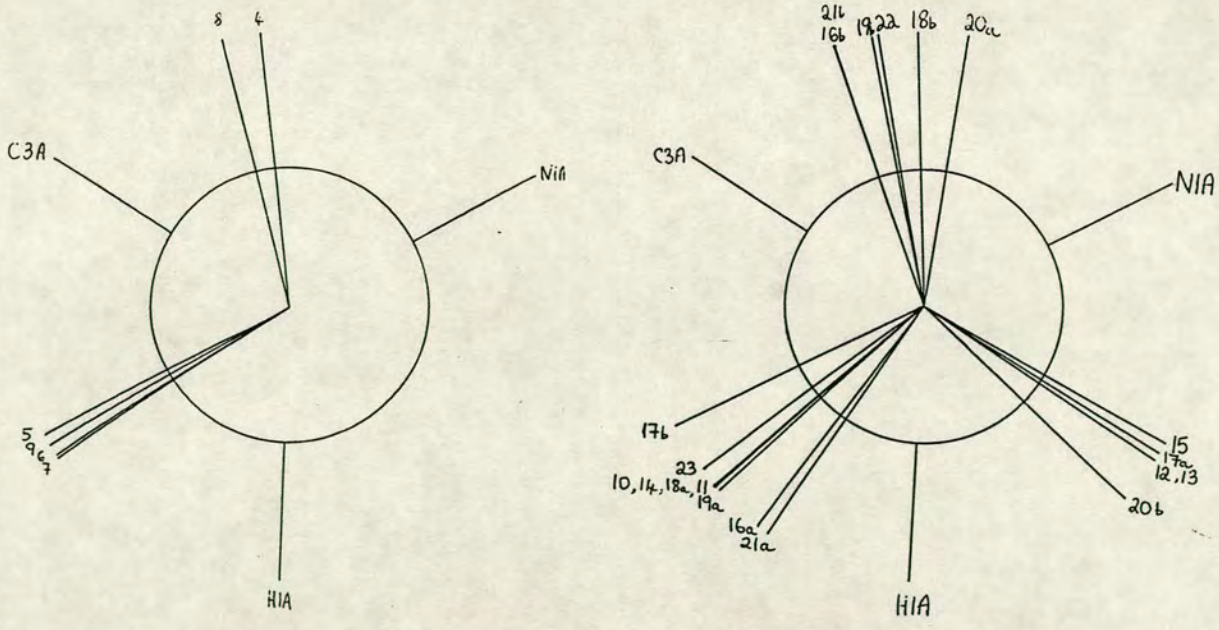
4.2.9 Side-chain conformations of the amino acids:

Descriptions of the three important torsion angles of the present structures are summarised below.

	χ_1	χ_2	χ_3
PHE-R-MAN	g+	90°	/
PHE-S-MAN	t	90°	/
ABA-R-MAN-A	t	/	/
ABA-R-MAN-B	t	/	/
MET-R-MAN-A	g+	t	g
MET-R-MAN-B	t	90°	g

The γ-carbon atom is not present in **ALA**. Surveys of the conformations[47,51,52,53] of the side-chains of the bulky non-polar amino acids **ILE, LEU, PHE,** and **VAL** in both small-molecule and protein crystal structures, show that they tend to adopt ideal staggered conformations, with the order of preference being gauche->trans>gauche+. The present structures, **MET** and **NOR**[37] also adopt the expected staggered conformation.

4.2.10 Comparison of χ_1 torsion angles in the amino acids.



The present structures fall into two sets, (a) trans: (i.e. C21A trans to N1A), and (b) gauche$^+$: C21A (gauche to both C3A and N1A). Most of the amino acids fall into the first group, except **S-PHE-R-MAN** and the A molecule of **S-MET-R-MAN**.

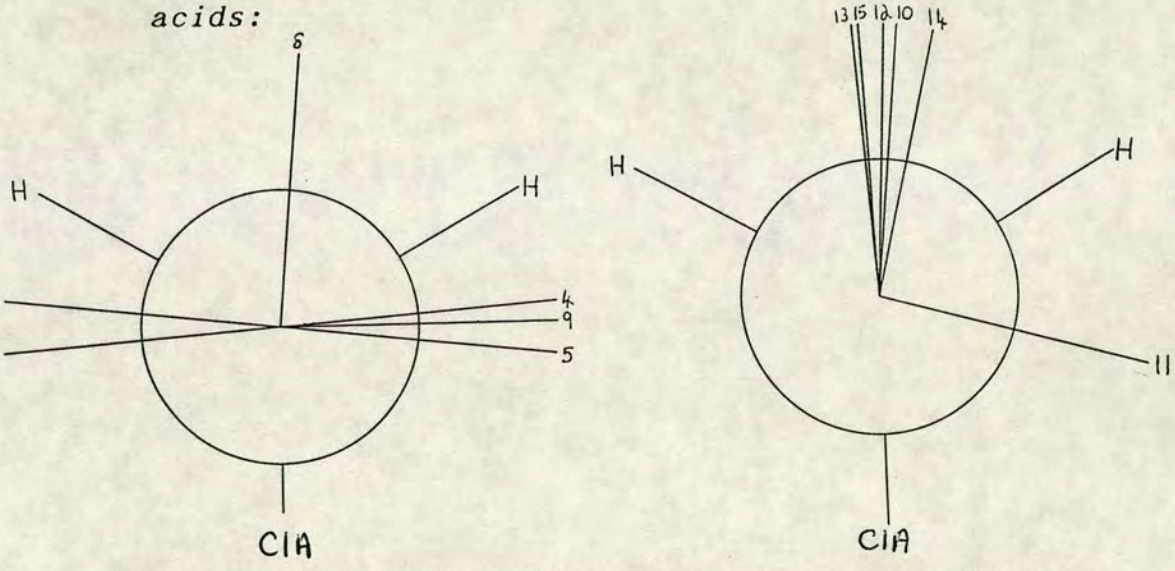
A small survey represented in the second diagram, reveals a simlar preference for the trans-conformation (which corresponds to tg$^+$ for **VAL** and **ILE** structures according to the nomenclature used in the literature for molecules having two γ-carbon atoms[51]). These all have in common that their amino acid molecules are not joined covalently to form a larger molecule. The trans preference is in contrast to the gauche$^-$ preference found in wider surveys[47,51,52,53], which include larger molecules incorporating amino acids and proteins. The trans conformation came second in these surveys.

In **R-CYS**[50], **S-VAL**[42] and **S-ILE**[41], the largest differences in conformation between two crystallographically independent molecules in crystals of each single amino acid occur about the Cα-Cβ bond, when one molecule may be rotated by about 100° about this bond. In **R-CYS**, one molecule is trans, and the other gauche$^+$. The molecule of **S-NOR** and both molecules of **S-MET** have the amino trans conformation and have very similar torsion angles about this bond, but there is a difference in χ_1 conformation of approximately 100° between the enantiomeric and the racemic compounds, in both cases. In the present structures, the amino acids of diastereomeric pair containing **PHE**, and the two disordered side chains of **MET**, each have one gauche and one trans arrangement, whereas in the structure containing **ABA**, both **ABA** molecules have the amino trans conformation about the Cα-Cβ bond. In the present structures, some of the amino acid side chains must need to fold at this point in order to prevent unfavourable close contacts of atoms of the side chain

with neighbouring side chains and the phenyl ring of mandelic acid. Indeed surveys[51] showed that this χ_1 conformation is most commonly gauche- for bulky side chains. **ABA** has the smallest of the side chains apart from **ALA** so it is reasonable that it should be able to stretch out in the amino trans conformation, with less liklihood of contacts that are too close.

Comparison of the packing arrangements in **S-PHE-R-MAN** and **S-PHE-S-MAN** reveal that the major alterationin the conformation of **PHE** molecules to accommodate **MAN** molecules of opposite hand is the rotation of the hydrophilic groups bonded to C1A (Cα), while the positions of C2A (Cβ) and C21A (Cγ) remain little changed.

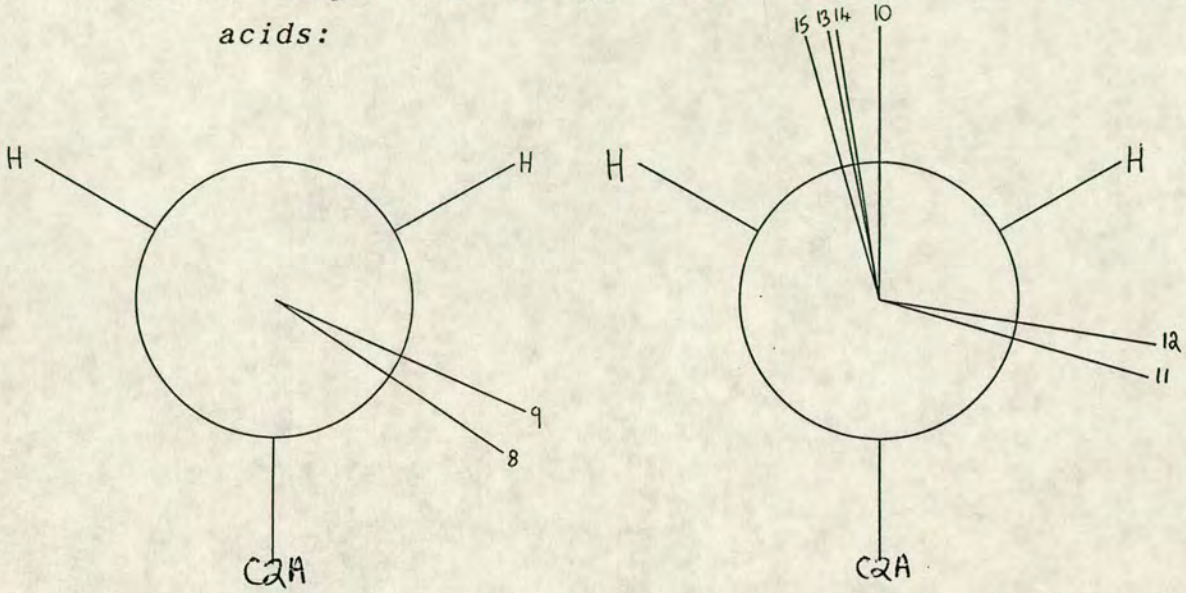
4.2.11 Comparison of χ_2 torsion angles in the amino acids:



In the present structures there are two types:-
(a) the sulphur atom trans to the C1A (**MET** only),
(b) the sulphur atom or the plane of the phenyl rings approximately at right angles to C1A (**MET** or **PHE**).
The major chain of the **MET** structure falls into the first category. Both **PHE** structures fall into the second category, together with S1B of the minor **MET** structure. The **PHE** phenyl ring planes are tilted in opposite directions. Surveys[51] of amino acid conformations show that **PHE**

always tends to adopt this ideal χ_2 conformation because of the phenyl ring, with a tolerance of ±15°. See below for a full discussion of MET side-chain conformation.

4.2.12 Comparison of χ_3 torsion angles in the amino acids:



In the present structures, both terminal methyl groups, carbon atoms, C1SA and C1SB are gauche to C2A and C2B, the β-carbon atoms. The conformations are similar at this point, although the sulphur atoms themselves are on different positions.

It is quite reasonable for the conformation to be gauche rather than trans to prevent too close contact with **MET** or **MAN** molecules across and within the bilayer. Torii and Iitaka[37] mention that if **MET** in the structure of **S-MET** was fully trans planar in both crystallographically independent molecules, then very short contacts of about 3.2Å would be observed between the C and S atoms of neighbouring side chains.

4.2.13 Comparison of methionine conformations:

A range of conformations occur in **MET** and **NOR** structures. The three torsion angles for **MET** in the present structures and **MET** and **NOR** in the literature are given below.

	χ_1	χ_2	χ_3
MET-R-MAN-A	g+	t	g
MET-R-MAN-B	t	90°	g
S-MET-A	t	t	t
S-MET-B	t	g	g
SR-MET-α	g	t	g
SR-MET-β	g	t	t
S-NOR	t	t	t
S-NOR	g-	t	t

All except the second **MET** molecule in the present structures adopt ideal staggered conformations along their side chain, in accord with surveys[51] of amino-acid side chain conformations in bulky hydrophobic side chains. Only two have the fully extended trans planar conformation[37], **S-NOR** and the A-molecule in **S-MET**. There is great variability in the conformations. The conformation of the A-molecule of **MET** in **MET-R-MAN** is most like that in the α-form of **SR-MET**, except **SR-MET-α** has a gauche- χ_1 whereas **MET-R-MAN-A** is gauche+; and in **MET-R-MAN-A** the Cα-N bond eclipses a C-O bond in the carboxylate group, unlike in **SR-MET-α**, where that torsion angle is approximately -30°. The conformation of **MET-R-MAN-B** is most similar to that in the B-molecule of **S-MET**, including at the hydrophilic end, but with the exception that χ_2 is +90° in **MET-R-MAN-B**, but truly gauche+ in **S-MET-B**. Thus the disordered side chains of **MET** in the present structures do not bear a direct relationship to the conformations found in pure **MET** and **NOR** structures.

4.2.14 Comparison of conformations of mandelic acid molecules, introductory comments:

MAN molecules in the present structures were compared with **MAN** molecules in structures in the Cambridge Crystallographic Database[35], and with **MAN** molecules in the diastereomeric pair of salts of **S** and **R-MAN** with naturally occurring ephedrine[54,55]. Of course the atomic labels were not consistent in this group of structures from a variety of sources. **S-MAN** molecules were first inverted to have the R-configuration, to allow comparisons. See section 2.13.3

It was necessary to ascertain which were the 'long' and 'short' C-O bonds in carboxylic acid and indeed in carboxylate groups where the **MAN** is dissociated. Each of the present structure contains undissociated acid functional groups, as does the structure of pure **MAN**, determined twice and given the codes **DLMAND**[20] and **DLMAND01**[21] in the Cambridge Crystallographic Database. The remainder of the **MAN** structures in the Database, together with the ephedrine salts, contain dissociated acid and should have C-O bonds of similar lengths. Only in **BERVUP**[54], **BERWAW**[54], **DMPYRM**[55] and **EPH-S-MAN**[57] are the actual lengths fairly similar in size. The significance of differences in these C-O bond lengths was not examined because the esd's on the bond lengths were not immediately available and it was not considered particularly important, because in the same functional group in amino acids, hydrogen bonding had already been found to stretch some C-O bonds. The torsion angle of the C-O bond which most nearly eclipses the hydroxyl group will be listed below.

Atomic labels in the present structures have been standardised according to an allowed range of torsion angles. See section 2.13. In the literature structures,

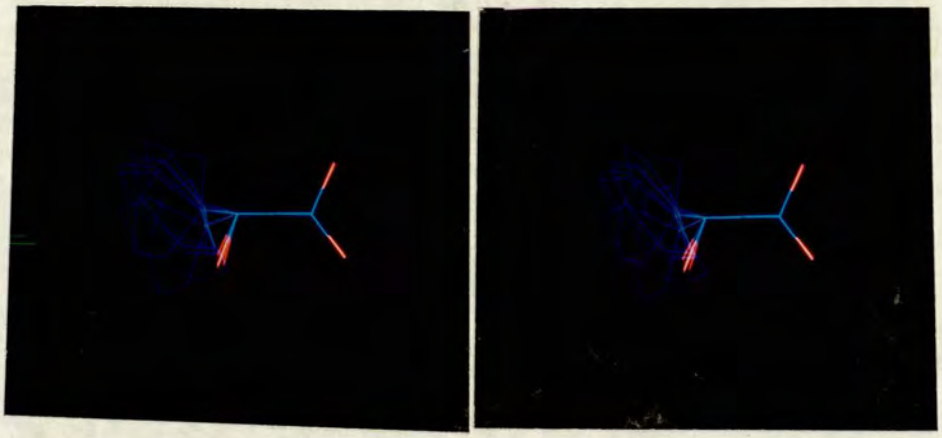
after inversion of **S-MAN** to **R-MAN**, the torsion angle selected, when there was ambiguity, was the one in the range required to conform to the conventions established for the present structures. Two torsion angles define the conformation of **MAN** molecules. These are listed below for the literature structures and those for the present structures may found listed in sections 4.2.1-6.

Table of torsion angles of R-MAN molecules from the Cambridge Crystallographic Database and the ephedrine-mandelic acid salts:

LABEL IN CDS[35]	{C12/C16-C11-C1-O1}	{O21/O22-C2-C1-O1}
BERVUP[54]	-70.34	13.75
BERWAW[54]	-50.05	22.51
CAMANX[19]	-22.71	19.08
DLMAND[20]	-68.03	24.32
DLMAND01[21]	-70.07	23.92
DMPYRM[55] inverted	-43.93	23.12
PEAMAN[56] inverted	-35.70	11.53
EPH-R-MAN[57]	-85.19	13.34
EPH-S-MAN[57] inverted	-16.92	42.07

Using an Evans and Sutherland Picture System, **MAN** molecules from the present structures, with coordinates of **S-MAN** molecules having first been inverted, were superimposed, with atoms C1, C2, O21 and O22 laid on top of one another. All hydrogen atoms were omitted for clarity. The following stereoscopic pair of photographs shows how their conformations compare. They are remarkably similar. The positions of the hydroxyl oxygen atom, O1, and the phenyl ring bridghead carbon atom, C11 vary slightly. The major variation is in the angle of the plane of the phenyl ring.

Mandelic acid molecules projected on C1-C2(O21)-O22

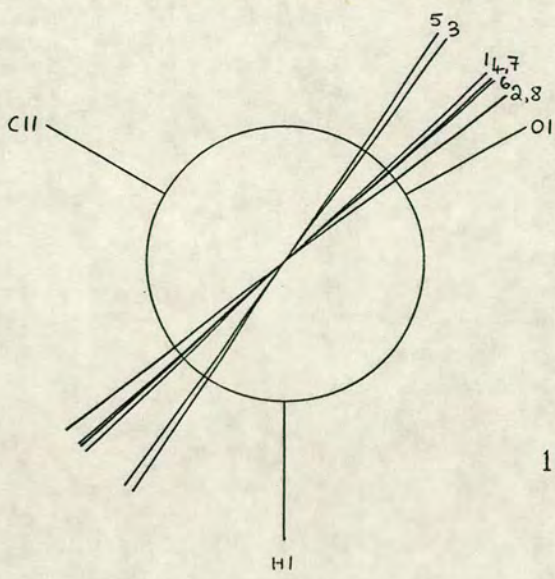


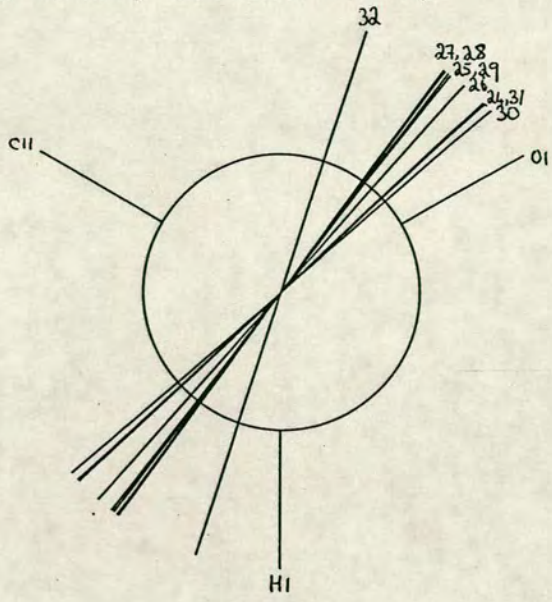
4.2.15 Orientation of the carboxylic acid (or carboxylate) group to the hydroxyl group in mandelic acid:

Key for mandelic acid diagrams

diagram code	abbreviated name	ref.	diagram code	abbreviated name	ref.
24	**BERVUP**	54	29	**DMPYRM**	55
25	**BERWAW**	54	30	**PEAMAN**	56
26	**CAMANX**	19	31	**EPH-R-MAN**	57
27	**DLMAND**	20	32	**EPH-S-MAN**	57
28	**DLMAND01**	21			

(See also codes in amino acid table, section 4.2.8)





The diagrams show that in each of the present structures and in those from the literature in which the **MAN** is undissociated, it is the short C-O bond which eclipses the hydroxyl group. in three of the dissociated **MAN** structures, **BERVUP, BERWAW** and **EPH-R-MAN**, it is again the 'short' C-O bond which eclipses the hydroxyl group. In the other four the dissociated **MAN** structures, **CAMANX, DMPYRM, PEAMAN** and **EPH-S-MAN**, it is the 'long' C-O bond which eclipses the hydroxyl group. thus regardless of whether the acid is dissociated or not, the 'short' C-O bond tends to eclipse the hydroxyl group. from amongst the four exceptions, it is only in **CAMANX** that the difference in C-O bond lengths is particularly large and probably significant. The bond lengths are 1.294 and 1.226Å. The longer one eclipses the hydroxyl group. It is perhaps the strong effect of the calcium ion on the hydrogen bonding and coordination of oxygen atoms to the calcium ion which upsets the usual pattern.

Since the hydroxyl group tends to eclipse a carboxylic acid oxygen atom, there is therefore the potential for an intramolecular hydrogen bond in the **MAN** molecule. However, certainly in the present structures, that hydroxyl hydrogen atom is usually donated to another hydrogen bond acceptor, as is the acid hydrogen atom, and there is no intramolecular bond. Less clear is **MAN-A** in **S-ABA-R-MAN**, where the hydroxyl hydrogen atom is involved in a bifurcated hydrogen bond; and in **S-MET-R-MAN**, where the hydroxyl hydrogen atom was not located and the hydroxyl group appears not to be a hydrogen bond donor at all. Also, none of the literature structures are reported to have such an intramolecular hydrogen bond.

Thus, with an intramolecular hydrogen bond excluded, there are appears to be no identifiable reason, which is internal to the **MAN** molecule, why this torsion angle should tend to be eclipsed. One would predict other conformations and indeed many of the molecules have this torsion angle approaching 30°, where the planar carboxylic acid group makes torsion angles of approximately 30° to the large atoms, C11 and O1, and of approximately 90° to the small atom H1. The fact that there remains this tendency for the torsion angle to be in the range 0°-30°, suggests some common feature of the packing arrangement or hydrogen bonding, which pulls the molecule around into that conformation.

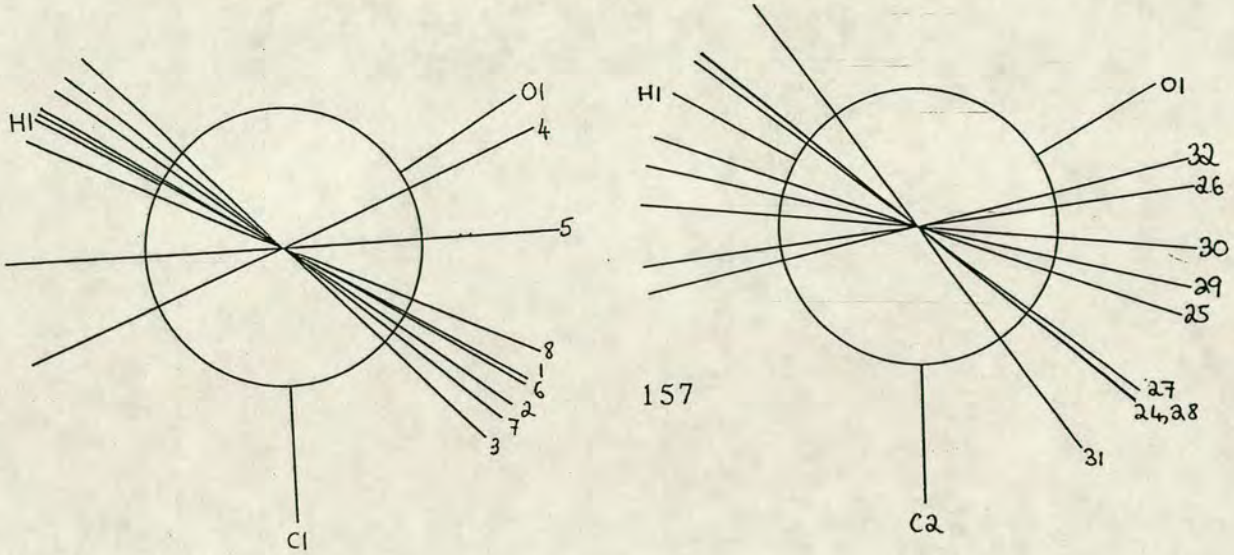
An answer might lie in that in the present structures, the hydroxyl is able to connect with molecules across a bilayer. At the same time, the oxygen atoms of the carboxylic acid group are in such an orientation that they can make hydrogen bonds along the bilayer using the acid oxygen atom, O21, and across the bilayer using the carboxyl oxygen atom, O22. If the carboxylic acid eclipsed the hydrogen atom, H11, it would be pointing up one side of the bilayer and could not make the valuable connections across the bilayer. (See the packing diagrams in section 4.3.)

In **ABA-S-MAN**, there is a bifurcated hydrogen bond in which the hydroxyl hydrogen atom appears to be donated not only to an amino acid carboxylate oxygen atom but also to O21 in an intramolecular fashion. Of course these atoms are close in any case because they are separated by only three bonds and there may be other factors which bring them close by coincidence. However, neither of the angles at the hydrogen atom, subtended by the proposed donors and acceptors, are sufficiently linear, which is consistent with a bifurcated hydrogen bond sharing this hydrogen atom. It does appear that H10 has indeed moved

into a position where it can be shared between O31B and O21. The torsion angle, O21-C2-C1-O1, in **S-ABA-R-MAN** is one of the smaller ones. However, this is the only csae where the assignment of an intramolecular hydrogen bonds appears justified.

The structure **EPH-R-MAN** has this eclipsing, which facilitates hydrogen bonded dimer formation btween one **MAN** molecule and the one symmetry related by a two fold rotation axis. In **EPH-S-MAN**, however, the corresponding torsion angle is almost gauche, at -42°, much larger than for any of the other structures, which never exceed ±30°. (The real, not the inverted torsion angle is mentioned here.) In both diastereomers the carboxylate oxygen atoms both accept two hydrogen bonds. One is hydrogen bonded to **EPH** and **MAN** hydroxyl atoms donated from molecules which are directly across the bilayer from each other. The other accepts hydrogen bonds from two ammonium groups, which are themselves in molecules related by the two fold screw axis, which passes up the bilayer. There is therefore a cross motif in the hydrogen bonding scheme made possible by the angle at which then carboxylate group slices between the **EPH** molecules which is adjacent and on the same side of the bilayer and the **MAN** molecule which is directly across the bilayer from the **EPH** molecule and related by a two fold screw to the first **MAN** molecule. (See packing diagrams in section 4.3)

4.2.16 Orientation of the phenyl ring in mandelic acid:



The present structures and the literature structures exhibit torsion angles in the same large range between -7.5 and -85.5° (after inversion of **S-MAN**). Comparisons may be made between the orientations of **MAN** phenyl rings in diastereometric pairs. One might expect a difference in the **MAN** conformation, in addition to the obvious difference because of the inversion of the hand (for which a correction has been made) when the oppositely hanced **MAN** molecules are cocrystallised with a single hand of the amino acid.

The only pair of structures in which there is a major difference between the torsion angles C12/C16-C11-C1-O1 is in the ephedrine structures. In **EPH-S-MAN**[57], the phenyl ring almost eclipses the hydroxyl group and in **EPH-R-MAN**[57], it is almost at 90° to it. This does not occur in any of the present structures.

In both stereoisomers of the **PHE-MAN** compounds, as in **EPH-S-MAN** and **CAMANX**[19], the phenyl rings in **MAN** molecules eclipse the hydroxyl groups. This puts an electronegative oxygen atom in the vicinity of the slightly positive phenyl ring edge, a favourable interaction. In the remaining structures, the hydroxyl group is twisted farther out of the plane of the phenyl ring and that interaction no longer occurs.

The two **PHE** structures are like the two **EPH** structures in that there are bilayers and that phenyl rings from both molecules interact within the hydrophobic bilayers. Where they differ is that, in the **PHE** structures, it is the **PHE** molecule which alters its conformation most to accommodate the change of hand of the **MAN** molecule (see sections 4.4.9 and 4.2.10). However, in the **EPH** structures, it is the **MAN** molecules which exhibit the greatest additional change in their conformations, while the **EPH** molecules remain little affected.

4.3 Molecular Packing Arrangement

4.3.1 Descriptions:

Diagrams of the packing arrangements of the molecules in the six crystal structures are given. The projections showing the molecules most clearly were chosen. They show one unit cell length in the direction of the projection and a little over one unit cell length in the other two. The projection direction corresponded to the shortest unit cell axis in each case, a view into the plate faces of the crystals.

In each, bilayers are clearly seen parallel to two unit cell axes. The hydrophobic ends of molecules point towards one another, making a hydrophobic sheet, and hydrophilic ends point together to make a hydrophilic sheet. In **S-ALA-R-MAN** and **S-ABA-R-MAN**, it is in these hydrophilic parts that the water molecules are found. Hydrophilic layers are held together by electrostatic forces and hydrogen bonds; hydrophobic layers by non-directional Van der Waals' forces.

The phenyl rings of **MAN** molecules are arranged in pairs across the bilayers, separated alternately by amino acid side chains which pinch in from either side of the bilayer. They vary in their hydrophobic interactions in these bilayers. These are not easily quantifiable and are probably of less importance than hydrogen bonds in determining which diastereomer is preferred over its opposite. Phenyl rings are at an angle to the unit cell edges which allows favourable stepped parallel ring interactions to occur between identical phenyl rings separated by a unit cell repeat.

In both **S-ALA** diastereomers the angles between the planes of phenyl rings are in the narrow range, 71° to 73°.

In the case of the **S-PHE** diastereomers the arrangements of phenyl rings are strikingly similar, the change in handedness of **MAN** having its effect in the hydrophilic hydrogen-bonded bilayer. The greatest differences in the hydrophilic bilayer occur in two of the angles between planes. The differences in angles between the phenyl ring planes in neighbouring **PHE** and **MAN** molecules along the same side of a bilayer, are 13° steeper for S-PHE-S-MAN at 53° than for **S-PHE-R-MAN** at 41°. Similarly, the former has an angle of 81°, 12° steeper than in the latter compound. The interaction is between amino acid and **MAN** phenyl rings back to back across a bilayer. The angle is very near the ideal 90° angle for the favourable face-edge interaction of phenyl rings and might a contribute to **S-PHE-S-MAN** being slightly favoured over its diastereomer as powder diffraction experiments show.

The packing in the **S-ABA-R-MAN** complex is most similar to the **S-ALA-R-MAN** complex in that they have four molecules and a water molecule in the asymmetric unit. In one the side chain of the amino acid is a methyl group; in the other an ethyl group. The major difference in the packing arrangement of these two structures is that for molecules to map onto one another, **ABA-R-MAN** must be rotated 180°, relative to **ALA-R-MAN**, around the shortest unit cell direction. The water molecules are then associated with 'different' mandelic acid molecules. The other complexes, except **S-MET-R-MAN**, have space group C2. In the present complexes the inclusion of a single water molecule reduces the symmetry, both by its location and by the effect it may have on the position and conformation of other molecules as they arrange and

contort themselves in order to accomplish the maximum hydrogen bonding and the minimum energy (maximum stability) of the lattice. In both, the water molecules are near to one of the **MAN** molecules. There are also differences in the hydrogen bonding schemes. The water molecule fits into the existing hydrogen bonding patterns, making long and therefore weak hydrogen bonds. (see section 4.5) The complex containing **S-ABA** has only a two-fold screw, space group $P2_1$, instead of a two-fold screw and a two-fold rotation, which are found in the C2 structures; and the complex, **S-ALA-R-MAN** has none, being in space group P1. Apart from differences in symmetry, there are detailed differences in molecular geometry. (see sections 4.1-4.2)

There is a relationship between the cell dimensions of these two structures, **S-ABA-R-MAN** and **S-ALA-R-MAN**. The a- and b- cell dimensions are similar : 5.999/5.969 and 8.196/8.441 Å.

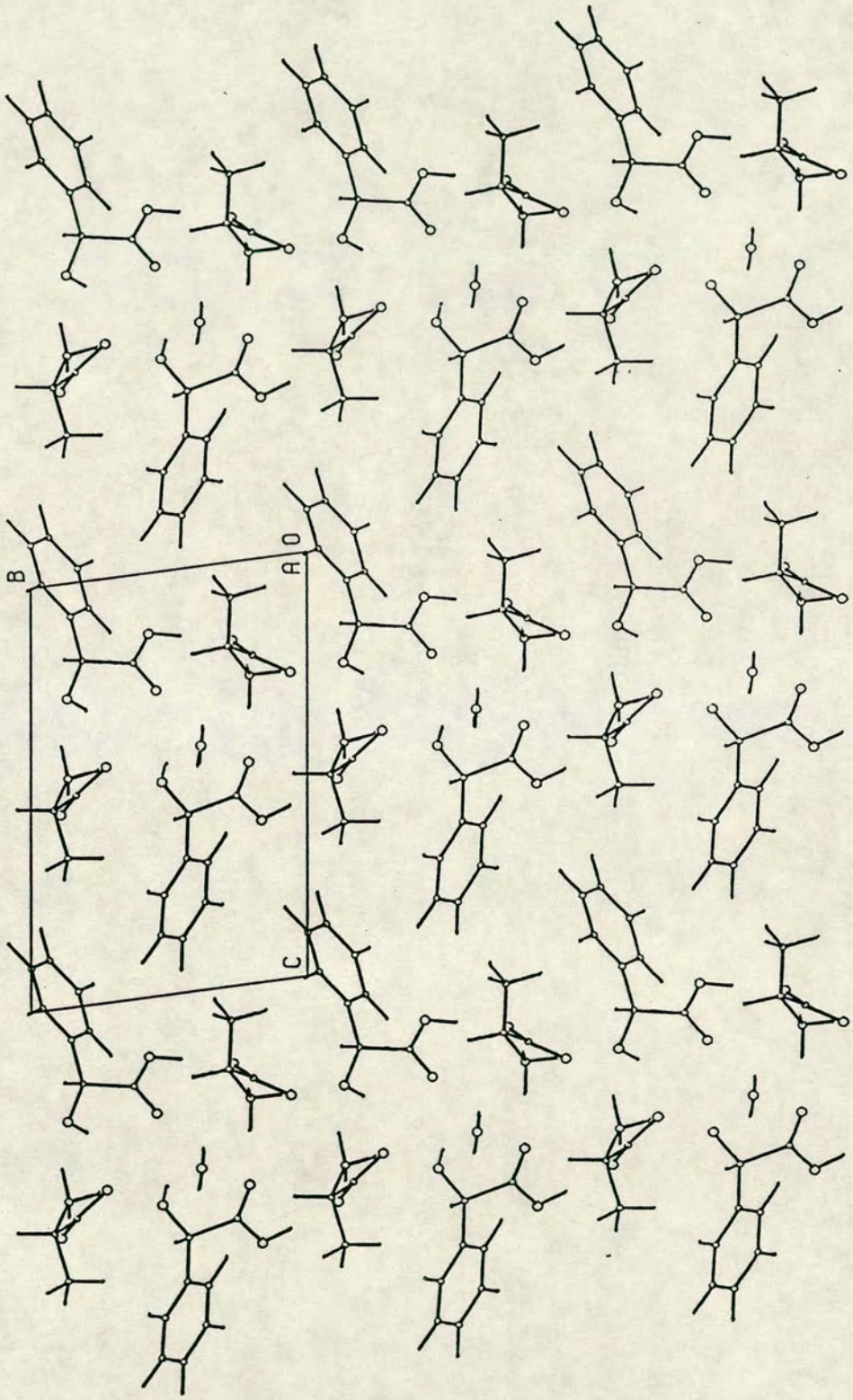
a is slightly compressed in S-ABA-R-MAN relative to **S-ALA-R-MAN**, but the β-angle is a little farther from 90° in **S-ABA-R-MAN**, which perhaps compensates. β-angles are **S-ABA-R-MAN/S-ALA-R-MAN** : 86.45/94.58 and departure from 90° : 3.55/4.58. *b* is stretched in **S-ABA-R-MAN** relative to **S-ALA-R-MAN**. The ethyl group in **S-ABA-R-MAN** is wider than the methyl group in **S-ALA-R-MAN**, which may perhaps contribute to to the effect on *b*.

Comparing the *c*-axes, it it apparent that *c* of **S-ABA-R-MAN** is more than twice *c* of **S-ALA-R-MAN** : 26.78/12.538. There are two effects:-
a) doubling because of the 2_1 screw axis in **S-ABA-R-MAN**
b) longer because the length of the ethyl group exceeds that of the methyl group and makes the hydrophobic bilayers of **S-ABA-R-MAN** wider than **S-ALA-R-MAN** in the *c*-direction.

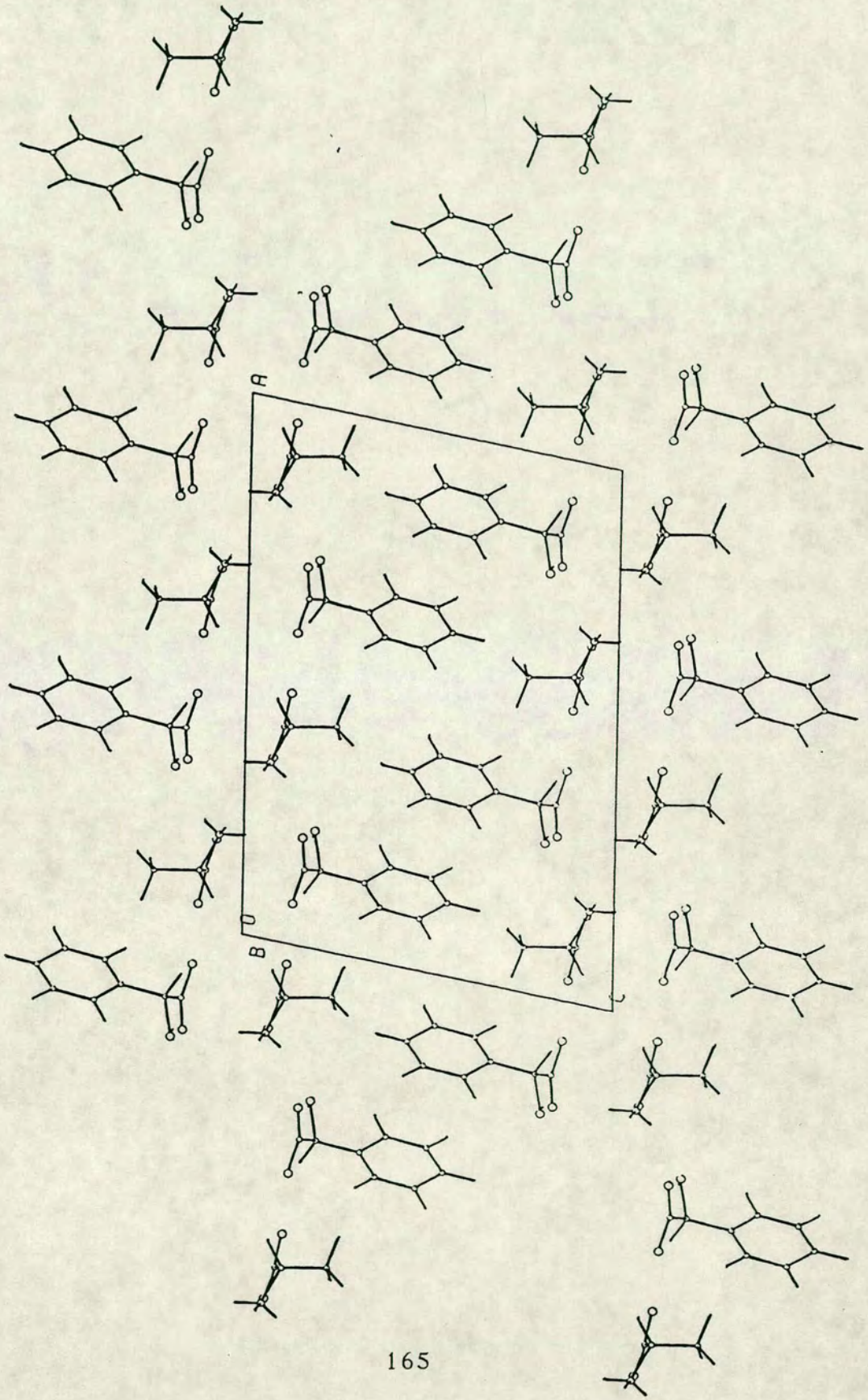
This is the major difference in the packing arrangement of these two structures. For molecules to map on to one another, **S-ABA-R-MAN** must be rotated 180° around the shortest unit cell direction relative to **S-ALA-R-MAN** and the water is then associated with the other amino acid molecule.

S-MET-R-MAN has space group $P2_1$ and an asymmetric unit containing only one **MAN**-amino acid pair. It is also a disordered structure, having two forms in a 70:30 ratio. This suggests that there is little constraint on how the side chain may lie in the hydrophobic bilayer.

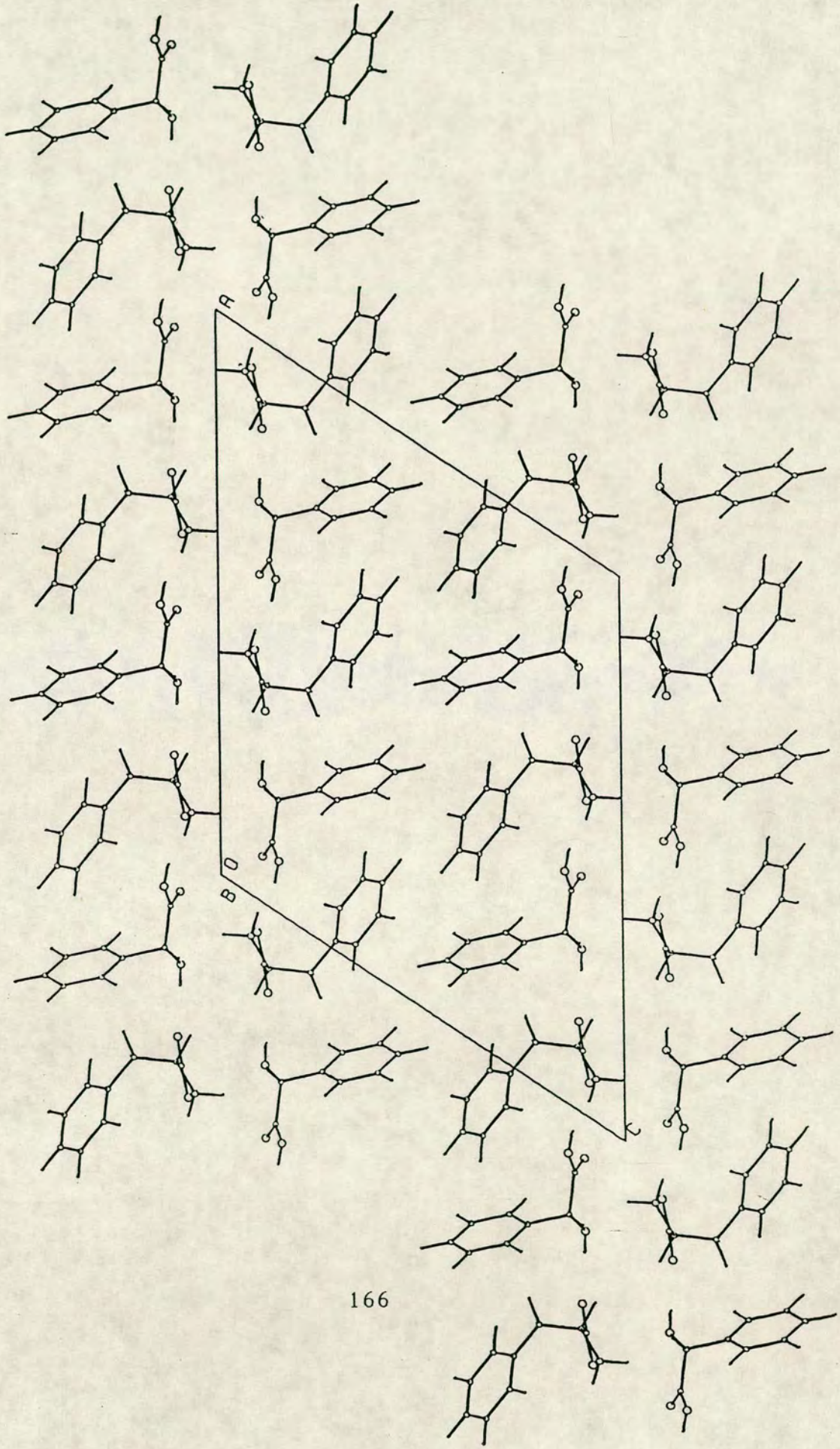
4.3.2 S-Alanine R-Mandelic Acid: View along a.



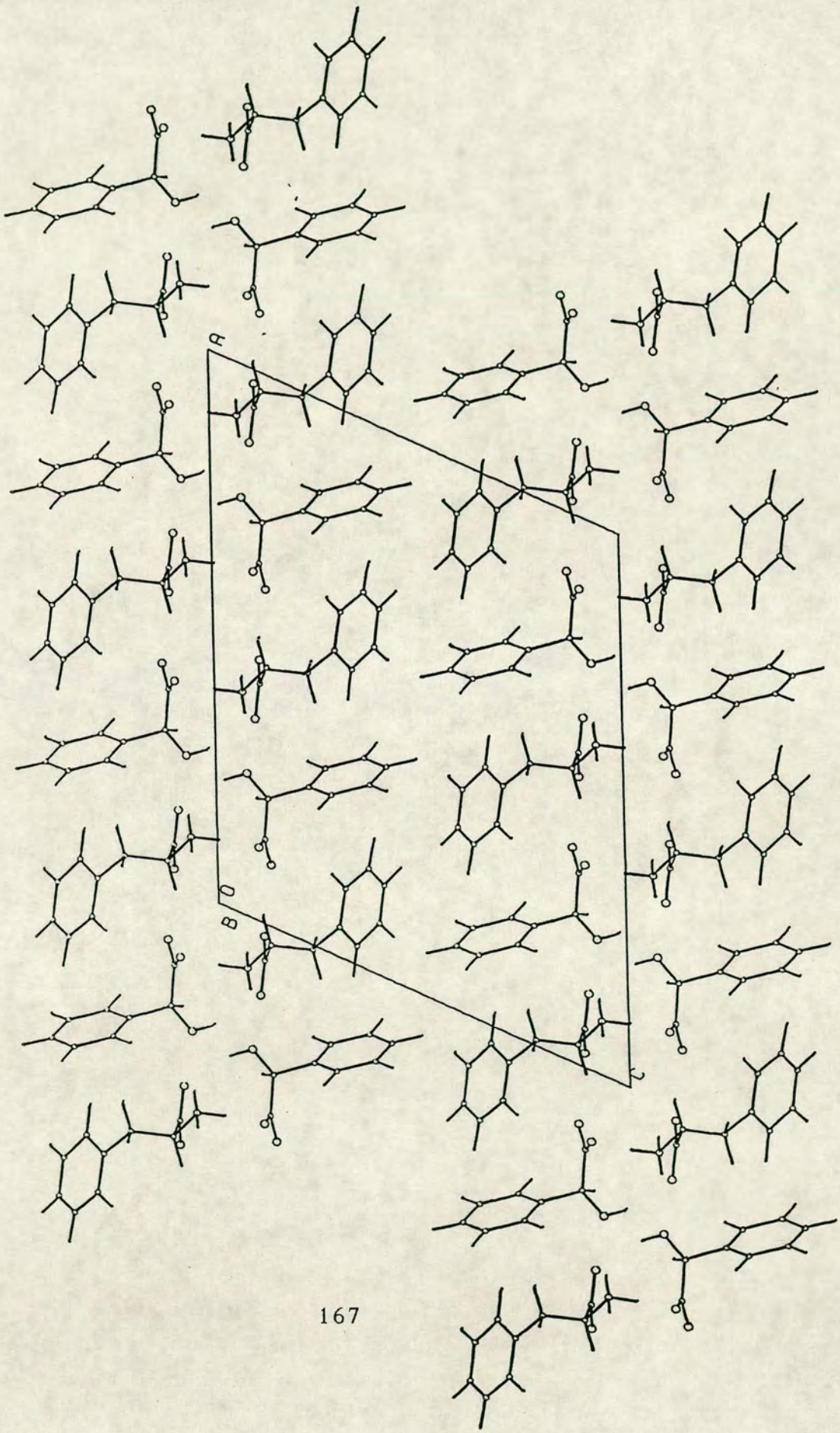
4.3.3 S-Alanine S-Mandelic Acid: View along b.



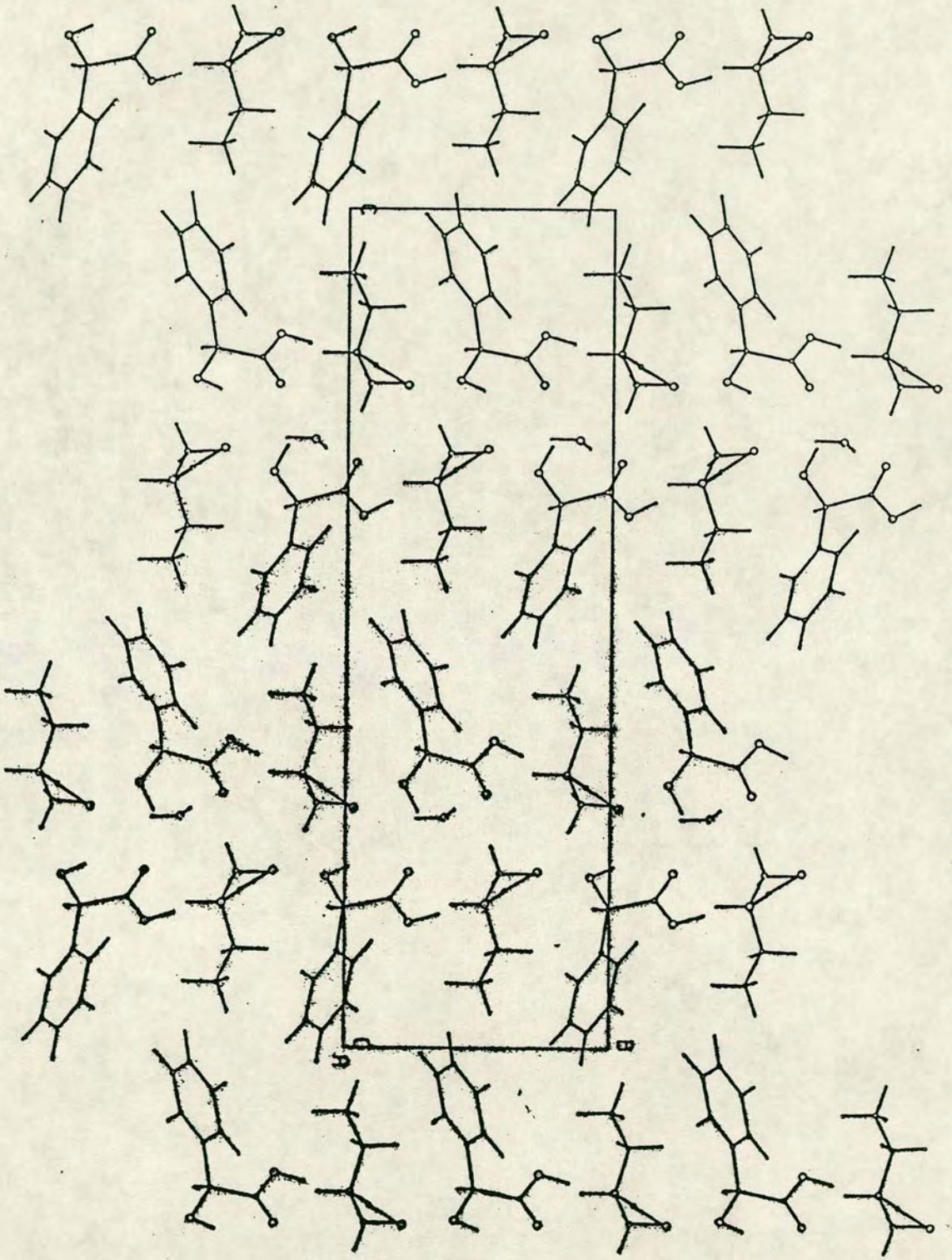
4.3.4 S-Phenylalanine R-Mandelic Acid: View along b.



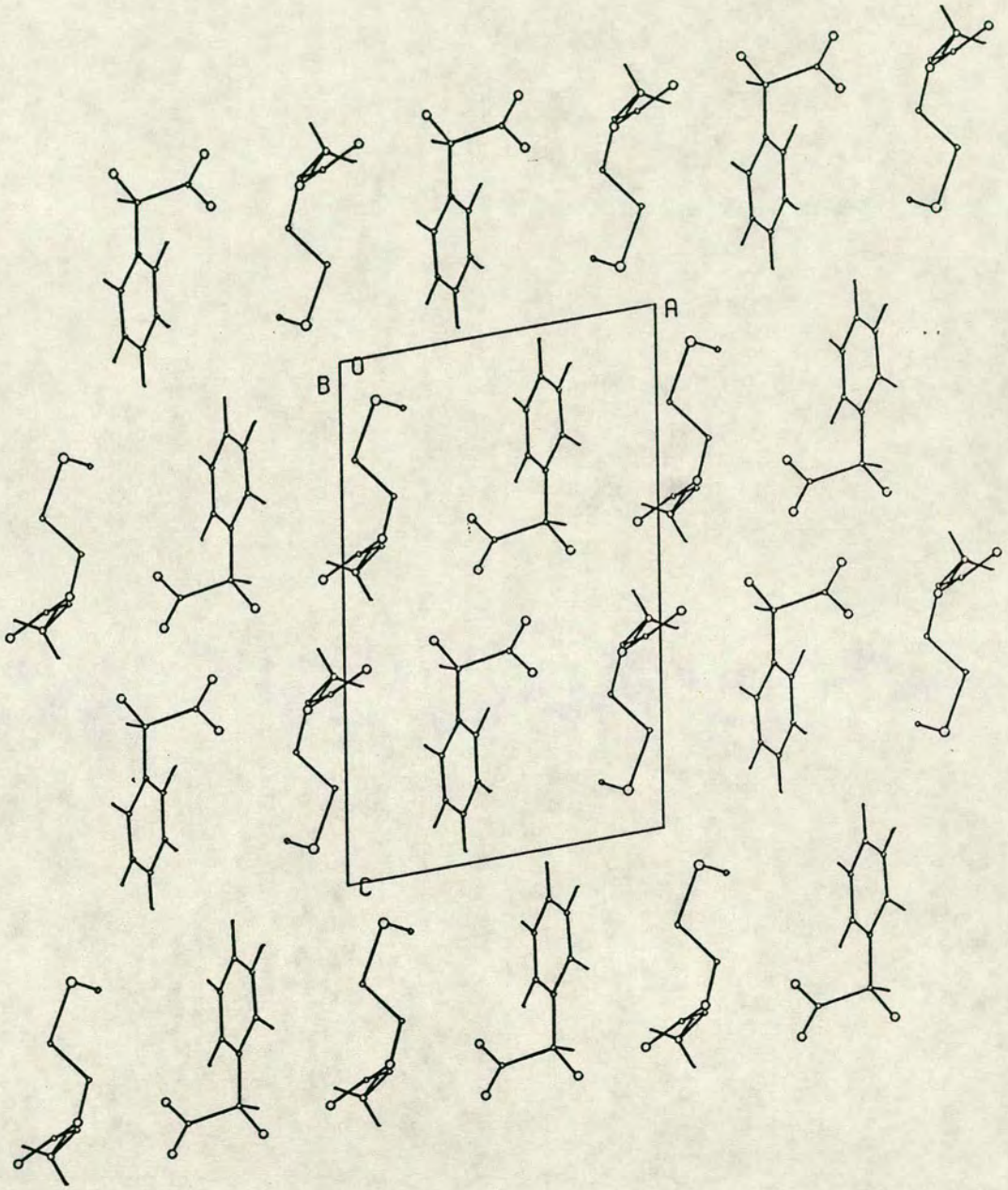
4.3.5 S-Phenylalanine S-Mandelic Acid: View along b.



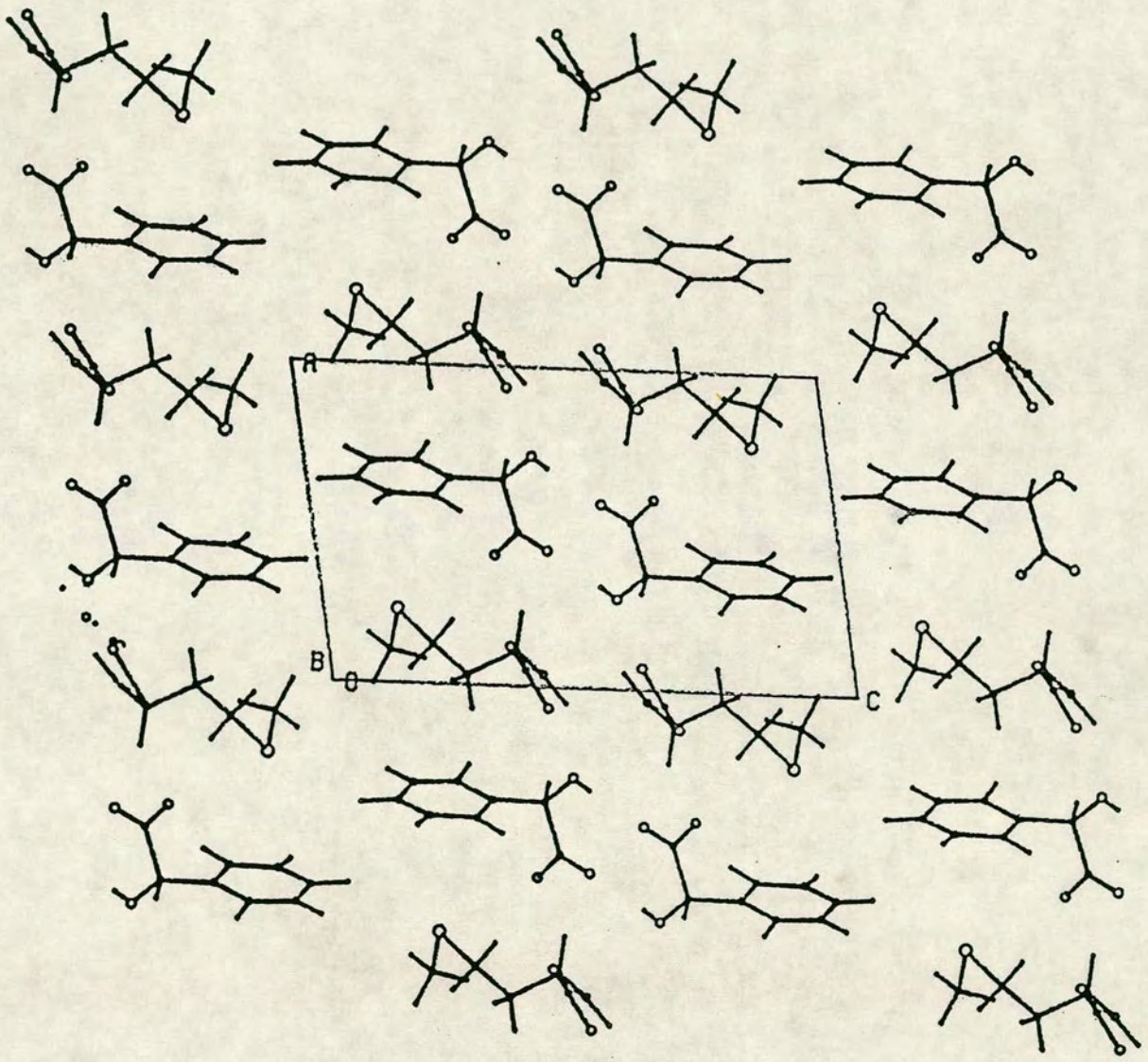
4.3.6 S-α-Aminobutyric Acid R-Mandelic Acid:
View along a.



4.3.7 S-Methionine R-Mandelic Acid:
View along b (major).



4.3.8 S-Methionine R-Mandelic Acid:
View along b (minor).



4.4 Hydrophobic interactions

4.4.1 Stepped parallel interactions between phenyl rings:

These tend to occur between molecules pointing the same way and related to one another by a unit cell repeat. The planes of the phenyl rings are, to all intents and purposes, parallel, lying within the range 1-5°. The stacking direction (parallel to the unit cell repeat direction) is at an angle to the planes of the ring to minimise replusions between like parts of the charge spread over the Van der Waals' surface of the molecule, between faces and between edges of phenyl rings. Favourable attractions occur between the slightly negatively charged area above or below the face of a phenyl ring and the slightly positively charged protons of the ring tip.

4.4.2 Face to edge interactions between phenyl rings:

This kind of interaction occurs between the negative part of the molecular surface above and below the phenyl ring faces and the positive area around the ring edge. The molecules taking part tend to point towards each other or to lie next to each other along a bilayer. The angle between the planes of the rings can be in the range 30-90°. In the ideal situation, when the rings are perpendicular the interaction is entirely attractive, but down to about 30° the interaction remains positive before repulsions between ring edges overcome attractions.

4.4.3 Other interactions:

Oxygen atoms may be expected to lie in the plane of phenyl rings, since there may be favourable interactions between electronegative oxygen atoms and the slightly positive hydrogen hydrogen atoms at the phenyl ring

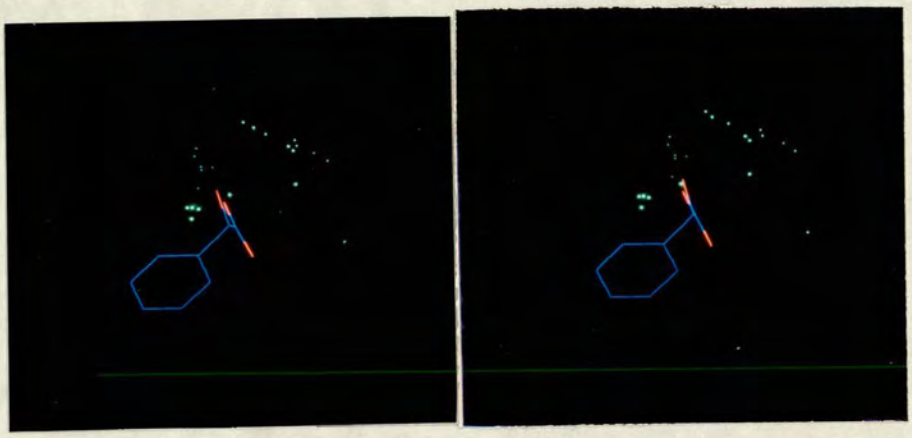
edges, and repulsion between oxygen atoms and the slightly negative ring faces. A survey[51] has shown that the elevations of oxygen atoms out of the plane of a phenyl ring tend to be in the range of 0-20° and to be more or less normally distributed in this range, with an additional maximum towards the top end.

Some atoms may be close enough to suggest that there may be an interaction between them, but there may be no such direct interaction to explain their proximity. One of the atoms may be covalently bonded to another atom which in turn interacts with the nearby atom. The first atom is thus drawn closer than it otherwise might be. An example is the carboxylate carbon atom of an amino acid which is relatively close to an electronegative atom to which an adjacent carboxylate oxygen atom is hydrogen bonded. Alkyl groups may interact positively with the slightly negative faces of phenyl rings.

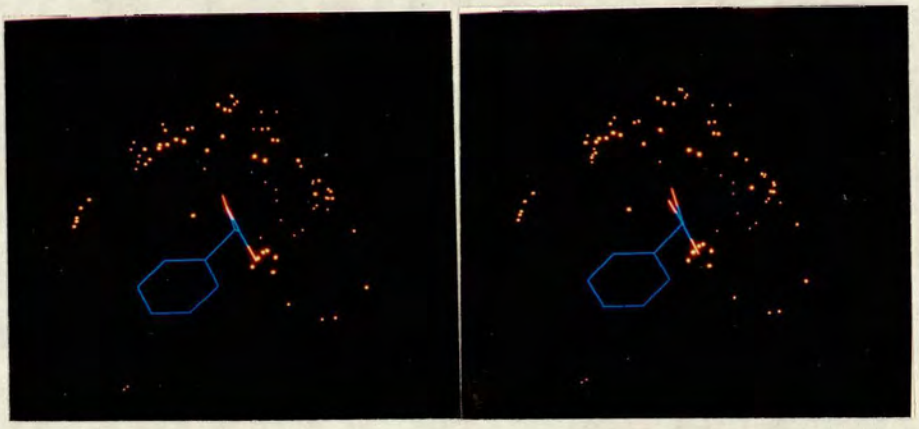
4.4.4 The environments of mandelic acid molecules:

Using the atomic positions of the mandelic acid from **S-PHE-R-MAN** as a template, the positions of certain types of atom from each of the six structures were plotted on the same diagram as stereoscopic pairs using an Evans and Sutherland Picture System.

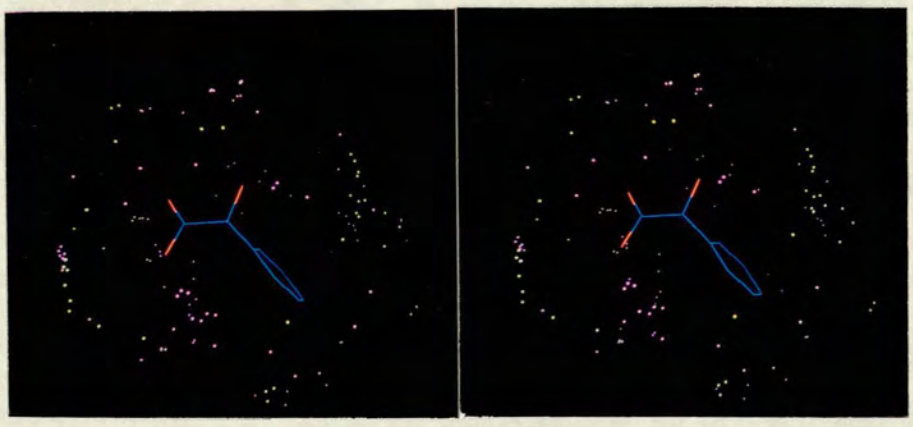
Nitrogen environment of a typical ***MAN*** *molecule:*



Oxygen environment of a typical ***MAN*** *molecule:*



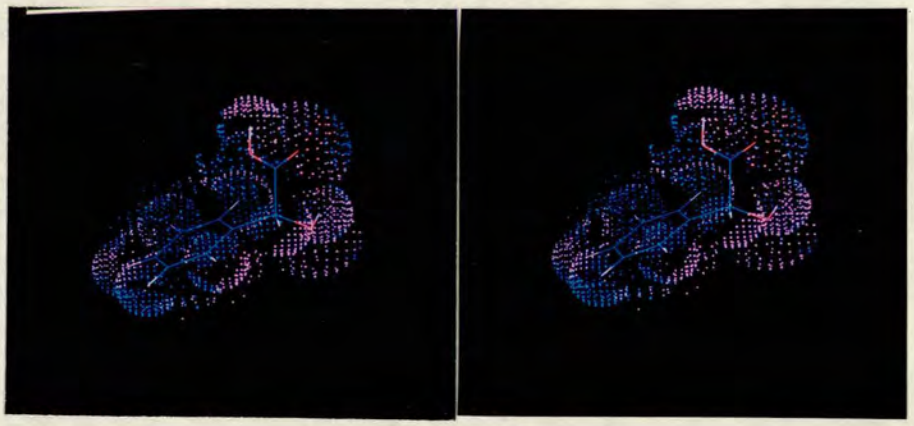
Carbon environment of a typical ***MAN*** *molecule:*



The most interesting feature displayed is the polar nature of the molecule. Nitrogen and oxygen atoms are to be found in association with the hydrophilic part of the molecule. There is a cluster of nitrogen atoms (from amino acid ammonium groups) above the hydroxyl oxygen atom and the carboxylate atom eclipsed by it. This corresponds to the commonly occurring hydrogen bonds between the ammonium group and these oxygen atoms. Some of the oxygen atoms are to be found in line with the phenyl ring edge.

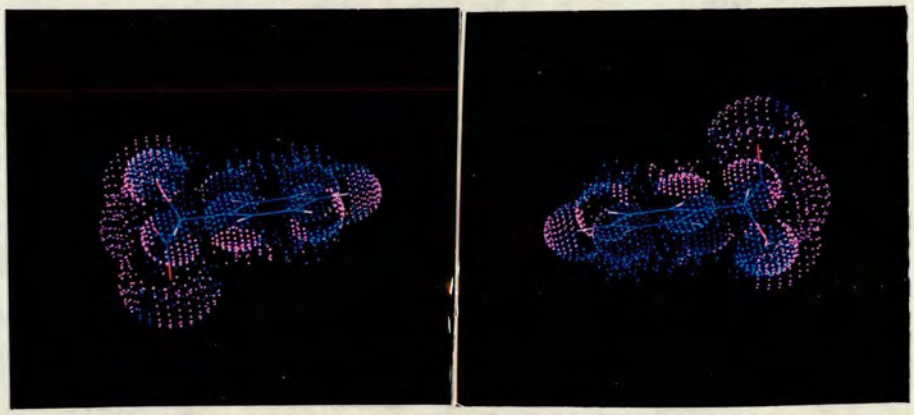
The following pictures show the Van der Waals' surfaces of mandelic acid molecules in the six crystal structures, colour coded according to the type of molecule in closest contact over the surface. Contact with other mandelic acid molecules is shown in blue, with an amino acid molecule in mauve, and with a molecule of water in red. Stereoscopic pairs are given. The top face of the phenyl ring is generally unhindered by functional groups, with the hydroxyl group at one end. The carboxylic acid group completes an L or wedge shape, hindering the bottom face of the phenyl ring to approach by hydrophobic parts of molecules.

*Environment of **MAN-A** in S-ALA-R-MAN:*

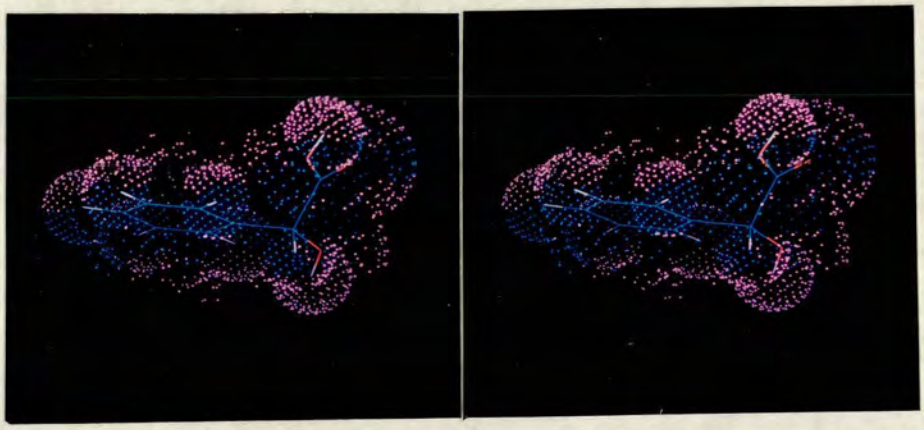


*Environment of **MAN-B** in S-ALA-R-MAN:*

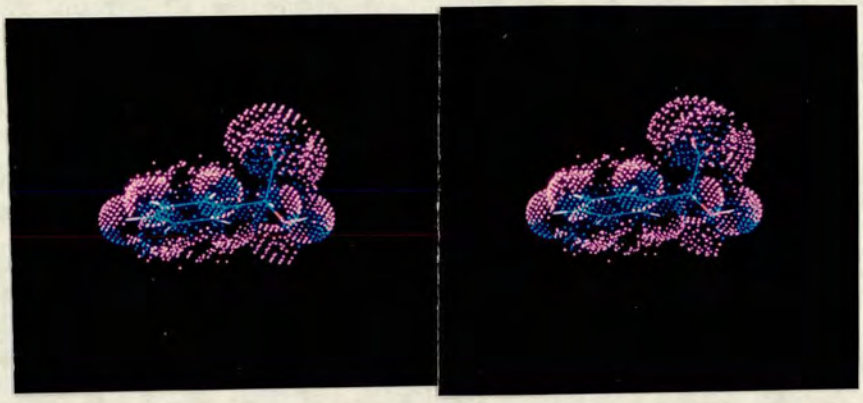
*Environment of **MAN** in S-ALA-S-MAN:*



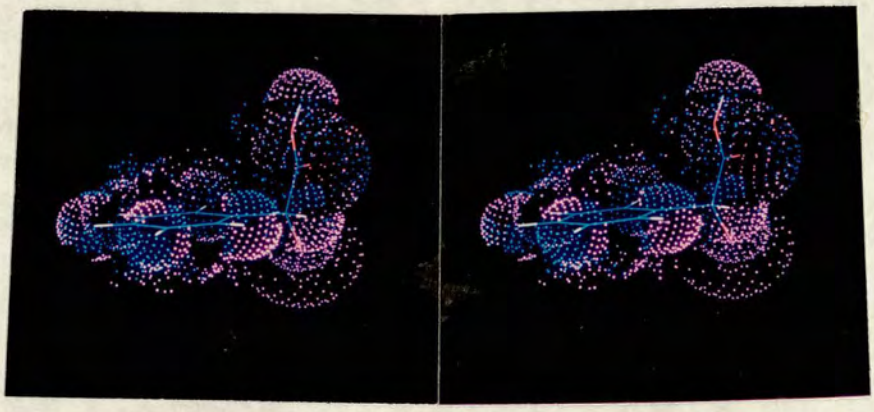
*Environment of **MAN** in S-PHE-R-MAN:*



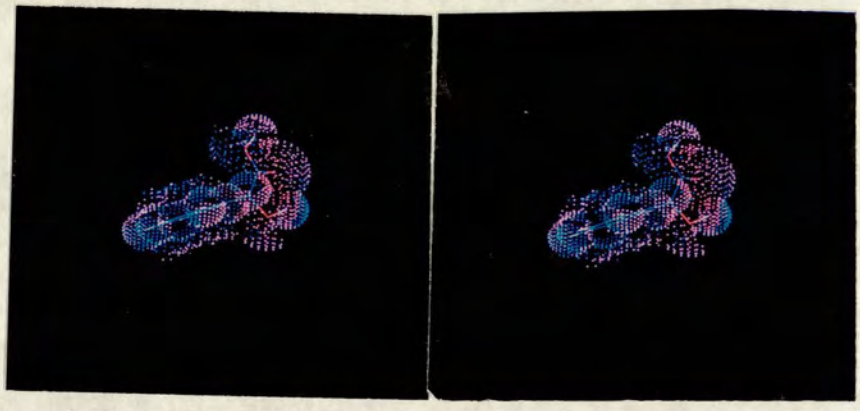
*Environment of **MAN** in S-PHE-S-MAN:*



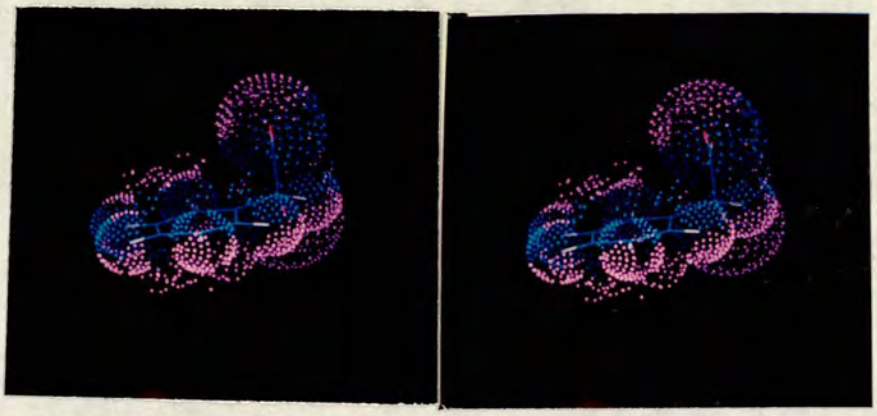
*Environment of **MAN-A** in S-ABA-R-MAN:*



*Environment of **MAN-B** in S-ABA-R-MAN:*



*Environment of **MAN** in S-MET-R-MAN major:*



4.4.5 Water contacts:

The two mandelic acid molecules in **S-ALA-R-MAN** differ in that one (with the prime in the atom labels) has more contact with the water molecule than the other in the hydrophilic end of the **MAN** molecule. This is because the water is situated closer to this one and joined to it by hydrogen bonding. The same is true for the **S-ABA-R-MAN** complex.

4.4.6 Hydrophilic portion of mandelic acid:

In every case there is some combination of contact with other **MAN** molecules and amino acid molecules.
The contact to water molecules has been discussed above.

4.4.7 Hydrophobic portion of mandelic acid in S-alanine-R-mandelic acid:

The intermolecular contacts in the two **MAN**'s molecules are similar. Each **MAN** molecule makes contact with other **MAN** molecules around their ring edges. This is on account of stepped parallel face-edge interactions between **MAN** molecules related by a unit cell repeat. The upper ring face, on the side of the wedge-shaped molecule

with the hydroxyl group in it, makes contact with an **ALA** molecule adjacent in the bilayer. The underside of the ring tip makes contact with an **ALA** molecule across the bilayer.

4.4.8 Hydrophobic portion of mandelic acid in S-alanine-S-mandelic acid:

The top face of the phenyl ring, on the side of the 'wedge' with the hydroxyl group in it, there is contact almost entirely with **MAN** molecules. This is partly because of the face-edge interaction with a symmetry related **MAN** molecule around a two-fold screw axis. It is also to do with the stepped parallel interaction between **MAN** molecules related by a unit cell repeat in the b-direction. The lower and upper edges of the ring tip are involved in this. **ALA** contacts occur around the edge on one side only. This is the side of the **MAN**, past which runs the two-fold rotation axis and the methyl side chains of **ALA** molecules pinch in to the bilayer from both sides. The **ALA** adjacent in the bilayer, which is hydrogen bonded to the **MAN**, makes contact with the edge of the phenyl ring and also underneath it close to the bridgehead atom.

4.4.9 Hydrophobic portion of mandelic acid in S-phenylalanine-R-mandelic acid and S-phenylalanine-S-mandelic acid:

The environments of these contrast markedly with that of the **MAN** molecules in the **ALA** complexes. The top and bottom faces of the wedge-shaped molecules make contact with amino acid only, the **MAN** contacts being restricted to a stripe around the edges. This stripe is particularly narrow for the **S-MAN** complex. The **MAN** contacts are principally to do with stepped parallel stacking of mandelic acids making the unit cell repeat, the rings

being at a steeper angle to the b-axis than in other complexes. In the **R-MAN** complex, but not in the **S-MAN** complex, the upper tip of the ring, on the face with the hydroxyl rather than the carboxylic acid, makes contact with another **MAN**, the one related by a two-fold rotation, across the bilayer.

Most hydrophobic contact comes in the form of face-edge interactions between amino acid and **MAN** molecules adjacent along bilayers on either side of the **MAN** molecule. These molecules are also hydrogen bonded along the bilayer. In both cases the **PHE** so contorts itself so as to present the methylene group, containing atom C21A, to the top face of the wedge-shaped **MAN** molecules, which are opposite in configuration. This is revealed in the large difference in the χ_1 torsion angle, described in section 4.2.10. (See also packing diagrams in section 4.3) In the **R-MAN** complex the ammonium donates a hydrogen bond to the **MAN** on the same side as it presents the methylene group, whereas in the **S-MAN** complex the ammonium group is twisted around to donate to the **MAN** on the other side along the bilayer.

4.4.10 Hydrophobic portion of mandelic acid in S-methionine-R-mandelic acid, major conformer:

The environment is most like that of **S-PHE-R-MAN**. There is an increased contact with other **MAN** molecules in the hydrophilic region and the contact around the edge of the ring is rather more towards the underside of the ring edge. The top face is again completely contacted by the amino acid adjacent in the bilayer, both because of hydrogen bonding and possible hydrophobic interactions. The methylene group of the side chain, with the atom C21A, is presented to the face of top face of the **MAN** molecule, with the hydroxyl group in it. The stepped parallel stacking interaction covers an area of the size of that in the **S-PHE-R-MAN** complex, much greater than that in the **S-PHE-S-MAN** complex. The **MET** contact under the ring, on the 'hindered' carboxylic acid side, from the centre to the tip is where the terminal methyl group points towards the **MAN** phenyl ring adjacent in the bilayer, or where the sulphur atom of the **MET** across the bilayer is close to the ring.

4.4.11 Hydrophobic portion of mandelic acid in S-α-aminobutyric acid-R-mandelic acid:

Water contacts have been discussed earlier. The pattern of the contacts around **MAN** in this complex is different again. There is the amino acid above and below the ring, with the **MAN** contact around the edge of the ring common to the **PHE** and **MET** structures, but it is not so clear cut. As in these the amino acids on either side adjacent in the bilayer make contact above an below the ring. These amino acids are hydrogen bonded to the **MAN** in the hydrophilic region. The larger contact comes from above the ring on the hydroxyl side of the wedge. The methylene group of the adjacent **ABA** points down towards the ring face covering the area between the bridgehead

carbon atom and the middle of the ring. Under the ring, on the carboxylic acid side of the wedge, the adjacent, hydrogen bonded **ABA** points up towards the ring making some degree of contact at the bridgehead end of the ring. The methyl group at the end of the side chain of an amino acid across the bilayer points towards the underside of the ring tip. Between these latter contacts the phenyl ring of a **MAN** across the bilayer inserts itself in a face-edge interaction. These two **MAN** molecules are related by a two fold screw along the bilayer. The **MAN** contact above the ring at the tip represents another face-edge interaction with the molecule related by a two fold screw, translated in the opposite direction. The **MAN** edge contact on the underside near the bridgehead carbon atom represents the stepped parallel stacking of **MAN** phenyl rings up the b-direction. The corresponding contact on the other side of the ring is obscured.

4.4.12 Discussion:

The apparent interaction between alkyl groups and the slightly negatively charged faces of phenyl rings is a prominent feature of the **PHE-MAN** structures, where the methylene protons of the **PHE** side chain point directly towards the **MAN** phenyl ring face adjacent along the bilayer. That the 1:1 molecular complexes occur at all is unexpected since there is no ionic electrostatic interaction between the two components. Van der Waals' bonding must surely supplement the hydrogen bonding which holds the molecules together. Some combinations of amino acid and **MAN** may have more directional attractions than Van der Waal's forces. Examples are the cases of **PHE** and of **MAN**, where there are face-edge interactions between the phenyl rings of adjacent amino acid and **MAN** molecules. The inclusion of the large, electronegative sulphur atom in the side chain of **MET** appears to interrupt the interactions leaving the **MET** freer to adopt more than one

conformation in this disordered structure. The diastereomeric complex appears to form crystals with an even more disordered structure which varies gradually over the crystal so that the crystals are unsuitable for single crystal x-ray structure determination. **S-ABA-S-MAN** forms only small, thin crystals, too small for structure determination, which suggests that the parts of molecules in the hydrophobic bilayers, which would be predicted to form the packing motif, do not pack as well as in the opposite diastereomer, whose structure was successfully determined.

The small methyl groups of the **ALA** complexes do not hinder hydrophobic interactions and indeed act like the methylene groups in the **PHE** structures and point towards neighbouring **MAN** phenyl rings.

4.5 Hydrogen Bonds

4.5.1 Tabular data:

In each of these six molecular complexes, there are sheets of hydrogen bonds holding together bilayers. The hydrogen bonding extends in a third direction to link together adjoining bilayers.

Tables listing the hydrogen bonds in each structure are given below. The symmetry operators given are those which move the acceptor atom from its position in the first asymmetric unit, (x,y,z), to the coordinates at which it accepts the hydrogen bond from the donor in the first aymmetric unit. In the case of bifurcated hydrogen bonds, the midpoint of the two acceptor atoms is given as X or Y.

donor	*acceptor*	*symmetry*	*D-A/Å*	*D-H-A/°*
S-ALA-R-MAN				
N(1A) -H(1NA)...O(21')		1+x,y,z	3.000(5)	123(4)
N(1A) -H(1NA)...O(1W)		x,y,z	2.953(6)	127(4)
N(1A) -H(1NA)...X			2.427(9)	149(5)
N(1A) -H(2NA)...O(1)		1+x,y-1,z	2.871(5)	174(6)
N(1A) -H(3NA)...O(32A)		1+x,y,z	2.871(5)	157(7)
N(1B) -H(1NB)...O(31A)		x,1+y,z	2.811(4)	136(4)
N(1B) -H(2NB)...O(1')		x,y,z	2.880(5)	144(5)
N(1B) -H(3NB)...O(32B)		x-1,y,z	2.824(5)	165(5)
O(1) -H(1O) ...O(31B)		x-1,y,z	2.903(4)	147(6)
O(1') -H(1O')...O(21)		x,y,z	2.850(5)	153(9)
O(22) -H(2O) ...O(32A)		x,y,z	2.481(4)	172(6)
O(22')-H(2O')...O(32B)		x-1,y-1,z	2.534(4)	177(6)
O(1W) -H(2W) ...O(1')		x,y,z	3.028(6)	139(5)
O(1W) -[ ] ...O(31B)		x,y,z	2.924(5)	---
S-ALA-S-MAN				
N(1A) -H(1NA)...O(21)		1-x,y,2-z	2.985(12)	176(8)
N(1A) -H(2NA)...O(1)		½+x,½+y,z	2.880(12)	160(9)
N(1A) -H(3NA)...O(31A)		x,1+y,z	2.713(12)	144(8)
O(1) -H(1O) ...O(21)		x,y-1,z	2.788(10)	167(9)
O(22) -[ ] ...O(32A)		x,y,z	2.436(10)	---
S-PHE-R-MAN				
N(1A)-H(1NA)...O(1)		½-x,½+y,-z	2.805(5)	143(3)
N(1A)-H(1NA)...O(21)		½-x,½+y,-z	3.043(5)	139(3)
N(1A)-H(1NA)...X			2.630(7)	167(4)
N(1A)-H(2NA)...O(21)		½+x,½+y,z	2.927(5)	166(4)
N(1A)-H(3NA)...O(31A)		x,-1+y,z	2.870(5)	167(4)
O(1)-H(1O)...O(32A)		x,-1+y,z	2.636(5)	162(4)
O(22)-H(2O)...O(31A)		-½+x,-½+y,z	2.610(4)	164(4)

S-PHE-S-MAN

N(1A)-H(2NA)...O(1)	x,1+y,z	2.880(17)	153(11)
N(1A)-H(1NA)...O(21)	½-x,½+y,-z	2.859(17)	141(9)
N(1A)-H(3NA)...O(32A)	x,1+y,z	2.717(17)	155(10)
O(1)-H(1O)...O(31A)	½-x,-½+y,-z	2.693(15)	140(10)
O(22)-[ ]...O(32A)	-½+x,-½+y,z	2.523(16)	---

S-ABA-R-MAN

N(1A)-H(1NA)...O(1)	x,y,z	2.951(6)	152.4(23)
N(1A)-H(2NA)...O(21')	-1+x,y,z	3.041(6)	116.9(20)
N(1A)-H(2NA)...O(1W)	x,y,z	2.962(7)	137.8(23)
N(1A)-H(2NA)...X		2.428(6)	153.9(26)
N(1A)-H(3NA)...O(32A)	-1+x,y,z	2.805(6)	173.9(26)
N(1B)-H(1NB)...O(1')	x,1+y,z	2.962(6)	144.4(14)
N(1B)-H(2NB)...O(31A)	x,y,z)	2.782(6)	158.1(16)
N(1B)-H(3NB)...O(32B)	1+x,y,z	2.773(6)	168.9(16)
O(1)-H(1O)...O(21)	x,y,z	2.661(9)	112.8(19)
O(1)-H(1O)...O(31B)	x,y,z	2.896(6)	129.1(20)
O(1)-H(1O)...Y		2.221(9)	145.2(25)
O(1')-H(1O')...O(21)	1+x,-1+y,z	2.916(6)	145.8(23)
O(22)-H(2O)...O(32A)	-1+x,1+y,z	2.511(6)	174.6(25)
O(22')-H(2O')...O(32B)	1+x,y,z	2.562(7)	175.8(26)
O(1W)-H(1W)...O(21')	x,y,z	3.178(7)	172(4)
O(1W)-H(2W)...O(31B)	x,-1+y,z	2.973(6)	166(4)

S-MET-R-MAN

N1A-H2NA...O1	1+x,-1+y,z	3.029(10)	149(3)
N1A-H3NA...O31A	2-x,-½+y,1-z	2.792(12)	115.0(25)
N1A-H1NA...O32A	x,-1+y,z	2.747(12)	127.4(25)
O22-[ ]...O32A	x,y,z	2.584(11)	---

4.5.2 Discussion:

Each structure utilises its full complement of hydrogen bond donors except **S-MET-R-MAN**, where the hydroxyl hydrogen atom is not involved in any hydrogen bonding. This hydrogen atom itself is not located and the only atom close enough to be hydrogen bonded is the nitrogen atom of the amino acid ammonium group, which donates a hydrogen atom to it. In these six structures the only type of atom capable of accepting a hydrogen bond but which never does is the carboxylic acid oxygen atom labelled O22 or O22'. The water molecules only accept hydrogen bonds as part of bifurcated hydrogen bonds, but each donate two hydrogen bonds.

Although the detailed arrangements vary, the pattern in the types of atom which accept hydrogen bonds from the ammonium groups fall into two categories:-

a) two carboxylate acceptors, either O31A or O31B and either O32A or O32B, one hydroxyl acceptor, either O1 or O1' (**ALA-R-MAN B, MET-R-MAN, ABA-R-MAN B**).

b) one carboxylate acceptor, one out of O31A, O31B, O32A or O32B; one hydroxyl aceptor, either O1 or O1'; one carboxyl acceptor, either O21 or O21', which shares in a bifurcated hydrogen bond with water in both cases where water is present. (**ALA-R-MAN A, ALA-S-MAN, PHE-R-MAN, PHE-S-MAN, ABA-R-MAN A**)

Additionally, in **PHE-R-MAN**, the hydroxyl oxygen atom shares in a bifurcated hydrogen bond with a second carboxyl oxygen atom. The ammonium groups of both complexes, **ALA-R-MAN** and **ABA-R-MAN** fall one into each category a) and b). No **S-MAN** complexes fall into catego-

ry a), which is altogether the less common category. In the diastereomeric pair, **PHE-R-MAN** and **PHE-S-MAN**, it is "opposite" carboxylate oxygen atoms, O31A and O32A which accept the hydrogen bond from the ammonium group. This reflects the change in handedness of the **MAN** between the two structures because of from where the **MAN** hydroxyl group is presented towards the ammonium group:- from across or along the bilayer. The ammonium then has to use the carboxylate oxygen atom in the direction of a spare ammonium hydrogen atom. In **PHE-R-MAN** the hydroxyl accepts an ammonium hydrogen bond from across the bilayer and donates to a carboxylate O32A along the bilayer. In **PHE-S-MAN** the hydroxyl accepts an ammonium hydrogen bond from along the bilayer and donates to a carboxylate O31A across the bilayer. **MAN** is hydrogen bonded only to **PHE**.

Although they vary as to the type of atom to which they donate their hydrogen atoms, the hydroxyl groups accept hydrogen bonds almost exclusively from ammonium groups. A photograph of the total environment of a **MAN** molecule highlights this. (See section 4.4.4.) One of these hydrogen bonds, in **PHE-R-MAN**, may be bifurcated. The exception is in **ALA-R-MAN** where the water molecule also donates a hydrogen bond to one of the two hydroxyl groups. It is unexpected to find such uniformity amongst the structures because there is no apparent reason for ammonium groups to prefer hydroxyl groups.

In every case, the **MAN** carboxylic acid oxygen atoms, O22 or O22', donate hydrogen bonds to only one type of atom, an amino acid carboxylate oxygen. The acceptor is usually O32A or O32B, which makes torsion angles with the ammonium group within the same defined range. The exception is in **PHE-R-MAN**, where the acceptor is O31A. However, no general explanation can be found in terms of other hydrogen bonds, as to why those particular atoms are persistently hydrogen bonded. Nevertheless, just as

the "opposite" carboxylate oxygen atoms O31A and O32A accept a hydrogen bond from the ammonium group in **PHE-R-MAN** and **PHE-S-MAN**, respectively, because the opposite hands of **MAN** are present, so opposite carboxylate atoms, O32A and O31A accept the **MAN** hydroxyl hydrogen bond, in this pair of structures.

Because of the charged nature of the ammonium and carboxylate groups, one would expect there to be some ion pairing between them. Within each bilayer there are columns of amino acid molecules in which carboxylate and ammonium groups alternate. In every case the ion pairing is expressed in hydrogen bonding between these groups, where an ammonium group donates a hydrogen bond to a carboxylate oxygen atom in the molecule one unit cell removed in the shortest cell dimension. In complexes in which a second ammonium-carboxylate hydrogen bond occurs (in category a) above), this hydrogen bond is between amino acids on opposite sides of the bilayer. In complexes in category b) above, this second hydrogen bond is replaced by the ammonium again donating across the bilayer, but to a carboxyl oxygen atom of a **MAN** across the bilayer. The exception is in **PHE-R-MAN**, where that hydrogen bond is bifurcated, the hydrogen atom of the ammonium group being shared by the carboxyl oxygen atom and the hydroxyl oxygen atom of the same **MAN** across the bilayer.

The overall pattern of types of atoms involved in hydrogen bonding is similar for **ALA-R-MAN** and **ABA-R-MAN**, except that one of the hydroxyl hydrogen atoms in **ABA-R-MAN**, is involved in a bifurcated hydrogen bond, being shared between a carboxylate oxygen atom and a carboxyl oxygen atom and that the water is a hydrogen bond donor to a carboxyl oxygen atom in **ABA-R-MAN**, but to a hydroxyl in **ALA-R-MAN**. In **ALA-R-MAN** the water is between the ammonium and the hydroxyl. As viewed in projection down the shortest axis, in **ABA-R-MAN** the ammonium and the

carboxyl are on the same side of the water. In both cases the water is between the ammonium and the carboxylate. So the water creates a different hydrogen bonding pattern in each case. The details of the hydrogen bonding patterns differ.

The hydrogen bond between the **MAN** carboxylic acid oxygen and an amino acid carboxylate oxygen atom, common to each structure, is particularly short in each case. Again this is surprising because this is not a charged interaction so there is no particular reason for them to be bonded. They are listed below in Å, extracted from the general tables above.

ALA-R-MAN:	2.481 and 2.534	**ALA-S-MAN:**	2.436
PHE-R-MAN:	2.610	**PHE-S-MAN:**	2.523
ABA-R-MAN:	2.562 and 2.584	**MET-R-MAN:**	2.511

This set of hydrogen bonds are all below 2.6Å except the one in the structure **PHE-R-MAN**. In every case, but one, it is the oxygen atom forming the longer of the two C-O bonds in the carboxylate group and the one with the N-C-C-O torsion angle nearest 180° which accepts the hydrogen bond. The exception is in **PHE-R-MAN**, where the atom involved, O(31A), forms the longer C-O bond, although the torsion angle is nearer to 0°. In each case, the hydrogen bonding takes place, between neighbouring molecules along the bilayer, not across.

Hydrogen bonds where a hydroxyl group is the donor vary in the range 2.636Å, in **PHE-R-MAN**, to 2.916Å in **ABA-R-MAN**. They are all of moderately short to long length. There is no particular pattern to discuss about the lengths.

Hydrogen bonds where an ammonium group is the donor vary in the range 2.713 to 3.043Å. They are all of medium length to very long. Excluding the bifurcated ones the longest, 3.029Å occurs in the complex **MET-R-MAN**. There is no particular pattern in the lengths to discuss.

Hydrogen bonds where a water molecule is the donor vary in the range 2.924 to 3.178Å. They are very long as are the two hydrogen bonds with water as an acceptor, which are 2.953 and 2.962Å.

4.6.1 Bonds, angles and torsion angles in S-alanine R-mandelic acid

C(1) - O(1)	1.415(3)	C(12')-C(13')	1.357(7)
C(1) - C(2)	1.517(4)	C(13')-C(14')	1.387(8)
C(1) -C(11)	1.508(4)	C(14')-C(15')	1.360(8)
O(1) -H(1O)	0.82(6)	C(15')-C(16')	1.370(7)
C(2) -O(21)	1.226(5)	C(1A) -N(1A)	1.474(5)
C(2) -O(22)	1.290(5)	C(1A) -C(3A)	1.535(5)
O(22) -H(2O)	0.94(6)	C(1A) -C(2A)	1.501(6)
C(11) -C(12)	1.389(6)	N(1A) -H(1NA)	0.97(6)
C(11) -C(16)	1.385(6)	N(1A) -H(2NA)	0.93(6)
C(12) -C(13)	1.370(8)	N(1A) -H(3NA)	0.72(6)
C(13) -C(14)	1.387(9)	C(3A) -O(31A)	1.219(5)
C(14) -C(15)	1.372(9)	C(3A) -O(32A)	1.260(5)
C(15) -C(16)	1.375(8)	C(1B) -N(1B)	1.476(5)
C(1') -O(1')	1.421(6)	C(1B) -C(3B)	1.529(5)
C(1') -C(2')	1.524(6)	C(1B) -C(2B)	1.507(6)
C(1') -C(11')	1.505(6)	N(1B) -H(1NB)	0.96(5)
O(1') -H(1O')	0.55(7)	N(1B) -H(2NB)	0.92(6)
C(2') -O(21')	1.200(5)	N(1B) -H(3NB)	0.88(6)
C(2') -O(22')	1.310(5)	C(3B) -O(31B)	1.226(5)
O(22')-H(2O')	0.93(6)	C(3B) -O(32B)	1.257(5)
C(11')-C(12')	1.376(6)	O(1W) -H(2W)	0.84(6)
C(11')-C(16')	1.388(6)		

O(1) - C(1) - C(2)	109.83(19)	C(12')-C(13')-C(14')	120.2(5)
O(1) - C(1) -C(11)	112.81(20)	C(13')-C(14')-C(15')	120.3(5)
C(2) - C(1) -C(11)	109.23(21)	C(14')-C(15')-C(16')	119.5(5)
C(1) - O(1) -H(1O)	114(4)	C(11')-C(16')-C(15')	120.7(5)
C(1) - C(2) -O(21)	120.3(3)	N(1A) -C(1A) -C(3A)	107.0(3)
C(1) - C(2) -O(22)	114.0(3)	N(1A) -C(1A) -C(2A)	111.3(3)
O(21) - C(2) -O(22)	125.6(4)	C(3A) -C(1A) -C(2A)	111.6(3)
C(2) -O(22) -H(2O)	105(4)	C(1A) -N(1A) -H(1NA)	117(3)
C(1) -C(11) -C(12)	119.8(3)	C(1A) -N(1A) -H(2NA)	110(4)
C(1) -C(11) -C(16)	120.8(3)	C(1A) -N(1A) -H(3NA)	112(5)
C(12) -C(11) -C(16)	119.3(4)	H(1NA)-N(1A) -H(2NA)	98(5)
C(11) -C(12) -C(13)	120.3(5)	H(1NA)-N(1A) -H(3NA)	121(6)
C(12) -C(13) -C(14)	119.7(6)	H(2NA)-N(1A) -H(3NA)	94(6)
C(13) -C(14) -C(15)	120.6(6)	C(1A) -C(3A) -O(31A)	119.1(3)
C(14) -C(15) -C(16)	119.6(5)	C(1A) -C(3A) -O(32A)	115.2(3)
C(11) -C(16) -C(15)	120.5(4)	O(31A)-C(3A) -O(32A)	125.4(3)
O(1') -C(1') -C(2')	109.2(3)	N(1B) -C(1B) -C(3B)	108.4(3)
O(1') -C(1') -C(11')	107.4(4)	N(1B) -C(1B) -C(2B)	110.0(3)
C(2') -C(1') -C(11')	112.0(3)	C(3B) -C(1B) -C(2B)	111.5(3)
C(1') -O(1') -H(1O')	117(70)	C(1B) -N(1B) -H(1NB)	120(3)
C(1') -C(2') -O(21')	122.1(4)	C(1B) -N(1B) -H(2NB)	115(4)
C(1') -C(2') -O(22')	113.0(3)	C(1B) -N(1B) -H(3NB)	106(5)
O(21')-C(2') -O(22')	125.0(4)	H(1NB)-N(1B) -H(2NB)	85(5)
C(2') -O(22')-H(2O')	107(4)	H(1NB)-N(1B) -H(3NB)	126(5)
C(1') -C(11')-C(12')	120.8(4)	H(2NB)-N(1B) -H(3NB)	100(5)
C(1') -C(11')-C(16')	120.1(4)	C(1B) -C(3B) -O(31B)	119.9(3)
C(12')-C(11')-C(16')	119.0(4)	C(1B) -C(3B) -O(32B)	114.3(3)
C(11')-C(12')-C(13')	120.3(4)	O(31B)-C(3B) -O(32B)	125.8(4)

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 C(2) - C(1) - O(1) -H(1O)  -28(5)
C(11) - C(1) - O(1) -H(1O)   94(5)
 O(1) - C(1) - C(2) -O(21)   13.6(4)
 O(1) - C(1) - C(2) -O(22) -167.5(3)
C(11) - C(1) - C(2) -O(21) -110.6(4)
C(11) - C(1) - C(2) -O(22)   68.3(4)
 O(1) - C(1) -C(11) -C(12)  -61.3(4)
 O(1) - C(1) -C(11) -C(16)  117.3(4)
 C(2) - C(1) -C(11) -C(12)   61.1(4)
 C(2) - C(1) -C(11) -C(16) -120.2(4)
 C(1) - C(2) -O(22) -H(2O) -173(4)
O(21) - C(2) -O(22) -H(2O)    6(4)
 C(1) -C(11) -C(12) -C(13)  179.9(4)
C(16) -C(11) -C(12) -C(13)    1.2(7)
 C(1) -C(11) -C(16) -C(15) -178.9(4)
C(12) -C(11) -C(16) -C(15)   -0.2(7)
C(11) -C(12) -C(13) -C(14)   -1.4(8)
C(12) -C(13) -C(14) -C(15)    0.8(9)
C(13) -C(14) -C(15) -C(16)    0.2(9)
C(14) -C(15) -C(16) -C(11)   -0.4(8)
C(2') -C(1') -O(1') -H(1O')  29(8)
C(11')-C(1') -O(1') -H(1O') 150(8)
O(1') -C(1') -C(2') -O(21')   7.6(6)
O(1') -C(1') -C(2') -O(22')-172.3(3)
C(11')-C(1') -C(2') -O(21')-111.2(4)
C(11')-C(1') -C(2') -O(22')  68.8(4)
O(1') -C(1') -C(11')-C(12') -67.4(5)
O(1') -C(1') -C(11')-C(16') 110.6(5)
C(2') -C(1') -C(11')-C(12')  52.5(5)
C(2') -C(1') -C(11')-C(16')-129.5(4)
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C(1') -C(2') -O(22')-H(2O') 178(4)
O(21')-C(2') -O(22')-H(2O')  -2(4)
C(1') -C(11')-C(12')-C(13') 178.6(4)
C(16')-C(11')-C(12')-C(13')   0.5(7)
C(1') -C(11')-C(16')-C(15')-177.2(4)
C(12')-C(11')-C(16')-C(15')   0.9(7)
C(11')-C(12')-C(13')-C(14')  -0.6(8)
C(12')-C(13')-C(14')-C(15')  -0.8(9)
C(13')-C(14')-C(15')-C(16')   2.1(9)
C(14')-C(15')-C(16')-C(11')  -2.2(8)
C(3A) -C(1A) -N(1A) -H(1NA) -60(4)
C(3A) -C(1A) -N(1A) -H(2NA)  51(4)
C(3A) -C(1A) -N(1A) -H(3NA) 154(5)
C(2A) -C(1A) -N(1A) -H(1NA) 178(4)
C(2A) -C(1A) -N(1A) -H(2NA) -71(4)
C(2A) -C(1A) -N(1A) -H(3NA)  32(5)
N(1A) -C(1A) -C(3A) -O(31A) -19.5(4)
N(1A) -C(1A) -C(3A) -O(32A) 165.8(3)
C(2A) -C(1A) -C(3A) -O(31A) 102.5(4)
C(2A) -C(1A) -C(3A) -O(32A) -72.2(4)
C(3B) -C(1B) -N(1B) -H(1NB) -59(4)
C(3B) -C(1B) -N(1B) -H(2NB)  41(4)
C(3B) -C(1B) -N(1B) -H(3NB) 151(4)
C(2B) -C(1B) -N(1B) -H(1NB) 179(4)
C(2B) -C(1B) -N(1B) -H(2NB) -81(4)
C(2B) -C(1B) -N(1B) -H(3NB)  28(4)
N(1B) -C(1B) -C(3B) -O(31B) -12.1(5)
N(1B) -C(1B) -C(3B) -O(32B) 168.7(3)
C(2B) -C(1B) -C(3B) -O(31B) 109.1(4)
C(2B) -C(1B) -C(3B) -O(32B) -70.1(4)
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4.6.2 Bonds, angles and torsion angles in S-alanine-S-mandelic acid.

C(1) - O(1)	1.433(11)	C(14) -C(15)	1.36(3)
C(1) - C(2)	1.517(12)	C(15) -C(16)	1.365(25)
C(1) -C(11)	1.490(13)	C(1A) -N(1A)	1.476(11)
O(1) -H(1O)	0.91(9)	C(1A) -C(3A)	1.488(11)
C(2) -O(21)	1.215(11)	C(1A) -C(2A)	1.533(11)
C(2) -O(22)	1.278(11)	N(1A) -H(1NA)	0.91(9)
C(11) -C(12)	1.384(18)	N(1A) -H(2NA)	0.70(10)
C(11) -C(16)	1.349(17)	N(1A) -H(3NA)	0.94(9)
C(12) -C(13)	1.384(24)	C(3A) -O(31A)	1.222(12)
C(13) -C(14)	1.37(3)	C(3A) -O(32A)	1.269(11)

O(1) - C(1) - C(2)	106.9(7)	C(11) -C(16) -C(15)	120.2(14)
O(1) - C(1) -C(11)	111.3(7)	N(1A) -C(1A) -C(3A)	109.7(7)
C(2) - C(1) -C(11)	109.7(7)	N(1A) -C(1A) -C(2A)	110.4(6)
C(1) - O(1) -H(1O)	100(6)	C(3A) -C(1A) -C(2A)	111.5(6)
C(1) - C(2) -O(21)	120.7(8)	C(1A) -N(1A) -H(1NA)	106(6)
C(1) - C(2) -O(22)	116.5(8)	C(1A) -N(1A) -H(2NA)	98(8)
O(21) - C(2) -O(22)	122.8(8)	C(1A) -N(1A) -H(3NA)	134(6)
C(1) -C(11) -C(12)	121.2(10)	H(1NA)-N(1A) -H(2NA)	127(10)
C(1) -C(11) -C(16)	121.2(10)	H(1NA)-N(1A) -H(3NA)	97(8)
C(12) -C(11) -C(16)	117.4(11)	H(2NA)-N(1A) -H(3NA)	99(10)
C(11) -C(12) -C(13)	120.8(14)	C(1A) -C(3A) -O(31A)	119.5(8)
C(12) -C(13) -C(14)	121.5(17)	C(1A) -C(3A) -O(32A)	116.0(8)
C(13) -C(14) -C(15)	115.4(16)	O(31A)-C(3A) -O(32A)	124.4(9)
C(14) -C(15) -C(16)	124.1(18)		

C(2) - C(1) - O(1) -H(1O)	-153(6)	C(11) -C(12) -C(13) -C(14)	4(3)
C(11) - C(1) - O(1) -H(1O)	87(6)	C(12) -C(13) -C(14) -C(15)	-5(3)
O(1) - C(1) - C(2) -O(21)	-24.6(11)	C(13) -C(14) -C(15) -C(16)	7(3)
O(1) - C(1) - C(2) -O(22)	156.2(8)	C(14) -C(15) -C(16) -C(11)	-7(3)
C(11) - C(1) - C(2) -O(21)	96.2(10)	C(3A) -C(1A) -N(1A) -H(1NA)	-52(6)
C(11) - C(1) - C(2) -O(22)	-83.1(10)	C(3A) -C(1A) -N(1A) -H(2NA)	80(8)
O(1) - C(1) -C(11) -C(12)	76.2(12)	C(3A) -C(1A) -N(1A) -H(3NA)	-168(8)
O(1) - C(1) -C(11) -C(16)	-99.9(12)	C(2A) -C(1A) -N(1A) -H(1NA)	-175(6)
C(2) - C(1) -C(11) -C(12)	-41.9(13)	C(2A) -C(1A) -N(1A) -H(2NA)	-43(8)
C(2) - C(1) -C(11) -C(16)	142.0(10)	C(2A) -C(1A) -N(1A) -H(3NA)	69(8)
C(1) -C(11) -C(12) -C(13)	-179.4(13)	N(1A) -C(1A) -C(3A) -O(31A)	-17.4(11)
C(16) -C(11) -C(12) -C(13)	-3.1(20)	N(1A) -C(1A) -C(3A) -O(32A)	164.2(8)
C(1) -C(11) -C(16) -C(15)	-178.9(13)	C(2A) -C(1A) -C(3A) -O(31A)	105.1(9)
C(12) -C(11) -C(16) -C(15)	4.9(20)	C(2A) -C(1A) -C(3A) -O(32A)	-73.3(9)

4.6.3 Bonds, angles and torsion angles in S-phenylalanine R-mandelic acid

C(1) - O(1)	1.406(5)	C(1A) -C(3A)	1.536(6)
C(1) - C(2)	1.512(6)	C(1A) -C(2A)	1.531(6)
C(1) -C(11)	1.530(6)	N(1A) -H(1NA)	0.99(4)
O(1) -H(1O)	0.76(4)	N(1A) -H(2NA)	0.92(4)
C(2) -O(21)	1.199(5)	N(1A) -H(3NA)	0.82(5)
C(2) -O(22)	1.314(5)	C(3A) -O(31A)	1.249(5)
O(22) -H(2O)	0.79(4)	C(3A) -O(32A)	1.235(5)
C(11) -C(12)	1.370(6)	C(2A) -C(21A)	1.510(6)
C(11) -C(16)	1.388(6)	C(21A)-C(22A)	1.377(6)
C(12) -C(13)	1.394(6)	C(21A)-C(26A)	1.388(6)
C(13) -C(14)	1.367(7)	C(22A)-C(23A)	1.386(7)
C(14) -C(15)	1.372(7)	C(23A)-C(24A)	1.368(8)
C(15) -C(16)	1.386(6)	C(24A)-C(25A)	1.355(8)
C(1A) -N(1A)	1.492(5)	C(25A)-C(26A)	1.395(7)

O(1) - C(1) - C(2)	105.0(3)	C(1A) -N(1A) -H(1NA)	112.6(23)
O(1) - C(1) -C(11)	113.8(3)	C(1A) -N(1A) -H(2NA)	112(3)
C(2) - C(1) -C(11)	111.5(3)	C(1A) -N(1A) -H(3NA)	112(3)
C(1) - O(1) -H(1O)	114(3)	H(1NA)-N(1A) -H(2NA)	99(4)
C(1) - C(2) -O(21)	123.2(4)	H(1NA)-N(1A) -H(3NA)	113(4)
C(1) - C(2) -O(22)	112.9(3)	H(2NA)-N(1A) -H(3NA)	107(4)
O(21) - C(2) -O(22)	123.9(4)	C(1A) -C(3A) -O(31A)	118.7(3)
C(2) -O(22) -H(2O)	106(3)	C(1A) -C(3A) -O(32A)	116.4(4)
C(1) -C(11) -C(12)	121.4(4)	O(31A)-C(3A) -O(32A)	124.9(4)
C(1) -C(11) -C(16)	119.4(4)	C(1A) -C(2A) -C(21A)	115.3(3)
C(12) -C(11) -C(16)	119.2(4)	C(2A) -C(21A)-C(22A)	121.3(4)
C(11) -C(12) -C(13)	120.4(4)	C(2A) -C(21A)-C(26A)	120.8(4)
C(12) -C(13) -C(14)	120.4(4)	C(22A)-C(21A)-C(26A)	117.9(4)
C(13) -C(14) -C(15)	119.1(4)	C(21A)-C(22A)-C(23A)	121.0(4)
C(14) -C(15) -C(16)	121.1(4)	C(22A)-C(23A)-C(24A)	120.5(5)
C(11) -C(16) -C(15)	119.6(4)	C(23A)-C(24A)-C(25A)	119.4(5)
N(1A) -C(1A) -C(3A)	110.0(3)	C(24A)-C(25A)-C(26A)	120.8(5)
N(1A) -C(1A) -C(2A)	111.9(3)	C(21A)-C(26A)-C(25A)	120.3(4)
C(3A) -C(1A) -C(2A)	111.5(3)		

C(2) - C(1) - O(1) -H(1O)	178(3)	C(3A) -C(1A) -N(1A) -H(2NA)	49(3)
C(11) - C(1) - O(1) -H(1O)	-59(4)	C(3A) -C(1A) -N(1A) -H(3NA)	169(3)
O(1) - C(1) - C(2) -O(21)	11.9(5)	C(2A) -C(1A) -N(1A) -H(1NA)	173.5(25)
O(1) - C(1) - C(2) -O(22)	-167.0(3)	C(2A) -C(1A) -N(1A) -H(2NA)	-76(3)
C(11) - C(1) - C(2) -O(21)	-111.7(4)	C(2A) -C(1A) -N(1A) -H(3NA)	45(3)
C(11) - C(1) - C(2) -O(22)	69.4(4)	N(1A) -C(1A) -C(3A) -O(31A)	-21.7(5)
O(1) - C(1) -C(11) -C(12)	-7.5(5)	N(1A) -C(1A) -C(3A) -O(32A)	160.1(4)
O(1) - C(1) -C(11) -C(16)	170.9(4)	C(2A) -C(1A) -C(3A) -O(31A)	103.0(4)
C(2) - C(1) -C(11) -C(12)	110.9(4)	C(2A) -C(1A) -C(3A) -O(32A)	-75.1(5)
C(2) - C(1) -C(11) -C(16)	-70.6(5)	N(1A) -C(1A) -C(2A) -C(21A)	68.2(4)
C(1) - C(2) -O(22) -H(2O)	178(3)	C(3A) -C(1A) -C(2A) -C(21A)	-55.5(5)
O(21) - C(2) -O(22) -H(2O)	-1(3)	C(1A) -C(2A) -C(21A)-C(22A)	94.7(5)
C(1) -C(11) -C(12) -C(13)	179.3(4)	C(1A) -C(2A) -C(21A)-C(26A)	-84.9(5)
C(16) -C(11) -C(12) -C(13)	0.8(6)	C(2A) -C(21A)-C(22A)-C(23A)	-179.4(4)
C(1) -C(11) -C(16) -C(15)	-179.7(4)	C(26A)-C(21A)-C(22A)-C(23A)	0.2(7)
C(12) -C(11) -C(16) -C(15)	-1.2(6)	C(2A) -C(21A)-C(26A)-C(25A)	179.0(4)
C(11) -C(12) -C(13) -C(14)	0.5(7)	C(22A)-C(21A)-C(26A)-C(25A)	-0.6(7)
C(12) -C(13) -C(14) -C(15)	-1.4(7)	C(21A)-C(22A)-C(23A)-C(24A)	-0.2(8)
C(13) -C(14) -C(15) -C(16)	1.0(7)	C(22A)-C(23A)-C(24A)-C(25A)	0.5(8)
C(14) -C(15) -C(16) -C(11)	0.3(7)	C(23A)-C(24A)-C(25A)-C(26A)	-1.0(9)
C(3A) -C(1A) -N(1A) -H(1NA)	-62.0(25)	C(24A)-C(25A)-C(26A)-C(21A)	1.0(8)

4.6.4 Bonds, angles and torsion angles in S-phenylalanine S-mandelic acid

C(1) - O(1)	1.403(17)	C(1A) -C(2A)	1.543(17)
C(1) - C(2)	1.535(20)	N(1A) -H(1NA)	0.99(11)
C(1) -C(11)	1.495(19)	N(1A) -H(2NA)	0.85(12)
O(1) -H(1O)	0.88(12)	N(1A) -H(3NA)	1.14(12)
C(2) -O(21)	1.182(19)	C(3A) -O(31A)	1.233(17)
C(2) -O(22)	1.350(19)	C(3A) -O(32A)	1.244(17)
C(11) -C(12)	1.357(20)	C(2A) -C(21A)	1.544(20)
C(11) -C(16)	1.377(21)	C(21A)-C(22A)	1.372(21)
C(12) -C(13)	1.412(23)	C(21A)-C(26A)	1.396(22)
C(13) -C(14)	1.39(3)	C(22A)-C(23A)	1.359(23)
C(14) -C(15)	1.36(3)	C(23A)-C(24A)	1.33(3)
C(15) -C(16)	1.392(25)	C(24A)-C(25A)	1.36(3)
C(1A) -N(1A)	1.501(16)	C(25A)-C(26A)	1.41(3)
C(1A) -C(3A)	1.522(17)		

O(1) - C(1) - C(2)	110.0(11)	C(1A) -N(1A) -H(1NA)	113(6)
O(1) - C(1) -C(11)	109.8(11)	C(1A) -N(1A) -H(2NA)	135(8)
C(2) - C(1) -C(11)	109.4(11)	C(1A) -N(1A) -H(3NA)	109(6)
C(1) - O(1) -H(1O)	122(8)	H(1NA)-N(1A) -H(2NA)	105(10)
C(1) - C(2) -O(21)	125.3(14)	H(1NA)-N(1A) -H(3NA)	92(9)
C(1) - C(2) -O(22)	109.9(12)	H(2NA)-N(1A) -H(3NA)	93(10)
O(21) - C(2) -O(22)	124.8(14)	C(1A) -C(3A) -O(31A)	117.4(12)
C(1) -C(11) -C(12)	121.2(13)	C(1A) -C(3A) -O(32A)	116.6(12)
C(1) -C(11) -C(16)	119.5(13)	O(31A)-C(3A) -O(32A)	126.0(13)
C(12) -C(11) -C(16)	119.3(13)	C(1A) -C(2A) -C(21A)	110.1(11)
C(11) -C(12) -C(13)	121.0(14)	C(2A) -C(21A)-C(22A)	119.8(13)
C(12) -C(13) -C(14)	119.1(16)	C(2A) -C(21A)-C(26A)	119.9(13)
C(13) -C(14) -C(15)	119.4(18)	C(22A)-C(21A)-C(26A)	120.3(14)
C(14) -C(15) -C(16)	120.9(17)	C(21A)-C(22A)-C(23A)	120.1(14)
C(11) -C(16) -C(15)	120.2(15)	C(22A)-C(23A)-C(24A)	121.3(17)
N(1A) -C(1A) -C(3A)	109.2(9)	C(23A)-C(24A)-C(25A)	120.8(20)
N(1A) -C(1A) -C(2A)	105.6(9)	C(24A)-C(25A)-C(26A)	120.3(19)
C(3A) -C(1A) -C(2A)	112.1(9)	C(21A)-C(26A)-C(25A)	117.2(15)

C(2) - C(1) - O(1) -H(1O)	-36(9)	C(3A) -C(1A) -N(1A) -H(3NA)	-166(6)
C(11) - C(1) - O(1) -H(1O)	-156(9)	C(2A) -C(1A) -N(1A) -H(1NA)	173(7)
O(1) - C(1) - C(2) -O(21)	-26.7(20)	C(2A) -C(1A) -N(1A) -H(2NA)	-41(12)
O(1) - C(1) - C(2) -O(22)	155.3(11)	C(2A) -C(1A) -N(1A) -H(3NA)	73(6)
C(11) - C(1) - C(2) -O(21)	94.0(18)	N(1A) -C(1A) -C(3A) -O(31A)	-35.9(15)
C(11) - C(1) - C(2) -O(22)	-83.9(14)	N(1A) -C(1A) -C(3A) -O(32A)	144.5(12)
O(1) - C(1) -C(11) -C(12)	29.3(18)	C(2A) -C(1A) -C(3A) -O(31A)	80.9(14)
O(1) - C(1) -C(11) -C(16)	-150.6(13)	C(2A) -C(1A) -C(3A) -O(32A)	-98.7(14)
C(2) - C(1) -C(11) -C(12)	-91.5(16)	N(1A) -C(1A) -C(2A) -C(21A)	179.5(10)
C(2) - C(1) -C(11) -C(16)	88.6(16)	C(3A) -C(1A) -C(2A) -C(21A)	60.6(13)
C(1) -C(11) -C(12) -C(13)	178.8(14)	C(1A) -C(2A) -C(21A)-C(22A)	83.8(16)
C(16) -C(11) -C(12) -C(13)	-1.3(23)	C(1A) -C(2A) -C(21A)-C(26A)	-94.5(15)
C(1) -C(11) -C(16) -C(15)	-178.7(14)	C(2A) -C(21A)-C(22A)-C(23A)	-179.0(14)
C(12) -C(11) -C(16) -C(15)	1.4(23)	C(26A)-C(21A)-C(22A)-C(23A)	-0.7(23)
C(11) -C(12) -C(13) -C(14)	0.0(25)	C(2A) -C(21A)-C(26A)-C(25A)	176.8(15)
C(12) -C(13) -C(14) -C(15)	1(3)	C(22A)-C(21A)-C(26A)-C(25A)	-1.5(23)
C(13) -C(14) -C(15) -C(16)	-1(3)	C(21A)-C(22A)-C(23A)-C(24A)	3(3)
C(14) -C(15) -C(16) -C(11)	-0(3)	C(22A)-C(23A)-C(24A)-C(25A)	-4(3)
C(3A) -C(1A) -N(1A) -H(1NA)	-66(7)	C(23A)-C(24A)-C(25A)-C(26A)	2(3)
C(3A) -C(1A) -N(1A) -H(2NA)	80(12)	C(24A)-C(25A)-C(26A)-C(21A)	1(3)

4.6.5 Bonds, angles and torsion angles in S-α-amino-butyric acid R-mandelic acid

C(1) - O(1)	1.415(5)	C(1A) -N(1A)	1.488(6)
C(1) - C(2)	1.508(6)	C(1A) -C(3A)	1.521(7)
C(1) -C(11)	1.508(6)	C(1A) -C(2A)	1.526(7)
O(1) -H(1O)	1.00(3)	N(1A) -H(1NA)	1.05(3)
C(2) -O(21)	1.216(7)	N(1A) -H(2NA)	0.97(3)
C(2) -O(22)	1.304(7)	N(1A) -H(3NA)	0.96(3)
O(22) -H(2O)	1.00(3)	C(3A) -O(31A)	1.226(6)
C(11) -C(12)	1.385(8)	C(3A) -O(32A)	1.258(6)
C(11) -C(16)	1.368(8)	C(2A) -C(21A)	1.510(8)
C(12) -C(13)	1.378(10)	C(21A)-H(23A)	1.080(19)
C(13) -C(14)	1.385(12)	C(21A)-H(24A)	1.080(19)
C(14) -C(15)	1.338(12)	C(21A)-H(25A)	1.080(19)
C(15) -C(16)	1.394(10)	C(1B) -N(1B)	1.476(6)
C(1') -O(1')	1.411(7)	C(1B) -C(3B)	1.525(7)
C(1') -C(2')	1.520(8)	C(1B) -C(2B)	1.533(7)
C(1') -C(11')	1.520(7)	N(1B) -H(1NB)	1.000(18)
O(1') -H(1O')	1.00(3)	N(1B) -H(2NB)	1.000(18)
C(2') -O(21')	1.198(7)	N(1B) -H(3NB)	1.000(18)
C(2') -O(22')	1.309(7)	C(3B) -O(31B)	1.232(6)
O(22')-H(2O')	1.00(3)	C(3B) -O(32B)	1.250(6)
C(11')-C(12')	1.375(8)	C(2B) -C(21B)	1.489(8)
C(11')-C(16')	1.371(8)	C(21B)-H(23B)	1.080(20)
C(12')-C(13')	1.378(8)	C(21B)-H(24B)	1.080(20)
C(13')-C(14')	1.377(10)	C(21B)-H(25B)	1.080(20)
C(14')-C(15')	1.358(10)	O(1W) -H(1W)	0.93(4)
C(15')-C(16')	1.384(10)	O(1W) -H(2W)	0.94(4)

O(1) - C(1) - C(2)	109.7(3)	C(1A) -N(1A) -H(2NA)	110.1(17)
O(1) - C(1) -C(11)	112.0(3)	C(1A) -N(1A) -H(3NA)	110.9(18)
C(2) - C(1) -C(11)	110.5(4)	H(1NA)-N(1A) -H(2NA)	107.5(23)
C(1) - O(1) -H(1O)	104.9(15)	H(1NA)-N(1A) -H(3NA)	107.7(23)
C(1) - C(2) -O(21)	122.3(5)	H(2NA)-N(1A) -H(3NA)	114.6(24)
C(1) - C(2) -O(22)	113.6(4)	C(1A) -C(3A) -O(31A)	118.1(4)
O(21) - C(2) -O(22)	124.1(5)	C(1A) -C(3A) -O(32A)	116.5(4)
C(2) -O(22) -H(2O)	105.6(16)	O(31A)-C(3A) -O(32A)	125.4(5)
C(1) -C(11) -C(12)	120.7(5)	C(1A) -C(2A) -C(21A)	114.3(5)
C(1) -C(11) -C(16)	120.2(5)	C(2A) -C(21A)-H(23A)	109.6(11)
C(12) -C(11) -C(16)	119.1(5)	C(2A) -C(21A)-H(24A)	110.2(11)
C(11) -C(12) -C(13)	119.7(6)	C(2A) -C(21A)-H(25A)	109.4(11)
C(12) -C(13) -C(14)	120.2(7)	H(23A)-C(21A)-H(24A)	109.1(15)
C(13) -C(14) -C(15)	120.1(8)	H(23A)-C(21A)-H(25A)	108.9(15)
C(14) -C(15) -C(16)	120.1(8)	H(24A)-C(21A)-H(25A)	109.6(15)
C(11) -C(16) -C(15)	120.6(6)	N(1B) -C(1B) -C(3B)	108.2(4)
O(1') -C(1') -C(2')	109.8(4)	N(1B) -C(1B) -C(2B)	109.0(4)
O(1') -C(1') -C(11')	108.3(4)	C(3B) -C(1B) -C(2B)	111.2(4)
C(2') -C(1') -C(11')	111.9(4)	C(1B) -N(1B) -H(1NB)	109.1(11)
C(1') -O(1') -H(1O')	105.5(17)	C(1B) -N(1B) -H(2NB)	109.3(11)
C(1') -C(2') -O(21')	122.5(5)	C(1B) -N(1B) -H(3NB)	109.6(11)
C(1') -C(2') -O(22')	112.9(5)	H(1NB)-N(1B) -H(2NB)	109.5(15)
O(21')-C(2') -O(22')	124.6(5)	H(1NB)-N(1B) -H(3NB)	109.8(15)

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C(2') -O(22')-H(2O') 104.9(16)
C(1') -C(11')-C(12') 120.0(5)
C(1') -C(11')-C(16') 120.5(5)
C(12')-C(11')-C(16') 119.4(5)
C(11')-C(12')-C(13') 119.9(5)
C(12')-C(13')-C(14') 120.6(6)
C(13')-C(14')-C(15') 119.1(7)
C(14')-C(15')-C(16') 120.8(7)
C(11')-C(16')-C(15') 120.1(6)
N(1A) -C(1A) -C(3A)  107.1(4)
N(1A) -C(1A) -C(2A)  109.5(4)
C(3A) -C(1A) -C(2A)  111.9(4)
C(1A) -N(1A) -H(1NA) 105.5(16)
H(2NB)-N(1B) -H(3NB) 109.5(15)
C(1B) -C(3B) -O(31B) 118.6(4)
C(1B) -C(3B) -O(32B) 115.6(4)
O(31B)-C(3B) -O(32B) 125.8(5)
C(1B) -C(2B) -C(21B) 115.4(5)
C(2B) -C(21B)-H(23B) 110.2(11)
C(2B) -C(21B)-H(24B) 110.2(11)
C(2B) -C(21B)-H(25B) 110.7(11)
H(23B)-C(21B)-H(24B) 108.5(15)
H(23B)-C(21B)-H(25B) 108.6(15)
H(24B)-C(21B)-H(25B) 108.5(15)
H(1W) -O(1W) -H(2W)  115(4)
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 C(2) - C(1) - O(1) -H(1O)  -27.5(16)
C(11) - C(1) - O(1) -H(1O)   95.6(16)
 O(1) - C(1) - C(2) -O(21)   11.4(6)
 O(1) - C(1) - C(2) -O(22) -170.2(4)
C(11) - C(1) - C(2) -O(21) -112.7(5)
C(11) - C(1) - C(2) -O(22)   65.8(5)
 O(1) - C(1) -C(11) -C(12)  -62.5(6)
 O(1) - C(1) -C(11) -C(16)  116.0(5)
 C(2) - C(1) -C(11) -C(12)   60.2(6)
 C(2) - C(1) -C(11) -C(16) -121.4(5)
 C(1) - C(2) -O(22) -H(2O) -178.9(16)
O(21) - C(2) -O(22) -H(2O)   -0.5(17)
 C(1) -C(11) -C(12) -C(13)  177.5(6)
C(16) -C(11) -C(12) -C(13)   -1.0(9)
 C(1) -C(11) -C(16) -C(15) -176.7(6)
C(12) -C(11) -C(16) -C(15)    1.8(9)
C(11) -C(12) -C(13) -C(14)    1.0(11)
C(12) -C(13) -C(14) -C(15)   -1.9(13)
C(13) -C(14) -C(15) -C(16)    2.8(13)
C(14) -C(15) -C(16) -C(11)   -2.7(11)
C(2') -C(1') -O(1') -H(1O')  33.2(18)
C(11')-C(1') -O(1') -H(1O') 155.7(17)
O(1') -C(1') -C(2') -O(21')  12.2(7)
O(1') -C(1') -C(2') -O(22')-168.8(4)
C(11')-C(1') -C(2') -O(21')-108.1(6)
C(11')-C(1') -C(2') -O(22')  70.9(6)
O(1') -C(1') -C(11')-C(12') -70.9(6)
O(1') -C(1') -C(11')-C(16') 107.2(6)
C(2') -C(1') -C(11')-C(12')  50.3(7)
C(2') -C(1') -C(11')-C(16')-131.6(5)
C(1') -C(2') -O(22')-H(2O') 170.4(17)
O(21')-C(2') -O(22')-H(2O') -10.6(18)
C(1') -C(11')-C(12')-C(13') 176.5(5)
C(16')-C(11')-C(12')-C(13')  -1.6(8)
C(1') -C(11')-C(16')-C(15')-176.6(6)
```

```
C(12')-C(11')-C(16')-C(15')   1.5(9)
C(11')-C(12')-C(13')-C(14')   1.2(9)
C(12')-C(13')-C(14')-C(15')  -0.6(11)
C(13')-C(14')-C(15')-C(16')   0.4(11)
C(14')-C(15')-C(16')-C(11')  -0.9(10)
C(3A) -C(1A) -N(1A) -H(1NA)  53.2(17)
C(3A) -C(1A) -N(1A) -H(2NA) -62.5(18)
C(3A) -C(1A) -N(1A) -H(3NA) 169.5(19)
C(2A) -C(1A) -N(1A) -H(1NA) -68.4(17)
C(2A) -C(1A) -N(1A) -H(2NA) 175.9(18)
C(2A) -C(1A) -N(1A) -H(3NA)  48.0(19)
N(1A) -C(1A) -C(3A) -O(31A) -26.0(6)
N(1A) -C(1A) -C(3A) -O(32A) 156.7(4)
C(2A) -C(1A) -C(3A) -O(31A)  94.1(5)
C(2A) -C(1A) -C(3A) -O(32A) -83.2(5)
N(1A) -C(1A) -C(2A) -C(21A)-174.2(4)
C(3A) -C(1A) -C(2A) -C(21A)  67.2(6)
C(1A) -C(2A) -C(21A)-H(23A) 179.3(11)
C(1A) -C(2A) -C(21A)-H(24A)  59.2(12)
C(1A) -C(2A) -C(21A)-H(25A) -61.4(12)
C(3B) -C(1B) -N(1B) -H(1NB)  52.8(12)
C(3B) -C(1B) -N(1B) -H(2NB) -66.9(12)
C(3B) -C(1B) -N(1B) -H(3NB) 173.1(11)
C(2B) -C(1B) -N(1B) -H(1NB) -68.3(12)
C(2B) -C(1B) -N(1B) -H(2NB) 172.0(11)
C(2B) -C(1B) -N(1B) -H(3NB)  52.0(12)
N(1B) -C(1B) -C(3B) -O(31B) -24.2(6)
N(1B) -C(1B) -C(3B) -O(32B) 155.9(4)
C(2B) -C(1B) -C(3B) -O(31B)  95.5(5)
C(2B) -C(1B) -C(3B) -O(32B) -84.4(5)
N(1B) -C(1B) -C(2B) -C(21B)-174.9(4)
C(3B) -C(1B) -C(2B) -C(21B)  65.9(6)
C(1B) -C(2B) -C(21B)-H(23B) -60.1(13)
C(1B) -C(2B) -C(21B)-H(24B)  59.7(12)
C(1B) -C(2B) -C(21B)-H(25B) 179.7(12)
```

4.6.6 Bonds, angles and torsion angles in S-methionine R-mandelic acid

C(1) - O(1)	1.416(12)	N(1A) -H(1NA)	0.95(3)
C(1) - C(2)	1.529(15)	N(1A) -H(2NA)	0.96(3)
C(1) -C(11)	1.528(15)	N(1A) -H(3NA)	0.96(3)
C(2) -O(21)	1.199(14)	C(3A) -O(31A)	1.247(12)
C(2) -O(22)	1.297(13)	C(3A) -O(32A)	1.278(12)
C(11) -C(12)	1.399(18)	C(2A) -C(21A)	1.501(23)
C(11) -C(16)	1.387(18)	C(21A)-S(1A)	1.829(20)
C(12) -C(13)	1.360(24)	S(1A) -C(1SA)	1.797(23)
C(13) -C(14)	1.37(3)	C(1B) -N(1A)	1.472(16)
C(14) -C(15)	1.39(3)	C(1B) -C(3A)	1.504(16)
C(15) -C(16)	1.32(3)	C(1B) -C(2B)	1.523(20)
C(1A) -N(1A)	1.462(14)	C(2B) -C(21B)	1.53(3)
C(1A) -C(3A)	1.503(14)	C(21B)-S(1B)	1.80(3)
C(1A) -C(2A)	1.494(18)	S(1B) -C(1SB)	1.80(5)

O(1) - C(1) - C(2)	109.9(8)	H(1NA)-N(1A) -H(2NA)	120.4(29)
O(1) - C(1) -C(11)	112.0(8)	H(1NA)-N(1A) -H(3NA)	119.8(29)
C(2) - C(1) -C(11)	109.8(9)	H(2NA)-N(1A) -H(3NA)	119.3(28)
C(1) - C(2) -O(21)	122.5(10)	C(1A) -C(3A) -O(31A)	120.0(8)
C(1) - C(2) -O(22)	112.9(9)	C(1A) -C(3A) -O(32A)	115.4(8)
O(21) - C(2) -O(22)	124.6(10)	O(31A)-C(3A) -O(32A)	124.0(9)
C(1) -C(11) -C(12)	121.0(10)	C(1A) -C(2A) -C(21A)	117.8(12)
C(1) -C(11) -C(16)	122.3(10)	C(2A) -C(21A)-S(1A)	112.6(12)
C(12) -C(11) -C(16)	116.7(11)	C(21A)-S(1A) -C(1SA)	99.8(10)
C(11) -C(12) -C(13)	122.2(14)	N(1A) -C(1B) -C(3A)	108.8(10)
C(12) -C(13) -C(14)	118.0(19)	N(1A) -C(1B) -C(2B)	110.0(11)
C(13) -C(14) -C(15)	121.2(22)	C(3A) -C(1B) -C(2B)	112.4(11)
C(14) -C(15) -C(16)	119.5(20)	C(1B) -N(1A) -H(1NA)	85.7(22)
C(11) -C(16) -C(15)	122.2(15)	C(1B) -N(1A) -H(2NA)	74.7(20)
N(1A) -C(1A) -C(3A)	109.4(8)	C(1B) -N(1A) -H(3NA)	102.5(20)
N(1A) -C(1A) -C(2A)	116.3(10)	C(1B) -C(3A) -O(31A)	115.8(9)
C(3A) -C(1A) -C(2A)	116.1(10)	C(1B) -C(3A) -O(32A)	119.7(9)
C(1A) -N(1A) -H(1NA)	87.6(21)	C(1B) -C(2B) -C(21B)	110.4(13)
C(1A) -N(1A) -H(2NA)	87.6(20)	C(2B) -C(21B)-S(1B)	108.6(15)
C(1A) -N(1A) -H(3NA)	87.3(20)	C(21B)-S(1B) -C(1SB)	100.4(20)

O(1) - C(1) - C(2) -O(21)	7.4(14)	N(1A) -C(1A) -C(3A) -O(31A)	-0.8(13)
O(1) - C(1) - C(2) -O(22)	-173.7(8)	N(1A) -C(1A) -C(3A) -O(32A)	170.7(8)
C(11) - C(1) - C(2) -O(21)	-116.2(11)	C(2A) -C(1A) -C(3A) -O(31A)	133.2(11)
C(11) - C(1) - C(2) -O(22)	62.7(11)	C(2A) -C(1A) -C(3A) -O(32A)	-55.4(13)
O(1) - C(1) -C(11) -C(12)	-55.2(14)	N(1A) -C(1A) -C(2A) -C(21A)	76.0(15)
O(1) - C(1) -C(11) -C(16)	124.0(12)	C(3A) -C(1A) -C(2A) -C(21A)	-54.8(16)
C(2) - C(1) -C(11) -C(12)	67.2(14)	C(1A) -C(2A) -C(21A)-S(1A)	175.4(10)
C(2) - C(1) -C(11) -C(16)	-113.6(12)	C(2A) -C(21A)-S(1A) -C(1SA)	56.6(15)
C(1) -C(11) -C(12) -C(13)	-178.4(14)	C(3A) -C(1B) -N(1A) -H(1NA)	-174.3(22)
C(16) -C(11) -C(12) -C(13)	2.4(21)	C(3A) -C(1B) -N(1A) -H(2NA)	62.6(22)
C(1) -C(11) -C(16) -C(15)	174.5(15)	C(3A) -C(1B) -N(1A) -H(3NA)	-54.7(22)
C(12) -C(11) -C(16) -C(15)	-6.3(21)	C(2B) -C(1B) -N(1A) -H(1NA)	62.3(23)
C(11) -C(12) -C(13) -C(14)	1.7(27)	C(2B) -C(1B) -N(1A) -H(2NA)	-60.8(22)
C(12) -C(13) -C(14) -C(15)	-2.3(33)	C(2B) -C(1B) -N(1A) -H(3NA)	-178.1(21)
C(13) -C(14) -C(15) -C(16)	-1.5(35)	N(1A) -C(1B) -C(3A) -O(31A)	-32.3(13)
C(14) -C(15) -C(16) -C(11)	5.9(29)	N(1A) -C(1B) -C(3A) -O(32A)	155.5(9)
C(3A) -C(1A) -N(1A) -H(1NA)	161.8(22)	C(2B) -C(1B) -C(3A) -O(31A)	89.7(13)
C(3A) -C(1A) -N(1A) -H(2NA)	41.3(21)	C(2B) -C(1B) -C(3A) -O(32A)	-82.5(13)
C(3A) -C(1A) -N(1A) -H(3NA)	-78.2(20)	N(1A) -C(1B) -C(2B) -C(21B)	-177.2(13)
C(2A) -C(1A) -N(1A) -H(1NA)	27.9(23)	C(3A) -C(1B) -C(2B) -C(21B)	61.4(16)
C(2A) -C(1A) -N(1A) -H(2NA)	-92.6(22)	C(1B) -C(2B) -C(21B)-S(1B)	90.5(16)
C(2A) -C(1A) -N(1A) -H(3NA)	147.9(21)	C(2B) -C(21B)-S(1B) -C(1SB)	66.3(23)

CHAPTER 5

THE DETERMINATION OF THE STRUCTURES OF CAMPHOR-10-SULPHONIC ACID SALTS

As in Chapter 3, structure determinations of seven compounds are here described, together with an account of attempts at the study of several other compounds.

5.1 Hydronium 1S-4R-Camphor-10-sulphonate

5.1.1 Crystal data:

Mo radiation on the STADI-2 diffractometer:

$H_3O^+.C_{10}H_{15}O_4S^-$ M_r=250.2, orthorhombic, $P2_12_12_1$, a = 6.792(4), b = 11.239(8), c = 15.628(12)Å, V = 1193.0Å^3, Z = 4, D_c = 1.393gcm^{-3}, MoK_α, λ = 0.71069Å, μ = 2.25cm^{-1}, F(000) = 536, T = 293K, final R,R_w = 0.049, 0.058 for 1627 observed reflections F>4σ(F), final max δ/σ = 0.206. Final difference Fourier max=0.50 min=-0.53 eÅ^{-3}.

Cu radiation on STADI-4 diffractometer:

$H_3O^+.C_{10}H_{15}O_4S^-$ M_r=250.2, orthorhombic, $P2_12_12_1$, a = 6.7792(17), b = 11.302(8), c = 15.703(3)Å, V = 1203.19Å^3, Z = 4, D_c = 1.381gcm^{-3}, CuK_α, λ = 1.5418Å, μ = 23.30cm^{-1}, F(000) = 536, T = 293K, final R,R_w = 0.043, 0.052 for 1537 observed reflections F>4σ(F), final max δ/σ = 0.176. Final difference Fourier max=0.47, min=-0.58 eÅ^{-3}.

5.1.2 Overview of structure determination:

Recrystallisation of 1S-4R-camphor-10-sulphonic acid from ethyl acetate yielded crystals suitable for data collection. Details are given in the table in section 2.15. Information about the method of structure determination is to be found in chapter 2.

They were elongated triangular prisms with an extinction direction in the long axis of the crystal, which turned out to be the a-axis, and along which the crystal selected was mounted. It was put in a Lindemann tube to prevent deliquescence. Its dimensions were 0.64x0.12x0.12mm.

Oscillation and Weissenberg photographs gave approximate unit cell dimensions and revealed that there were two alternatives for the space group, $P2_12_12_1$ or $P2_12_12$. The former was the more likely, being the most common non-centrosymmetric orthorhombic space group. Successful structure solution in the former later confirmed it; also the second dataset measured on the STADI-4 and also when a manual search for reflections was made along the 0k0 row, when refining the size of the mounting axis on the STADI-2.

Cell dimensons were refined using both diffractometers. $P2_12_12_1$ is a four-fold space group. Estimation of the number of non-hydrogen atoms at 18Å^3 per atom corresponded to approximately four camphor-10-sulphonate molecules per unit cell in this four-fold space group and thus one in the asymmetric unit.

Data were first collected on the STADI-2 two-circle diffractometer using MoK_α radiation and secondly on the STADI-4 four-circle diffractometer using CuK_α radiation, with the purpose of determining the absolute configura-

tion. The structure was solved using the Mo dataset and those coordinates passed to the Cu dataset.

In the Cu case, parallel refinements were carried out, one having the coordinates inverted. The one with the lower R-factor was the correct hand of CSA. See section 2.12 for details of the method. It turned out that the correct hand was indeed the inverted version and indeed upon inspection of the difference maps from both datasets, it was observed that the "wrong" enantiomorph had been selected by the program in both cases. Refinement proceeded in parallel for the two datasets, using the inverted coordinates.

5.1.3 Structure solution and refinement for the Mo data:

The mounting axis was known as the b-axis at this point. The crystal was placed on the STADI-2 two circle diffractometer and set up manually for data collection and the unit cell refined. It is normal only to collect data in an octant of space because of equivalences. However, since the intention was subsequently to collect data for the determination of the absolute configuration and two octants would be required then to show up the inequivalence of Friedel pairs, two octants were collected here for completeness, although with the Mo radiation and a sulphur atom as the heaviest atom, the effect of anomalous dispersion would be very small indeed.

2349 data were collected using the method of ω-scans, with $2\theta_{max} = 50°$ and $0 \leq h \leq 12$, $0 \leq k \leq 7$ and $-18 \leq l \leq 18$. Two intensity standards showed that crystal decay was negligible.

The sulphur atom was located by SHELX76[29] Patterson and DIRDIF[30] phase refinement located the remainder of the non-hydrogen atoms. An interchange of axes and

reflection labels was carried out when reading the data into SHELX76 for the Patterson so that they would correspond to the Cu dataset. The a and b axes were interchanged, as were the h and k indices, the direction of the c-axis inverted and the l indices being made negative to preserve the handedness of the unit cell. Thus the new name of the mounting axis is a.

2054 data remained after rejection of systematically absent reflections and merging equivalent reflections. The merging R-factor was 0.024. h,k,l reflections were not merged with h,k,-l because they are not equivalent, although the amplitudes of the structure factors are negligibly different.

A version of the dataset was created for use with DIRDIF, which required a single octant of the data. Wherever the l-index was negative it was made positive so that the SHELX76 MERG command would effectively merge h,k,l with h,k,-l. 1203 'unique' reflections remained, with a merging R-factor of 0.024.

DIRDIF located all the expected non-hydrogen atoms of the basis of the sulphur position. The R-factor before SHELX76 least squares refinement was quite acceptable at 0.287. Unexpectedly a lone peak was found which might represent a water oxygen atom, but it was not passed on to the subsequent SHELX76 least squares refinement with the other atoms. The densities with and without a water molecule were calculated as 1.393 and 1.293 gcm^{-3} respectively and did not reveal whether or not there ought to be a water molecule. However, the fact that CSA was deliquescent did make it likely that there should be water associated with it. The water may have come from wet ethylacetate solvent or the acid crystals may already have contained. The water peak came up again in the difference map after the first few cycles of refinement

and was added to the list of atoms. This reduced the R-factor to 0.120. The equivalent sulphur-oxygen bond lengths made its clear that the acid was dissociated, which suggested that the water molecule would in fact be a hydronium ion, H_3O^+.

The non-hydrogen atoms were refined with three positional parameters and one isotropic thermal parameter initially. All the hydrogen atoms bonded to carbon atoms were assigned to peaks in the difference maps at first and their coordinates allowed to refine freely and with a fixed isotropic thermal parameter of 0.05Å^3. However, the bond lengths were frequently small and the peaks might actually represent anisotropic thermal parameters of non-hydrogen atoms. In particular, around some oxygen and sulphur atoms, there were some peaks of electron density which were ascribed to anisotropic thermal parameters yet to be refined. The two apparent hydrogen atoms on the water molecule were 180° apart, which supports the anisotropy point of view. Including these peaks as hydrogen atoms lowered the R-factor by about 1%, but that is perhaps because they might be mopping up anisotropy, not representing hydrogen atom positions. Refinement continued and it was hoped that good hydrogen atom positions might result from these beginnings. The R-factor steadied at 0.940, but the apparent hydrogen atoms were obviously not real because of the way their thermal parameters behaved, some going large and others small. The output coordinates of this set of refinements were used with the Cu dataset to determine the absolute configuration of the camphor-10-sulphonic acid. The apparent protons were left in meantime.

5.1.4 The determination of absolute configuration using the Cu dataset:

The crystal was transfered to the STADI-4 four circle diffractometer. 2052 data were collected, two octants of the available data, positive and negative l being collected to enable the determination of the absolute configuration. The maximum value of 2θ was 117.3°; the ranges of h, k, and l, were as before, except the axes were interchanged relative to the first dataset. The scan technique was ω/2θ scans and two intensity standards, measured periodically showed that there was no significant overall decay in the data. The unit cell was determined after an automatic reflection search.

In two sets of calculations kept apace, a structure factor calculation and several cycles of refinement were carried out using the Cu dataset with, in one case, CSAAED, the coordinates from the Mo dataset and in the other, CSAAEDI, the same coordinates transformed through an inversion centre at the origin.

Merging equivalent reflections reduced the number to 1719 with a merging R-factor of 0.047. The first R-factors, before any least squares refinement, were 0.093 and 0.086 for CSAAED and CSAAEDI respectively. This suggested that the inverted coordinates gave values of the calculated structure factors which more nearly corresponded to the observed values than original coordinates. Further tandem refinement was carried out to verify this.

During this refinement the omit level was changed to 4 and the number of observed, unique reflections dropped to 1538. The R-factors dropped to 0.076 and 0.069 respectively and the configurations were examined. The R-factor was lower for the inverted coordinates by 0.007 and thus

the actual configuration of the (+)-CSA used was 1S-4R, which confirmed the assignment given in the suppliers' catalogues.[14]

5.1.5 Parallel refinement of the structure using the two datasets:

Two sets of refinement were continued in tandem: CSAAEDI, Cu data with the current, inverted, coordinates; and CSA, Mo data, starting from the same, inverted, coordinates.

The hydrogen atoms were not entirely satisfactory. Their bond lengths were too large or too small and the thermal parameters and shifts/esds were frequently large. Their current coordinates were replaced by ideal calculated ones and allowed to ride on their attached carbon atom in the usual way. The exception was the methyl hydrogen atoms which were retained and continued to be refined freely. This was unusual in the CSA structures, where the methyl groups were usually refined as rigid groups.

In both refinements non-hydrogen atoms were allowed to refine anisotropically. This was set up in two stages, sulphur and oxygen atoms first, followed by carbon atoms. Before the carbon atoms were allowed to do this attempts were made to locate the three hydrogen atoms of the water (hydronium) molecule, with some success.

In order to verify the water hydrogen atom coordinates, details of the geometry around the water oxygen atom, involving the bonded hydrogen atoms and hydrogen bonded oxygen atoms were determined using the program CALC[32]. The H_3O^+ ion would be expected to be a tetrahedron with only three of the vertices occupied by

hydrogen atoms. The oxygen atoms to which it is linked by hydrogen bonds would similarly be expected to make tetrahedral angles at the hydronium oxygen, but with larger variations being acceptable. This proved to be true in both cases.

After the carbon atoms began to refine anisotropically and the structures were approaching convergence, it became apparent that it was necessary to omit one reflection from each of the refinements, for different reasons. In CSAAEDI, 2 0 0, a strong, low angle reflection, had $F_o<F_c$ because of extinction. In many of the high angle reflections of CSA had $F_o>F_c$. In 2 9 12 this was particularly marked.

The weighting schemes applied were: $W^{-1} = \sigma^2(F) + 0.004452F$ for the Cu dataset and $W^{-1} = \sigma^2(F) + 0.000693F$ for the Mo dataset. In both cases the variances in $\sqrt{F/F_{max}}$ levelled out over all the reflections as a result.

In the last cycle the shifts/esd's were low, mostly less than 0.05, although the largest were 0.21 for a methyl hydrogen atom coordinate and 0.18 for a water hydrogen atom coordinate. The H_3O^+ hydrogen atoms refined into satisfactory positions.

5.1.6 Results of Crystal Structure Determination:

Fractional coordinates of non-hydrogen atoms, six anisotropic thermal parameters for each and fractional coordinates of hydrogen atoms are listed in the following tables. Isotropic thermal parameters for all hydrogen atoms were fixed at 0.05Å. The asymmetric unit consists of one water molecule as a hydronium ion and one 1-S-4-R-camphor-10-sulphonate ion. Only the three water hydrogen atoms were located in difference maps and the six methyl

hydrogen atoms were refined with three positional parameters. The remainder of the hydrogen atoms bound to carbon atoms were placed in ideal calculated positions. In the structure obtained from Mo radiation, esd's on fractional coordinates ranged from 0.00014 to 0.0010 and tended to be smaller for heavier atoms. The range of the values of principal anisotropic thermal parameters was 0.0252(21) to 0.075(2). The methyl carbon atoms exhibited some of the larger thermal parameters. In the structure obtained from Cu radiation, esd's on fractional coordinates ranged from 0.00005 to 0.0010 and also tended to be smaller for heavier atoms. The range of the values of principal anisotropic thermal parameters was 0.0274(15) to 0.091(4). Again the methyl carbon atoms exhibited some of the larger thermal parameters. There are electrostatic forces and hydrogen bonding to cause the salt to hold together. See section 6.4 for details. It was only the crystal structure detemination that revealed a molecule of water as an integral part of the crystal structure, and indeed that the camphor-10-sulphonic acid was dissociated, having given up its acid hydrogen atom to the water molecule.

Figure 5.1 Hydronium Camphor-10 Sulphonate

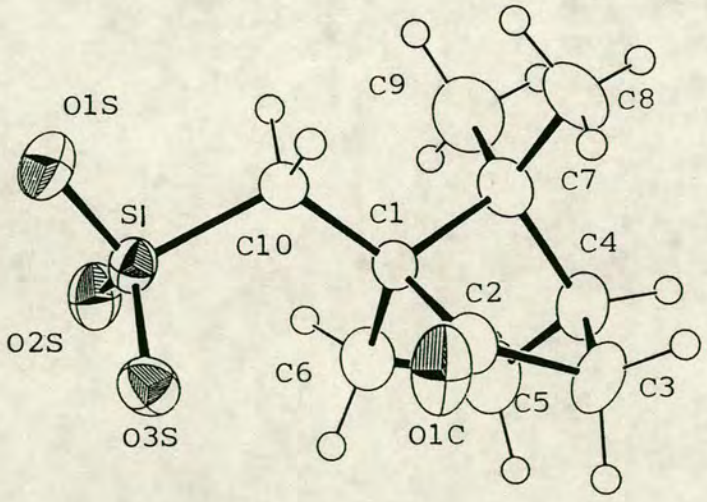


Table 5.1.1 Fractional coordinates with isotropic thermal parameters in Å² (U_{iso} for H fixed at 0.05Å²) ***Mo data***

	x	y	z	U_{iso}
C(1)	-0.3034(6)	0.1389(4)	-0.14852(24)	0.0282(22)
C(2)	-0.5196(7)	0.1735(4)	-0.1353(3)	0.036(3)
O(1C)	-0.6514(5)	0.1123(3)	-0.10908(22)	0.0544(22)
C(3)	-0.5387(8)	0.3000(4)	-0.1682(4)	0.049(3)
C(4)	-0.3340(7)	0.3239(4)	-0.2048(3)	0.043(3)
C(5)	-0.1982(9)	0.3437(4)	-0.1293(4)	0.055(3)
C(6)	-0.1844(7)	0.2200(4)	-0.0873(3)	0.041(3)
C(7)	-0.2692(8)	0.1991(3)	-0.2370(3)	0.0376(23)
C(8)	-0.4047(10)	0.1500(6)	-0.3077(4)	0.053(4)
C(9)	-0.0588(9)	0.1938(7)	-0.2684(5)	0.064(4)
C(10)	-0.2638(7)	0.0066(3)	-0.14560(22)	0.0320(23)
S(1)	-0.22909(14)	-0.05922(8)	-0.04462(7)	0.0298(5)
O(1S)	-0.2230(6)	-0.18511(22)	-0.06331(19)	0.0483(19)
O(2S)	-0.0434(4)	-0.0153(3)	-0.01007(20)	0.0425(19)
O(3S)	-0.3927(4)	-0.0259(3)	0.00974(19)	0.0383(18)
O(1W)	-0.2210(5)	-0.3747(3)	0.02486(22)	0.0479(20)
	x	y	z	
H(31)	-0.6509	0.3064	-0.2168	
H(32)	-0.5727	0.3607	-0.1171	
H(4)	-0.3313	0.3951	-0.2506	
H(51)	-0.0547	0.3737	-0.1500	
H(52)	-0.2604	0.4076	-0.0857	
H(61)	-0.0329	0.1912	-0.0828	
H(62)	-0.2498	0.2207	-0.0246	
H(81)	-0.338(7)	0.074(4)	-0.324(3)	
H(82)	-0.363(7)	0.199(4)	-0.357(3)	
H(83)	-0.525(8)	0.149(4)	-0.284(3)	
H(91)	0.018(9)	0.216(5)	-0.230(4)	
H(92)	-0.024(7)	0.103(4)	-0.290(3)	
H(93)	-0.036(7)	0.242(4)	-0.322(3)	
H(101)	-0.3878	-0.0370	-0.17528	
H(102)	-0.1322	-0.0098	-0.18248	
H(1W)	-0.116(8)	-0.415(4)	0.000(3)	
H(2W)	-0.341(7)	-0.419(4)	0.027(3)	
H(3W)	-0.220(8)	-0.307(4)	-0.006(3)	

Table 5.1.2 Anisotropic thermal parameters in Å² ***Mo data***

	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
C(1)	0.0334(23)	0.0258(21)	0.0252(21)	0.0005(16)	-0.0046(18)	0.0018(18)
C(2)	0.0318(23)	0.042(3)	0.034(3)	0.0077(22)	0.0010(20)	0.0022(21)
O(1C)	0.0343(18)	0.0585(23)	0.070(3)	0.0267(20)	0.0027(17)	0.0008(16)
C(3)	0.047(3)	0.035(3)	0.064(4)	0.0080(25)	-0.001(3)	0.0127(24)
C(4)	0.049(3)	0.0269(24)	0.051(3)	0.0105(21)	-0.0039(23)	-0.0047(21)
C(5)	0.066(4)	0.033(3)	0.066(3)	0.0024(24)	-0.019(3)	-0.0072(25)
C(6)	0.042(3)	0.038(3)	0.045(3)	-0.0008(21)	-0.0134(22)	-0.0047(21)
C(7)	0.041(3)	0.0391(23)	0.0327(22)	0.0086(19)	0.0049(24)	-0.0053(23)
C(8)	0.073(4)	0.054(4)	0.031(3)	0.006(3)	-0.008(3)	-0.009(3)
C(9)	0.055(4)	0.075(5)	0.061(4)	0.017(4)	0.019(3)	-0.005(3)
C(10)	0.039(3)	0.0314(21)	0.0252(22)	-0.0006(16)	0.0014(22)	0.0081(22)
S(1)	0.0264(5)	0.0289(5)	0.0341(5)	0.0044(5)	0.0017(5)	0.0021(4)
O(1S)	0.0622(22)	0.0293(15)	0.0535(20)	0.0054(14)	0.0024(19)	0.0068(16)
O(2S)	0.0317(17)	0.0478(21)	0.0479(19)	0.0085(17)	-0.0061(15)	0.0041(13)
O(3S)	0.0325(16)	0.0474(20)	0.0349(17)	0.0012(15)	0.0046(13)	0.0007(13)
O(1W)	0.0346(17)	0.0359(17)	0.073(3)	0.0123(17)	-0.0004(19)	-0.0034(16)

Table 5.1.3 Fractional coordinates with isotropic thermal parameters in Å² (U_{iso} for H fixed at 0.05Å²) ***Cu data***

	x	y	z	U_{iso}
C(1)	-0.3044(5)	0.1395(3)	-0.14820(20)	0.0296(16)
C(2)	-0.5197(6)	0.1732(4)	-0.13492(24)	0.0397(20)
O(1C)	-0.6516(4)	0.1119(3)	-0.10894(21)	0.0597(19)
C(3)	-0.5401(7)	0.3008(4)	-0.1685(3)	0.053(3)
C(4)	-0.3346(6)	0.3231(3)	-0.2046(3)	0.0457(23)
C(5)	-0.1984(8)	0.3440(4)	-0.1289(3)	0.057(3)
C(6)	-0.1851(6)	0.2195(3)	-0.0878(3)	0.0460(23)
C(7)	-0.2703(6)	0.1986(3)	-0.23699(22)	0.0380(18)
C(8)	-0.4076(10)	0.1507(5)	-0.3064(3)	0.060(3)
C(9)	-0.0565(8)	0.1930(5)	-0.2674(4)	0.066(4)
C(10)	-0.2634(6)	0.0066(3)	-0.14618(19)	0.0347(18)
S(1)	-0.22910(12)	-0.05924(7)	-0.04475(5)	0.0326(4)
O(1S)	-0.2236(5)	-0.18575(20)	-0.06349(17)	0.0513(16)
O(2S)	-0.0425(4)	-0.01530(25)	-0.00998(18)	0.0439(15)
O(3S)	-0.3928(4)	-0.02537(25)	0.00961(17)	0.0408(14)
O(1W)	-0.2203(4)	-0.3746(3)	0.02513(20)	0.0493(16)

	x	y	z
H(31)	-0.5745	0.3619	-0.1178
H(32)	-0.6516	0.3068	-0.2175
H(4)	-0.3309	0.3940	-0.2506
H(51)	-0.0551	0.3744	-0.1495
H(52)	-0.2610	0.4075	-0.0852
H(61)	-0.2493	0.2199	-0.0248
H(62)	-0.0336	0.1904	-0.0839
H(81)	-0.333(7)	0.087(4)	-0.324(3)
H(82)	-0.363(6)	0.192(4)	-0.358(3)
H(83)	-0.560(7)	0.144(4)	-0.281(3)
H(91)	0.012(8)	0.235(4)	-0.235(3)
H(92)	-0.018(6)	0.097(4)	-0.288(3)
H(93)	-0.040(7)	0.242(4)	-0.313(3)
H(101)	-0.3866	-0.0372	-0.17625
H(102)	-0.1312	-0.0090	-0.18287
H(1W)	-0.109(7)	-0.428(4)	0.010(3)
H(2W)	-0.335(7)	-0.411(4)	0.021(3)
H(3W)	-0.227(7)	-0.311(4)	-0.007(3)

Table 5.1.4 Anisotropic thermal parameters in Å² ***Cu data***

	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
C(1)	0.0332(18)	0.0279(16)	0.0276(16)	-0.0003(14)	-0.0045(14)	0.0044(14)
C(2)	0.0393(19)	0.0393(21)	0.0406(20)	0.0088(18)	0.0000(17)	0.0060(18)
O(1C)	0.0370(16)	0.0617(20)	0.0805(22)	0.0285(17)	0.0034(15)	0.0008(14)
C(3)	0.058(3)	0.0353(22)	0.066(3)	0.0122(20)	-0.0017(21)	0.0144(21)
C(4)	0.057(3)	0.0286(19)	0.0514(23)	0.0087(17)	-0.0035(18)	-0.0020(18)
C(5)	0.072(3)	0.0312(18)	0.069(3)	0.0002(20)	-0.0145(25)	-0.0093(20)
C(6)	0.052(3)	0.0380(21)	0.0477(21)	0.0018(17)	-0.0097(19)	-0.0079(19)
C(7)	0.0459(21)	0.0358(17)	0.0324(17)	0.0075(14)	0.0047(17)	-0.0025(18)
C(8)	0.091(4)	0.054(3)	0.0345(23)	0.0042(20)	-0.0143(23)	-0.013(3)
C(9)	0.066(3)	0.063(3)	0.069(4)	0.013(3)	0.022(3)	-0.002(3)
C(10)	0.0475(22)	0.0292(17)	0.0274(15)	0.0021(13)	-0.0012(17)	0.0043(18)
S(1)	0.0330(4)	0.0287(4)	0.0361(4)	0.0049(3)	0.0014(4)	0.0021(3)
O(1S)	0.0720(19)	0.0280(13)	0.0539(16)	0.0033(11)	0.0037(15)	0.0061(14)
O(2S)	0.0295(14)	0.0483(17)	0.0541(15)	0.0083(13)	-0.0104(11)	0.0013(11)
O(3S)	0.0322(13)	0.0496(17)	0.0407(14)	0.0016(12)	0.0071(10)	0.0043(11)
O(1W)	0.0363(14)	0.0385(15)	0.0731(19)	0.0117(14)	-0.0020(15)	0.0001(12)

5.2 Ammonium (+)-1S-1R-Camphor-10-sulphonate:

5.2.1 Crystal data:

$NH_4^+.C_{10}H_{15}O_4S^-$, M_r = 249.3, monoclinic, I2, *a*) =17.135(7), *b* = 7.3774(22), *c* =19.959(3)Å, β = 101.07(3)°, *V* = 2476.17Å^3, *Z* = 8, D_c = 1.337gcm^{-3}, CuK_α, λ = 1.5418Å, μ = 23.00cm^{-1}, *F*(000) = 1072, *T* = 293K, final *R* = 0.069 for 1856 observed reflections F>4σ(F) final max δ/σ = 0.454. Final difference Fourier max=0.35 min=-0.76 eÅ^{-3}.

5.2.2 Structure solution and refinement:

Details of preparation and crystallisation are to be found in the table in section 2.15, under the code $CSNH_4$. An elongated triangular prism, 0.65x0.2x0.2mm was mounted in a capillary tube with the long axis, along which there was an extinction direction, parallel to the oscillation axis. This turned out to be the unique monoclinic axis, b. Oscillation and Weissenberg photographs revealed that the space group was I2 and that the crystal was a strong diffractor. 2042 data, a quarter of those of those available, were measured on the AED-2 four circle diffractometer using ω/2θ scans, with $2\theta_{max}$ of 119° and 0≤h≤19, 0≤k≤8 and -22≤l≤22. 1949 remained after merging, when the merging R-factor was 0.044. Three intensity standards verified that there was no significant crystal decay. 1856 data with F<4σ(F) were used for structure refinement (although, at the start 1900 relections with F<6σ(F) were used for structure solution and refinement). The number of ammonium camphor-10-sulphonate ion pairs in the unit cell was indicated by the calculated density. The density was 1.337gcm^{-3} for eight molecules per unit cell, which lies in the expected range of 1.2 to 1.5 g cm^{-3} and which corresponded, in this four fold space group, to an asymmetric unit containing two ion pairs. A

Patterson map would be complicated, with eight sulphur atoms, so direct methods was tried first. The structure was successfully solved by SHELX86[28] direct methods and a single sulphur atom of one molecule and the sulphonate group and bonded carbon atom of the other, were located in the E-map. No peak list refinement was carried out because this was not an equal atom structure. DIRDIF[30] phase refinement allowed many of the remaining non-hydrogen atoms to be located. For one camphor-10-sulphonate molecule all the carbon atoms were found at this stage, but only one five membered ring for the other. The carbonyl oxygen atoms, which define the hand of the camphor-10-sulphonate molecule were not yet located. At this point the R-factor was 0.31, which was reasonable given that nine carbon atoms and two oxygens remained unaccounted for.

The y-coordinate of one of the sulphur atoms was at first fixed to define an origin and six cycles of least squares refinement carried out in which the remaining atoms were located in successive steps. One molecule was completed first. Its hand was 1S-4R-, which indicated that the correct enantiomorph had been selected by the program. Nine strong low angle reflections had deviations/sigma greater than 5, with F_o less than F_c in each case. Extinction was the probable cause of this and they were specifically omitted from the structure refinement, despite the risk that while the model remained incomplete there was likely to be a large deviation between calculated and observed structure factors. More were omitted later for the same reason. The final non-hydrogen atoms to be located were those of the two methyl group in each molecule and the R-factor had successfully reduced to 0.13. Non-hydrogen atoms were allowed to refine with six anisotropic thermal parameters, beginning with the two sulphur atoms, then the rest. Alkyl hydrogen atoms were placed in calculated positions because few good hydrogen

locations appeared in difference maps. The R-factor fell to 0.074. The methyl groups were refined as rigid groups. Also, many reflections had earlier been specifically omitted from the refinement because they had values of deviation/sigma greater than 5. The deviation F_o from F_c relative to the precision of F_o is likely to be large when reflections are affected by extinction. It is amongst strong, low angle reflections that extinction tends to show itself, if it occurs. At an early stage in refinement it is the case that, since the model is not yet complete, there are likely to be deviations of F_o from F_c which will later be resolved. Most of the omitted reflections were probably affected by extinction and to verify which required to be omitted on the basis of a good model structure, that is good values of F_c, they were all desuppressed. The R-factor rose from approximately 0.065 to 0.088 after a Fourier calculation. During subsequent cycles of refinement many did indeed again show large values of deviation/sigma and in every case this could be attributable to extinction. It was noticeable that many of them were reflections with k=7. There was an unusually large variance between F_o and F_c in this subset of the data. Those with deviation/sigma greater than 5 were specifically suppressed from use in Fourier calculations. The geometry of the hydrogen bonding region was studied and the hydrogen bonds appeared to be poorly directional. Attempts were made to find better positions for the ammonium hydrogen atoms. The carbon skeleton and the attached hydrogen atoms were kept fixed while the hydrogen bonded region was allowed to refine. Free refinement of the coordinates of the ammonium hydrogen atoms failed. They drifted too close to or too far away from the nitrogen atoms. The angles at the nitrogen atoms made by the surrounding oxygen atoms varied from tetrahedral. Some fitted better than others. In both cases the carbonyl oxygen atoms could be excluded from the hydrogen bonding pattern because the N...O

separations tended to be long and the angles at the nitrogen atoms made to other oxygen atoms tended to be consistently far from tetrahedral. Seven peaks in a difference map were located which made satisfactory hydrogen bonds. All except one were nearly linear. Refinement of all atoms followed, with the ammonium groups constrained to have N-H bond lengths of 1.08Å and separations between the hydrogen atom and the acceptor atom of 1.76Å to hold the angle at the nitrogen atom to be as near as possible to the ideal tetrahedral angle. The eighth hydrogen atom was not found after refinement so its position was calculated to complete the tetrahedral ammonium group. The weighting scheme applied was $W^{-1} = \sigma^2(F) + 0.00039F^2$.

The final R-factor was 0.069 with a weighted R-factor of 0.096; the shift/esd values final cycle were mainly less than 0.1 with many less than 0.05; and the maximum and minimum peaks in the final difference Fourier were 0.35 and 0.76 $eÅ^{-3}$.

5.2.3 Results of Crystal Structure Determination:

Fractional coordinates of non-hydrogen atoms, six anisotropic thermal parameters for each and fractional coordinates of hydrogen atoms are listed in the following tables. Isotropic thermal parameters for all hydrogen atoms were fixed at 0.05Å. The asymmetric unit consists of two ammonium ions and two 1-S-4-R-camphor-10-sulphonate ions. They are crystyallographically independent. Some ammonium hydrogen atoms were located in difference maps and the remainder placed between their hydrogen bond donors and acceptors. Hydrogen atoms bound to carbon atoms were placed in ideal calculated positions. Esd's on fractional coordinates ranged from 0.00007 to 0.003 and tended to be smaller for z-coordinates. The range of the values of principal anisotropic thermal parameters was

0.024(3) to 0.223(18)). The present structure was isomorphous with the potassium salt.

There are electrostatic forces and hydrogen bonding to cause the salt to hold together. See section 6.4 for details.

Figure 5.2 Ammonium Camphor-10 Sulphonate

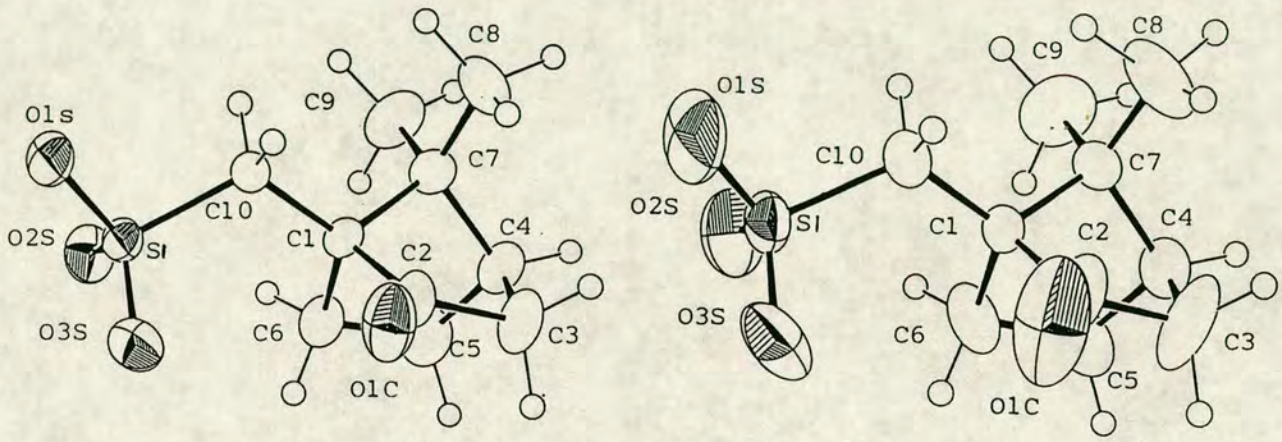


Table 5.2.1 Fractional coordinates with isotropic thermal parameters in Å² (U_{iso} for H fixed at 0.05Å²)

	x	y	z	U_{iso}
C(1)	0.2314(4)	0.1756(9)	0.1257(3)	0.028(3)
C(2)	0.2145(4)	-0.0321(11)	0.1294(4)	0.040(4)
O(1C)	0.2592(3)	-0.1529(8)	0.1207(3)	0.061(4)
C(3)	0.1315(4)	-0.0498(13)	0.1434(5)	0.057(5)
C(4)	0.1042(4)	0.1466(12)	0.1431(4)	0.045(4)
C(5)	0.1484(4)	0.2290(16)	0.2112(4)	0.056(5)
C(6)	0.2356(4)	0.2421(15)	0.1999(3)	0.048(4)
C(7)	0.1465(4)	0.2371(13)	0.0897(3)	0.041(4)
C(8)	0.1215(4)	0.1685(17)	0.0178(4)	0.065(5)
C(9)	0.1367(5)	0.4452(12)	0.0875(5)	0.061(5)
C(10)	0.2982(3)	0.2212(12)	0.0878(3)	0.036(4)
S(1)	0.39604(8)	0.23694(20)	0.13781(7)	0.0329(8)
O(1S)	0.44565(25)	0.2547(11)	0.08587(21)	0.052(3)
O(2S)	0.3998(3)	0.4023(9)	0.1791(3)	0.049(3)
O(3S)	0.4120(3)	0.0711(8)	0.1784(3)	0.050(3)
C(1')	0.1905(4)	0.6784(10)	-0.1422(3)	0.032(3)
C(2')	0.1773(5)	0.4701(13)	-0.1435(6)	0.068(6)
O(1C')	0.2271(5)	0.3567(12)	-0.1358(6)	0.121(7)
C(3')	0.0879(6)	0.4430(15)	-0.1584(8)	0.094(8)
C(4')	0.0566(4)	0.6378(14)	-0.1655(4)	0.052(5)
C(5')	0.0722(5)	0.716(3)	-0.0934(4)	0.096(8)
C(6')	0.1638(4)	0.7403(22)	-0.0767(4)	0.073(6)
C(7')	0.1184(4)	0.7355(14)	-0.1979(3)	0.044(4)
C(8')	0.1247(5)	0.663(3)	-0.2682(4)	0.104(9)
C(9')	0.1061(7)	0.9380(18)	-0.2037(7)	0.098(9)
C(10')	0.2721(4)	0.7313(15)	-0.1525(3)	0.044(4)
S(1')	0.34841(10)	0.76306(20)	-0.08013(9)	0.0481(10)
O(1S')	0.4181(3)	0.7904(19)	-0.1077(4)	0.113(7)
O(2S')	0.3281(5)	0.9305(10)	-0.0468(4)	0.083(5)
O(3S')	0.3473(5)	0.6094(11)	-0.0340(4)	0.076(4)
N(1A)	0.4208(3)	0.7324(10)	0.1080(3)	0.041(3)
N(1B)	0.3983(3)	0.2560(10)	-0.0587(3)	0.043(3)

	x	y	z
H(31)	0.0940	-0.1276	0.1040
H(32)	0.1321	-0.1124	0.1924
H(4)	0.0403	0.1613	0.1344
H(51)	0.1253	0.3615	0.2197
H(52)	0.1442	0.1418	0.2538
H(61)	0.2742	0.1557	0.2354
H(62)	0.2569	0.3800	0.2057
H(81)	0.1338	0.0257	0.014C
H(82)	0.1547	0.2444	-0.0136
H(83)	0.0587	0.1925	0.0005
H(91)	0.1592	0.4794	0.1403
H(92)	0.0759	0.4909	0.0730
H(93)	0.1727	0.5106	0.0556
H(101)	0.2989	0.1171	0.0499
H(102)	0.2842	0.3502	0.0628
H(31')	0.0684	0.3669	-0.2048
H(32')	0.0688	0.3747	-0.1164
H(4')	-0.0045	0.6489	-0.1920
H(51')	0.0422	0.845	-0.0917
H(52')	0.0530	0.623	-0.0581
H(61')	0.1904	0.6564	-0.0340
H(62')	0.1794	0.8803	-0.0654
H(81')	0.1315	0.519	-0.2768
H(82')	0.1794	0.732	-0.2712
H(83')	0.0771	0.716	-0.3067
H(91')	0.1038	0.9499	-0.1502
H(92')	0.0468	0.9520	-0.2337
H(93')	0.1438	1.0431	-0.2176
H(103)	0.2919	0.6269	-0.1834
H(104)	0.2659	0.8577	-0.1804
H(1NA)	0.4804	0.7608	0.1013
H(2NA)	0.3859	0.7227	0.0571
H(3NA)	0.4003	0.8528	0.1314
H(4NA)	0.4176	0.6120	0.1386
H(1NB)	0.3581	0.3644	-0.0780
H(2NB)	0.4182	0.2582	-0.0039
H(3NB)	0.4517	0.2427	-0.0796
H(4NB)	0.3764	0.1189	-0.0636

Table 5.2.2 Anisotropic thermal parameters in Å²

	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
C(1)	0.027(3)	0.031(3)	0.026(3)	0.0001(25)	0.0119(24)	0.000(3)
C(2)	0.025(3)	0.046(4)	0.048(4)	-0.004(3)	0.011(3)	-0.004(3)
O(1C)	0.036(3)	0.048(3)	0.097(5)	-0.005(3)	0.019(3)	0.003(3)
C(3)	0.029(4)	0.059(5)	0.082(6)	0.011(5)	0.020(4)	-0.005(4)
C(4)	0.033(4)	0.051(4)	0.052(4)	0.005(4)	0.023(3)	0.001(3)
C(5)	0.047(4)	0.075(6)	0.048(4)	-0.012(5)	0.028(3)	-0.003(5)
C(6)	0.045(4)	0.069(5)	0.029(3)	-0.011(4)	0.017(3)	-0.019(4)
C(7)	0.028(3)	0.056(4)	0.038(3)	0.010(4)	0.013(3)	0.005(4)
C(8)	0.028(4)	0.117(8)	0.045(4)	0.002(5)	0.000(3)	-0.001(5)
C(9)	0.051(5)	0.047(5)	0.086(6)	0.025(5)	0.031(4)	0.020(4)
C(10)	0.024(3)	0.060(5)	0.025(3)	0.006(3)	0.0062(23)	-0.006(3)
S(1)	0.0263(7)	0.0455(9)	0.0266(7)	-0.0011(8)	0.0084(5)	-0.0021(7)
O(1S)	0.0302(22)	0.093(4)	0.0347(22)	-0.001(3)	0.0172(18)	-0.002(3)
O(2S)	0.047(3)	0.057(3)	0.042(3)	-0.020(3)	0.0111(25)	-0.010(3)
O(3S)	0.044(3)	0.052(3)	0.051(3)	0.009(3)	0.000(3)	0.003(3)
C(1')	0.026(3)	0.040(4)	0.030(3)	-0.003(3)	0.0047(25)	-0.003(3)
C(2')	0.044(5)	0.040(5)	0.115(8)	0.009(5)	-0.003(5)	-0.004(4)
O(1C')	0.064(5)	0.063(5)	0.220(10)	-0.007(6)	-0.024(6)	0.016(4)
C(3')	0.047(5)	0.051(6)	0.174(12)	0.023(7)	-0.007(6)	-0.019(5)
C(4')	0.024(3)	0.078(6)	0.052(4)	0.001(4)	0.005(3)	-0.002(4)
C(5')	0.040(4)	0.203(16)	0.047(4)	-0.013(8)	0.018(3)	-0.013(8)
C(6')	0.030(3)	0.152(10)	0.038(4)	-0.022(7)	0.011(3)	-0.009(6)
C(7')	0.034(3)	0.061(5)	0.036(3)	0.007(4)	0.001(3)	-0.004(4)
C(8')	0.042(5)	0.223(18)	0.043(5)	-0.023(8)	0.003(4)	0.001(7)
C(9')	0.072(7)	0.086(9)	0.126(10)	0.062(8)	-0.009(7)	0.010(6)
C(10')	0.031(3)	0.065(5)	0.035(3)	-0.010(4)	0.007(3)	-0.003(4)
S(1')	0.0292(8)	0.0646(13)	0.0476(10)	-0.0029(10)	0.0011(7)	-0.0037(9)
O(1S')	0.029(3)	0.209(12)	0.097(5)	-0.011(7)	0.010(3)	-0.011(5)
O(2S')	0.085(5)	0.067(5)	0.090(5)	-0.033(4)	0.002(4)	-0.008(4)
O(3S')	0.087(5)	0.074(5)	0.056(4)	0.004(3)	-0.022(3)	0.012(4)
N(1A)	0.036(3)	0.042(3)	0.044(3)	0.002(3)	0.0120(23)	0.002(3)
N(1B)	0.035(3)	0.048(3)	0.045(3)	-0.003(3)	0.0135(22)	-0.001(3)

5.3 Potassium 1S-4R-Camphor-10-sulphonate

5.3.1 Crystal data:

$K^+.C_{10}H_{15}O_4S^-$, M_r = 270.4, monoclinic, I2, a =16.855(10), b = 7.237(4), c =19.916(16)Å, β = 100.80(6)°, V = 2386.3Å^3, Z = 8, D_c = 1.505gcm^{-3}, MoK_α, λ = 0.71069Å, μ = 5.71cm^{-1}, F(000) = 1144, T = 293K, final R = 0.054 for 1123 observed reflections F>4σ(F) final max δ/σ = 0.307. Final difference Fourier max=0.43 min=-0.60 eÅ^{-3}.

5.3.2 Structure solution and refinement:

The details of preparation and the recrystallisation procedure are to be found in the table in section 2.15, under the code CSK5(iv). The crystals were elongated and triangular, though rather flattened, in cross section. Previously (see under code CSK2) one of a crop of crystals was photographed. They were elongated and rhombic in cross section. The crystal turned out to to be twinned, each spot on the Weissenberg photographs being repeated 5° away along the film, in ω. In that case the two portions of the crystal were identical in alignment, sharing the unique, b, mounting axis, except that they were rotated to different degrees about it. They did not have the other axes coincident and the identical diffraction patterns were displaced relative to one another. The first crystal was monoclinic b-mounted with an F2 unit cell.

The crystal from which data were collected, an elongated trianglar prism of dimensions 0.95x0.2x0.15mm, was mounted in a 0.5mm Lindemann tube and fixed with araldite with the needle axis parallel to the tube. This corresponded to an optical extinction direction of the crystal.

Oscillation and Weissenberg photographs were directly superimposable on the photographs of ammonium 1S-4R-camphor-10-sulphonate and indicated that the space group was I2. The two structures were isomorphous and there were differences in the intensities of some spots because of the different contributions to the structure factors of the potassium ion in the present case and the NH_4^+ ion. The diffraction was fairly weak so relatively long exposure times were required and for data collection, the power of the X-rays was increased to 1800W instead of the normal 1500W.

1769 reflections were measured on the AED-2 four-circle diffractometer, with $-18<h<18$, $0<k<7$ and $0<l<18$, out to a $2\theta_{max}$ of 45°, using $\omega/2\theta$ scans. Thus a quarter of the data for this four fold space group were collected. Two intensity standards verified that there was no crystal decay. 1506 data remained after merging, for which the merging R-factor was 0.048. Reflections with $F<4\sigma(F)$ were suppressed to leave 1123 to be used for structure solution and refinement.

Since this structure was isomorphous with that of $CSNH_4$, it was solved by a structure factor calculation using the program SHELX76,[29] based on the coordinates from the structure $CSNH_4$. The initial R-factor was 0.22. The input model included non-hydrogen atoms with their six anisotropic thermal parameters and calculated hydrogen atoms, with the ammonium group replaced by the potassium ion. The methyl groups on the camphor-10-sulphonate molecules were again refined ar rigid groups. After several cycles of least squares refinement at the start, during which several atoms were non-positive definite at first, the R-factor reduced to 0.055. The largest peak on the difference map amounted to 0.39 $eÅ^{-3}$ and was associated with one of the two sulphur atoms and was probably related to its being fixed in the value of

the y-coordinate in this polar space group. Also the ratio between the shifts and the esds for each refining parameter dropped to small values, mainly below 0.05. The values for each y-coordinate shift tended to be noticeably larger than the others. The fixation of the origin had hitherto been achieved solely by fixing the y-coordinate of one of the sulphur atoms. The situation was altered to depend on both and to allow the values of the y-coordinates to refine. By adding the same small number less than 1 to each fractional y-coordinate, the sulphur y-coordinates were made to have the sum 1. The sulphur y-coordinates were then allowed to refine together, with the restriction that their sum is always unity. The shifts/esds of the y-coordinates were no longer greater than other shifts after this change was made.

A weighting scheme of the form $W^{-1} = \sigma^2(F) + 0.00242F^2$ was applied. The shifts/esd in the final cycles were mainly below 0.05, although the largest was 0.307, and was associated with one of the rotational parameters of a methyl carbon atom. The final R-factor was 0.054 and the final weighted R-factor was 0.063.

5.3.3 Results of Crystal Structure Determination:

Fractional coordinates of non-hydrogen atoms, six anisotropic thermal parameters for each and fractional coordinates of hydrogen atoms are listed in the following tables. Isotropic thermal parameters for all hydrogen atoms were fixed at 0.05Å. The asymmetric unit consists of two potassium ions and two 1-S-4-R-camphor-10-sulphonate ions. They are crystallographically independent. Hydrogen atoms bound to carbon atoms were placed in ideal calculated positions. Esd's on fractional coordinates ranged from 0.00014 to 0.005 and tended to be smaller for heavier atoms, except on the y-coordinates, which were noticeably larger. The range of the values of principal

anisotropic thermal parameters was 0.015(7) to 0.37(3). The present salt was isomorphous with the ammonium salt.

There are electrostatic forces to cause the salt to hold together and no hydrogen bonding, because there were no hydrogen bond donors in the structure. See section 6.4 for details.

Figure 5.3 Potassium Camphor-10 Sulphonate

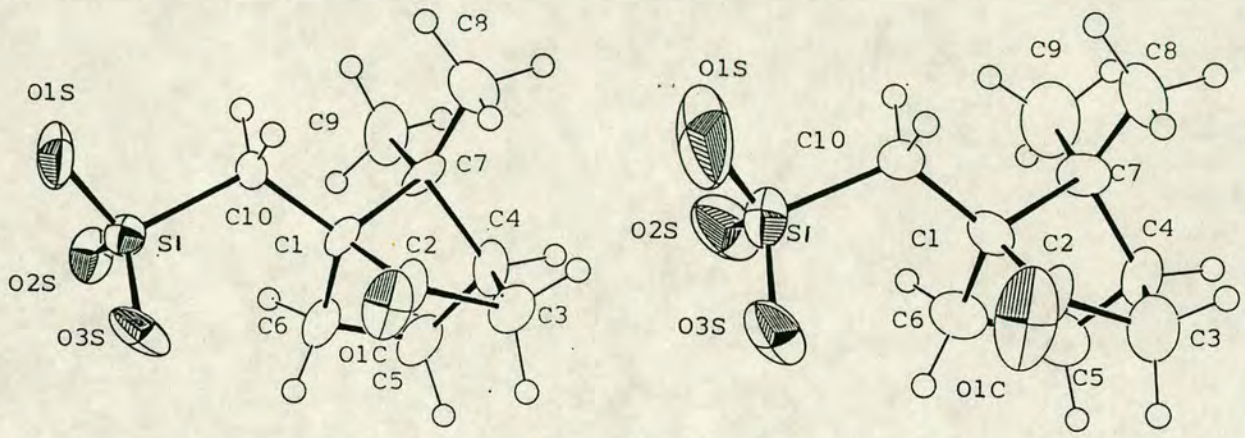


Table 5.3.1 Fractional coordinates with isotropic thermal parameters in Å² (U_{iso} for H fixed at 0.05Å²)

	x	y	z	U_{iso}
C(1)	0.2325(7)	0.1737(18)	0.1240(6)	0.028(8)
C(2)	0.2164(8)	-0.0326(21)	0.1275(7)	0.039(9)
O(1C)	0.2619(5)	-0.1572(15)	0.1187(5)	0.047(6)
C(3)	0.1326(8)	-0.0504(23)	0.1434(8)	0.048(10)
C(4)	0.1053(7)	0.1486(20)	0.1460(7)	0.036(8)
C(5)	0.1535(7)	0.225(3)	0.2127(7)	0.044(9)
C(6)	0.2392(7)	0.243(3)	0.1992(6)	0.040(7)
C(7)	0.1463(6)	0.241(3)	0.0910(6)	0.040(8)
C(8)	0.1184(9)	0.167(3)	0.0180(8)	0.056(11)
C(9)	0.1366(8)	0.4491(22)	0.0896(9)	0.053(11)
C(10)	0.2986(6)	0.226(3)	0.0840(6)	0.032(8)
S(1)	0.40067(16)	0.2448(5)	0.13162(14)	0.0283(17)
O(1S)	0.4488(4)	0.2578(25)	0.0779(4)	0.054(6)
O(2S)	0.4051(7)	0.4109(15)	0.1720(6)	0.042(8)
O(3S)	0.4180(8)	0.0784(15)	0.1723(6)	0.042(7)
C(1')	0.1956(7)	0.6755(20)	-0.1385(7)	0.034(9)
C(2')	0.1832(9)	0.4695(22)	-0.1378(8)	0.049(11)
O(1C')	0.2333(6)	0.3520(16)	-0.1291(8)	0.081(9)
C(3')	0.0936(10)	0.446(3)	-0.1512(10)	0.072(14)
C(4')	0.0592(8)	0.6395(22)	-0.1627(8)	0.044(9)
C(5')	0.0746(8)	0.730(4)	-0.0918(7)	0.066(12)
C(6')	0.1675(7)	0.753(4)	-0.0735(6)	0.053(9)
C(7')	0.1235(7)	0.730(3)	-0.1969(7)	0.037(8)
C(8')	0.1290(9)	0.656(3)	-0.2655(8)	0.069(12)
C(9')	0.1105(12)	0.945(3)	-0.2055(11)	0.080(15)
C(10')	0.2789(7)	0.735(3)	-0.1491(6)	0.037(7)
S(1')	0.35824(17)	0.7552(5)	-0.07553(16)	0.0414(20)
O(1S')	0.4284(6)	0.765(5)	-0.1037(6)	0.162(14)
O(2S')	0.3458(10)	0.9230(18)	-0.0416(8)	0.074(10)
O(3S')	0.3507(8)	0.6009(16)	-0.0283(7)	0.062(9)
K(1)	0.41594(15)	0.7452(9)	0.10315(15)	0.0399(16)
K(2)	0.39765(15)	0.2666(8)	-0.06231(14)	0.0355(16)

	x	y	z
H(31)	0.0934	-0.1260	0.1037
H(32)	0.1342	-0.1184	0.1919
H(4)	0.0408	0.1670	0.1404
H(51)	0.1517	0.131	0.2544
H(52)	0.1303	0.358	0.2244
H(61)	0.2591	0.385	0.2041
H(62)	0.2805	0.157	0.2341
H(81)	0.1360	0.026	0.0206
H(82)	0.1458	0.235	-0.0191
H(83)	0.0545	0.176	0.0030
H(91)	0.1710	0.5112	0.1347
H(92)	0.0752	0.4912	0.0834
H(93)	0.1600	0.4905	0.0455
H(101)	0.2987	0.122	0.0450
H(102)	0.2825	0.358	0.0602
H(31')	0.0745	0.363	-0.1962
H(32')	0.0744	0.383	-0.1079
H(4')	-0.0030	0.6472	-0.1887
H(51')	0.0451	0.863	-0.0935
H(52')	0.0533	0.643	-0.0550
H(61')	0.1842	0.896	-0.0651
H(62')	0.1926	0.674	-0.0287
H(81')	0.1456	0.515	-0.2609
H(82')	0.1736	0.731	-0.2855
H(83')	0.0722	0.670	-0.2996
H(91')	0.0896	1.035	-0.1700
H(92')	0.0729	0.958	-0.2553
H(93')	0.1708	0.980	-0.2087
H(103)	0.2985	0.636	-0.1831
H(104)	0.2721	0.869	-0.1735

Table 5.3.2 Anisotropic thermal parameters in Å²

	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
C(1)	0.025(7)	0.029(8)	0.032(8)	0.007(6)	0.014(6)	-0.004(6)
C(2)	0.024(8)	0.031(9)	0.059(10)	0.006(8)	0.006(7)	-0.008(7)
O(1C)	0.040(6)	0.018(5)	0.082(8)	-0.006(5)	0.023(5)	0.006(5)
C(3)	0.022(7)	0.062(11)	0.060(11)	0.027(10)	0.015(7)	0.008(7)
C(4)	0.015(7)	0.028(7)	0.064(10)	-0.003(8)	0.013(7)	0.006(6)
C(5)	0.053(8)	0.031(10)	0.049(8)	-0.004(8)	0.025(6)	-0.010(8)
C(6)	0.038(7)	0.040(8)	0.043(7)	-0.003(12)	0.019(5)	-0.013(10)
C(7)	0.028(6)	0.030(8)	0.061(9)	0.040(11)	0.012(6)	0.009(9)
C(8)	0.044(9)	0.082(13)	0.038(9)	-0.007(8)	0.001(7)	-0.006(9)
C(9)	0.022(8)	0.040(11)	0.094(14)	0.013(10)	0.010(8)	0.017(7)
C(10)	0.016(5)	0.043(11)	0.034(7)	0.016(8)	0.000(5)	-0.003(7)
S(1)	0.0283(15)	0.0283(18)	0.0277(16)	-0.002(3)	0.0071(12)	-0.0013(25)
O(1S)	0.026(4)	0.083(7)	0.054(6)	-0.024(9)	0.017(4)	-0.017(8)
O(2S)	0.040(7)	0.037(7)	0.049(8)	-0.017(6)	0.015(6)	-0.009(5)
O(3S)	0.053(7)	0.016(6)	0.048(8)	0.002(6)	-0.026(6)	0.007(5)
C(1')	0.030(7)	0.045(10)	0.025(8)	0.005(6)	0.002(6)	0.010(6)
C(2')	0.045(10)	0.023(10)	0.073(13)	0.008(8)	-0.009(9)	-0.018(8)
O(1C')	0.057(7)	0.022(6)	0.152(13)	-0.008(7)	-0.018(7)	0.019(6)
C(3')	0.066(12)	0.067(14)	0.073(14)	0.016(11)	-0.018(10)	-0.020(10)
C(4')	0.021(7)	0.050(10)	0.058(11)	-0.006(8)	0.003(7)	-0.003(7)
C(5')	0.043(8)	0.105(17)	0.050(9)	0.008(14)	0.012(6)	0.003(13)
C(6')	0.039(7)	0.080(11)	0.038(7)	0.009(15)	0.015(6)	0.012(14)
C(7')	0.027(6)	0.038(10)	0.043(8)	0.025(10)	0.003(5)	0.019(8)
C(8')	0.035(8)	0.127(17)	0.042(10)	-0.016(10)	-0.002(8)	-0.013(10)
C(9')	0.069(13)	0.055(14)	0.106(18)	0.016(13)	-0.017(11)	0.010(10)
C(10')	0.036(6)	0.047(9)	0.027(6)	0.003(9)	0.009(5)	-0.006(10)
S(1')	0.0314(16)	0.0432(22)	0.0478(20)	-0.014(3)	0.0049(14)	-0.003(3)
O(1S')	0.032(6)	0.37(3)	0.083(8)	-0.069(22)	0.019(6)	-0.037(18)
O(2S')	0.122(13)	0.047(9)	0.047(8)	-0.007(7)	-0.006(8)	-0.009(8)
O(3S')	0.095(11)	0.029(7)	0.052(9)	0.014(6)	-0.027(7)	-0.004(7)
K(1)	0.0352(14)	0.0338(17)	0.0495(16)	-0.002(3)	0.0099(12)	-0.0030(21)
K(2)	0.0355(14)	0.0304(19)	0.0397(15)	-0.0013(21)	0.0094(11)	0.0059(20)

5.4 Calcium Di-1S-4R-Camphor-10-sulphonate Tetrahydrate

5.4.1 Crystal data:

$Ca^{2+}.2C_{10}H_{15}O_4S^-.4H_2O$, M_r = 574.6, orthorhombic, $C222_1$, a = 7.650(4), b = 11.042(4), c = 32.533(16)Å, V = 2748.10Å^3, Z = 4, D_c = 1.389gcm^{-3}, MoK_α, λ = 0.71069Å, μ = 4.15cm^{-1}, $F(000)$ = 1488, T = 293K, final R = 0.038 for 1190 observed reflections F>4σ(F) final max δ/σ = 0.714. Final difference Fourier max=0.31 min=-0.32 eÅ^{-3}.

5.4.2 Structure solution and refinement:

The details of crystal preparation are given in the table in section 2.15, under the code CSCA2. See chapter 2 for details of the method of structure determination. A thin, broken plate, 1.5x0.56x0.12mm, was mounted parallel to the plate face and its longest dimension. Oscillation and Weissenberg photographs indicated that it was an a-mounted orthorhombic crystal, with space group $C222_1$, and that it was a good diffractor. 1360 reflections were collected on the STADI-2 diffractometer with $2\theta_{max}$ = 60° and 0<h<8, 0<k<12 and 0<l<38. The ranges in h, k and l were such as to collect an eigth of the data, the maximum required for orthorhombic space groups. 1336 data remained after merging, when R = 0.05, and of these, 1190 with F<4σ(F) were used for structure determination and refinement. Structure solution was achieved by SHELX76[29] Patterson. The cell volume was similar to that of ammonium and potassium camphor-10-sulphonate, which suggested that there were likewise eight camphor-10-sulphonate molecules in the unit cell. The Ca^{2+} ion must therefore lie on a special position in this eight-fold space group. The two possibilities were that it would lie on a two-fold rotation axis parallel to a, when the coordinates would be of the form (x,0,0) and (x,0,0.5); or on a two fold parallel to b, when the coordinates would be of the

form (0,y,0.25) and (0,y,0.75). Large Patterson vectors between calcium ions located on the latter were observed and coordinates in the first of these were accepted because this set of coordinates lies within the eighth of the unit cell bounded by the origin and +0.5 in each direction, the portion of the difference map to be calculated. One molecule of the camphor-10-sulphonate is found in this portion, the other related to it by the two fold rotation axis on which the calcium ion sits. This calcium ion position was input to SHELX76[29] with the x and z coordinates fixed and the site occupancy fixed as a half atom because this atom must lie on the two fold rotation axis. After a Fourier calculation the R-factor was shown to be 0.675. After two cycles of least squares refinement it fell to 0.520. This is comparable with the value for a random non-centrosymmetric structure.

All expected non-hydrogen atoms were located in stages and refined isotropically. However, at first, the carbonyl oxygen atom, which determines the enantiomorph, was ambiguous and it was put in in the wrong place. It was later moved to its correct position. Two peaks in the difference map near the calcium ion were attributed to water molecules as an integral part of the crystal lattice. All non-hydrogen atoms were allowed to refine with six anisotropic thermal parameters. The first and third cross terms of the anisotropic thermal parameter tensor for the calcium ion were fixed to be zero to comply with the symmetry restrictions of an atom on a special position on a two fold rotation axis. Hydrogen atoms on the camphorsulphonate molecule were placed in ideal positions in the usual way. Three rotational parameters for the methyl groups on the camphorsulphonate molecule were refined. Their shift/esd in the subsequent refinements were rather larger than for other atoms because the orientation of methyl groups is poorly defined. This may be either simply because it is hard to

locate hydrogen atom electron density or because there may be some disorder or thermal motion.

Two hydrogen atoms on each water molecule, located in a difference map, were allowed to refine freely with a fixed isotropic thermal parameter of 0.05Å², the assigned value of the thermal parameter for every hydrogen atom. In subsequent refinement some water protons began to drift, but were replaced by other more suitable peaks from the difference map, which exhibited peaks of up to 0.3 eÅ^{-3}.

Geometrical parameters were determined to verify the calcium coordination and the hydrogen bonding scheme, before a weighting scheme was refined.

Final refinement of the entire structure was carried out with the weighting scheme $W^{-1} = \sigma^2(F) + 0.000410F^2$ applied. The final R-factor was 0.038 based on 1190 observed data and the final weighted R-factor,0.046. The largest shift/esd in the final cycle was 0.714, for a methyl rotational parameter, but most were less than 0.1. The maximum peak or trough in the difference map amounted to 0.3 eÅ^{-3}.

5.4.3 Results of Crystal Structure Determination:

Fractional coordinates of non-hydrogen atoms, six anisotropic thermal parameters for each and fractional coordinates of hydrogen atoms are listed in the following tables. Isotropic thermal parameters for all hydrogen atoms were fixed at 0.05Å². The asymmetric unit consists of a calcium ion situated on a two-fold rotation axis at 0,y,¼, a 1-S-4-R-camphor-10-sulphonate ion and two molecules of water. The calcium atom in the asymmetric unit was assigned half occupancy. All water hydrogen atoms were located in difference maps and hydrogen atoms

bound to carbon atoms were placed in ideal calculated positions. Esd's on fractional coordinates ranged from 0.00010 to 0.0010 and tended to be smaller for z-coordinates. The range of the values of principal anisotropic thermal parameters was 0.0237(5) to 0.115(4), with certain cross terms for calcium fixed to zero because it was on a special position, see 5.4.2.

Figure 5.4 Calcium Camphor-10 Sulphonate

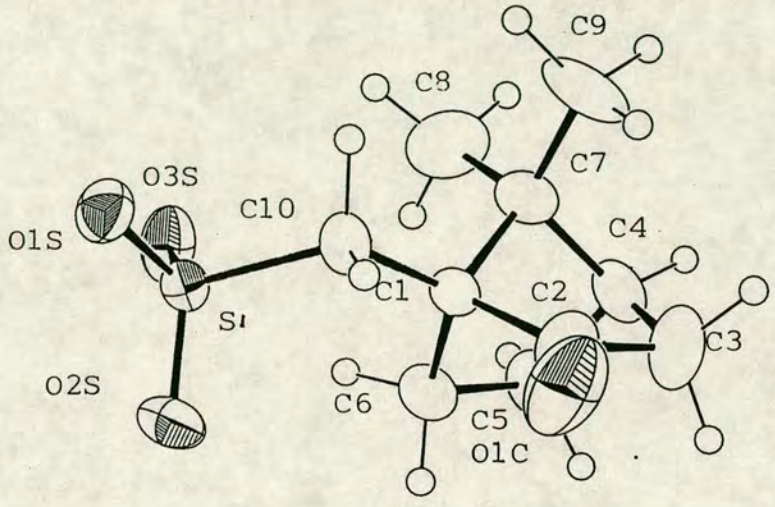


Table 5.4.1 Fractional coordinates with isotropic thermal parameters in Å² (U_{iso} for H fixed at 0.05Å²)

	x	y	z	U_{iso}
C(1)	0.2806(5)	0.2647(4)	0.39811(12)	0.0303(20)
C(2)	0.3889(7)	0.2919(6)	0.43691(15)	0.053(3)
O(1C)	0.5471(6)	0.2808(5)	0.44074(13)	0.083(3)
C(3)	0.2611(10)	0.3350(5)	0.46916(17)	0.070(4)
C(4)	0.0846(8)	0.3268(4)	0.44663(15)	0.049(3)
C(5)	0.0802(9)	0.4307(4)	0.41547(16)	0.061(3)
C(6)	0.2204(8)	0.3922(4)	0.38317(14)	0.048(3)
C(7)	0.1074(6)	0.2154(4)	0.41821(15)	0.0450(24)
C(8)	-0.0400(8)	0.1955(6)	0.38711(22)	0.072(4)
C(9)	0.1377(11)	0.0970(5)	0.44162(19)	0.081(5)
C(10)	0.3815(7)	0.1820(4)	0.36892(12)	0.0372(23)
S(1)	0.39765(13)	0.21625(10)	0.31550(3)	0.0281(5)
O(1S)	0.4924(5)	0.1119(3)	0.29905(9)	0.0441(18)
O(2S)	0.2179(4)	0.2243(4)	0.29954(9)	0.0495(18)
O(3S)	0.4916(5)	0.3304(3)	0.31119(10)	0.0451(18)
CA(1)	0.0000	0.21939(11)	0.2500	0.0256(5)
O(1W)	0.1524(5)	0.0653(4)	0.21567(13)	0.0493(21)
O(2W)	0.1521(5)	0.3722(4)	0.21335(12)	0.0491(21)

	x	y	z
H(31)	0.2630	0.2763	0.49570
H(32)	0.2889	0.4268	0.47859
H(41)	-0.0250	0.3258	0.46756
H(51)	-0.0476	0.4390	0.40168
H(52)	0.1156	0.5154	0.42983
H(61)	0.1628	0.3865	0.35292
H(62)	0.3282	0.4553	0.38260

H(81)	-0.0637	0.2797	0.37120
H(82)	-0.1535	0.1718	0.40513
H(83)	-0.0144	0.1247	0.36498
H(91)	0.2517	0.1059	0.46095
H(92)	0.1538	0.0200	0.42148
H(93)	0.0234	0.0839	0.46058
H(101)	0.5136	0.1763	0.38043
H(102)	0.3202	0.0941	0.37086
H(1W)	0.132(8)	0.011(5)	0.2054(16)
H(2W)	0.247(9)	0.075(5)	0.2094(17)
H(3W)	0.099(7)	0.444(5)	0.2127(15)
H(4W)	0.241(9)	0.371(5)	0.2032(16)

Table 5.4.2 Anisotropic thermal parameters in Å²

	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
C(1)	0.0376(21)	0.0244(19)	0.0290(19)	0.0052(17)	-0.0005(17)	0.0027(19)
C(2)	0.055(3)	0.059(3)	0.046(3)	-0.007(3)	-0.0081(24)	0.002(3)
O(1C)	0.060(3)	0.115(4)	0.074(3)	-0.027(3)	-0.0242(21)	0.003(3)
C(3)	0.098(5)	0.073(4)	0.040(3)	-0.011(3)	-0.001(3)	0.016(4)
C(4)	0.064(3)	0.042(3)	0.040(3)	0.0084(22)	0.020(3)	0.011(3)
C(5)	0.090(4)	0.036(3)	0.055(3)	0.0079(24)	0.019(3)	0.026(3)
C(6)	0.072(4)	0.0274(22)	0.044(3)	0.0070(21)	0.010(3)	0.008(3)
C(7)	0.0462(24)	0.0332(23)	0.055(3)	0.0018(25)	0.0168(23)	0.002(3)
C(8)	0.046(3)	0.074(4)	0.096(5)	-0.013(4)	0.001(3)	-0.014(3)
C(9)	0.106(6)	0.040(3)	0.098(5)	0.029(3)	0.058(5)	0.011(4)
C(10)	0.049(3)	0.0348(23)	0.0283(20)	0.0046(18)	-0.0001(21)	0.0115(21)
S(1)	0.0243(4)	0.0335(5)	0.0264(4)	0.0014(5)	-0.0006(4)	-0.0001(5)
O(1S)	0.0439(19)	0.0446(18)	0.0436(17)	-0.0094(15)	0.0071(16)	0.0011(18)
O(2S)	0.0354(15)	0.0777(23)	0.0353(15)	-0.0058(18)	-0.0093(13)	0.0062(20)
O(3S)	0.0406(19)	0.0360(16)	0.0588(20)	0.0079(15)	0.0110(18)	-0.0051(16)
CA(1)	0.0237(5)	0.0229(5)	0.0300(5)	0.0000	-0.0039(4)	0.0000
O(1W)	0.0423(20)	0.0392(19)	0.0663(24)	-0.0179(18)	0.0094(20)	0.0026(19)
O(2W)	0.0391(21)	0.0352(17)	0.0728(25)	0.0118(19)	0.0123(20)	-0.0007(18)

Each part of the asymmetric unit has an image related by the two fold axis, so that there are two camphor-10-sulphonate molecules per calcium and four water molecules in this salt. There are electrostatic forces and hydrogen bonding to cause the salt to hold together. See section 6.4 for details.

5.5 Copper(II) Di-1S-4R-Camphor-10-Sulphonate Hexa-hydrate:

5.5.1. Crystal data:

$Cu^{2+}.2C_{10}H_{15}O_4S^-.6H_2O$, M_r = 634.1, monoclinic, $P2_1$, a =11.768(8), b = 7.070(4), c =17.181(9)Å, β = 93.95(5)°, V = 1479.54Å^3, Z = 2, D_c = 1.477gcm^{-3}, MoK_α, λ = 0.71069Å, μ = 9.34cm^{-1}, $F(000)$ = 668, T = 293K, final R = 0.037 for 1981 observed reflections F>4σ(F), final max δ/σ = 0.789. Final difference Fourier max = 0.29 min = -0.66 eÅ^{-3}.

5.5.2 Structure solution and refinement:

The details of the preparation and crystallisation of the copper salt are given in section 2.15, under code CSCU(ii) for the first crystal and CSCU3 for the second. The first crystal selected decayed during data collection, probably through loss of water. It was a thick, blue plate, mounted on a glass fibre and fixed using araldite. The second crystal for which diffraction data was collected was protectively covered in nail varnish with which it was also stuck to the glass fibre. It was an irregular fragment rendered more irregular by its coating. The overall dimensions were 0.8x0.7x0.5mm. There was no expectation that it could be aligned for photographs. The two crystal had identical structures.

Oscillation and Weissenberg photographs of the first crystal revealed that it was monoclinic, primitive and mounted about the unique axis. Data collection on a CAD-4 four-circle diffractometer revealed the systematically absent reflections which indicated that the space group was $P2_1$. The festoons of diffraction spots on the Weissenberg photographs alternated in intensity such that reflections for which h+k=2n were strong and h+k=2n+1 were weak. This intensity pattern became more accentuated at higher 2θ-values. This is consistent with the Cu atoms alone having a C-centred arrangement within the unit cell, their contribution to the scattering increasing with 2θ. That the second crystal had the same structure was shown by the identical unit cell and space group determined on the AED-2 diffractometer.

Structure solution was attempted using the first dataset despite the decay in intensities of standard reflections. From the pseudo C-centring, an approximate starting copper position was available, so it was not necessary to use a Patterson map. Equating the symmetry

operators for the 2_1 screw and C-centring gave the approximate position of a copper atom and operating either symmetry operations on it gave the second. The positions were x=0.25 or 0.75, any value of y, and z=0. These positions were compatible both with 2_1 screw and C-centring symmetry operations, both of which would have the same effect on an atom at these points. DIRDIF[30] phase refinement was carried out based on the first copper position and SHELX76[29] difference Fourier maps calculated. The data were sufficient only to determine that there were six water oxygen atoms associated with the copper ion, responsible for the blue colour and to obtain the positions of the sulphur atoms and some of the sulphonate oxygen atoms.

Using the second crystal, 2046 reflections were measured on an AED-2 four-circle diffractometer by a learnt profile method with $2\theta_{max}$ of 44.98°. There was negilible decay of the reflection intensities. A semi-empirical absorption correction was carried out, required because of the heavy, copper atom. 2021 data remained after merging, when the merging R-factor was very low at 0.0095. 1989 with F>4s(F) were used for structure solution and refinement. The position of the copper atom close to the expected "C-centred" position, as determined by the first, CAD-4, dataset, was input to DIRDIF phase refinement on the current, AED-2, dataset. The oxygen atoms of the hexaquo Cu^{2+} ion were located in the E-map, as were both sulphonate groups of the CSA molecules to which were attached the beginnings of the CSA cages. Further DIRDIF phase refinement, during which parts of the CSA cages were located, revealed that there was a pseudo mirror plane in one of the CSA molecules necessitating raising the space group to $P2_1/m$ and fixing atoms on the pseudo mirror plane for SHELX76 least squares refinement and analysis of difference maps until the remainder of the structure was located. The mirror plane

had y=0.25, hence the precise value of the copper y-coordinate, which was held fixed to determine the origin during refinement in the true space group of $P2_1$.

To ensure that both CSA molecules were given coordinates to repesent the same enantiomorph, one molecule was deleted to be found again in a difference map on the basis of the enantiomorph of the other. All alkyl hydrogen atoms were place in calculated positions, refining the positions of those on the meythl groups by roation as rigid groups. All twelve water molecules associated with the copper atom were located on difference maps. Anisotropic refinement was introduced in stages for all non-hydrogen atoms, beginning with the copper and the sulphur atoms, then the oxygen atoms and finally the carbon atoms after hydrogen atoms had been placed in calculated positions in the normal way. The weighting scheme applied was of the form $W^{-1} = \sigma^2(F) + 0.004738F^2$.

5.5.3 Results of Crystal Structure Determination:

Fractional coordinates of non-hydrogen atoms, six anisotropic thermal parameters for each and fractional coordinates of hydrogen atoms are listed in the following tables. Isotropic thermal parameters for all hydrogen atoms were fixed at 0.05Å. The asymmetric unit consists of one hexaquo copper ion and two 1-S-4-R-camphor-10-sulphonate ions, which are crystyallographically independent. Hydrogen atoms bound to carbon atoms were placed in ideal calculated positions. Esd's on fractional coordinates ranged from 0.00003 to 0.0009. The range of the values of principal anisotropic thermal parameters was 0.0276(5) to 0.127(4). There are electrostatic forces to cause the salt to hold together and hydrogen bonding. CSA molecules coordinate to the copper atom only via hydrogen bonds to the water molecules. See section 6.4 for details.

It was the structure determination which revealed the presence of the six molecules which coordinate to the copper ion. The bright blue colour of the crystal was consistent with familiar hydrated copper salts.

Figure 5.5 Copper(II) Camphor-10 Sulphonate

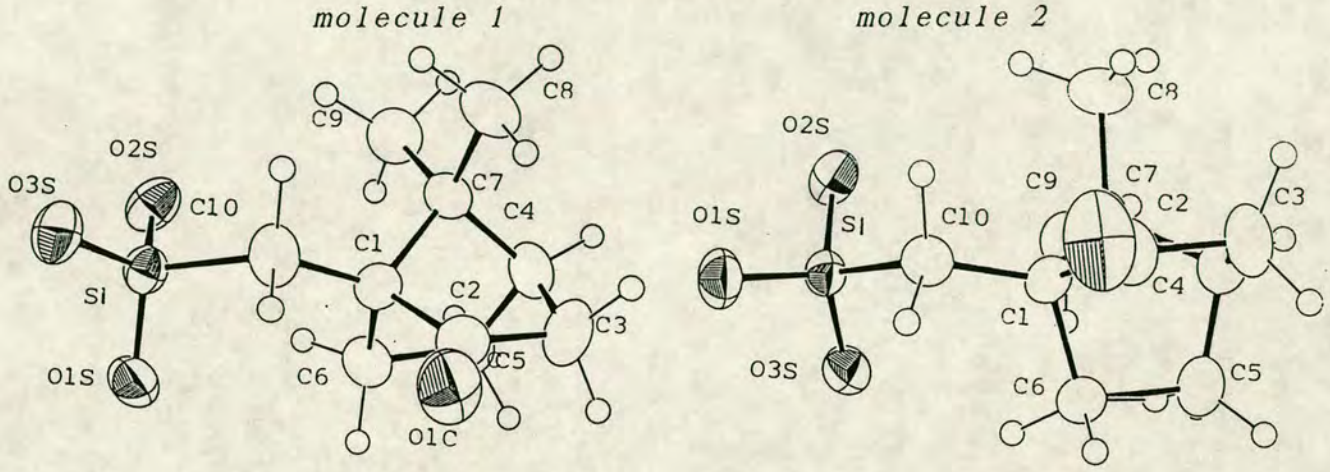


Table 5.5.1 Fractional coordinates with isotropic thermal parameters in Å² (U_{iso} for H fixed at 0.05Å²)

	x	y	z	U_{iso}
C(1)	0.5322(3)	0.2539(8)	0.29864(22)	0.0359(20)
C(2)	0.5327(4)	0.1300(7)	0.3717(3)	0.048(3)
O(1C)	0.4674(4)	0.0057(7)	0.38435(23)	0.0710(25)
C(3)	0.6332(5)	0.1951(9)	0.4253(3)	0.060(3)
C(4)	0.6810(4)	0.3597(9)	0.3787(3)	0.050(3)
C(5)	0.7403(3)	0.2642(9)	0.3122(3)	0.053(3)
C(6)	0.6382(4)	0.1870(7)	0.2576(3)	0.0447(24)
C(7)	0.5729(3)	0.4439(6)	0.33807(25)	0.0365(23)
C(8)	0.4894(4)	0.5245(8)	0.3945(4)	0.054(3)
C(9)	0.5955(5)	0.6015(8)	0.2800(3)	0.051(3)
C(10)	0.4156(3)	0.2463(9)	0.25419(22)	0.0422(22)
S(1)	0.40720(8)	0.24622(19)	0.15052(6)	0.0338(6)
O(1S)	0.28513(22)	0.2389(7)	0.12788(17)	0.0495(17)
O(2S)	0.4612(3)	0.4191(5)	0.12585(24)	0.0468(20)
O(3S)	0.4663(4)	0.0782(5)	0.12578(25)	0.0475(21)
C(1')	1.0074(3)	0.7447(7)	0.32497(21)	0.0321(19)
C(2')	0.9766(4)	0.8018(8)	0.4072(3)	0.051(3)
O(1C')	0.8817(3)	0.8322(8)	0.42645(20)	0.076(3)
C(3')	1.0869(4)	0.8087(9)	0.45803(24)	0.056(3)
C(4')	1.1742(4)	0.7495(9)	0.40088(24)	0.0447(23)
C(5')	1.1579(4)	0.5394(8)	0.3873(3)	0.051(3)
C(6')	1.0398(4)	0.5325(7)	0.3363(3)	0.0398(23)
C(7')	1.1264(3)	0.8396(7)	0.32242(24)	0.0363(21)
C(8')	1.1182(5)	1.0558(8)	0.3232(4)	0.060(3)
C(9')	1.1962(3)	0.7822(8)	0.25374(24)	0.0476(25)
C(10')	0.9062(3)	0.7862(6)	0.26766(23)	0.0356(21)
S(1')	0.91504(7)	0.75528(19)	0.16614(5)	0.0315(6)
O(1S')	0.79646(23)	0.7613(6)	0.13556(16)	0.0456(16)
O(2S')	0.9804(3)	0.9146(6)	0.13932(23)	0.0448(18)
O(3S')	0.9689(3)	0.5740(5)	0.15322(21)	0.0430(18)
CU(1)	0.75728(3)	0.2500	0.005780(20)	0.0324(4)
O(1W)	0.6696(3)	0.0346(6)	0.05157(24)	0.0470(21)
O(2W)	0.6652(4)	0.4791(7)	0.0584(3)	0.0597(25)
O(3W)	0.8688(3)	0.2441(6)	0.09698(23)	0.0638(22)
O(4W)	0.6452(3)	0.2505(6)	-0.08466(21)	0.0578(20)
O(5W)	0.8525(4)	0.0234(7)	-0.0481(3)	0.0579(24)
O(6W)	0.8456(3)	0.4704(6)	-0.04013(24)	0.0478(20)

	x	y	z
H(31)	0.6052	0.2440	0.4804
H(32)	0.6949	0.0833	0.4356
H(41)	0.7356	0.4554	0.4130
H(51)	0.7888	0.3664	0.2816
H(52)	0.7957	0.1510	0.3335
H(61)	0.6413	0.0345	0.2542
H(62)	0.6385	0.2459	0.1996
H(81)	0.4656	0.4107	0.4320
H(82)	0.4148	0.5739	0.3602
H(83)	0.5253	0.6394	0.4296
H(91)	0.6601	0.5505	0.2436
H(92)	0.6274	0.7235	0.3125
H(93)	0.5203	0.6409	0.2439
H(101)	0.3758	0.1168	0.27147
H(102)	0.3669	0.3657	0.27260
H(31')	1.1038	0.9493	0.48058
H(32')	1.0860	0.7099	0.50590
H(41')	1.2605	0.7880	0.41989
H(51')	1.2260	0.4813	0.3557
H(52')	1.1530	0.4643	0.4417
H(61')	0.9819	0.4642	0.3736
H(62')	1.1259	0.5190	0.3617
H(81')	1.0320	0.4668	0.2769
H(82')	1.0646	1.1062	0.3673
H(83')	1.0862	1.1083	0.2669
H(91')	1.1723	1.1080	0.34081
H(92')	1.2027	0.6303	0.24814
H(93')	1.2766	0.8383	0.27767
H(103)	0.8378	0.6964	0.28450
H(104)	0.8841	0.9325	0.27654
H(11W)	0.6079(23)	0.020(9)	0.065(3)
H(12W)	0.714(3)	-0.035(7)	0.072(3)
H(21W)	0.693(4)	0.566(6)	0.082(3)
H(22W)	0.607(3)	0.463(9)	0.077(3)
H(31W)	0.910(4)	0.158(5)	0.109(3)
H(32W)	0.883(4)	0.335(5)	0.122(3)
H(41W)	0.618(4)	0.342(5)	-0.105(3)
H(42W)	0.592(3)	0.183(6)	-0.088(3)
H(51W)	0.907(3)	0.025(9)	-0.0725(25)
H(52W)	0.814(4)	-0.060(6)	-0.066(3)
H(61W)	0.899(3)	0.444(9)	-0.064(3)
H(62W)	0.810(4)	0.536(7)	-0.070(3)

Table 5.5.2 Anisotropic thermal parameters in Å²

	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
C(1)	0.0366(19)	0.0365(21)	0.0345(19)	0.0023(23)	0.0050(16)	0.0028(22)
C(2)	0.065(3)	0.0379(24)	0.040(3)	0.0054(22)	0.0044(21)	-0.001(3)
O(1C)	0.095(3)	0.0626(23)	0.0553(24)	0.0136(19)	0.0034(20)	-0.0219(23)
C(3)	0.064(3)	0.069(3)	0.047(3)	0.0127(24)	-0.0121(23)	0.000(3)
C(4)	0.0425(23)	0.060(3)	0.0451(24)	-0.0141(24)	-0.0084(19)	-0.0012(25)
C(5)	0.0355(21)	0.064(3)	0.059(3)	-0.013(3)	-0.0094(18)	0.009(3)
C(6)	0.0394(22)	0.0488(25)	0.0458(23)	-0.0087(20)	0.0022(18)	0.0001(18)
C(7)	0.0326(20)	0.0347(23)	0.0422(23)	-0.0055(20)	0.0044(17)	-0.0026(18)
C(8)	0.056(3)	0.051(3)	0.057(3)	-0.0175(25)	0.0088(22)	-0.0018(23)
C(9)	0.050(3)	0.045(3)	0.058(3)	0.001(3)	0.0045(22)	-0.0113(24)
C(10)	0.0321(18)	0.059(3)	0.0358(20)	0.001(3)	0.0063(15)	-0.0110(25)
S(1)	0.0276(5)	0.0377(7)	0.0359(6)	0.0002(7)	-0.0016(4)	-0.0022(6)
O(1S)	0.0312(14)	0.0643(21)	0.0522(17)	0.0011(20)	-0.0064(12)	-0.0015(19)
O(2S)	0.0352(19)	0.0479(18)	0.0570(22)	0.0142(17)	0.0002(16)	-0.0015(15)
O(3S)	0.0433(21)	0.0458(20)	0.0525(23)	-0.0148(18)	-0.0046(17)	-0.0005(16)
C(1')	0.0304(18)	0.0342(20)	0.0318(19)	0.0064(22)	0.0046(14)	0.0002(21)
C(2')	0.052(3)	0.064(3)	0.0360(23)	-0.0060(22)	0.0094(21)	-0.0014(23)
O(1C')	0.0475(20)	0.127(4)	0.0533(20)	-0.0170(24)	0.0197(16)	0.0136(23)
C(3')	0.056(3)	0.078(4)	0.0329(21)	-0.0094(24)	-0.0048(18)	0.0018(24)
C(4')	0.0442(21)	0.0473(24)	0.0419(22)	-0.0013(25)	-0.0032(17)	0.008(3)
C(5')	0.048(3)	0.060(3)	0.045(3)	0.0089(24)	-0.0100(21)	-0.0038(24)
C(6')	0.0408(21)	0.0353(23)	0.0428(24)	0.0042(19)	-0.0013(18)	-0.0024(19)
C(7')	0.0320(21)	0.0408(21)	0.0357(20)	-0.0023(20)	-0.0023(16)	-0.0021(19)
C(8')	0.061(3)	0.036(3)	0.082(4)	0.006(3)	-0.003(3)	-0.016(3)
C(9')	0.0299(19)	0.060(3)	0.0526(24)	0.0036(24)	0.0090(18)	-0.0033(23)
C(10')	0.0309(18)	0.0379(24)	0.0384(20)	-0.0026(19)	0.0087(15)	0.0019(18)
S(1')	0.0286(5)	0.0338(6)	0.0317(5)	0.0001(6)	-0.0007(4)	0.0009(6)
O(1S')	0.0345(14)	0.0558(19)	0.0454(16)	0.0037(19)	-0.0096(11)	-0.0010(18)
O(2S')	0.0328(16)	0.0510(19)	0.0503(19)	0.0157(17)	0.0020(15)	-0.0026(15)
O(3S')	0.0467(19)	0.0393(18)	0.0422(18)	-0.0067(16)	-0.0029(15)	0.0014(15)
CU(1)	0.0332(4)	0.0304(4)	0.0334(4)	0.0002(3)	-0.00014(24)	-0.0009(3)
O(1W)	0.0436(21)	0.0497(22)	0.0476(21)	0.0104(18)	0.0072(16)	0.0081(18)
O(2W)	0.0488(22)	0.0636(25)	0.068(3)	-0.0205(22)	0.0218(19)	-0.0117(21)
O(3W)	0.0843(25)	0.0337(18)	0.0699(23)	-0.0048(23)	-0.0386(19)	0.0024(24)
O(4W)	0.0704(21)	0.0367(17)	0.0636(22)	0.0042(23)	-0.0280(17)	-0.0100(21)
O(5W)	0.0523(24)	0.059(3)	0.0631(24)	-0.0096(21)	0.0172(19)	-0.0168(21)
O(6W)	0.0383(19)	0.0558(22)	0.0496(20)	0.0094(18)	0.0090(16)	0.0081(17)

5.6 R-phenylglycinum 1S-4R-Camphor-10-sulphonate

5.6.1 Crystal data:

$C_8H_{10}NO_2^+.C_{10}H_{15}O_4S^-$, M_r = 383.4, orthorhombic, $P2_12_12_1$, a = 6.908(3), b = 15.245(6), c =17.514(6)Å, V = 1844.4Å^3, Z = 4, D_c = 1.381gcm^{-3}, CuK_α, λ = 1.5418Å, μ = 18.18cm^{-1}, $F(000)$ = 816, T = 293K, final R = 0.071 for 2331 observed reflections $F>4\sigma(F)$, final max δ/σ = 0.36. Final difference Fourier max = 0.96, min = -0.65 eÅ^{-3}.

5.6.2 Structure solution and refinement:

Section 2.14 records the method of crystal preparation under D-PHG/(+)-CSA. The method of crystal structure determination is found in chapter 2. NMR suggested the product was a 1:1 compound (see section 2.16). A 2mm equant chunk was cut up into smaller fragments to produce crystals small enough for structure determination. The crystal selected, a thin flake, 0.65x0.38mm at its longest and widest, was mounted in a Lindemann tube, which was sealed with beeswax, and fixed with araldite. An oscillation photograph confirmed that it was a single crystal too poorly aligned for cell and unit cell determination from photography. It was transfered to the STADI-4 four-circle diffractometer for data collection. The Laue group of this primitive unit cell was mmm. Of the two holoaxial possibilities $P2_12_12_1$ and $P2_12_12$, the former was shown to be the actual space group by absent reflections along row lines in the data collection output.

3129 data, with $2\theta_{max}$ = 119° were measured using Cu radiation employing $\omega/2\theta$-scans. Although the cell was orthorhombic and normally the minimum proportion of the data it would be required to collect is one eighth, a quarter were collected because of anomalous dispersion.

The ranges in h, k, and l were -7-7, 0-17 and 0-19, collected in two overlapping portions, 0-h in each direction. Two intensity standards,remeasured frequently throughout data collection, indicated that there was no significant decay of the crystal.

Psi scans were performed to determine an absorption correction. However, one of the reflections used had an exceptionally low intensity recorded at one position, probably because the goniometer head blocked the measurement. The transmission factors calculated were incorrect, but had only a small effect on the intensities of the dataset. Three very strong reflections required filters when they were collected. The filter factors applied were, erroneously, those for Mo radiation. These data were suppressed during refinement.

A calculated density within the expected range showed that the there was one ion-pair in the asymmetric unit of this four fold space group.

Out of 3129 data 105 were rejected because they were innaccessible and 49 because they had relative intensities that were negative or essentially zero. Merging equivalent reflections reduced the number to 2500 with a merging R-factor of 0.044. The reduction was so great because the data collection method meant that the 0kl zone was measured twice. Also, when a reflection was innaccessible because of restrictions on the diffractometer circle angles, its 'Friedel' was measured instead, provided that it was itself accessible. This was a feature of the diffractometer software. The alternative reflection was not strictly equivalent to the first in this non-centrosymmetric space group, but was, however, equivalent to a reflection in the other octant also measured. It was these equivalent reflections that were merged.

2331 observed data with $F>4\sigma(F)$ were used for structure solution and refinement, although 2289 reflections with $F>6\sigma(F)$ were used in the initial stages. The structure was solved using Patterson search techniques. Orthogonalised coordinates of the non-hydrogen atoms in the camphor-10-sulphonate molecule of the hydronium camphor-10-sulphonate salt, CSA, were input to the programs ORIENT and TRADIR in the DIRDIF[30] suite of programs and a similar molecule located in the unit cell of the phenylglycinium salt. All of the non-hydrogen atoms of the associated phenylglycinium molecule were located in the resulting Fourier map.

The R-factor after the first Fourier synthesis carried out by SHELX76[29] was 0.272, based on 2289 reflections with $F>6\sigma(F)$. Two cycles of least squares refinement reduced the R-factor to 0.182. Atomic separations confirmed that the acid function in the amino acid was undissociated. The variance of intensities in reflections with h=0 or 3, k=0, or 2 and l= 2,3,10 or 12 were all greater than 1000. Deviations/sigma for several reflections were large. Three of these were accounted for by incorrect filter factors. For the others, F_o was far in excess of F_c, probably on account of the large variances of reflections with indices in the categories mentioned above. A couple of reflections were apparently affected by secondary extinction. All of these were suppressed as they became apparent. The variances reduced accordingly when the worst reflections were omitted.

All non-hydrogen atoms were allowed to refine with six anisotropic thermal parameters. During refinement hydrogen atoms were placed in calculated positions to ride on their attached carbon atom in the normal way. Exceptions were ammonium, acid and methyl hydrogen atoms. It was hoped initially, to find them in difference maps.

However, methyl hydrogen atoms were eventually treated in the usual way, by refining rotational parameters for the methyl carbon atoms.

Refinement was continued and the three ammonium hydrogen atoms were located in difference maps. When the structure had converged, the following weighting scheme applied was $W^{-1} = \sigma^2(F) + 0.000146F^2$.

The highest peak in the difference map was, consistently, a peak near both the sulphur and one of the sulphonate oxygen atoms. The thermal parameters for this oxygen atom were large. A difference map was calculated with it excluded from the atom list in order to ascertain whether or not there was some disorder here. However, it appeared that there was genuinely only one position for the atom, which could be assigned. It was replaced and allowed to refine anistropically again.

After the final cycles of refinement, the R-factor was 0.071 and the weighted R-factor, 0.081. The maximum shift/esd in the final cycle was 0.36, for an ammonium proton coordinate, (although they were in general less than 0.1). The largest peak in the electron density map was 0.964 $eÅ^{-3}$ and the lowest trough, 0.652. The highest peak was near the sulphur and one of the sulphonate oxygen atoms and therefore associated with them.

5.6.3 Results of Crystal Structure Determination:

Fractional coordinates of non-hydrogen atoms, six anisotropic thermal parameters for each and fractional coordinates of hydrogen atoms are listed in the following tables. Isotropic thermal parameters for all hydrogen atoms were fixed at $0.05Å^2$. The asymmetric unit consists of one phenylglycinium ion and one 1-R-4-S-camphor-10-sulphonate ions. The three ammonium and single carboxylic

acid hydrogen atoms were located in difference maps and refined freely, with fixed isotropic thermal parameters of 0.05Å². Hydrogen atoms bound to carbon atoms were placed in ideal calculated positions, refining three rotational parameters for each methyl group. Esd's on fractional coordinates ranged from 0.00008 to 0.0010. The range of the values of principal anisotropic thermal parameters was 0.026(3) to 0.273(8)Å². They tended to be larger amongst atoms of the sulphonate group and indeed they were so large for O2S that possible disorder was investigated, It was not possible to resolve separate positions for this atom and it was retained as a single atom with large thermal parameters.

There are electrostatic forces and hydrogen bonding to cause the salt to hold together. See section 6.4 for details.

Figure 5.6 R-Phenylglycinium Camphor-10-sulphonate
phenylglycinium camphor-10-sulphonate

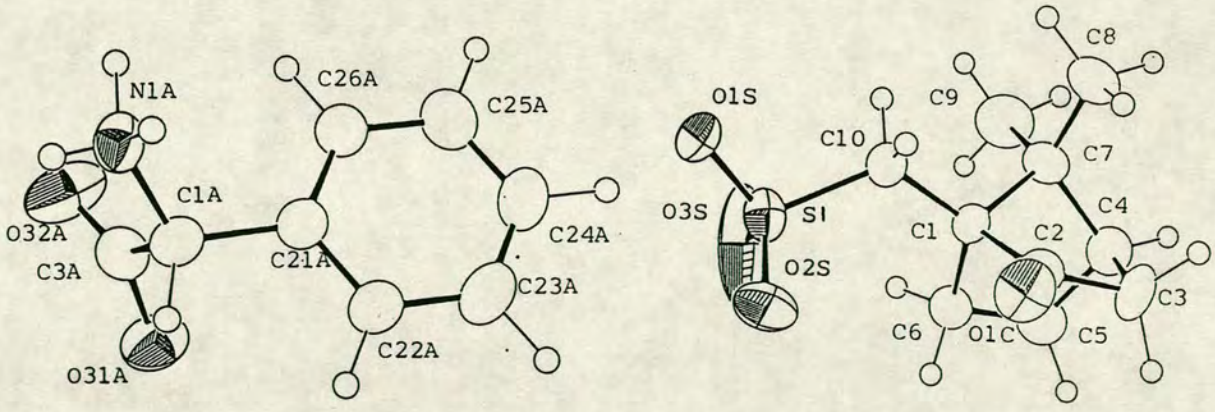


Table 5.6.1 Fractional coordinates with isotropic thermal parameters in Å² (U_{iso} for H fixed at 0.05Å²)

	x	y	z	U_{iso}
C(1)	-0.6096(7)	0.4684(3)	0.4769(3)	0.0295(25)
C(2)	-0.7006(8)	0.4172(4)	0.4114(3)	0.040(3)
O(1C)	-0.8711(5)	0.4155(3)	0.39391(24)	0.055(3)
C(3)	-0.5417(9)	0.3641(4)	0.3737(3)	0.049(3)
C(4)	-0.3659(8)	0.3886(4)	0.4226(3)	0.046(3)
C(5)	-0.3120(8)	0.4823(4)	0.4012(4)	0.050(3)
C(6)	-0.4802(8)	0.5365(3)	0.4343(3)	0.040(3)
C(7)	-0.4578(8)	0.3985(4)	0.5035(3)	0.040(3)
C(8)	-0.5525(10)	0.3161(4)	0.5357(4)	0.056(4)
C(9)	-0.3156(10)	0.4335(5)	0.5625(4)	0.060(4)
C(10)	-0.7518(10)	0.4991(4)	0.5374(3)	0.049(3)
S(1)	-0.83709(20)	0.60720(9)	0.53953(8)	0.0418(7)
O(1S)	-0.9676(7)	0.6111(3)	0.60360(22)	0.062(3)
O(2S)	-0.6763(7)	0.6658(4)	0.5420(5)	0.135(5)
O(3S)	-0.9385(9)	0.6225(3)	0.46849(25)	0.089(4)
C(1A)	-0.1048(8)	0.2531(3)	0.1696(3)	0.040(3)
N(1A)	-0.1873(8)	0.2897(3)	0.0977(3)	0.043(3)
C(3A)	-0.0634(9)	0.3309(4)	0.2222(3)	0.047(3)
O(31A)	0.0386(8)	0.3038(3)	0.2815(3)	0.063(3)
O(32A)	-0.1162(8)	0.4026(3)	0.2118(3)	0.082(3)
C(21A)	-0.2401(8)	0.1877(3)	0.2062(3)	0.036(3)
C(22A)	-0.1712(9)	0.1060(4)	0.2259(3)	0.044(3)
C(23A)	-0.2923(9)	0.0471(4)	0.2623(3)	0.049(4)
C(24A)	-0.4812(10)	0.0680(4)	0.2779(3)	0.049(4)
C(25A)	-0.5491(9)	0.1500(4)	0.2574(3)	0.050(4)
C(26A)	-0.4310(8)	0.2097(4)	0.2220(3)	0.043(3)

	x	y	z
H(31)	-0.5717	0.2947	0.3767
H(32)	-0.5220	0.3831	0.3147
H(41)	-0.2453	0.3439	0.4178
H(51)	-0.1753	0.5011	0.4263
H(52)	-0.3044	0.4896	0.3400
H(61)	-0.4264	0.5852	0.4737
H(62)	-0.5612	0.5684	0.3895
H(81)	-0.6646	0.2915	0.4984
H(82)	-0.6098	0.3237	0.5927
H(83)	-0.4331	0.2704	0.5368
H(91)	-0.2526	0.4971	0.5512
H(92)	-0.2017	0.3856	0.5691
H(93)	-0.4002	0.4366	0.6143
H(101)	-0.8779	0.4577	0.5318
H(102)	-0.6837	0.4872	0.5919
H(1A)	0.0263	0.2168	0.1582
H(1NA)	-0.108(9)	0.318(4)	0.076(3)
H(2NA)	-0.314(8)	0.338(4)	0.107(3)
H(3NA)	-0.216(10)	0.250(4)	0.072(3)
H(31A)	0.051(10)	0.343(4)	0.316(3)
H(22A)	-0.0235	0.0880	0.2131
H(23A)	-0.2376	-0.0167	0.2783

Table 5.6.2 Anisotropic thermal parameters in Å²

	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
C(1)	0.027(3)	0.0329(25)	0.0281(25)	-0.0014(21)	0.0014(23)	0.0018(21)
C(2)	0.042(3)	0.040(3)	0.037(3)	-0.0023(25)	-0.008(3)	-0.003(3)
O(1C)	0.0341(22)	0.071(3)	0.058(3)	-0.0081(23)	-0.0136(22)	-0.0044(21)
C(3)	0.054(4)	0.052(3)	0.043(3)	-0.020(3)	0.008(3)	0.003(3)
C(4)	0.036(3)	0.053(3)	0.048(3)	0.000(3)	0.001(3)	0.015(3)
C(5)	0.036(3)	0.055(4)	0.059(4)	0.008(3)	0.011(3)	0.001(3)
C(6)	0.044(3)	0.035(3)	0.041(3)	0.0022(24)	0.004(3)	-0.005(3)
C(7)	0.036(3)	0.043(3)	0.041(3)	0.007(3)	-0.007(3)	0.006(3)
C(8)	0.068(4)	0.042(3)	0.060(4)	0.012(3)	0.006(4)	0.000(3)
C(9)	0.046(4)	0.075(4)	0.059(4)	0.004(3)	-0.026(3)	-0.001(4)
C(10)	0.061(3)	0.043(3)	0.041(3)	0.005(3)	0.016(3)	0.019(3)
S(1)	0.0355(7)	0.0356(7)	0.0544(8)	-0.0064(6)	0.0053(7)	-0.0001(6)
O(1S)	0.080(3)	0.0563(24)	0.0499(24)	0.0039(21)	0.0319(24)	0.022(3)
O(2S)	0.049(3)	0.081(4)	0.273(8)	-0.102(5)	0.025(5)	-0.020(3)
O(3S)	0.126(5)	0.090(4)	0.050(3)	0.022(3)	-0.011(3)	0.053(4)
C(1A)	0.045(3)	0.033(3)	0.041(3)	-0.0006(24)	-0.008(3)	0.001(3)
N(1A)	0.055(3)	0.039(3)	0.036(3)	0.0003(21)	-0.005(3)	-0.012(3)
C(3A)	0.045(3)	0.046(3)	0.050(3)	-0.002(3)	-0.007(3)	-0.007(3)
O(31A)	0.075(3)	0.054(3)	0.060(3)	-0.0058(22)	-0.030(3)	-0.0013(25)
O(32A)	0.116(4)	0.0408(24)	0.089(3)	-0.0163(24)	-0.052(3)	0.011(3)
C(21A)	0.043(3)	0.040(3)	0.026(3)	-0.0020(24)	-0.004(3)	-0.001(3)
C(22A)	0.049(3)	0.038(3)	0.046(3)	0.000(3)	-0.005(3)	0.003(3)
C(23A)	0.074(5)	0.039(3)	0.035(3)	0.000(3)	-0.009(3)	0.001(3)
C(24A)	0.066(4)	0.045(3)	0.037(3)	0.003(3)	0.001(3)	-0.009(3)
C(25A)	0.051(4)	0.060(4)	0.040(3)	-0.005(3)	0.008(3)	-0.004(3)
C(26A)	0.044(3)	0.041(3)	0.044(3)	-0.003(3)	0.000(3)	0.002(3)

5.7 S-Methioninium 1S-4R-Camphor-10-sulphonate

5.7.1 Crystal data:

$C_5H_{12}NO_2S^+.C_{10}H_{15}O_4S^-$, M_r = 381.47, monoclinic, $P2_1$, a =11.933(5), b = 6.933(3), c =12.219(3)Å, β = 113.28(3)°, V = 928.6Å^3, Z = 2, D_c = 1.364gcm^{-3}, CuK_α, λ = 1.5418Å, μ = 28.12cm^{-1}, $F(000)$ = 408, T = 293K, final R = 0.066 for 1392 observed reflections F>4σ(F), final max δ/σ = 0.144. Final difference Fourier max=0.82 min=-0.64 eÅ^{-3}.

5.7.2 Structure solution and refinement:

The method of structure determination is discussed in chapter 2 and details of the preparation of crystals are given in section 2.14. An equant block of edge 0.6mm, crystallised from a gel, was mounted on a glass fibre and covered with araldite for protection. NMR was not carried out because of difficulties in separating the

small amount of crystals from the gel. Attempts to mount the crystal parallel to an extinction direction and to align it using oscillation photographs failed because it was so far from alignment. It was transfered to the AED-2 diffractometer where copper radiation was used to take a rotation photograph. In the time it took to measure the coordinates of ten spots, only four reflections were located in a systematic search. The crystal was large and strongly diffracting. Positions of reflections obtained from the two sources were combined to determine the cell dimensions and space group. The data collection output revealed systematic absences which showed that the space group was $P2_1$. After data collection the cell was redetermined using 24 reflections, which included 9 different reflections and some of their symmetry equivalent reflections. That the cell was different from either the unit cell of S-MET or of 1S-4R-CSA was indicative that the crystal contained a new salt. A density within the required range was calculated for two ion pairs in the unit cell, which is consistent with this two fold space group.

1423 reflections with $2\theta_{max} = 118.5°$ and $-13<h<13$, $0<k<7$ and $0<l<13$, were collected, making up a quarter of the available data. Two intensity standards measured frequently throughout the data collection verified that there was no crystal decay. 1417 unique data remained after merging, when the merging R-factor was 0.009. 1403 data with $F>6\sigma(F)$ were used for structure solution but during refinement the omit level was lowered to 4, and certain reflections omitted because of secondary extinction leaving 1392 reflections.

The structure was successfully solved using SHELX86[28] Patterson, finding the location of both of the sulphur atoms of the asymmetric unit. The advantage of SHELX86 Patterson over SHELX76[29] Patterson was that it

calculated a sharpened Patterson map in which vectors between heavier atoms were upweighted on the basis of their greater contribution to structure factors at higher values of 2θ. Vectors between sulphur atoms were upweighted relative to the others, in particular the sulphur-oxygen vectors, which made it easier to identify the four sulphur-sulphur vectors amongst the sulphur-oxygen vectors. An indicaton of the vector lengths were also given which further served to distinguish intra- and intermolecular interatomic vectors. In space group $P2_1$, symmetry related sulphur atoms in like molecules are separated by vectors of the form (2x,0.5,2y). The y-coordinates, y and y' must be 0.5 apart, by symmetry. Sulphur atoms in unlike molecules are separated by the vectors, $(x_1-x_2, y_1-y_2, z_1-z_2)$ and $(x_1+x_2, 0.5+y_1-y_2, z_1+z_2)$. It so happened that all of the v-components in the top section of the Patterson vector list were 0 or 0.5. Thus the y-coordinates of two non-symmetry related sulphur atoms, y_1 and y_2 in neighbouring molecules appear to be either 0 or 0.5. Since the Patterson map has mirror symmetry, the space group in the Patterson map is $P2_1/m$. There is therefore mirror plane passing through origin and one of the sulphur atoms in the asymmetric unit, y_1, will have y-coordinate of 0 and the other, y_2, therefore of 0.5. This also constitutes some pseudo-centring in the sulphur atom positions alone.

SHELX86[28] tangent expansion was carried out for the expansion of this partial structure. 200 reflections with large E-values were used and the two sulphur atom positions input were used in the calculation of an E-map after 2 cycles of peak list optimisation. The result is a difference Fourier map which represents the electron density. Sulphur atoms and peaks of electron density interpreted as point atoms were observed. The atoms which formed part of a CSA molecule were all on or near the plane with y=0, on which lay the sulphur atom. A psuedo

mirror plane may be identified in the CSA molecule with the following atoms in the plane, O1S, S1, C10, C1, C2, O1C, C3, C4, with C7 and C9 lying near the plane. The RMS deviation of atoms from the plane is 0.091, with C7 and C9 elevated out of the plane by a small amount, whereas the other atoms of that molecule are much farther out of the plane. The two remaining sulphonate oxygen atoms are mirrored in the plane. This also requires the other methyl carbon atom to be mirrored by the C5-C6 ethyl moiety. This conformation was later confirmed upon analysis of the torsion angles and is similar to the conformation of one of the CSA molecules in the copper salt.

The sulphonate group and some of the atoms near to the pseudo mirror plane in the camphor-10-sulphonate molecule were located in the map as well as the methionine molecule. Using these positions, a difference Fourier map was calculated by the program SHELX76. 14 reflections with $F<6\sigma(F)$ were suppressed to leave 1403. The R-factor was very high at 0.339. The remaining five carbon atoms of the CSA molecules were located readily in the map. There was electron density near the current atomic positions, on to which the atoms were expected to refine. With all non-hydrogen atoms located, two cycles of least squares refinement were carried out. The y-coordinate of the CSA sulphur atom was held still to fix an origin in this polar space group. Isotropic thermal parameters were refined to start with, beginning, as usual, at $0.05Å^2$. The value of the R-factor dropped sharply to 0.159.

All alkyl hydrogen atoms, including methyl groups, were placed in calculated positions and allowed to ride on the carbon atoms to which they were bonded, as they refined. Those on methyl groups were later refined as rigid groups in the normal way. The omit level was

changed to 4 at this stage, which only reduced the number of suppressed reflections to 10. Three possible ammonium protons were located which made a reasonably tetrahedral arrangment with the amino acid α-carbon atom. No position for the acid proton was discernable, although it was clear that the acid function must be undissociated. These atoms were not included in the atom list at this stage.

At this point in the refinement, deviations of individual observed and calculated structure factor amplitudes was meaningful. Six had deviation/sigma greater than 5 and were suppressed in the subsequent refinements. These reflections were all low angle data, of medium to strong intensity, with $F_o < F_c$. This suggests that they were affected by secondary extinction. As refinement progressed, more such reflections became apparent and were also omitted.

Rotational parameters for the three methyl groups were refined and subsequently every carbon atom was allowed to refine with six anisotropic thermal parameters.

Efforts were made to locate the ammonium and acid protons. A position for the acid protons was allowed to refine freely. The contribution of protons to the calculation of the difference map was upweighted. Two possible ammonium protons were located and the N-H bonds and the separations of the carbon and the two hydrogen atoms were constrained in the following refinement. The third ammonium proton was not located in the difference maps.

When the structure was near convergence, shift/esd remaining above 0.1, the weighting scheme applied was $W^{-1} = \sigma^2(F) + 0.000338F^2$.

The third ammonium proton was placed in an ideal position and refined constrained in the same manner as the original protons. The final few cycles of refinement reduced shift/esd values to mostly below 0.02, although the largest was 0.144, a methyl rotation parameter. The final difference Fourier contained a maximum peak of 0.82 and a minimum trough of 0.64. 1392 data were used, the R-factor was 0.066 and the weighted R-factor was 0.084.

In order to verify the hydrogen bonding proton postions, the molecular geometry near the acid and ammonium functional groups was analysed. Each was quite acceptable. See section 6.4. Angles subtended at the proposed hydrogen atoms by atoms between which they were expected to lie in hydrogen bonds, were not far from linear except in the case of one of the ammonium protons, H2NA. H2NA was probably involved in a bifurcated hydrogen bond to the MET acid carboxyl and the CSA carbonyl oxygen atoms. Indeed the midpoint of the two atoms fitted well into a tetrahedral arrangement of hydrogen bond acceptors around the ammonium group.

5.7.3 Results of Crystal Structure Determination:

Fractional coordinates of non-hydrogen atoms, six anisotropic thermal parameters for each and fractional coordinates of hydrogen atoms are listed in the following tables. Isotropic thermal parameters for all hydrogen atoms were fixed at 0.05Å^2. The asymmetric unit consists of one methioninium ion and one 1-S-4-R-camphor-10-sulphonate ion. Two of the three ammonium hydrogen atoms were located in difference maps and the third was placed in a calculated position and they were refined constrained to hold them in a tetrahedral arrangement. The single carboxylic acid hydrogen atom was located in a difference map and refined freely, with fixed isotropic thermal parameters of 0.05Å^2. Hydrogen atoms bound to

carbon atoms were placed in ideal calculated positions, refining three rotational parameters for each methyl group. Esd's on fractional coordinates ranged from 0.00011 to 0.0016. They tended to be larger in the y-coordinates. The range of the values of principal anisotropic thermal parameters was 0.020(3) to 0.169(8)Å². There are electrostatic forces and hydrogen bonding to cause the salt to hold together. See section 6.4 for details.

Figure 5.7 S-Methioninium 1S-4R-Camphor-10 Sulphonate

methioninium *camphor-10-sulphonate*

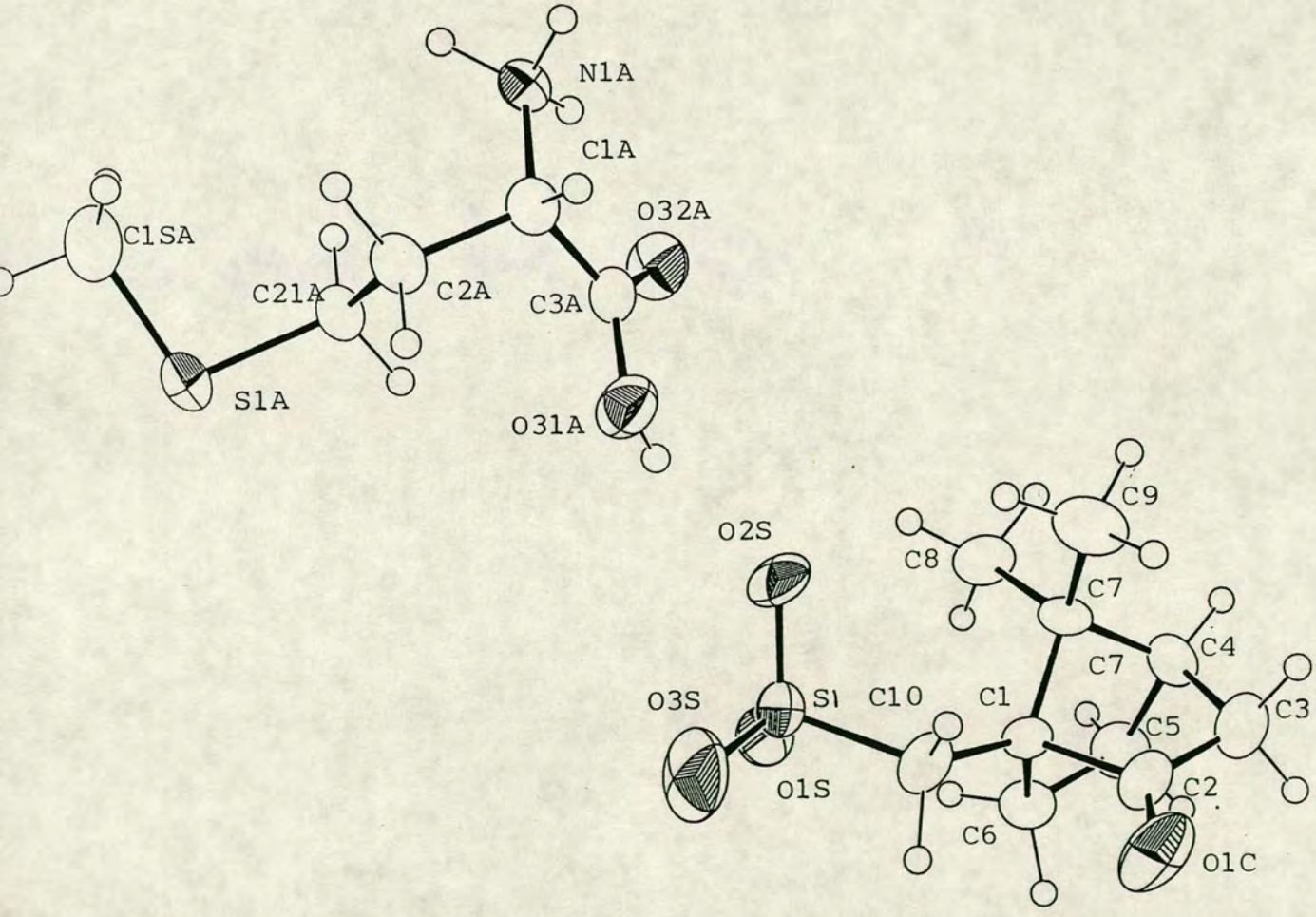


Table 5.7.1 Fractional coordinates with isotropic thermal parameters in Å² (U_{iso} for H fixed at 0.05Å²)

	x	y	z	U_{iso}
C(1)	0.8093(4)	0.0350(8)	0.4666(4)	0.027(3)
C(2)	0.8856(5)	-0.0015(12)	0.5992(4)	0.043(3)
O(1C)	0.9962(4)	-0.0108(12)	0.6443(4)	0.066(3)
C(3)	0.8008(5)	-0.0173(13)	0.6610(5)	0.055(4)
C(4)	0.6764(5)	0.0187(11)	0.5596(5)	0.044(3)
C(5)	0.6767(6)	0.2354(10)	0.5287(6)	0.050(4)
C(6)	0.7669(6)	0.2491(9)	0.4684(6)	0.042(4)
C(7)	0.6921(5)	-0.0802(8)	0.4524(5)	0.033(3)
C(8)	0.7129(8)	-0.2967(11)	0.4646(8)	0.066(5)
C(9)	0.5802(5)	-0.0434(12)	0.3363(5)	0.048(4)
C(10)	0.8860(4)	-0.0021(12)	0.3965(4)	0.040(3)
S(1)	0.82012(12)	0.0000	0.23802(11)	0.0429(9)
O(1S)	0.9219(5)	0.0087(16)	0.2040(5)	0.111(5)
O(2S)	0.7493(5)	-0.1789(7)	0.1992(4)	0.057(3)
O(3S)	0.7431(5)	0.1708(8)	0.1982(4)	0.055(3)
C(1A)	0.2038(4)	-0.0387(10)	0.0142(4)	0.032(3)
N(1A)	0.1729(4)	-0.0126(8)	-0.1163(4)	0.0346(25)
C(3A)	0.0911(5)	-0.0084(10)	0.0368(5)	0.038(3)
O(31A)	0.1112(3)	-0.0318(9)	0.1491(3)	0.052(3)
O(32A)	-0.0074(3)	0.0292(8)	-0.0410(3)	0.050(3)
C(2A)	0.3093(4)	0.0941(10)	0.0909(5)	0.035(3)
C(21A)	0.2720(5)	0.3053(10)	0.0838(5)	0.035(3)
S(1A)	0.39348(13)	0.4646(4)	0.17512(13)	0.0519(11)
C(1SA)	0.4872(6)	0.4712(14)	0.0915(7)	0.065(5)

	x	y	z
H(31)	0.8050	-0.1589	0.6992
H(32)	0.8207	0.0905	0.7299
H(41)	0.5993	-0.0257	0.5788
H(51)	0.7068	0.3225	0.6084
H(52)	0.5869	0.2813	0.4688
H(61)	0.7228	0.3049	0.3789
H(62)	0.8433	0.3402	0.5189
H(81)	0.7896	-0.3440	0.5428
H(82)	0.7222	-0.3510	0.3858
H(83)	0.6294	-0.3508	0.4678
H(91)	0.5640	0.1090	0.3188
H(92)	0.5081	-0.1043	0.3578
H(93)	0.5819	-0.1140	0.2581
H(101)	0.9569	0.1061	0.4237
H(102)	0.9264	-0.1429	0.4229
H(1A)	0.2363	-0.1839	0.0401
H(1NA)	0.200(6)	-0.153(4)	-0.136(5)
H(2NA)	0.0799(23)	0.038(10)	-0.149(5)
H(3NA)	0.220(5)	0.083(7)	-0.153(5)
H(31A)	0.059(6)	0.002(13)	0.168(6)
H(21A)	0.3826	0.0810	0.0607
H(22A)	0.3407	0.0479	0.1826
H(23A)	0.2420	0.3515	-0.0077
H(24A)	0.1974	0.3174	0.1124
H(1SA)	0.5569	0.5740	0.1409
H(2SA)	0.4372	0.5248	0.0024
H(3SA)	0.5293	0.3352	0.0872

Table 5.7.2 Anisotropic thermal parameters in Å²

	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
C(1)	0.0233(21)	0.020(3)	0.0305(24)	0.0003(21)	0.0048(19)	0.0033(21)
C(2)	0.045(3)	0.042(4)	0.028(3)	0.004(3)	0.0011(23)	0.006(3)
O(1C)	0.0355(21)	0.099(5)	0.0450(23)	-0.007(4)	-0.0080(17)	0.015(3)
C(3)	0.059(3)	0.059(5)	0.035(3)	0.002(4)	0.012(3)	0.002(4)
C(4)	0.038(3)	0.046(4)	0.040(3)	0.011(3)	0.0141(23)	-0.002(3)
C(5)	0.050(3)	0.036(4)	0.057(4)	-0.005(3)	0.029(3)	0.009(3)
C(6)	0.046(3)	0.022(3)	0.049(3)	-0.004(3)	0.021(3)	0.0025(25)
C(7)	0.031(3)	0.019(3)	0.040(3)	0.0015(23)	0.0102(23)	-0.0033(22)
C(8)	0.080(5)	0.026(4)	0.074(5)	0.011(4)	0.022(4)	-0.004(3)
C(9)	0.029(3)	0.051(4)	0.051(3)	-0.002(3)	0.0042(24)	-0.004(3)
C(10)	0.0292(24)	0.050(4)	0.0303(25)	-0.003(3)	0.0034(20)	0.012(3)
S(1)	0.0442(8)	0.0443(9)	0.0356(7)	-0.0047(7)	0.0214(6)	-0.0019(7)
O(1S)	0.083(3)	0.169(8)	0.080(3)	-0.032(6)	0.062(3)	-0.015(6)
O(2S)	0.079(3)	0.0316(23)	0.048(3)	-0.0179(21)	0.023(3)	-0.0108(24)
O(3S)	0.072(3)	0.0362(24)	0.042(3)	0.0151(21)	0.0135(24)	0.0018(24)
C(1A)	0.0297(23)	0.028(3)	0.0319(24)	0.0042(25)	0.0079(19)	0.0036(23)
N(1A)	0.0344(21)	0.032(3)	0.0294(20)	-0.0022(23)	0.0080(17)	-0.0004(22)
C(3A)	0.038(3)	0.032(3)	0.038(3)	-0.001(3)	0.0158(22)	-0.008(3)
O(31A)	0 0370(20)	0.067(3)	0.0452(22)	0.0033(25)	0.0192(18)	-0.0054(23)
O(32A)	0.0255(17)	0.066(3)	0.0483(23)	0.0049(24)	0.0057(18)	0.0026(22)
C(2A)	0 0249(25)	0.035(3)	0.036(3)	-0.002(3)	0.0037(21)	0.0043(24)
C(21A)	0.028(3)	0.031(3)	0.039(3)	-0.006(3)	0.0098(22)	-0.0016(24)
S(1A)	0.0484(9)	0.0503(12)	0.0484(9)	-0.0203(8)	0.0199(7)	-0.0192(8)
C(1SA)	0.049(3)	0.063(5)	0.071(4)	-0.009(5)	0.023(3)	-0.014(4)

5.8 S-Methioninium (1R)-(4S)-Camphor-10-sulphonate

5.8.1 Crystal data:

$C_5H_{12}NO_2S^+.C_{10}H_{15}O_4S^-$, M_r = 381.47, monoclinic, $P2_1$, a =14.035(10), b = 10.342(5), c = 6.593(3)Å, β = 90.36(12)°, V = 957.0Å³, Z = 2, D_c = 1.324gcm^{-3}, MoK_α, λ = 0.71069Å, μ = 2.93cm^{-1}, $F(000)$ = 408, T = 293K, final R = 0.037 for 1805 observed reflections F>4σ(F), final max δ/σ = 0.41. Final difference Fourier max=0.23 min= -0.36 eÅ^{-3}.

5.8.2 Structure solution and refinement:

A description of the method of crystal preparation is given in section 2.14, under L-MET/(-)-CSA and the method of structure solution and refinement in chapter 2.

Crystals grew from a gel which formed in the container. They were large rectangular blocks, fragments of which were mounted on glass fibres. Despite difficulties in separating crystals from the gel, NMR was carried out, and suggested that they contained a 1:1

compound (see section 2.16). The first crystal was shown to be non-single, possibly being a aggregate of four crystalites. Diffraction spots on a zero layer Weissenberg film were divided into four, and spots on an oscillation photograph were doubled, particularly at higher 2θ angles. Photographs of a second crystal, an almost equant, but irregularly shaped, block, showed that it was single. The diffraction spots were extended widely along the Weissenberg photographs in the direction of translation during exposure, which was indicative of disorder.

The space group was determined from oscillation and Weissenberg photographs and could be narrowed down to either P2 or $P2_1$. The systematic absences along the row line 0k0, which indicate that there is a two fold screw along the, unique, mounting axis, became apparent when the crystal was set up for data collection on the STADI-2 diffractometer. A refined unit cell was obtained from manual measurement of the 020 and 040 reflections and by the least squares refinement method on the basis of 13 strong reflections located during an automated reflection search.

1913 data were collected on a STADI-2 two circle diffractometer using MoK_α radiation by the ω-scan technique. $2\theta_{max}$ was 50° and h,k and l were in the ranges $-17 \leq h \leq 17$, $0 \leq k \leq 11$, and $0 \leq l \leq 8$ and a quarter of the data were collected. An uneven background correction was carried out on 654 reflections during data reduction, to counteract the effect of the very wide diffracted beams. 1893 data remained after merging of equivalent reflections, when the merging R-factor was 0.004. Of these 1778, with F>6sigma(F), were used in the initial stages of structure determination.

The structure was solved by SHELX86[28] direct methods. The solution with the lowest combined figure of merit, automatically selected by the program gave a satisfactory arrangement of atoms in the E-map after one cycle of peak list optimisation. Many other "solutions", with figure of merits only a little higher than the automatically selected solution were observed. The list of semi-invariants for many of these showed that they were effectively the same as the one selected. Every non-hydrogen atom apart from the CSA C3, C5 and the MET terminal methyl carbon atom were located and input to the next stage. There was a quite strong peak of electron density not far, 1.06Å, from the MET sulphur atom. The possibility existed that it represented a severely librationally shortened sulphur to carbon bond, due to two, or more, disordered positions of the terminal methyl group. The alternative was that it may have represented a second, disordered, sulphur position, because it was a strong peak, although it was not bound to the atom C21A. The peak height was a little under a half that of the sulphur atom of the CSA molecules. Disorder was expected on the basis of photographs. The peak was simply ignored at this stage.

A SHELX76[29] difference map was plotted. The R-factor was 0.288, on the basis of 1778 reflections with $F>6\sigma(F)$. There were peaks in the electron density map near the current atom positions and the two remaining CSA carbon atoms were located. With these atoms added, two cycles of least squares refinement were carried out refining positions and isotropic thermal parameters for each atom, apart from the y-coordinate of the sulphur atom in the CSA molecule. which was not allowed to refine in order to provide a reference point for the refinement of other y-coordinates in this holoaxial space group. The R-factor reduced satisfactorily to 0.164. The thermal parameter of the MET sulphur atom was noticeably larger than other

atoms, a result of the as yet unidentified carbon atom bonded to it and possibly also to disorder in the region. There was a large peak in the electron density of 4.5 eÅ^{-3} very near to the MET sulphur atom. It was possible that this represented a disordered position for this sulphur atom, particularly since a feasible position for the methyl carbon atom bound to it was also located. Most peaks amounted to no more than 1.5 eÅ^{-3}. The separation between C21A and the apparent sulphur was rather large, but might be accounted by the fact that the structure was, as yet, far from convergence. Only the position for the methyl carbon atom, C1SA, bonded to the current sulphur atom was added to the atom list at this stage. The configuration of the molecules was the same as the absolute configurations. The omit level was changed to 4, which raised the number of 'observed reflections to 1810.

The R-factor, even after a couple of cycles of refinement rose slightly to 0.179 and there were noticeable deviation/sigma values for several reflections. These were not omitted because of the still poor model.

All hydrogen atoms on the carbon skeleton of the model were placed in calculated positions and treated in the usual way. This included the hydrogen atoms of the CSA methyl groups, but not those of the terminal methyl group of the MET molecule. Refinement reduced the R-factor to 0.160, but the isotropic thermal parameters in the region of the disorder were very large. All non-hydrogen atoms were next allowed to refine with six anisotropic thermal parameters and the R-factor fell to 0.089. C21A, and S1A had large thermal parameters, C1SA became non-positive definite.

In order to identify the arrangement of the disordered atoms and their frequency, only the current sulphur and terminal atoms of the MET molecule were

allowed to refine. The position and site occupancy were refined while keeping thermal parameters fixed. They were fixed originally at values near to the average of the anisotropic thermal parameters they were assigned previously. Using a series of such refinements and difference maps, two MET side chains were identified, diverging at the C21A carbon atom, each with a sulphur and a methyl carbon atom. With U_{iso} fixed at 0.1Å² for all four refining atoms, free refinement of the site occupancies, beginning at half occupancies led to the identification of a major and a minor chain. The terminal methyl carbon atom of the latter, C1SA, had a low site occupancy which was consistent with further disorder or thermal motion. The site occcupancies of the two pairs of atoms forming the two disordered chains were refined again, but with site occupancy kept the same within a chain and the sum of the chain site occupancy fixed at unity. The ratio of the first chain, labelled with a suffix, A, to the second, labelled with a suffix, B, was approximately 40:60. With the site occupancies fixed at the new values, isotropic thermal parameters for each of these four atoms were refined, while continuing to refine their positions, and keeping the remainder of the atoms entirely unrefined. The R-factor after refinement was 0.079 and the minor methyl group had a large, but not excessive, thermal parameter of 0.096Å². When these four atoms were allowed to refine with six anisotropic thermal parameters, the R-factor fell to 0.057. One of the thermal parameters of the less well defined carbon atom was very large, at 0.37Å².

Attempts were made to place hydrogen atoms in feasible places while refining the entire structure. Three possible ammonium protons, located in a difference map before the structure was fixed to analyse the disorder, were added to the atom list and refined freely with fixed isotropic thermal parameters of 0.05Å². A carboxy-

lic acid proton was located in a difference map and refined similarly. Assignment of protons in the disordered region was eventually abandoned. The site occupancy of the disordered atoms was mostly kept constant and restrained, as before, although it was redetermined, but remained about 40:60. The thermal parameters of the terminal methyl groups were eventually refined with only isotropic thermal parameters because the anisotropic thermal parameters were quite large and no real hydrogen atoms could be placed.

The weighting scheme applied was $W^{-1} = \sigma^2(F) + 0.000334F^2$. The final R-factor was 0.037, with a weighted R-factor of 0.047, based on 1805 reflections with $F>\sigma(F)$ and 243 refining parameters. A few reflections, probably affected by secondary extinction, were specifically omitted. The largest value of the shift/esd in the final cycle of least squares refinement was 0.41, for a CSA methyl carbon atom rotational parameter, although they were mostly less than 0.05.

5.8.3 Results of Crystal Structure Determination:

Fractional coordinates of non-hydrogen atoms, six anisotropic thermal parameters for most, one isotropic thermal parameter for terminal methyl groups on the methionine molecule and fractional coordinates of hydrogen atoms are listed in the following tables. Isotropic thermal parameters for all hydrogen atoms were fixed at 0.05Å. The asymmetric unit consists of one methioninium ion and one 1-R-4-S-camphor-10-sulphonate ions. There was a two-fold disorder in the sulphur atom and terminal methyl group in the methionine molecule. Hydrogen atoms on the terminal methyl group and the γ-methylene group were not included because of the disorder. The three ammonium and single carboxylic acid hydrogen atoms were located in difference maps and refined freely, with fixed

isotropic thermal parameters of 0.05Å². Hydrogen atoms bound to carbon atoms were placed in ideal calculated positions, refining three rotational parameters for each methyl group. Esd's on fractional coordinates ranged from 0.00005 to 0.007. They tended to be larger on refined hydrogen atoms, of course. The range of the values of principal anisotropic thermal parameters was 0.0211(4) to 0.116(4)Å², the larger ones being in the methionine side chain, particularly on C2A and the disordered atoms. The sulphonate group, the ammonium group and the carboxylic acid group, in the region fixed by hydrogen bonding, tended to have smaller thermal parameters.

There are electrostatic forces and hydrogen bonding to cause the salt to hold together. See section 6.4 for details.

Figure 5.7 S-Methioninium (1R)(4S)Camphor-10 Sulphonate

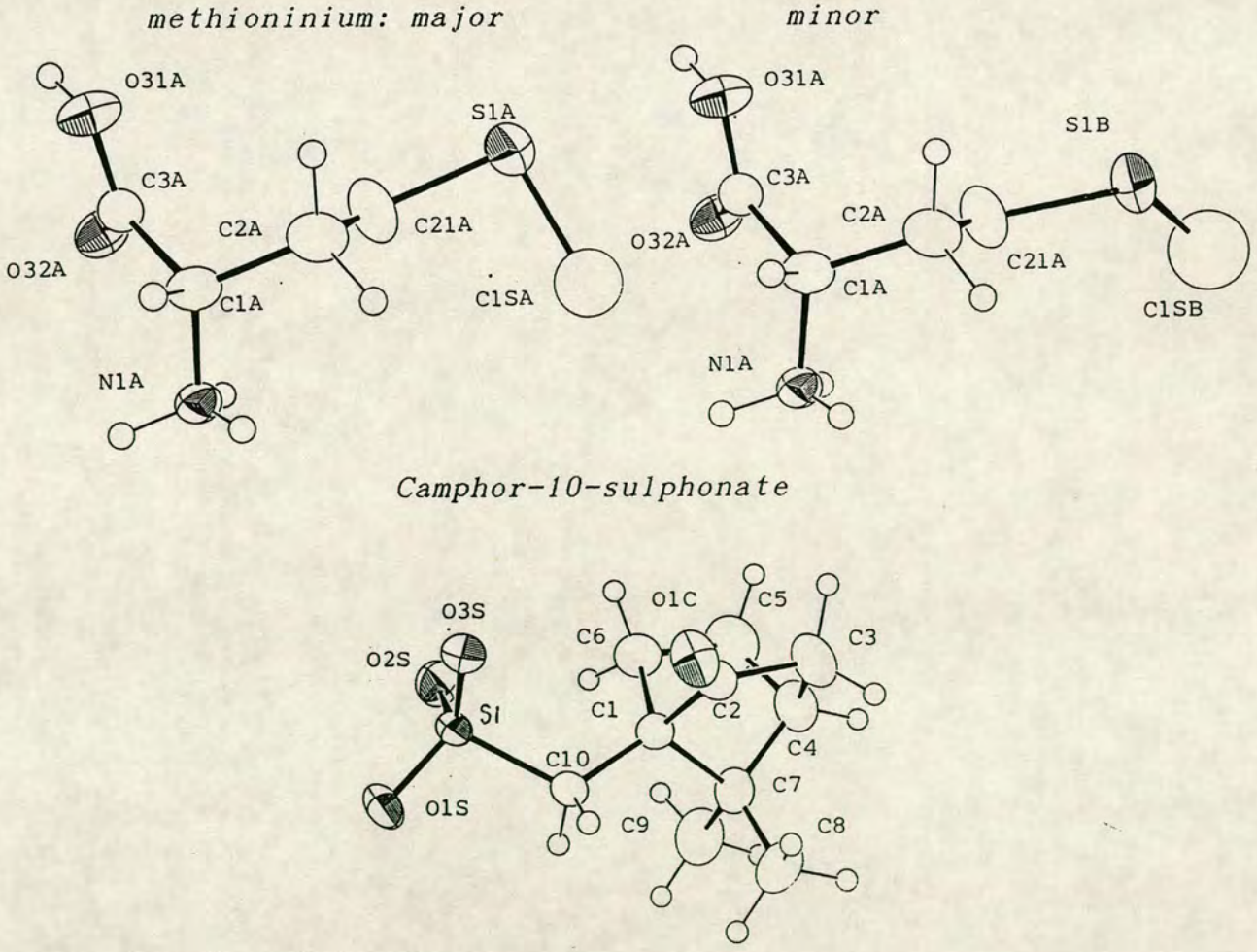


Table 5.8.1 Fractional coordinates with isotropic thermal parameters in Å² (U_{iso} for H fixed at 0.05Å²)

	x	y	z	U_{iso}
C(1)	0.29382(22)	0.5185(3)	0.2094(5)	0.0307(15)
C(2)	0.27343(22)	0.4173(4)	0.0493(5)	0.0351(17)
O(1C)	0.19905(17)	0.4010(3)	-0.0443(4)	0.0461(14)
C(3)	0.3651(3)	0.3415(4)	0.0149(7)	0.0537(24)
C(4)	0.43406(25)	0.4112(4)	0.1610(7)	0.0500(23)
C(5)	0.4075(3)	0.3694(5)	0.3770(8)	0.064(3)
C(6)	0.31016(25)	0.4380(4)	0.4091(5)	0.0436(19)
C(7)	0.39976(22)	0.5533(4)	0.1502(6)	0.0405(20)
C(8)	0.4071(3)	0.6147(6)	-0.0575(6)	0.0592(24)
C(9)	0.4494(3)	0.6425(5)	0.3054(8)	0.062(3)
C(10)	0.22568(21)	0.6333(3)	0.2148(5)	0.0322(15)
S(1)	0.11879(5)	0.62010	0.35925(11)	0.0298(4)
O(1S)	0.07416(18)	0.7470(3)	0.3432(4)	0.0413(13)
O(2S)	0.06068(17)	0.5169(3)	0.2647(4)	0.0382(13)
O(3S)	0.14620(18)	0.5850(3)	0.5644(4)	0.0449(14)
C(1A)	0.06720(23)	1.0539(3)	0.2458(6)	0.0344(18)
N(1A)	-0.01325(20)	0.9753(3)	0.1636(5)	0.0311(15)
C(3A)	0.04116(23)	1.1970(3)	0.2225(5)	0.0310(17)
O(31A)	0.09802(18)	1.2698(3)	0.3337(4)	0.0432(14)
O(32A)	-0.02055(17)	1.23583(24)	0.1105(4)	0.0394(13)
C(2A)	0.1614(3)	1.0225(4)	0.1410(9)	0.0601(25)
C(21A)	0.1639(3)	1.0627(7)	-0.0821(9)	0.082(4)
S(1A)	0.29083(19)	0.9840(4)	-0.1134(6)	0.0590(18)
S(1B)	0.26906(16)	1.03716(25)	-0.2335(4)	0.0668(14)
C(1SA)	0.2750(13)	0.9212(23)	-0.364(3)	0.104(5)
C(1SB)	0.2424(6)	0.8691(10)	-0.3069(15)	0.0687(22)

	x	y	z
H(31)	0.3567	0.2407	0.0542
H(32)	0.3886	0.3492	-0.1403
H(4)	0.5081	0.3935	0.1275
H(51)	0.4002	0.2657	0.3879
H(52)	0.4598	0.4023	0.4862
H(61)	0.2538	0.3680	0.4284
H(62)	0.3130	0.5009	0.5398
H(81)	0.3581	0.5728	-0.1659
H(82)	0.4794	0.5965	-0.1052
H(83)	0.3952	0.7177	-0.0485
H(91)	0.4381	0.6149	0.4614
H(92)	0.4247	0.7404	0.2823
H(93)	0.5244	0.6368	0.2711
H(101)	0.2650	0.7146	0.2749
H(102)	0.2048	0.6532	0.0600
H(1A)	0.0775	1.0312	0.4043
H(1NA)	0.011(3)	0.913(4)	0.171(6)
H(2NA)	-0.071(3)	0.991(5)	0.240(7)
H(3NA)	-0.028(3)	0.999(3)	0.029(5)
H(31A)	0.079(3)	1.352(5)	0.310(7)
H(21A)	0.2180	1.0723	0.2205
H(22A)	0.1730	0.9194	0.1501

Table 5.8.2 Anisotropic thermal parameters in Å²

	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
C(1)	0.031(1)	0.028(1)	0.034(2)	0.001(1)	0.002(1)	-0.001(1)
C(2)	0.035(2)	0.031(2)	0.040(2)	-0.002(1)	0.002(1)	0.001(1)
O(1C)	0.038(1)	0.050(2)	0.050(1)	-0.014(1)	-0.008(1)	0.005(1)
C(3)	0.041(2)	0.045(2)	0.076(3)	-0.016(2)	0.000(2)	0.006(2)
C(4)	0.031(2)	0.051(2)	0.068(3)	-0.007(2)	-0.001(2)	0.007(2)
C(5)	0.050(2)	0.068(3)	0.075(3)	0.014(2)	-0.013(2)	0.021(2)
C(6)	0.043(2)	0.044(2)	0.044(2)	0.010(2)	-0.006(2)	0.005(2)
C(7)	0.028(2)	0.044(2)	0.049(2)	-0.009(2)	0.004(1)	-0.004(2)
C(8)	0.056(2)	0.063(3)	0.059(2)	-0.007(3)	0.021(2)	-0.016(2)
C(9)	0.042(2)	0.070(3)	0.074(3)	-0.022(3)	0.003(2)	-0.017(2)
C(10)	0.037(2)	0.024(2)	0.036(2)	0.000(2)	0.008(1)	0.001(1)
S(1)	0.0373(4)	0.0211(4)	0.0311(4)	-0.0007(4)	0.0067(3)	0.0020(3)
O(1S)	0.048(1)	0.029(1)	0.047(1)	-0.004(1)	0.006(1)	0.011(1)
O(2S)	0.041(1)	0.029(1)	0.044(1)	-0.001(1)	0.006(1)	-0.003(1)
O(3S)	0.056(1)	0.047(2)	0.032(1)	0.003(1)	0.009(1)	0.007(1)
C(1A)	0.031(2)	0.025(2)	0.048(2)	0.003(2)	-0.004(1)	-0.001(1)
N(1A)	0.029(1)	0.021(1)	0.043(2)	0.001(1)	0.002(1)	0.001(1)
C(3A)	0.034(2)	0.024(2)	0.035(2)	0.003(1)	0.006(2)	-0.001(1)
O(31A)	0.050(2)	0.028(1)	0.052(2)	-0.002(1)	-0.008(1)	-0.009(1)
O(32A)	0.047(1)	0.025(1)	0.046(1)	0.003(1)	-0.006(1)	0.004(1)
C(2A)	0.031(2)	0.034(2)	0.116(4)	-0.005(2)	0.006(2)	0.001(2)
C(21A)	0.049(2)	0.102(4)	0.097(4)	-0.047(4)	0.036(3)	-0.018(3)

5.9 S-Valinium (1R)-(4S)-Camphor-10-sulphonate

5.9.1 Crystal data:

$C_5H_{12}NO_2^+.C_{10}H_{15}O_4S^-$ M=349.5, monoclinic, $P2_1$, a = 11.793(4), b = 7.009(3), c = 11.833(3)Å, β = 108.07(3)°, V = 929.84Å^3, Z = 2, D_c = 1.248 gcm^{-3}, MoK$_\alpha$, λ = 0.71069Å, μ = 1.60gcm-1, $F(000)$ = 376, T = 293K, final R,R_w = 0.0464, 0.0505 for 1375 observed reflections $F>4\sigma(F)$, final max δ/σ = 0.125. Final difference Fourier max=-0.17, min=-0.32 eÅ^{-3}.

5.9.2 Structure solution and refinement:

Details of the cocrystallisation are found in section 2.14, under the code L-VAL/(-)-CSA1 and the method of structure solution and refinement is described in chapter 2.

A number of elongated plates, basically rectangular in shape, grew on the surface of a gel. They extinguished sharply and there were striations prallel to the plates,

when observed through crossed polars. Difficulties in separating the small amount of crystals from the gel prevented NMR from being carried out. One plate, rectangular except that it had one slant, short edge, of dimensions, 0.85x0.3x0.05mm, was mounted in a Lindemann tube along the long axis, parallel to an extinction direction, which turned out to be the unique monoclinic axis.

Oscillation and Weissenberg photographs gave approximate cell dimensions and suggested that the space group was $P2_1$. The crystal was transfered to the STADI-2 diffractometer, where the space group as signment was confirmed and the cell dimensions were refined using the automatic method. 1716 data were collected, using ω-scans and molybdenum radiation, with a $2\theta_{max}$ of 28.4 and $-14 \leq h \leq 14$, $0 \leq k \leq 8$ and $0 \leq l \leq 14$. 1642 data remained after merging, when the merging R-factor was 0.0065. Various reflections were employed as intensity standard and showed negligible decay. 1375 data with F>4sig(F) were used for structure determination. The number of VAL and CSA ion pairs in the unit cell was determined from the calculated density. A density within the expected range was found for two ion pairs. The structure was solved by SHELX86[28] direct methods, when all non-hydrogen atoms were located. There was a peak bridging the ammonium and sulphonate groups, which might have represented a water molecule, but it was quickly discounted. The first R-factor was 0.257. The structure was refined using SHELX76[29] least squares. The enantimorph was checked by inspection and it was observed that the program had selected the opposite enatiomorph. The coordinates were inverted before refinement was continued. There was essentially no difference between the R-factors of the original and the inverted coordinates, because anomalous dispersion is not significant with the Mo radiation.

All hydrogen atoms bonded to carbon atoms were then placed in ideal positions and allowed to ride on their attached carbon atoms. Rotational parameters for the two methyl groups on the CSA molecules and the two VAL methyl groups, were later refined.

Peaks representing the three ammonium and the single carboxylic acid hydrogen atoms were located in difference maps. All non-hydrogen atoms were first refined with three positional and one isotropic thermal parameters, except the sulphur atom in CSA whose y-coordinate was kept constant to fix the origin. They were subsequently refined anisotropically.

One reflection, 2 0 0, with a large δ/σ was omitted. This was probably due to secondary extinction. The weighting scheme applied was $W^{-1} = \sigma^2(F) + 0.000273F^2$. The shifts/esd's in the final cycle were mainly below 0.05. The largest was for an O(1C) thermal parameter. See section 5.9.1 for final agreement parameters.

5.9.3 Results of crystal structure determination: Fractional coordinates and six anisotropic thermal parmeters of non-hydrogen atoms are listed in the tables which follow. Isotropic parameters of hydrogen atoms were fixed at 0.05Å^2. The asymmetric unit consists of an ion pair of S-VAL and (1R)-(4S)-CSA. Hydrogen atoms bound to carbon atoms were placed in ideal, calculated positions. Esd's on fractional coordinates ranged from 0.00010 to 0.00958 and tended to be larger on y-coordinates and on non-calculated hydrogen atoms. The range of the values of principal anistropic thermal parameters was 0.029(3) to 0.148(8), with the larger values on the more extreme atoms, as expected.

Electrostatic forces and hydrogen bonds hold the structure together. See section 6.4 for details.

Figure 5.9 S-Valinium (1R)(4S)Camphor-10 Sulphonate

valinium *camphor-10-sulphonate*

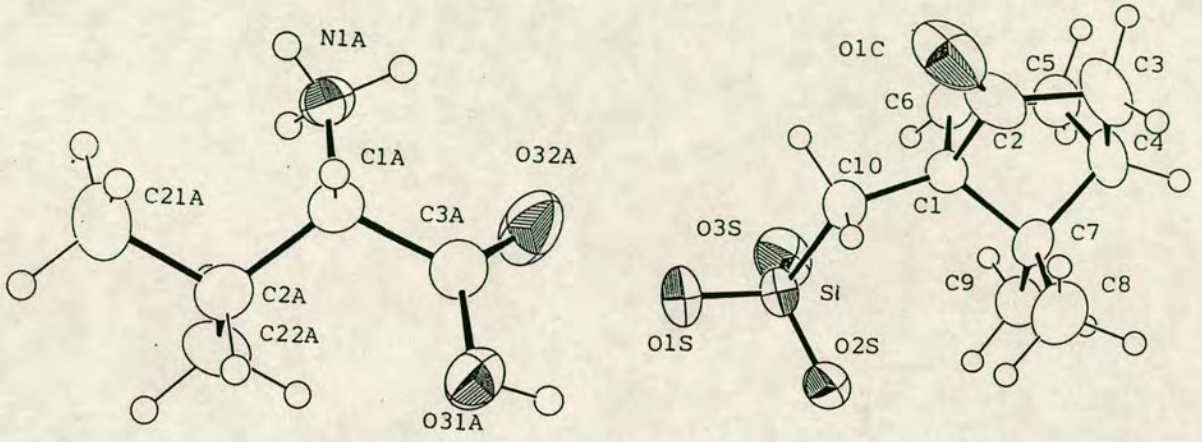


Table 5.9.1 Fractional coordinates with isotropic thermal parameters in Å² (U_{iso} for H fixed at 0.05Å²)

	x	y	z	Ueq
C(1)	-0.1864(4)	-0.5327(8)	-0.5132(4)	0.036(3)
C(2)	-0.1091(4)	-0.4989(11)	-0.3842(4)	0.056(4)
O(1C)	-0.0025(3)	-0.4726(11)	-0.3521(3)	0.084(3)
C(3)	-0.1885(4)	-0.5087(12)	-0.3058(4)	0.072(4)
C(4)	-0.3095(4)	-0.5549(9)	-0.3984(4)	0.052(3)
C(5)	-0.3008(5)	-0.7618(9)	-0.4352(5)	0.055(4)
C(6)	-0.2140(4)	-0.7515(8)	-0.5101(5)	0.050(3)
C(7)	-0.3059(4)	-0.4413(8)	-0.5113(4)	0.041(3)
C(8)	-0.2976(7)	-0.2259(10)	-0.4956(7)	0.079(5)
C(9)	-0.4139(4)	-0.4888(12)	-0.6183(4)	0.058(3)
C(10)	-0.1183(3)	-0.4705(9)	-0.5968(3)	0.0401(24)
S(1)	-0.18727(10)	-0.46685(0)	-0.75384(10)	0.0484(7)
O(1S)	-0.0901(3)	-0.4223(8)	-0.8011(3)	0.083(3)
O(2S)	-0.2429(4)	-0.6513(7)	-0.7893(4)	0.072(3)
O(3S)	-0.2735(3)	-0.3130(7)	-0.7801(4)	0.057(3)
C(1A)	-0.1970(4)	-1.0599(8)	-1.0004(4)	0.038(3)
N(1A)	-0.1792(4)	-1.0039(8)	-0.8730(4)	0.041(3)
C(3A)	-0.0909(4)	-0.9883(10)	-1.0333(4)	0.045(3)
O(31A)	-0.1036(3)	-1.0176(7)	-1.1482(3)	0.0549(24)
O(32A)	-0.0059(3)	-0.9161(8)	-0.9635(3)	0.072(3)
C(2A)	-0.3183(4)	-0.9966(11)	-1.0831(4)	0.050(3)
C(21A)	-0.4201(5)	-1.0849(15)	-1.0461(6)	0.093(5)
C(22A)	-0.3323(5)	-0.7805(12)	-1.0908(5)	0.070(5)

	x	y	z
H(31)	-0.1607	-0.6201	-0.2400
H(32)	-0.1909	-0.3741	-0.2621
H(4)	-0.3846	-0.5263	-0.3671
H(51)	-0.2653	-0.8519	-0.3583
H(52)	-0.3869	-0.8149	-0.4879
H(61)	-0.1336	-0.8311	-0.4682
H(62)	-0.2557	-0.8058	-0.5987
H(81)	-0.2135	-0.2002	-0.4277
H(82)	-0.3697	-0.1752	-0.4652
H(83)	-0.2990	-0.1511	-0.5758
H(91)	-0.4101	-0.6375	-0.6410
H(92)	-0.4145	-0.4013	-0.6936
H(93)	-0.4941	-0.4629	-0.5949
H(101)	-0.0878	-0.3269	-0.5712
H(102)	-0.0424	-0.5647	-0.5802
H(1A)	-0.2003	-1.2131	-1.0108
H(1NA)	-0.098(4)	-1.004(9)	-0.829(4)
H(2NA)	-0.210(5)	-1.079(9)	-0.840(5)
H(3NA)	-0.217(5)	-0.895(10)	-0.870(5)
H(31A)	-0.036(4)	-0.970(9)	-1.152(4)
H(2A)	-0.3228	-1.0475	-1.1705
H(21A)	-0.3966	-1.2337	-1.0470
H(22A)	-0.5060	-1.0604	-1.1114
H(23A)	-0.4243	-1.0472	-0.9590
H(24A)	-0.2597	-0.7241	-1.1181
H(25A)	-0.3255	-0.7281	-1.0031
H(26A)	-0.4162	-0.7355	-1.1528

Table 5.9.2 Anisotropic thermal parameters in Å²

	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
C(1)	0.030(2)	0.040(3)	0.036(2)	0.003(2)	0.010(2)	-0.001(2)
C(2)	0.051(3)	0.067(5)	0.041(2)	0.008(3)	0.004(2)	-0.022(3)
O(1C)	0.051(2)	0.137(5)	0.052(2)	0.018(4)	-0.003(2)	-0.031(4)
C(3)	0.079(3)	0.093(6)	0.039(2)	-0.002(4)	0.024(2)	-0.015(4)
C(4)	0.051(3)	0.061(4)	0.044(3)	-0.004(3)	0.027(2)	-0.010(3)
C(5)	0.053(3)	0.048(4)	0.062(4)	0.006(3)	0.028(3)	-0.005(3)
C(6)	0.047(3)	0.040(3)	0.060(3)	0.008(3)	0.025(3)	0.000(3)
C(7)	0.042(2)	0.029(3)	0.049(2)	-0.005(3)	0.022(2)	0.001(3)
C(8)	0.092(5)	0.051(4)	0.091(5)	0.001(4)	0.051(4)	0.012(4)
C(9)	0.034(2)	0.080(5)	0.057(3)	0.014(4)	0.018(2)	0.006(4)
C(10)	0.031(2)	0.044(3)	0.042(2)	0.001(3)	0.014(2)	-0.007(3)
S(1)	0.0513(7)	0.0536(8)	0.0390(6)	0.0036(9)	0.0241(5)	0.0051(8)
O(1S)	0.074(2)	0.104(4)	0.074(2)	0.027(3)	0.054(2)	0.022(3)
O(2S)	0.095(3)	0.065(3)	0.048(3)	-0.018(2)	0.020(2)	-0.006(3)
O(3S)	0.050(2)	0.062(3)	0.056(3)	0.018(2)	0.024(2)	0.008(2)
C(1A)	0.038(2)	0.043(3)	0.030(2)	0.000(2)	0.011(2)	-0.005(2)
N(1A)	0.041(2)	0.043(3)	0.035(2)	0.004(2)	0.012(2)	-0.004(2)
C(3A)	0.041(2)	0.052(4)	0.038(2)	-0.006(3)	0.014(2)	0.001(3)
O(31A)	0.043(2)	0.079(3)	0.040(2)	-0.002(2)	0.020(1)	-0.005(2)
O(32A)	0.051(2)	0.110(4)	0.052(2)	-0.018(3)	0.020(2)	-0.034(2)
C(2A)	0.043(3)	0.066(5)	0.036(2)	0.004(3)	0.010(2)	-0.013(3)
C(21A)	0.042(3)	0.148(8)	0.078(4)	0.027(5)	0.007(3)	-0.018(4)
C(22A)	0.059(4)	0.098(6)	0.047(3)	0.022(4)	0.013(3)	0.028(4)

5.10 Crystallisation attempts which failed to produce crystals for data collection

Crystallisation attempts are described in section 2.14. Most attempts were unsuccessful and they are listed here, together with a few comments. Nmr spectra were made and the melting points obtained where possible to ascertain whether or not an deposited crystals might be a salt with CSA and an amino acid co-crystallised together (see sections 2.16 and 2.17).

S-ALA/1S-4R-CSA The product was a few fragments of crystals in a gel, not suitable for structure determination.

S-ALA/1R-4S-CSA No crystals were produced, only a gel.

GLY/1R-4S-CSA The product was a small amount of fragments of crystals in a gel, not suitable for structure determination.

S-ILE/1S-4R-CSA A small amount of fragments of crystals, were produced in a gel, and were not suitable for structure determination.

S-ILE/1R-4S-CSA A small amount of fragments of crystals, were produced in a gel, and were not suitable for structure determination.

S-LEU/1S-4R-CSA A small amount of fragments of crystals, were produced in a gel, and were not suitable for structure determination.

S-LEU/1R-4S-CSA A small amount of fragments of crystals, were produced in a gel, and were not suitable for structure determination.

S-PHE/1S-4R-CSA usually no crystals, some product which was soluble in water. Probably CSA.

S-PHE/1R-4S-CSA No crystals.

D-PHG/1R-4S-CSA All techniques suggest that the product consist entirely of D-PHG. It decomposes at a temperature similar to PHG, the NMR shows there is only PHG and the crystals are very insoluble in water, like PHG.

S-VAL/1S-4R-CSA Deposited crystals were mainly fragments in gels. Mp suggested that there was a new compound and nmr suggested a 1:1 compound. However crystals were misplaced before structure determination and, since it was so hard to get crystals, further attempts were abandoned.

CHAPTER 6

MOLECULAR GEOMETRY, CRYSTAL PACKING ARRANGEMENT AND HYDROGEN BONDS IN CAMPHOR-10-SULPHONIC ACID STRUCTURES

6.1 Bond Lengths and Angles

There is little to note about bond lengths and angles since they were as expected for the molecules in these structures. The S-O bonds in sulphonate groups in most of the compounds were clearly not significantly different, as expected. Some, in the calcium, the potassium, and both methionine salts were strictly significantly different. In all of these except S-MET-1R-4S-CSA, some of the atoms have large thermal parameters, which might explain some differences in bond lengths. Also, hydrogen bonds might stretch some S-O bonds. C-O bond lengths in amino acids were clearly significantly different showing that they were undissociated.

6.2 Torsion Angles

The major torsion angles of relevance in camphor-10-sulphonate are the orientation of the sulphur atom to the cage, represented by S1-C10-C1-C2 and the sulphonate oxygen atoms about the S-C bond, represented by O1S-S1-C10-C1. It was necessary to specify the labels for certain atoms in the camphor-sulphonate molecules according to the range of the torsion angles it should adopt. The methyl carbon atoms, which did not have have freedom in their conformation, were to have the following approximate torsion angles for the C9 carbon atom:

C9-C7-C1-C2 180°
C9-C7-C1-C6 60° in 1S-4R-CSA and -60° in 1R-4S-CSA

The sulphonate oxygen atoms were to have the following approximate torsion angles:

O1S-S1-C10-C1 180°
O2S-S1-C10-C1 -60°
O3S-S1-C10-C1 60°

There were a few exceptions in which CSA conformations were not as specified. The labels on the methyl groups of CSA in CSCA, the calcium salt are switched. O2S and O3S in salts containing 1R-4S-CSA, CSAMET and CSAVAL are as specified, but upon inversion of the molecules for comparison, their torsion angles are reversed. These are not among the important torsion angles in any case.

Amino acid conformations have been specified in section 4.2. The carboxylic acid oxygen atom was labelled O31A and the carboxyl oxygen atom O32A. There are some exceptions in the molecule of PHG. There were two γ-carbon atoms in PHG, the ortho-carbon atoms of the phenyl ring, labelled C22A and C26A, and the β-carbon atom was labelled C21A.

The conformations in each structure will be described separately, then compared.

6.2.1 Hydronium 1S-4R-Camphor-10-sulphonate:

torsion angle	value/degrees	
	MoK_α	CuK_α
S1-C10-C1-C2	-84.3(4)	-84.2(2)
O1S-S1-C10-C1	172.3(3)	171.7(3)

The torsion angles in the structures determined using the two type of radiation are not significantly different. The sulphonate sulphur atom is gauche to both C2 and C6 and the farthest from eclipsing C6 out of the twelve CSA molecules. The sulphonate oxygen atoms are staggered, within 10°, with respect to the the methylene group which joins the sulphonate group to the cage and in the middle of the range of the structures.

6.2.2 Ammonium 1S-4R-Camphor-10-sulphonate:

torsion angle	value/degrees
S1-C10-C1-C2	-91.3(6)
O1S-S1-C10-C1	172.0(5)
S1'-C10'-C1'-C2'	-92.7(8)
O1S'-S1'-C10'-C1'	173.5(7)

Both sulphur atoms are at right angles to C2, lying between C6 and C2. The second molecule has the sulphur atom marginally closer to C6 and both have torsion angles similar to several of the structures. The sulphonate oxygen atoms are within 10° of the ideal staggered arrangement and are in the middle of the range shown by the twelve molecules. These are minor conformational differences in otherwise identical molecules and must be created by differences in the hydrogen bonds exhibited by the two molecules. See section 6.4 for further details.

6.2.3 Potassium 1S-4R-Camphor-10-sulphonate:

torsion angle	value/degrees
S1-C10-C1-C2	-91.3(13)
O1S-S1-C10-C1	168.9(10)
S1'-C10'-C1'-C2'	-87.0(14)
O1S'-S1'-C10'-C1'	165.5(14)

Both of the sulphur atoms lie at about right angles to C2, between C2 and C6, in the middle of the range of torsion angles of several of the molecules. The second molecule is insignificantly different from one of the molecules in the ammonium salt in this respect. The oxygen atoms of the sulphonate group again occupy a staggered conformation with respect to the rest of the molecule, a little over 10° from the ideal conformation. The second molecule has torsion angles at one extreme of the twelve structures.

6.2.4 Calcium 1S-4R-Camphor-10-sulphonate:

torsion angle	value/degrees
S1-C10-C1-C2	-132.2(4)
O1S-S1-C10-C1	-176.3(3)

The sulphur atom of the sulphonate group nearly eclipses C6 and is rotated into the sector which is trans to C2. The sulphonate oxygen atoms are in a staggered arrangement, within 5° of the ideal torsion angle, to the atoms bound to C10 and at one extreme of the range exhibited in the structures.

6.2.5 Copper 1S-4R-Camphor-10-sulphonate:

torsion angle	value/degrees
S1-C10-C1-C2	-142.6(4)
O1S-S1-C10-C1	179.8(3)
S1'-C10'-C1'-C2'	175.0(3)
O1S'-S1'-C10'-C1'	165.8(3)

The positions of the sulphur atom in the two molecules of the copper salt are quite different from one another and from the bulk of the other structures. In the

first molecule it tends to eclipse the atom C6, though not closely and lies between C6 and C7, farther round than in the calcium salt. The other molecue has the sulphur atom trans to C2 and gauche to both C6 and C7. This and the orientation of the oxygen atoms of the sulphonate group create a pseudo mirror plane in the second molecule. The "on-plane" atoms are O1S-S1-C10-C1-C2-O1C-C3-C4, with C7 and C9 close to the pseudo mirror plane. C5 and C6 may be envisaged as reflecting in the plane onto C8 or perhaps the whole isopropyl group, C7, C8 and C9. The remaining sulphonate oxygen atoms map more precisely on to one another by reflection in the pseudo mirror plane. This pseudo mirror plane made it feasible to solve the structure in a higher space group. See section 5.5 for details.

6.2.6 R-Phenylglycinium 1S-4R-Camphor-10-sulphonate:

torsion angle	value/degrees
camphor-10-sulphonic acid	
S1-C10-C1-C2	-100.6(5)
O1S-S1-C10-C1	179.7(4)
phenylglycine	
N1A-C1A-C3A-O32A	11.1(8)
N1A-C1A-C21A-C22A	128.2(5)
N1A-C1A-C21A-C26A	-53.5(7)

In the camphor-10-sulphonate molecule the sulphur atom is at one extreme of a group of structures which have the sulphur atom about 90° from C2 and it tends to eclipse C6, though not closely. The oxygen atoms of the sulphonate group are trans to C1, occupying the ideal staggered conformation.

In common with other amino acid molecules the acid group eclipses and is trans to the nitrogen atom. It is

the carbonyl oxygen atom which eclipses the nitrogen atom. The plane of the phenyl ring, the ortho-carbon atoms of which are β-carbon atoms of the amino acid, is gauche to both C3A and N1A, eclipsing the hydrogen atom, very much as expected.

6.2.7 S-Methioninium 1S-4R-Camphor-10-sulphonate:

torsion angle	value/degrees
camphor-10-sulphonic acid	
S1-C10-C1-C2	-172.7(4)
O1S-S1-C10-C1	165.8(5)
methionine	
N1A-C1A-C3A-O32A	0.06(8)
N1A-C1A-C2A-C21A	71.9(7)
C1A-C2A-C21A-S1A	179.0(4)
C2A-C21A-S1A-C1SA	73.4(5)

In the CSA molecule, the sulphur atom is trans to C2, and gauche to both C6 and C7. This is very similar to the valine salt and the second molecule of the copper salt and quite different from other CSA molecules. The oxygen atoms of the sulphonate group adopt the ideal staggered arrangement ,but almost at the extreme of the range of the twelve structures.

In the methionine molecule the carbonyl oxygen atom eclipses the nitrogen atom very closely and the carboxylic acid oxygen atom is trans to it. This and S-VAL-1R-4S-CSA are the only structures to have the carboxylic acid group rotated around to the other side of the ammonium group.

6.2.8 S-Methioninium 1R-4S-Camphor-10-sulphonate:

torsion angle	value/degrees
camphor-10-sulphonic acid	
S1-C10-C1-C2	86.5(3)
O1S-S1-C10-C1	176.40(24)
methionine	
N1A-C1A-C3A-O32A	-17.7(5)
N1A-C1A-C2A-C21A	67.2(5)
C1A-C2A-C21A-S1A	-175.7(3)
C2A-C21A-S1A-C1SA	142.4(7)
C1A-C2A-C21A-S1B	178.9(4)
C2A-C21A-S1B-C1SB	85.2(5)

The torsion angles are listed above. The torsion angles of 1R-4S-CSA were then inverted for comparison with other CSA molecules. The sulphur atom was at 90° to C2 and lay between C2 and C6 in a similar conformation to several other CSA molecules. The oxygen atoms of the sulphonate group adopted the ideal staggered conformation with respect to the cage, within 5° and at one extreme of the range observed in the present structures.

It was not necessary to invert the S-MET molecule to compare its conformation with other amino acids. In common with the other amino acids, the carbonyl oxygen atom tended to eclipse the nitrogen atom and the carboxylic acid acid oxygen atom was trans to it. The β-carbon atom was gauche to both N1A and C3A as in the two other CSA-amino acid structures and closer to C3A than N1A. The MET side chain was disordered in the sulphur atom and terminal methyl group. Both sulphur atoms were trans to the α-carbon atom, the conformation of S1B being almost identical to that in the opposite diastereomer. The terminal methyl groups adopt quite different conformations. The terminal methyl of the B-chain was again very

like that in the opposite diastereomer, being gauche+ (or at right angles) to the β-carbon atom. The C1SA of the A-chain was almost trans to C2A.

6.2.9 S-Valinium 1R-4S-Camphor-10-sulphonate:

torsion angle	value/degrees
camphor-10-sulphonic acid	
S1-C10-C1-C2	-173.4(4)
O1S-S1-C10-C1	-173.5(4)
valine	
N1A-C1A-C3A-O32A	5.9(7)
N1A-C1A-C2A-C21A	-59.5(6)
N1A-C1A-C2A-C22A	64.5(6)

The relevant torsion angles are listed above,. Torsion angles for 1R-4S-CSA were inverted for comparisons and are shown on the diagram in section 6.2.10. S1 is trans to C2, very similar to only 3 out of 12 CSA molecules in the present structures. The sulphonate oxygen atoms take up the ideal staggered conformation, in the middle of the observed range.

In common with all the other amino acids observed, the 'short' C-O bond of the VAL carboxylate group tends to eclipse the nitrogen atom. However, this O32A is 5.8° farther gauche+ than O32A in S-MET-1R-4S-CSA, both molecules being highly unusual in this respect. Terminal methyl groups are gauche+ and gauche- to the nitrogen atom, labelled g^+g^- in the summary table, which is the least common of the three possible VAL conformations as surveys have shown. The bulky counterion, CSA must affect the VAL conformation.

6.2.10 Comparison of Camphor-10-sulphonate Conformations:

Most of the structures contained 1S-4R-CSA so the torsion angles of the 1R-4S-CSA molecules in S-MET-1R-4S-CSA and S-VAL-1R-4S-CSA were inverted for comparison. The atomic labelling scheme is described in section 2.13. Torsion angles of the cage were as expected. The only two areas where there was any freedom in conformation was about the two bonds, C10-C1 and S1-C10, and they are shown in the diagrams below. There were few structures in the literature with which to compare them and the conformation of the CSA molecule itself was not often described, the CSA having been used to resolve a racemic mixture or allow the determination of an absolute configuration. An example is the canadinium salt of of 1S-1R-CSA.[59] This work therefore included some simple salts to provide a background to the amino acid salts.

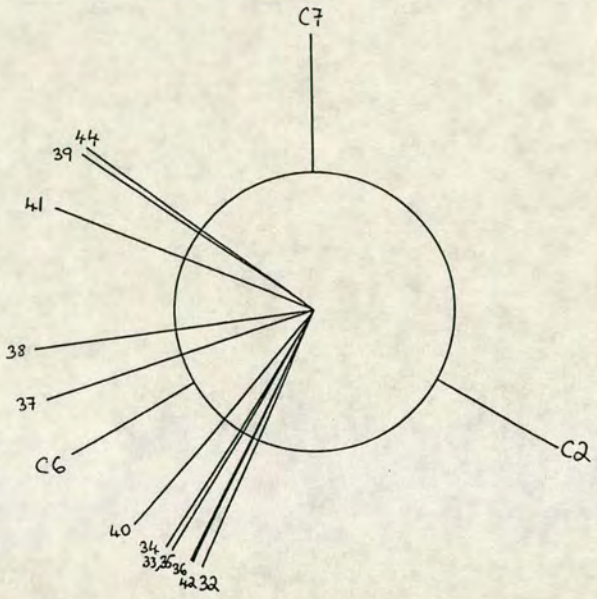
Key to the simple salts in this work:

diagram code	abbreviated name	full name
32	CSA	hydronium 1S-4R-camphor-10-sulphonate
33	$CSNH_4$ A	ammonium 1S-4R-camphor-10-sulphonate
34	$CSNH_4$ B	ammonium 1S-4R-camphor-10-sulphonate
35	CSK A	potassium 1S-4R-camphor-10-sulphonate
36	CSK B	potassium 1S-4R-camphor-10-sulphonate
37	CSCA	calcium 1S-4R-camphopr-10-sulphonate
38	CSCU A	copper 1S-4R-camphor-10-sulphonate
39	CSCU B	copper 1S-4R-camphor-10-sulphonate

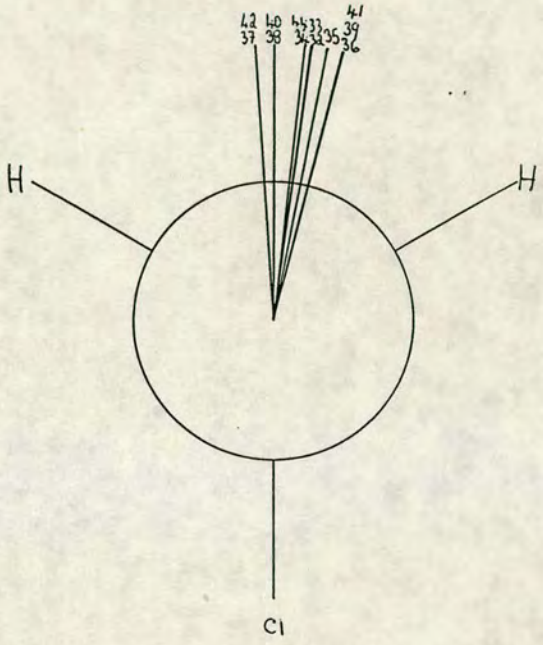
Key to the amino acid salts in this work:

diagram code	*abbreviated name*	*diagram code*	*abbreviated name*
40	R-PHG-1S-4R-CSA	42	S-MET-1R-4S-CSA A
41	S-MET-1S-4R-CSA	43	S-MET-1R-4S-CSA B
		44	S-VAL-1R-4S-CSA

view{S1-C10-C1-C2}



view{O1S-S1-C10-C1}



The rotations of the oxygen atoms of the sulphonate group were within 15° of the ideal arrangement and mostly rotated clockwise out of the ideal confomation. In CSCA, CSCU-A and inverted S-MET-1R-4S-CSA these oxygen atoms are rotated anticlockwise (although CSCU-A is almost exactly in the ideal conformation).

The most variability in the conformations occurred in the rotation of the sulphur atom around the C10-C1 bond. It is always gauche to (or near eclipsed with) the atom C6, on either side of it. They are mostly gauche+ and often within about 30° of C6. Three molecules have the sulphur atom trans to C2, the carbonyl group.

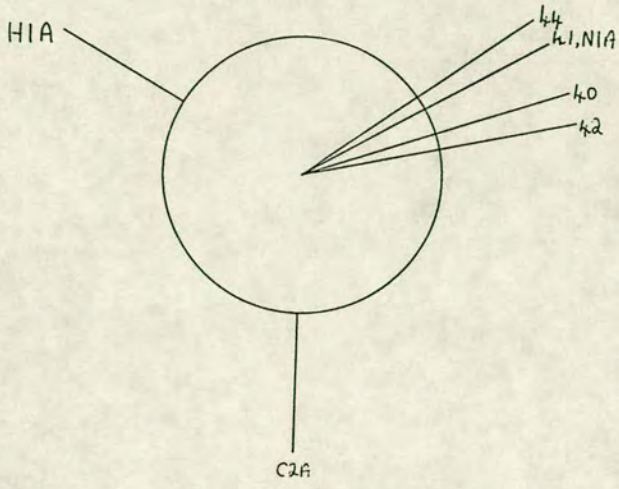
6.2.11 Comparison of Amino Acid Conformations:

The natures of ϕ_2, χ_1, χ_2, χ_3 are listed for the amino acids in the present structures and should be compared with those given in chapter 4 for amino acids in mandelic acid structures. Newman projection diagrams will then be given (see key in section 6.2.10) followed by a discussion of the conformations, during which reference will be made to amino acid conformations from this work and from the literature, more fully discussed in section 4.2.

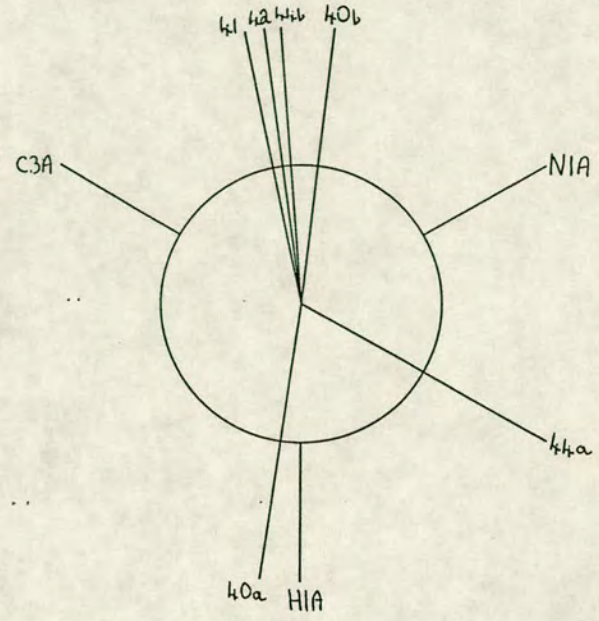
ϕ_2 is N1A-C1A-C3A-O32A
(contrast O31A in MAN structures)
χ_1 is N1A-C1A-C2A-C21A
(contrast N1A-C1A-C21A-C22A in R-PHG-1S-4R-CSA)
(also N1A-C1A-C2A-C22A in S-VAL-1R-4S-CSA)
χ_2 is C1A-C2A-C21A-S1A
(contrast C1A-C2A-C21A-S1B in the minor disordered chain in S-MET-1R-4S-CSA)
χ_3 is C2A-C21A-S1A-C1SA
(contrast C2A-C21A-S1B-C1SB in the minor disordered chain in S-MET-1R-4S-CSA)

compound	ϕ_2	χ_1	χ_2	χ_3
R-PHG-1S-4R-CSA (inverted to S-PHG)	e	g+	/	/
S-MET-1S-4R-CSA	≈e(+)	g+	t	g+(90°)
S-MET-1R-4S-CSA A	e	g+	t	g+
S-MET-1R-4S-CSA B	e	g+	t	t(120°)
S-VAL-1R-4S-CSA	≈e(+)	g-g+	/	/

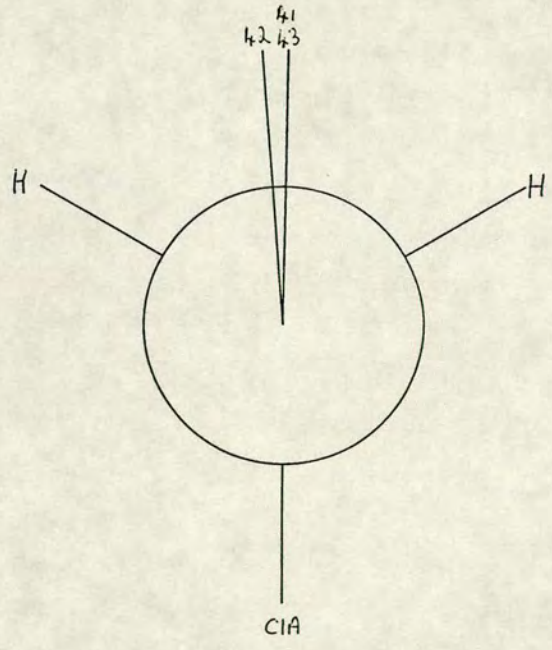
view{N1A-C1A-C3A-O32A}



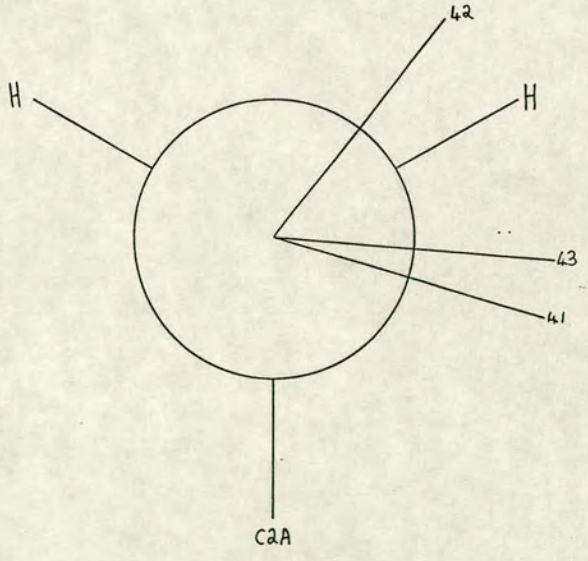
view{N1A-C1A-C2A-C21A}, χ_1



view{C1A-C2A-C21A-S1A}, χ_2



view{C2A-C21A-S1A-C1SA}, χ_3



ϕ_2 is N1A-C1A-C3A-O32A in the camphor-10-sulphonate structures because O32A is the oxygen atom nearest to eclipsing the ammonium group. C3A-O32A is the short, carbonyl bond. As in the mandelic acid compounds, it is the short C-O bond in the carboxylic acid or carboxylate group which eclipses the bond to the ammonium group. Amino acid molecules in camphor-10-sulphonate compounds

are similar to those in mandelic acid structures and in pure amino acid structures in that that ϕ_2 is between 0 and -30°. There are two exceptions which have a slightly positive values, one of which is within one esd of zero.

All of the amino acid molecules in these structures adopt ideal staggered conformation along their side chains, in accord with surveys of bulky hydrophobic amino acid side chains. Exceptions arise in χ_3 of the minor (B) MET chain in S-MET-1R-4S-CSA, where the torsion angle is approximately 120°, and in χ_3 of S-MET-1S-4R-CSA, where the terminal S-C bond is at right angles to the rest of the side chain.

R-PHG-1S-4R-CSA has the phenyl ring gauche to both large atoms and eclipsing the small hydrogen atom.

None of the MET molecules adopt the full trans planar conformation. The minor disordered side chain in S-MET-1R-4S-CSA is gauche, trans, trans like SR-MET-β,[44] SR-NORLEUCINE[37] and the major disordered side chain of S-MET-R-MAN. The remaining two MET molecules in CSA salts are gauche, trans, gauche, like the major disordered side chain in S-MET-R-MAN, SR-MET-α,[44] except that χ_3 is actually 90° in the fully ordered CSA salt. Thus again, The MET χ_2 conformation is always trans in the CSA salts, in common with the structures discussed in section 4.2, where there are two exceptions: in a MAN compound and a pure MET structure. There is great variability in the MET side chain conformations.

VAL, in S-VAL-1R-4S-CSA, occupies the least common of the three possibilities for χ_1

6.3 Molecular Packing Arrangements

Packing diagrams for each of the eight structures are given at the end of section 6.3. These show a view perpendicular to two axes, usually along the reciprocal axis corresponding to the shortest real axis. When necessary, additional diagrams are given in section 6.4, showing only atoms involved in hydrogen bonding and their immediate neighbours.

6.3.1 Hydronium 1S-4R-Camphor-10-sulphonate:

The packing motif consists of ribbons containing two CSA molecules and two water molecules in the form of hydronium ions, H_3O^+, zig-zagging parallel to the a-axis of the crystallographic unit cell. The CSA molecules are hydrogen bonded to hydronium ions, which link CSA molecules across the middle of the ribbon and along the length of the ribbon in a spiral. The pair of C8, C9 methyl groups and the C5, C6 part of the cage point towards the hydrogen bonded ribbon on both sides, but do not approach it closely. The carbonyl oxygen atoms, O1C, point in the general direction of the hydrogen bonded central spine of the ribbon, rather than out into the hydrophobic edge of the ribbon.

6.3.2 Ammonium 1S-4R-Camphor-10-sulphonate:

The structure is isomorphous with potassium 1S-4R-camphor-10-sulphonate, with the nitrogen atom of the ammonium group occupying the position corresponding to the potassium atom. The ammonium groups are hydrogen bonded to nearly tetrahedrally arranged sulphonate oxygen atoms.

6.3.3 Potassium 1S-4R-Camphor-10-sulphonate:

The structure is isomorphous with ammonium 1S-4R-camphor-10-sulphonate. The packing motif is a chequer-board of hydrophilic and hydrophobic square columns. The structure has two independent ion pairs in the asymmetric unit. Four ion pairs are arranged around a 2-fold rotation axis, forming a column. The hydrophilic columns contain the potassium ions, one to each CSA molecule. Sulphonate and carbonyl oxygen atoms coordinate to the potassium ions, five in one case and six in the other.

6.3.4 Calcium 1S-4R-Camphor-10-sulphonate:

The structure is composed of hydrophilic and hydrophobic bilayers normal to the c-axis. Two sulphonate oxygen atoms and four water molecules are octahedrally coordinated around each calcium ion at distances between 2.32 and 2.37A. Calcium ions are located on the 2-fold axes and on the central plane of the hydrophilic bilayers. Sulphonate oxygen atoms and water molecules on the same side of the bilayer are hydrogen bonded into infinite layers normal to c. Opposite sides of the bilayers are symmetry related by the 2-fold rotation axis running along the centre of the bilayer, through the calcium ion and parallel to b.

6.3.5 Copper(II) 1S-4R-Camphor-10-sulphonate:

This structure is composed of hydrophilic and hydrophobic bilayers. There are two independent CSA molecules in each asymmetric unit, the sulphonate groups of which are hydrogen bonded to the water molecules which, in turn, coordinate to the copper atoms. The copper atoms are found in the middle of the hydrophilic bilayers, but not on special positions. Six water molecules coordinate to each copper atom in a Jahn-Teller distorted arrangement. This octahedral arrangement of water molecules around the copper atom gives the crystal its blue colour.

6.3.6 R-Phenylglycinium 1S-4R-Camphor-10-sulphonate:

The phenylglycine salt is somewhat similar to the hydronium salt. The ammonium group of the phenylglycine cation, corresponds to the hydronium cation. Symmetry related pairs of CSA molecules are hydrogen bonded into a ribbon, as before, around the two-fold screw axis parallel to the to the a-axis. In addition the phenylglycine molecules stick out from the ribbon in a propellor-like arrangement. The carboxylic acid group hydrogen bonds to neighbouring CSA molecules,giving rise to a more extended hydrogen bonding network, linking each molecule, unlike the hydronium salt.

6.3.7 S-Methioninium 1S-4R-Camphor-10-sulphonate:

The structure is composed of hydrophilic and hydrophobic bilayers parallel to the bc-plane. There is hydrogen bonding in the hydrophilic bilayer and the carbonyl oxygen atom points into this bilayer. 2_1 screw axes are located in the centre of bilayers. The short unit cell axis is the b-axis and a diagram showing the packing arrangement normal to the b-axis is given. The side chain of the methionine molecule sticks out from the hydrogen bonded layer in the direction of the a-axis, with the ammonium and carboxylic acid groups fixed in the hydrogen bonded layer, and spread out in a plane normal to the b-axis. The two bonds in the chain C1-C10-S1 are extended along the c-direction within the hydrogen bonded layers. The extended CSA molecule lying along the c-direction makes the c-axis about the same length as the a-axis, which has extended MET molecules meeting back to back across the bilayers. The b-axis is the short axis because none of the molecules extend themselves in that direction.

The short axis is the direction in which neither molecule extends itself. It is related to the 'thickness' of the globular part of the CSA molecule.

6.3.8 S-Methioninium 1R-4S-Camphor-10-sulphonate:

Hydrophilic and hydrophobic bilayers parallel to the bc-plane compose this structure, which is very similar to the diastereomer described above. The β-angle is very close to 90° in this monoclinic space group. A view normal to the ab-plane is shown, because this view, down the short axis, allows the clearest presentation of the molecules. As in the diastereomeric structure, the MET side chains, in both disordered forms, project out from the hydrogen bonded layer in the a-direction in general. An exception is that the terminal methyl group curls round in the present structure, whereas it continues to extend along the a-direction in the diastereomeric structure. A major difference between the packing arrangements in the diastereomeric pair is that the CSA molecules tend to extend in the a-direction, out from the hydrogen bonded layer, rather than along that layer. It is this feature of the present structure that give it the long a-axis of 14Å and short c-axis of 6.5Å, compared to the a-axis of 12Å and c-axis of 12Å in the diastereomer.

The ammonium and carboxylic acid groups are held in the hydrogen bonded layer, and spread out in a plane normal to the c-axis. This is similar to the diastereomer in that this plane is also normal to the short axis.

The short axis is again determined by the 'thickness' of the globular part of the CSA molecule, and the fact that neither of the molecules extend themselves in that direction.

6.3.9 S-Valinium 1R-4S-Camphor-10-sulphonate:

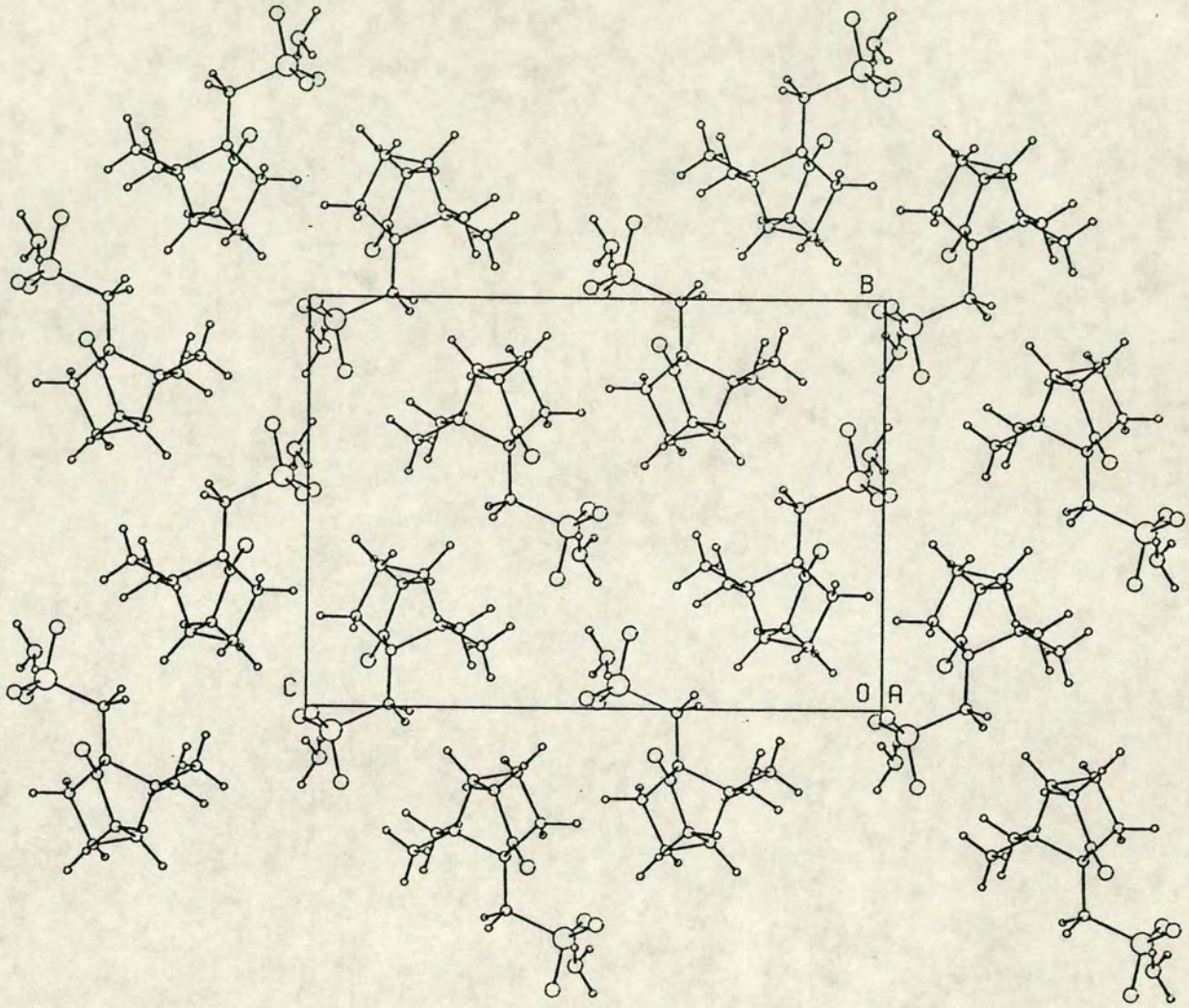
The packing diagram shows a projection down the b-axis, the mounting axis, which turned out to be the unique monoclinic axis. The structure consists of alternating hydrophilic and hydrophobic bilayers parallel to the ac-plane. Also, there are alternate sheets of VAL molecules and CSA molecules running in the ab-plane. Like molecules are related by 2_1-screw axes and the unit cell repeat.

O1C, the CSA carbonyl oxygen atom points into the hydrogen bonded hydrophilic bilayer, and, unusually, is involved in the hydrogen bonding. O1C takes part in a bifurcated hydrogen bond in which an ammonium hydrogen atom is donated equally to an O1C across the bilayer and, making an intramolecular connection, to a carboxylate oxygen atom which the nitrogen atom eclipses.

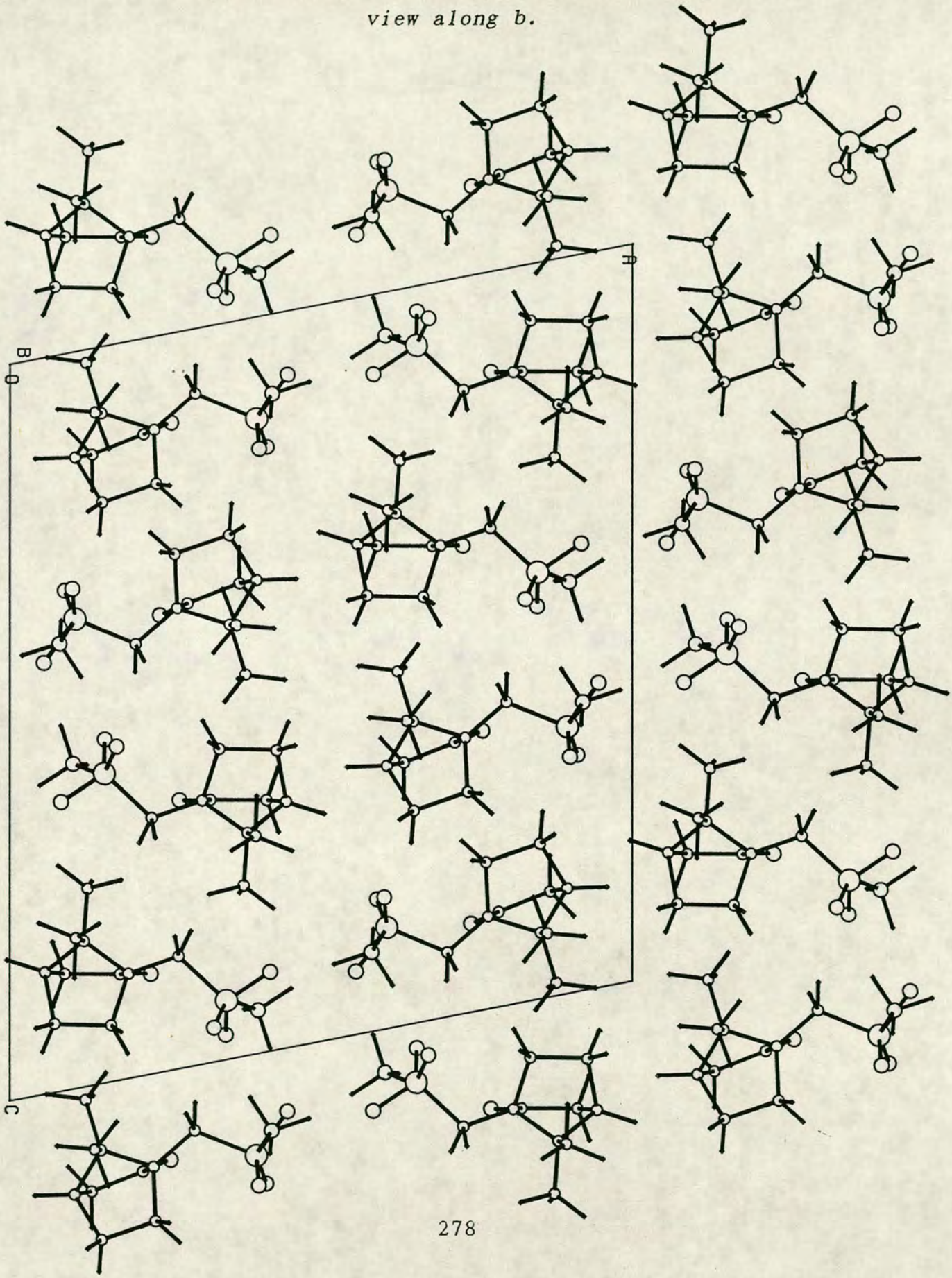
Each VAL is hydrogen bonded to two CSA molecules on the same side of the bilayer (one up and one down) and to two CSA molcules across the bilayer, separated by another VAL molecule. There are no hydrogen bonds between different VAL molecules, although they were a possibility.

The conformations and arrangement of molecules causes the a- and c-axes to be of similar lengths. CSA molecules have the atoms O1C-C2-C1-C10-S1-O1S in an approximately trans-planar conformation, stretched out along the c-direction. The VAL molecules, by contrast, extend in the a-direction, with the hydrophilic moiety extended in the c-direction, the H1NA-N1A-C3A(O32A)-O31A-H31A, approximately planar, parallel to the ac-plane.

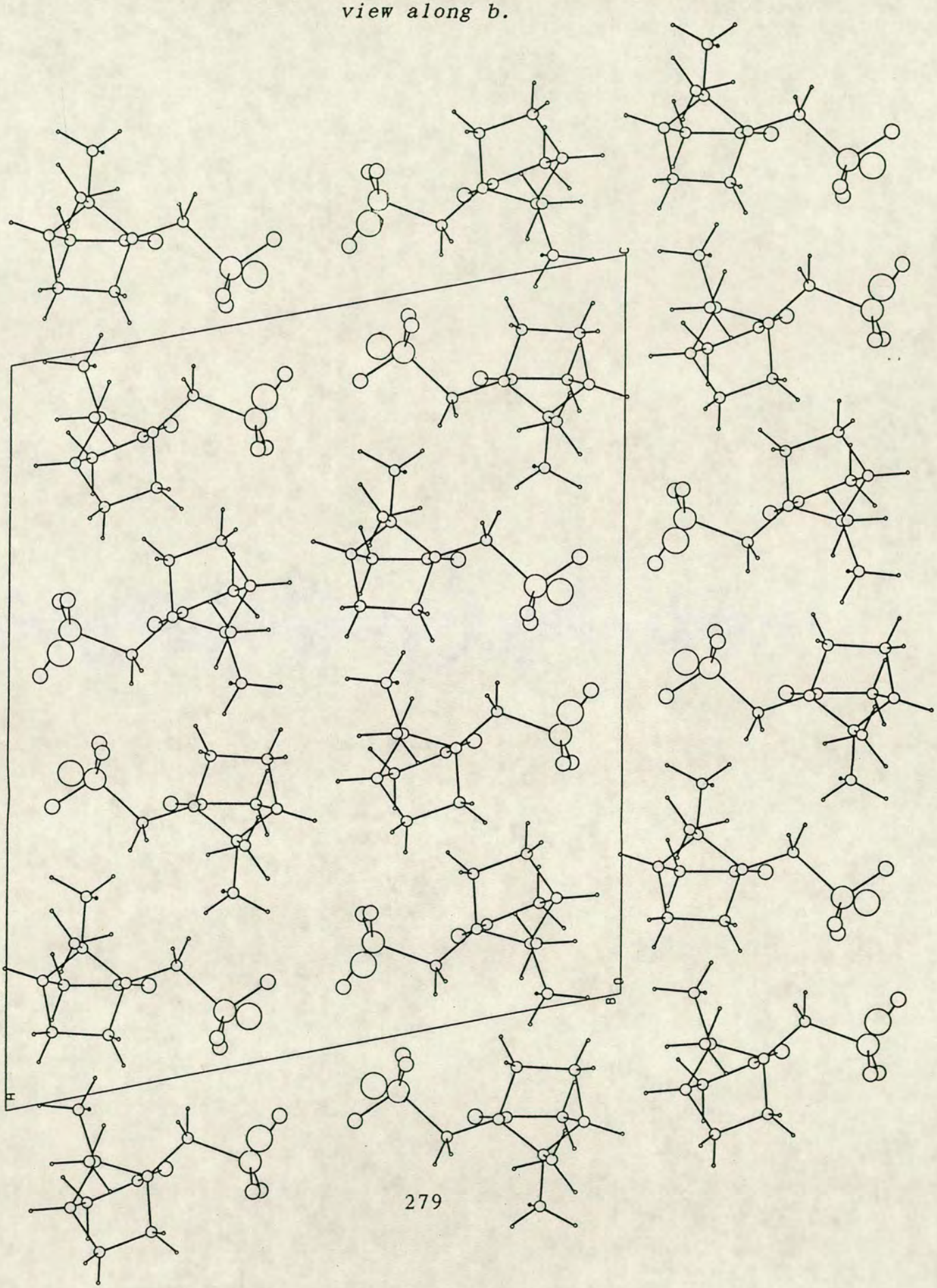
6.3.10 Hydronium 1S-4R-Camphor-10-sulphonate: view along a.



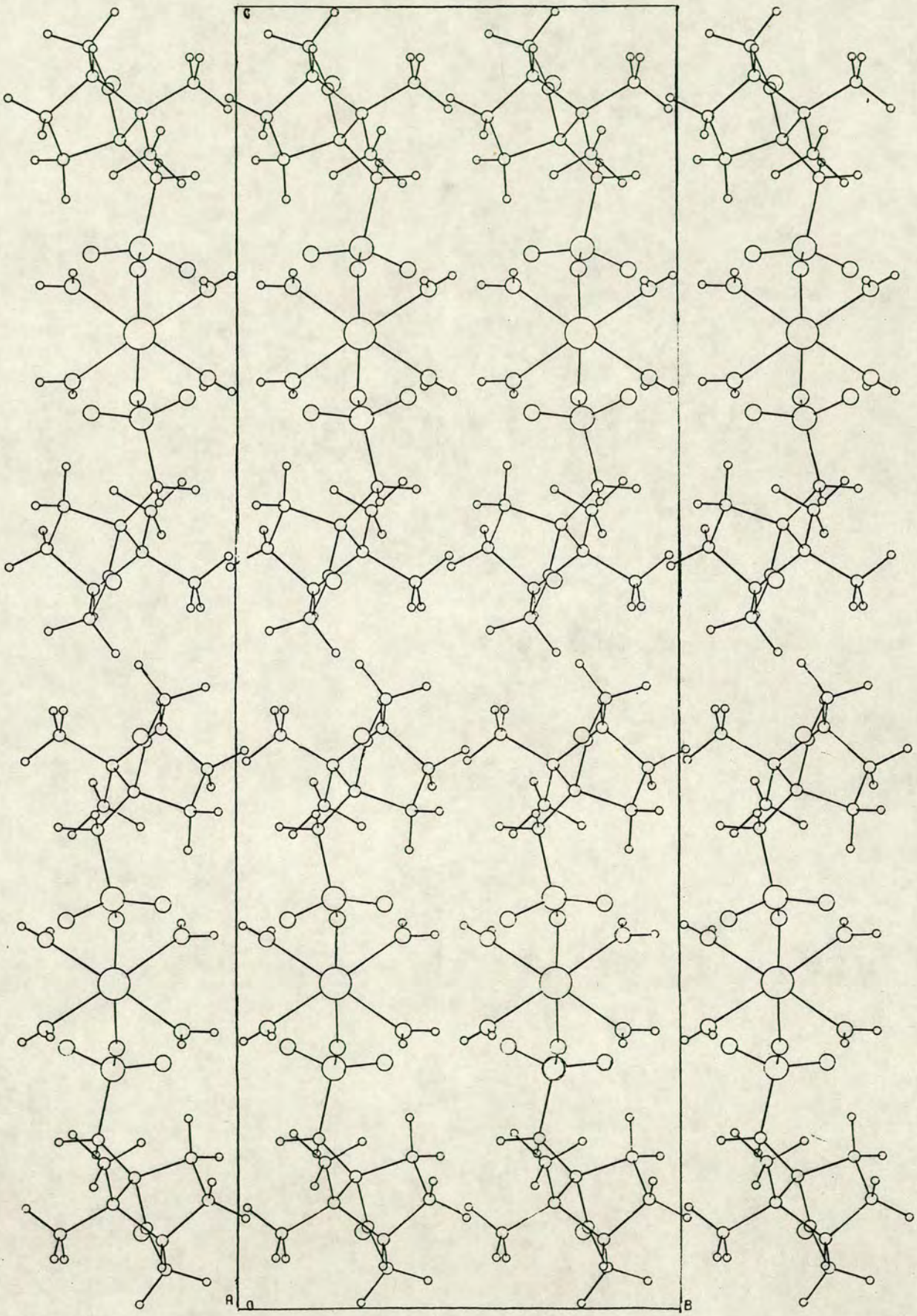
6.3.11 Ammonium 1S-4R-Camphor-10-sulphonate: view along b.



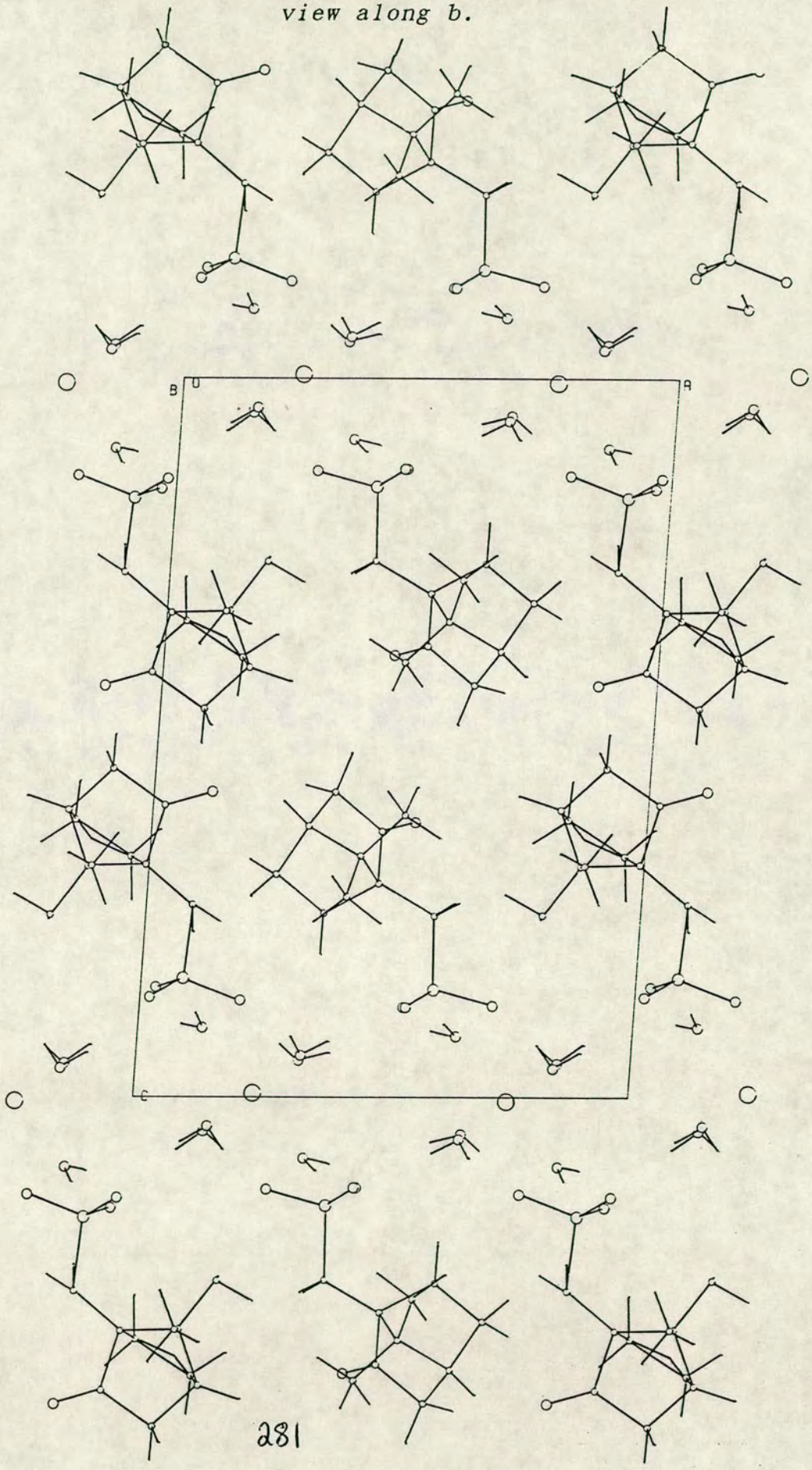
6.3.12 Potassium 1S-4R-Camphor-10-sulphonate: view along b.



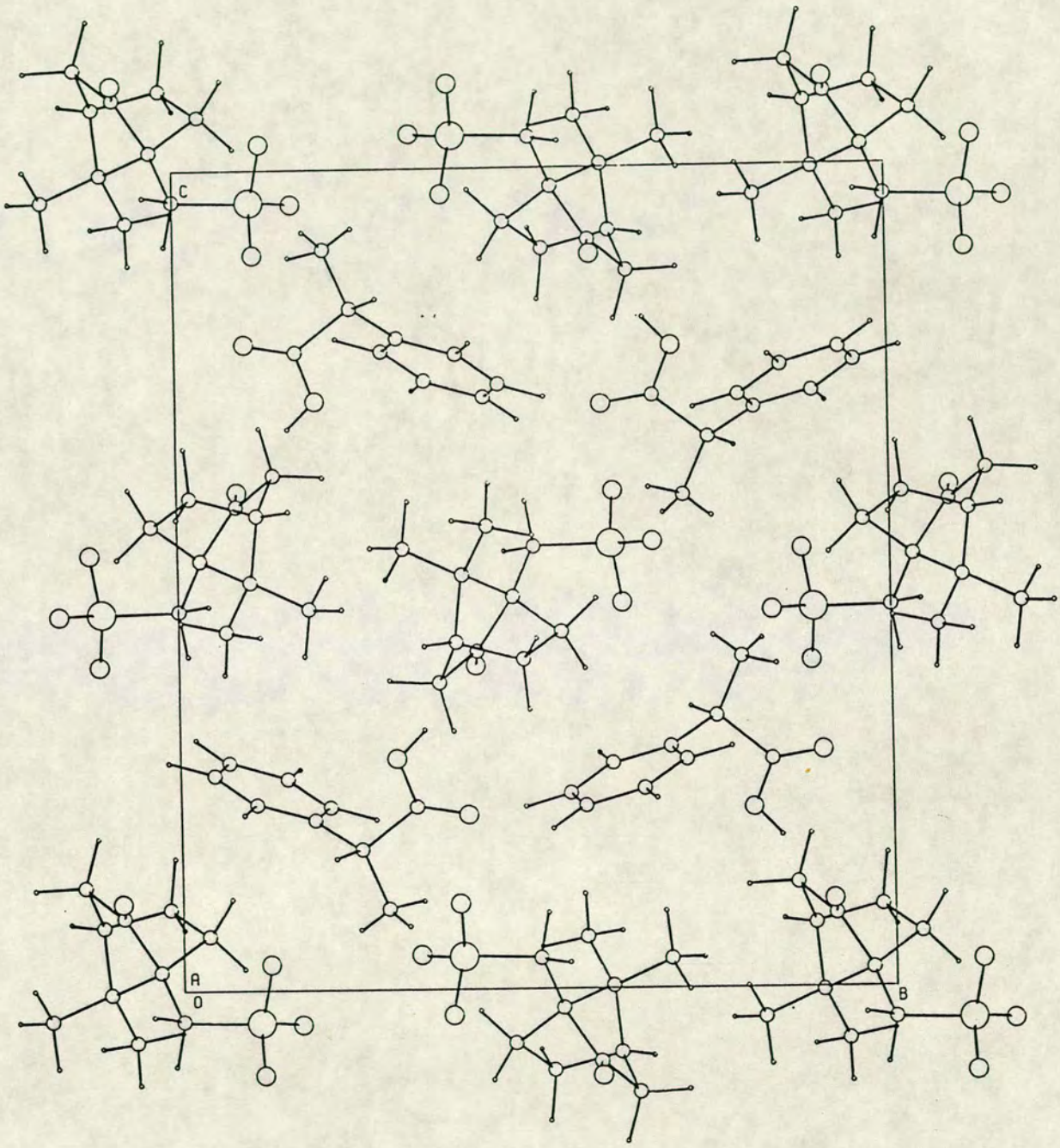
6.3.13 Calcium 1S-4R-Camphor-10-sulphonate: view along a.



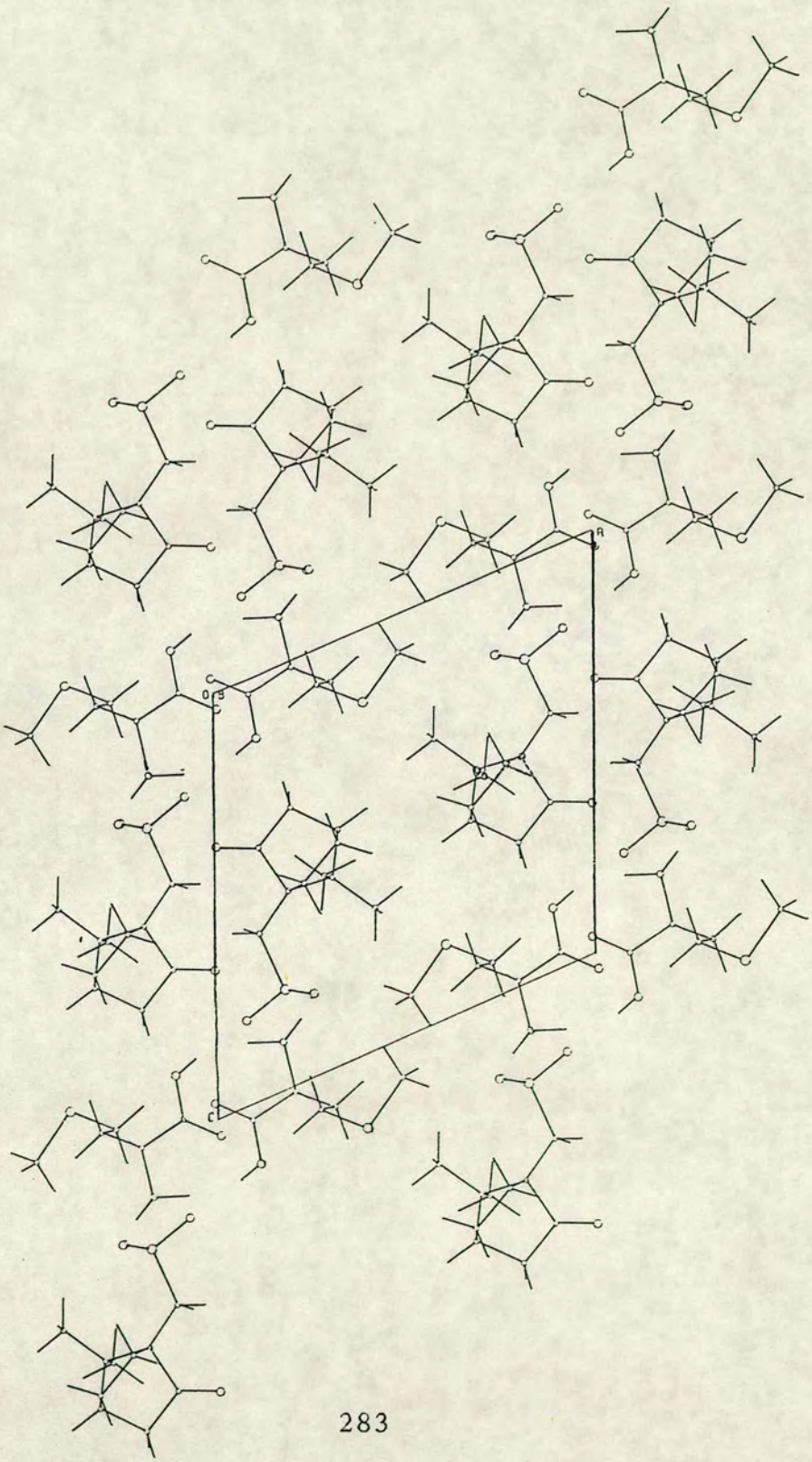
6.3.14 Copper 1S-4R-Camphor-10-sulphonate:
view along b.



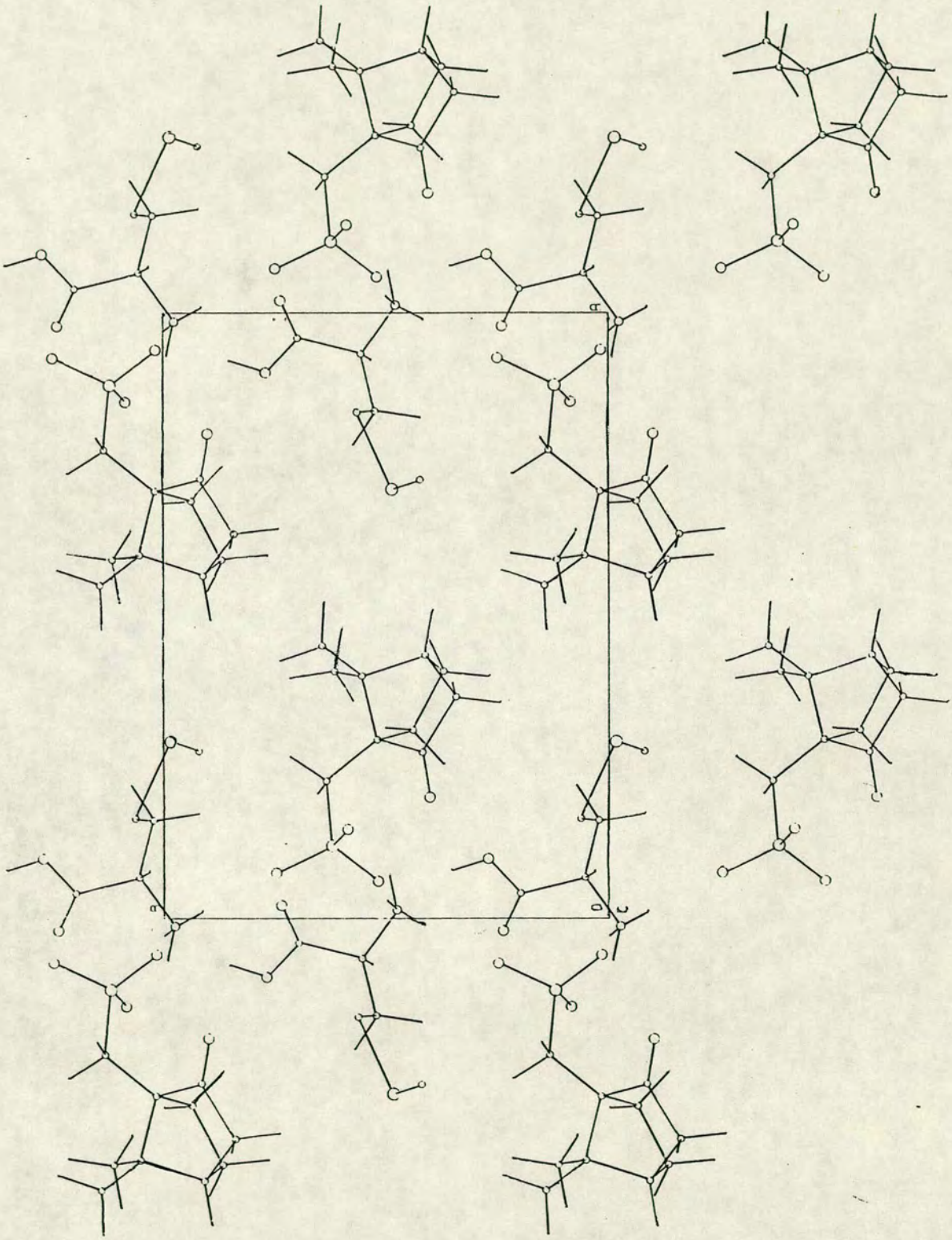
6.3.15 R-Phenylglycinium 1S-4R-Camphor-10-sulphonate: view along a.



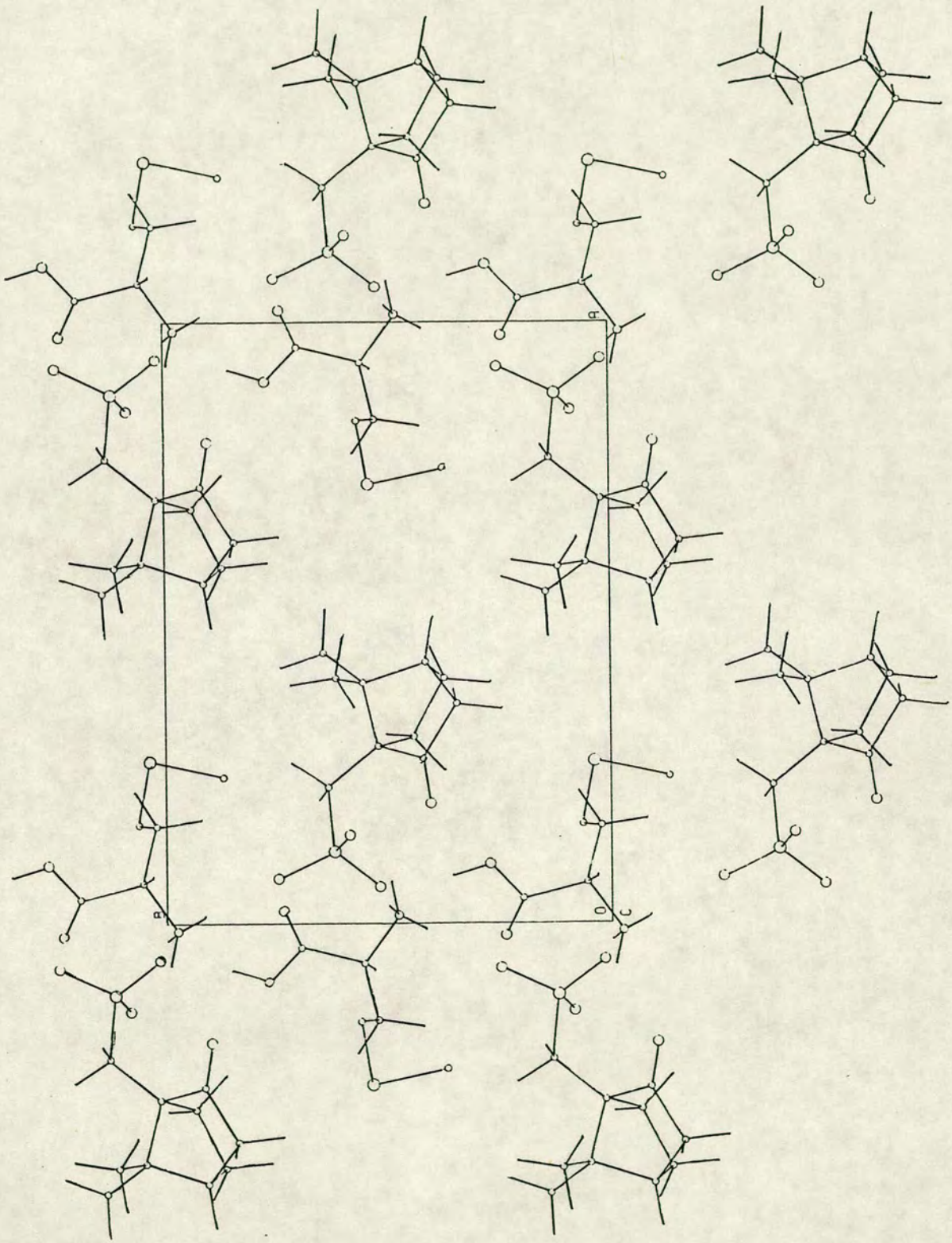
6.3.16 S-Methioninium 1S-4R-Camphor-10-sulphonate: view along b.



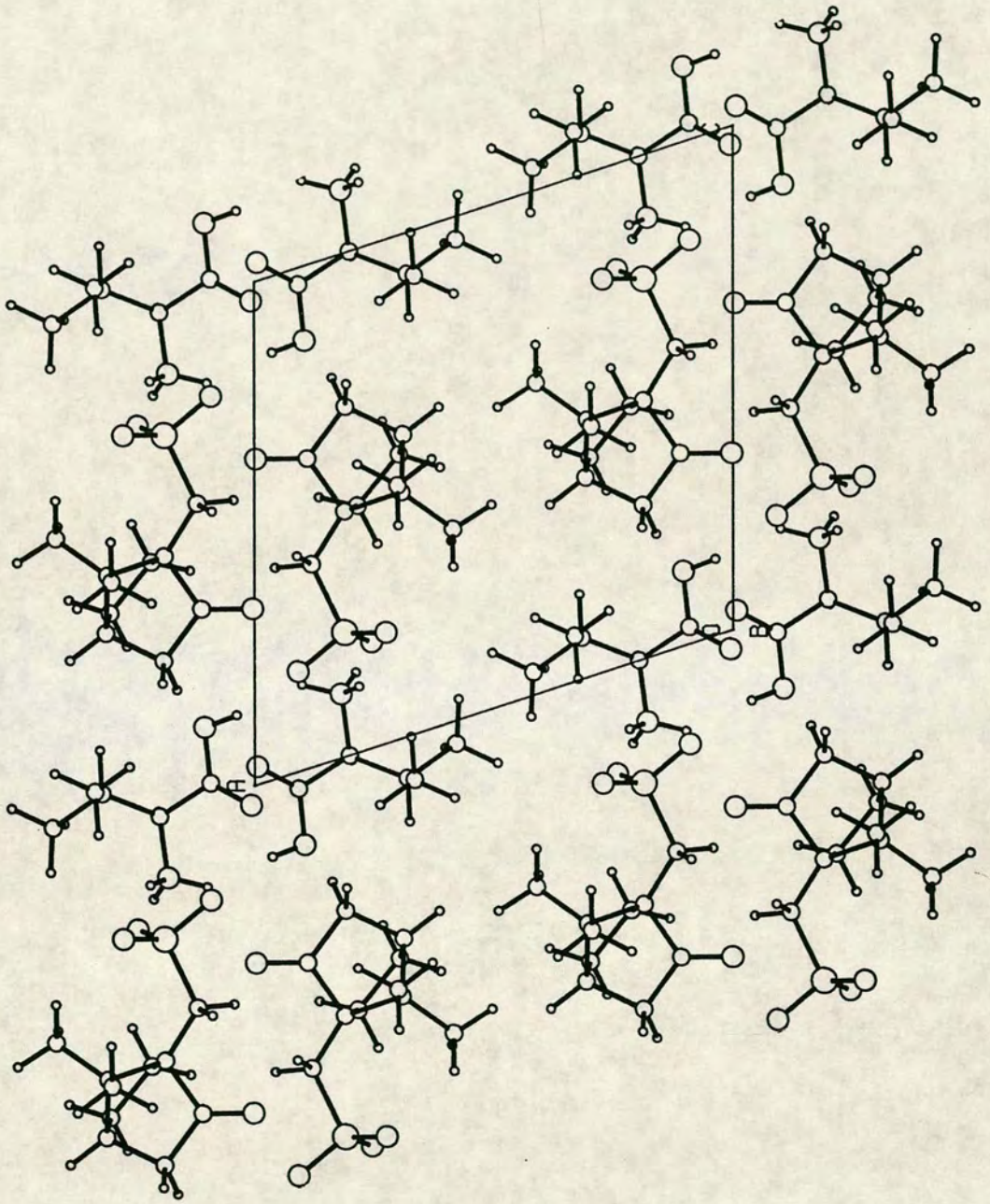
6.3.17 S-Methioninium 1R-4S-Camphor-10-sulphonate: view along c (major form).



6.3.18 S-Methioninium 1R-4S-Camphor-10-sulphonate: view along c (minor form).



6.3.19 S-Valinium 1R-4S-Camphor-10-sulphonate: view along b.



6.4 Hydrogen Bonds

6.4.1 Tabular Data:

In these salts there are a variety of packing arrangements and, correspondingly a variety of hydrogen bonding patterns. In certain of the compounds coordination of oxygen atoms in water and CSA molecules to metal cations also takes place and will be discussed alongside the hydrogen bonds. Listed below are tables of the hydrogen bonds and metal ion coordination.

donor	acceptor	symmetry	D-A/Å	D-H-A/°
CSA				
O1W-H1W...O3S		1/2+x,-1/2-y,-z	2.552(5)	159(5)
O1W-H2W...O2S		-1/2+x,-1/2-y,-z	2.526(5)	168(5)
O1W-H3W...O1S		x,y,z	2.551(5)	179(5)
O1W...O1C		1/2+x,-1/2-y,-z	3.031(5)	---
$CSNH_4$				
N1A-H1NA...O1S		1-x,y,-z	2.795(12)	168.2(5)
N1A-H2NA4..O3S'		x,y,z	3.011(9)	156.1(4)
N1A-H3NA...O3S		x,1+y,z	2.885(9)	155.5(4)
N1A-H4NA...O2S		x,y,z	2.876(8)	171.2(4)
N1B-H1NB...O3S'		x,y,z	2.824(10)	127.6(4)
N1B-H1NB...O1C'		x,y,z	3.130(12)	130.6(4)
N1B-H2NB...O1S		x,y,z	2.844(8)	176.7(4)
N1B-H3NB...O1S		1-x,y,z	2.828(8)	160.0(4)
N1B-H4NB...O2S'		x,-1+y,z	2.717(10)	159.0(4)

donor	acceptor	symmetry	D-A/Å	D-H-A/°
CSK	coordination			
K1...O1S'		1-x,y,-z	2.625(23)	/
K1...O1C		x,1+y,z	2.763(11)	/
K1...O3S		x,1+y,z	2.773(13)	/
K1...O2S		x,y,z	2.804(13)	/
K1...O3S'		x,y,z	2.842(14)	/
K1...O2S'		x,y,z	3.175(16)	/
K2...O1S		1-x,y,-z	2.665(13)	/
K2...O3S'		x,y,z	2.672(14)	/
K2...O2S'		x,-1+y,z	2.693(16)	/
K2...O1S		x,y,z	2.765(13)	/
K2...O1C'		x,y,z	2.905(13)	/
CSCA	coordination			
CA1...O2S		-x,y,1/2-z	2.319(3)	/
CA1...O1W		-x,y,1/2-z	2.345(4)	/
CA1...O2W		-x,y,1/2-z	2.371(4)	/
	hydrogen bonds			
O1W-H1W...O3S		1/2-x,-1/2+y,1/2-z	2.951(5)	168(6)
O1W-H2W...O1S		1-x,y,1/2-z	2.807(5)	171(7)
O2W-H3W...O1S		1/2-x,1/2+y,1/2-z	2.897(5)	166(7)
O2W-H4W...O3S		1-x,y,1/2-z	2.877(5)	156(6)
CSCU				
O1W-H11W...O1S		x,y,z	2.805(5)	156(5)
O1W-H12W...O1S'		x,-1+y,z	2.784(5)	167(5)
O2W-H21W...O1S'		x,y,z	2.801(5)	176(5)
O2W-H22W...O2S		x,y,z	2.770(6)	179(5)
O3W-H31W...O2S'		x,-1+y,z	2.748(5)	168(5)
O3W-H32W...O3S'		x,y,z	2.757(5)	156(5)
O4W-H41W...O1S		1-x,1/2+y,-z	2.731(5)	163(5)
O4W-H42W...O2S		1-x,-1/2+y,-z	2.727(5)	142(5)
O5W-H51W...O3S'		2-x,-1/2+y,-z	2.886(5)	167(5)
O5W-H52W...O3S		1-x,-1/2+y,-z	2.871(5)	172(5)
O6W-H61W...O2S'		2-x,-1/2+y,-z	2.871(5)	169(5)
O6W-H62W...O3S		1-x,1/2+y,-z	2.815(5)	168(5)

donor	acceptor	symmetry	D-A/Å	D-H-A/°
R-PHG-1S-4R-CSA				
N1A-H1NA...O2S		-½-x,1-y,-½+z	2.779(9)	149(6)
N1A-H2NA...O1S		-1½-x,1-y,-½+z	2.826(7)	163(5)
N1A-H3NA...O3S		-1-x,-½+y,½-z	2.931(7)	135(6)
O31A-H31A...O1C		1+x,y,z	2.676(6)	168(6)
S-MET-1S-4R-CSA				
N1A-H1NA...O3S		1-x,-½+y,-z	2.761(7)	161(5)
N1A-H2NA...O1C		-1+x,y,-1+z	2.851(8)	107(3)
N1A-H2NA...O32A		x,y,z	2.670(7)	118(4)
N1A-H3NA...O2S		1-x,½+y,-z	2.825(7)	152(5)
O31A-H31A...O1S		-1+x,y,-z	2.613(10)	163(9)
S-MET-1R-4S-CSA				
N1A-H2NA...O1C		-x,½+y,-z	2.826(4)	106(3)
N1A-H2NA...O3S		-x,½+y,1-z	2.833(4)	153(4)
N1A-H3NA...O2S		-x,½+y,-z	2.929(4)	170(4)
O31A-H31A...O2S		x,1+y,z	2.648(4)	172(4)
S-VAL-1R-4S-CSA				
N1A-H1NA...O1C		-x,-½+y,-1-z	2.862(7)	136(4)
N1A-H1NA...O32A		x,y,z	2.658(6)	104(4)
N1A-H2NA...O3S		x,-1+y,z	2.810(6)	166(6)
N1A-H3NA...O2S		x,y,z	2.848(7)	153(7)
O31A-H31A...O1S		-x,-½+y,-2-z	2.622(6)	162(5)

6.4.2 Discussion:

In salts with metal ions, there is no potential for hydrogen bonding unless there is water of crystallisation. The potassium salt is of that sort and the calcium and copper salts are of the other. Potential hydrogen bond acceptors are the sulphonate oxygen atoms, the carbonyl oxygen atom, and any water molecules or the hydronium ion in the camphor sulphonic acid structure.

The ammonium ion ,water molecules or hydronium ion are the hydrogen bond donors.

The amino acid structures have three ammonium and one carboxylic acid hydrogen atoms available for donation in hydrogen bonds. None of them have any water of crystallisation. The three sulphonate oxygen atoms are the chief acceptors, with O1C and O32A having some involvement. O31A, the carboxylic acid oxygen never accepts hydrogen bonds in any of the structures. Whenever O32A or O1C accept a hydrogen bond from the ammonium group, it is usually a bifurcated hydrogen bond, as the angles at hydrogen atoms show. The O32A which accepts that bifurcated hydrogen bond is in the same amino acid molecule as the ammonium group. So there is some intramolecular influence on the hydrogen bond. Torsion angles show that bonds to N1A and O32A are eclipsed. See section 6.2. The carboxylic acid hydrogen atom is donated to various oxygen atoms, usually to a sulphonate oxygen atom, O1S or O2S, not O3S. In R-PHG-1S-4R-CSA, this hydrogen atom is donated to the carbonyl oxygen atom of a CSA molecule.

In every structure, each hydrogen atom which can be, is indeed involved in hydrogen bonding. It is reasonable that most of the hydrogen bonding in the amino acid and ammonium and hydronium structures should be between the positively charged ammonium or hydronium groups and the negatively charged sulphonate group. In the same way, these oxygen atoms coordinate to the potassium and calcium ions in those structures. Four out of six oxygen atom which coordinate to the calcium ion are water molecules, each of which make hydrogen bonds with two sulphonate oxygen atoms. In two out of six cases, CA1 coordinates directly to a sulphonate oxygen atom. In the copper structure, six oxygen atoms coordinate to the copper ion, each of which are, in turn, hydrogen bonded

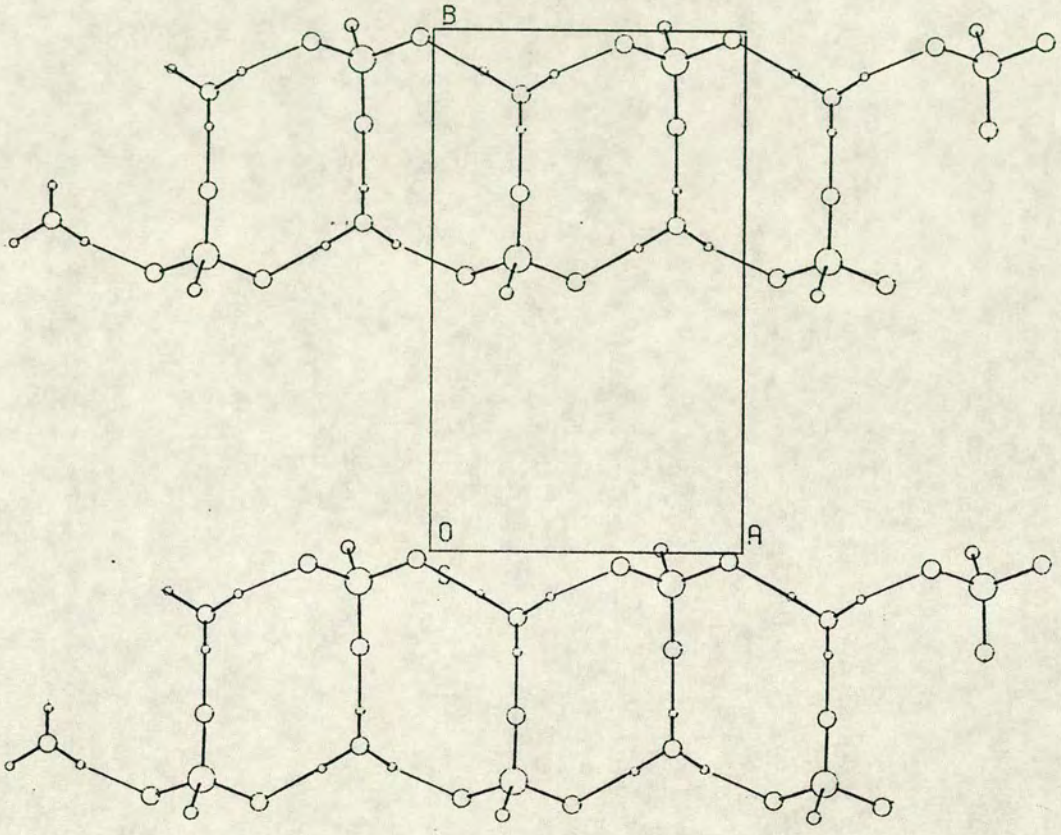
to sulphonate oxygen atoms and there is no direct coordination of sulphonate oxygen atoms to the copper atom.

Of the atoms capable of accepting a hydrogen bond, O1C, the CSA carbonyl oxygen atom is rarely clearly involved. Packing diagrams and interatomic distances show that it tends to point towards areas of hydrogen bonding and may, on occasion influence the hydrogen bonding scheme. Interatomic separation involving O1C are included in the lists of hydrogen bonds for completeness and to show the bifurcated nature of some hydrogen bonds. The water molecules and carboxylic acid oxygen atoms never accept hydrogen bonds.

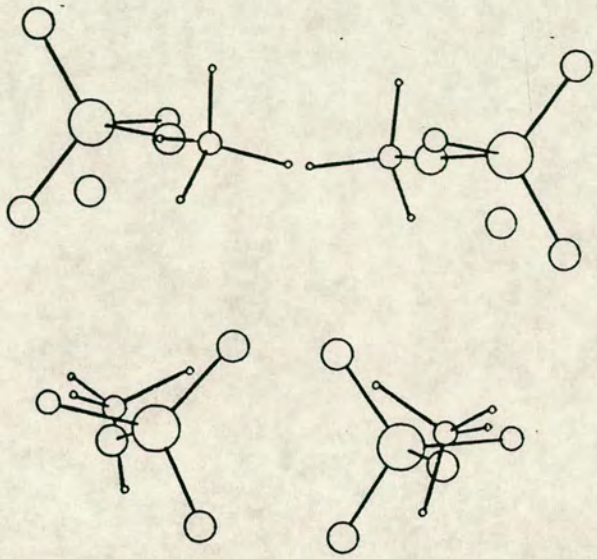
In $CSNH_4$, one ammonium donates three directional hydrogen bonds and the other has three directional ones and one bifurcated one, where the hydrogen atom is shared by a sulphonate oxygen atom and a CSA carbonyl atom. In the isomorphous CSK, six oxygen atoms coordinate to the first K^+ ion, in a pattern similar to that around the first ammonium ion, with two additions. The second K^+ ion has five oxygen atoms coordinating to it, in a pattern broadly similar to the second $CSNH_4$ ammonium ion. The only difference in the pattern apart from the internuclear separations, is the symmetry operators for one of the O1S atoms. The oxygen atoms are much closer to the potassium ion than to the ammonium ion. The lengths of the internuclear separations in CSK are in the range 2.625(23)-3.175(16)Å and the hydrogen bonds in $CSNH_4$ are in the range 2.717(19)- 3.130(12)Å.

Diagrams showing atoms in the hydrogen bonded regions of the CSA salts are given. The remainder of the atoms have been excluded for clarity.

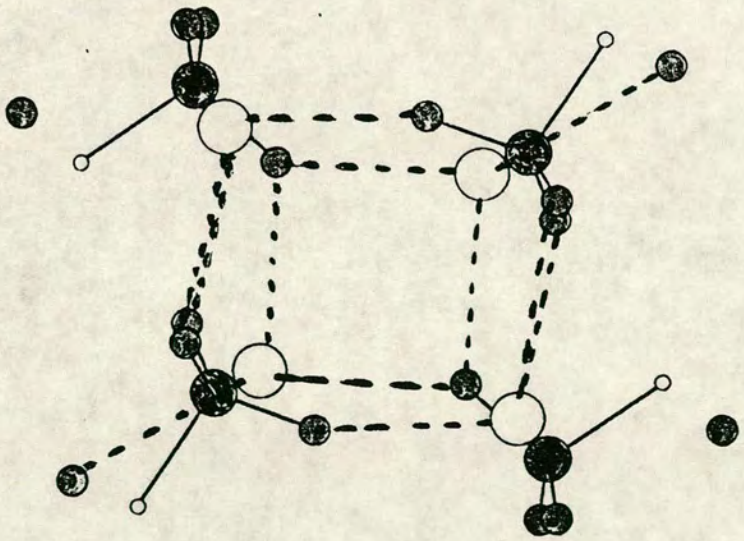
6.4.3 Hydronium 1S-4R-Camphor-10-sulphonate: hydrogen bonding ribbons viewed along c.



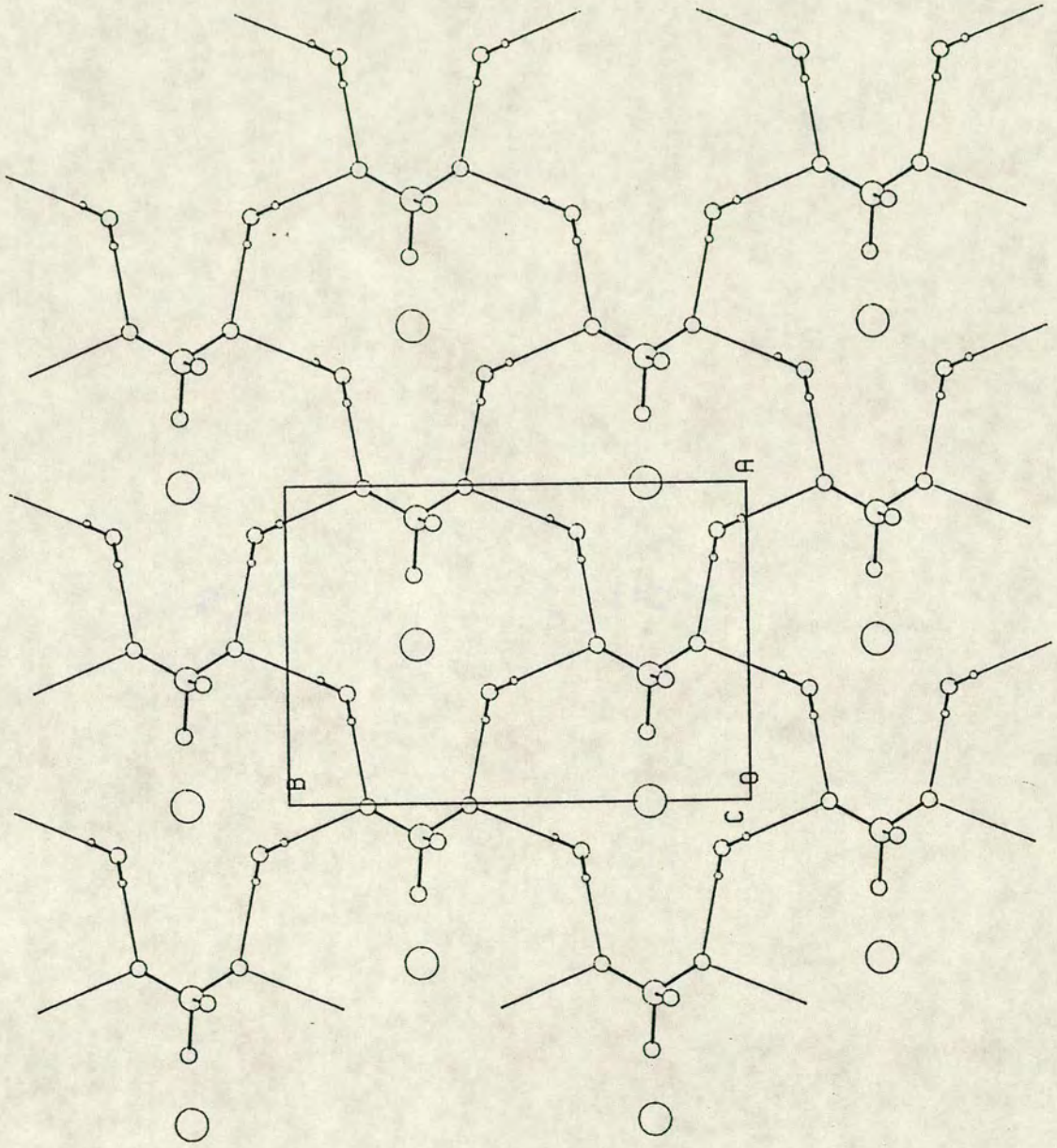
6.4.4 Ammonium 1S-4R-Camphor-10-sulphonate: hydrogen bonding columns viewed along a.



6.4.5 Potassium 1S-4R-Camphor-10-sulphonate: potassium coordination viewed along c.



6.4.6 Calcium 1S-4R-Camphor-10-sulphonate:
hydrogen bonding and calcium coordination viewed along c.



6.5.1 Bonds, angles and torsion angles in Hydronium 1S-4R-camphor-10-sulphonate (Mo data)

C(1) - C(2)	1.531(6)	C(8) -H(82)	0.99(5)
C(1) - C(6)	1.554(6)	C(8) -H(83)	0.90(5)
C(1) - C(7)	1.564(6)	C(9) -H(91)	0.84(6)
C(1) -C(10)	1.519(6)	C(9) -H(92)	1.11(5)
C(2) -O(1C)	1.203(6)	C(9) -H(93)	1.02(5)
C(2) - C(3)	1.526(7)	C(10) - S(1)	1.767(4)
C(3) - C(4)	1.526(7)	S(1) -O(1S)	1.453(3)
C(4) - C(5)	1.517(7)	S(1) -O(2S)	1.458(3)
C(4) - C(7)	1.562(6)	S(1) -O(3S)	1.450(3)
C(5) - C(6)	1.549(7)	O(1W) -H(1W)	0.93(5)
C(7) - C(8)	1.545(8)	O(1W) -H(2W)	0.96(5)
C(7) - C(9)	1.511(8)	O(1W) -H(3W)	0.90(5)
C(8) -H(81)	1.00(5)		

C(2) - C(1) - C(6)	105.2(3)	C(7) - C(8) -H(82)	101(3)
C(2) - C(1) - C(7)	98.7(3)	C(7) - C(8) -H(83)	104(3)
C(2) - C(1) -C(10)	114.6(3)	H(81) - C(8) -H(82)	99(4)
C(6) - C(1) - C(7)	102.5(3)	H(81) - C(8) -H(83)	120(4)
C(6) - C(1) -C(10)	118.0(3)	H(82) - C(8) -H(83)	127(4)
C(7) - C(1) -C(10)	115.4(3)	C(7) - C(9) -H(91)	110(4)
C(1) - C(2) -O(1C)	127.6(4)	C(7) - C(9) -H(92)	110(3)
C(1) - C(2) - C(3)	106.0(4)	C(7) - C(9) -H(93)	113(3)
O(1C) - C(2) - C(3)	126.3(4)	H(91) - C(9) -H(92)	112(5)
C(2) - C(3) - C(4)	102.5(4)	H(91) - C(9) -H(93)	110(5)
C(3) - C(4) - C(5)	106.5(4)	H(92) - C(9) -H(93)	102(4)
C(3) - C(4) - C(7)	102.6(4)	C(1) -C(10) - S(1)	117.7(3)
C(5) - C(4) - C(7)	102.5(4)	C(10) - S(1) -O(1S)	103.57(19)
C(4) - C(5) - C(6)	103.6(4)	C(10) - S(1) -O(2S)	107.80(19)
C(1) - C(6) - C(5)	103.8(4)	C(10) - S(1) -O(3S)	108.48(19)
C(1) - C(7) - C(4)	93.7(3)	O(1S) - S(1) -O(2S)	112.57(19)
C(1) - C(7) - C(8)	113.3(4)	O(1S) - S(1) -O(3S)	113.28(18)
C(1) - C(7) - C(9)	114.4(4)	O(2S) - S(1) -O(3S)	110.68(18)
C(4) - C(7) - C(8)	113.0(4)	H(1W) -O(1W) -H(2W)	114(4)
C(4) - C(7) - C(9)	114.0(4)	H(1W) -O(1W) -H(3W)	101(4)
C(8) - C(7) - C(9)	108.2(4)	H(2W) -O(1W) -H(3W)	118(4)
C(7) - C(8) -H(81)	103(3)		

C(6) - C(1) - C(2) -O(1C)	-117.5(5)	C(3) - C(4) - C(7) - C(8)	62.3(5)
C(6) - C(1) - C(2) - C(3)	66.4(4)	C(3) - C(4) - C(7) - C(9)	-173.7(4)
C(7) - C(1) - C(2) -O(1C)	136.9(5)	C(5) - C(4) - C(7) - C(1)	55.4(4)
C(7) - C(1) - C(2) - C(3)	-39.1(4)	C(5) - C(4) - C(7) - C(8)	172.6(4)
C(10) - C(1) - C(2) -O(1C)	13.8(6)	C(5) - C(4) - C(7) - C(9)	-63.4(5)
C(10) - C(1) - C(2) - C(3)	-162.3(4)	C(4) - C(5) - C(6) - C(1)	4.3(5)
C(2) - C(1) - C(6) - C(5)	-71.8(4)	C(1) - C(7) - C(8) -H(81)	-79(3)
C(7) - C(1) - C(6) - C(5)	30.9(4)	C(1) - C(7) - C(8) -H(82)	179(3)
C(10) - C(1) - C(6) - C(5)	158.9(4)	C(1) - C(7) - C(8) -H(83)	47(4)
C(2) - C(1) - C(7) - C(4)	55.9(4)	C(4) - C(7) - C(8) -H(81)	176(3)
C(2) - C(1) - C(7) - C(8)	-61.1(5)	C(4) - C(7) - C(8) -H(82)	74(3)
C(2) - C(1) - C(7) - C(9)	174.3(4)	C(4) - C(7) - C(8) -H(83)	-58(3)
C(6) - C(1) - C(7) - C(4)	-51.9(4)	C(9) - C(7) - C(8) -H(81)	49(3)
C(6) - C(1) - C(7) - C(8)	-168.8(4)	C(9) - C(7) - C(8) -H(82)	-53(3)
C(6) - C(1) - C(7) - C(9)	66.6(5)	C(9) - C(7) - C(8) -H(83)	175(3)
C(10) - C(1) - C(7) - C(4)	178.4(3)	C(1) - C(7) - C(9) -H(91)	-49(4)
C(10) - C(1) - C(7) - C(8)	61.5(5)	C(1) - C(7) - C(9) -H(92)	74(3)
C(10) - C(1) - C(7) - C(9)	-63.1(5)	C(1) - C(7) - C(9) -H(93)	-173(3)
C(2) - C(1) -C(10) - S(1)	-84.3(4)	C(4) - C(7) - C(9) -H(91)	57(4)
C(6) - C(1) -C(10) - S(1)	40.5(5)	C(4) - C(7) - C(9) -H(92)	-180(3)
C(7) - C(1) -C(10) - S(1)	162.1(3)	C(4) - C(7) - C(9) -H(93)	-66(3)
C(1) - C(2) - C(3) - C(4)	4.6(5)	C(8) - C(7) - C(9) -H(91)	-177(4)
O(1C) - C(2) - C(3) - C(4)	-171.5(5)	C(8) - C(7) - C(9) -H(92)	-53(3)
C(2) - C(3) - C(4) - C(5)	-75.2(5)	C(8) - C(7) - C(9) -H(93)	60(3)
C(2) - C(3) - C(4) - C(7)	32.0(4)	C(1) -C(10) - S(1) -O(1S)	172.3(3)
C(3) - C(4) - C(5) - C(6)	69.1(5)	C(1) -C(10) - S(1) -O(2S)	-68.2(3)
C(7) - C(4) - C(5) - C(6)	-38.2(5)	C(1) -C(10) - S(1) -O(3S)	51.7(4)
C(3) - C(4) - C(7) - C(1)	-54.9(4)		

6.5.2 Bonds, angles and torsion angles in Hydronium 1S-4R-camphor-10-sulphonate (Cu data)

C(1) - C(2)	1.523(5)	C(8) -H(82)	0.99(5)
C(1) - C(6)	1.540(5)	C(8) -H(83)	1.11(5)
C(1) - C(7)	1.563(5)	C(9) -H(91)	0.84(5)
C(1) -C(10)	1.528(5)	C(9) -H(92)	1.17(5)
C(2) -O(1C)	1.203(5)	C(9) -H(93)	0.91(5)
C(2) - C(3)	1.542(6)	C(10) - S(1)	1.774(4)
C(3) - C(4)	1.524(6)	S(1) -O(1S)	1.460(3)
C(4) - C(5)	1.523(6)	S(1) -O(2S)	1.465(3)
C(4) - C(7)	1.559(5)	S(1) -O(3S)	1.452(3)
C(5) - C(6)	1.551(6)	O(1W) -H(1W)	1.00(5)
C(7) - C(8)	1.533(7)	O(1W) -H(2W)	0.88(5)
C(7) - C(9)	1.527(7)	O(1W) -H(3W)	0.88(5)
C(8) -H(81)	0.92(5)		

C(2) - C(1) - C(6)	105.8(3)	C(7) - C(8) -H(82)	103(3)
C(2) - C(1) - C(7)	99.1(3)	C(7) - C(8) -H(83)	109.9(24)
C(2) - C(1) -C(10)	114.7(3)	H(81) - C(8) -H(82)	88(4)
C(6) - C(1) - C(7)	102.8(3)	H(81) - C(8) -H(83)	124(4)
C(6) - C(1) -C(10)	117.9(3)	H(82) - C(8) -H(83)	128(4)
C(7) - C(1) -C(10)	114.3(3)	C(7) - C(9) -H(91)	108(4)
C(1) - C(2) -O(1C)	128.0(4)	C(7) - C(9) -H(92)	110.0(22)
C(1) - C(2) - C(3)	105.8(3)	C(7) - C(9) -H(93)	108(3)
O(1C) - C(2) - C(3)	126.1(4)	H(91) - C(9) -H(92)	125(4)
C(2) - C(3) - C(4)	101.5(3)	H(91) - C(9) -H(93)	94(5)
C(3) - C(4) - C(5)	106.9(3)	H(92) - C(9) -H(93)	108(4)
C(3) - C(4) - C(7)	103.1(3)	C(1) -C(10) - S(1)	117.08(24)
C(5) - C(4) - C(7)	103.0(3)	C(10) - S(1) -O(1S)	103.50(16)
C(4) - C(5) - C(6)	102.7(3)	C(10) - S(1) -O(2S)	107.80(16)
C(1) - C(6) - C(5)	104.2(3)	C(10) - S(1) -O(3S)	108.49(16)
C(1) - C(7) - C(4)	93.0(3)	O(1S) - S(1) -O(2S)	112.64(16)
C(1) - C(7) - C(8)	113.2(3)	O(1S) - S(1) -O(3S)	113.35(16)
C(1) - C(7) - C(9)	113.7(3)	O(2S) - S(1) -O(3S)	110.60(16)
C(4) - C(7) - C(8)	112.4(3)	H(1W) -O(1W) -H(2W)	112(4)
C(4) - C(7) - C(9)	113.9(4)	H(1W) -O(1W) -H(3W)	113(4)
C(8) - C(7) - C(9)	109.8(4)	H(2W) -O(1W) -H(3W)	106(4)
C(7) - C(8) -H(81)	99(3)		

C(6) - C(1) - C(2) -O(1C)	-117.7(4)	C(3) - C(4) - C(7) - C(8)	61.0(4)
C(6) - C(1) - C(2) - C(3)	66.8(4)	C(3) - C(4) - C(7) - C(9)	-173.3(4)
C(7) - C(1) - C(2) -O(1C)	136.2(4)	C(5) - C(4) - C(7) - C(1)	55.5(3)
C(7) - C(1) - C(2) - C(3)	-39.4(4)	C(5) - C(4) - C(7) - C(8)	172.1(4)
C(10) - C(1) - C(2) -O(1C)	14.1(6)	C(5) - C(4) - C(7) - C(9)	-62.2(4)
C(10) - C(1) - C(2) - C(3)	-161.5(3)	C(4) - C(5) - C(6) - C(1)	3.7(4)
C(2) - C(1) - C(6) - C(5)	-71.8(4)	C(1) - C(7) - C(8) -H(81)	-87(3)
C(7) - C(1) - C(6) - C(5)	31.6(4)	C(1) - C(7) - C(8) -H(82)	-176(3)
C(10) - C(1) - C(6) - C(5)	158.4(3)	C(1) - C(7) - C(8) -H(83)	44.3(25)
C(2) - C(1) - C(7) - C(4)	56.3(3)	C(4) - C(7) - C(8) -H(81)	169(3)
C(2) - C(1) - C(7) - C(8)	-59.7(4)	C(4) - C(7) - C(8) -H(82)	80(3)
C(2) - C(1) - C(7) - C(9)	174.1(4)	C(4) - C(7) - C(8) -H(83)	-59.5(25)
C(6) - C(1) - C(7) - C(4)	-52.3(3)	C(9) - C(7) - C(8) -H(81)	41(3)
C(6) - C(1) - C(7) - C(8)	-168.3(3)	C(9) - C(7) - C(8) -H(82)	-48(3)
C(6) - C(1) - C(7) - C(9)	65.5(4)	C(9) - C(7) - C(8) -H(83)	172.6(25)
C(10) - C(1) - C(7) - C(4)	178.7(3)	C(1) - C(7) - C(9) -H(91)	-66(3)
C(10) - C(1) - C(7) - C(8)	62.7(4)	C(1) - C(7) - C(9) -H(92)	73.0(24)
C(10) - C(1) - C(7) - C(9)	-63.5(4)	C(1) - C(7) - C(9) -H(93)	-168(3)
C(2) - C(1) -C(10) - S(1)	-84.2(3)	C(4) - C(7) - C(9) -H(91)	39(4)
C(6) - C(1) -C(10) - S(1)	41.5(4)	C(4) - C(7) - C(9) -H(92)	177.9(24)
C(7) - C(1) -C(10) - S(1)	162.44(24)	C(4) - C(7) - C(9) -H(93)	-63(3)
C(1) - C(2) - C(3) - C(4)	4.4(4)	C(8) - C(7) - C(9) -H(91)	166(4)
O(1C) - C(2) - C(3) - C(4)	-171.3(4)	C(8) - C(7) - C(9) -H(92)	-54.9(24)
C(2) - C(3) - C(4) - C(5)	-75.5(4)	C(8) - C(7) - C(9) -H(93)	64(3)
C(2) - C(3) - C(4) - C(7)	32.7(4)	C(1) -C(10) - S(1) -O(1S)	171.7(3)
C(3) - C(4) - C(5) - C(6)	70.3(4)	C(1) -C(10) - S(1) -O(2S)	-68.7(3)
C(7) - C(4) - C(5) - C(6)	-38.1(4)	C(1) -C(10) - S(1) -O(3S)	51.1(3)
C(3) - C(4) - C(7) - C(1)	-55.6(3)		

6.5.3 Bonds, angles and torsion angles in Ammonium 1S-4R-camphor-10-sulphonate

C(1) - C(2)	1.564(10)	C(1') -C(2')	1.553(12)
C(1) - C(6)	1.548(10)	C(1') -C(6')	1.535(13)
C(1) - C(7)	1.561(10)	C(1') -C(7')	1.552(11)
C(1) -C(10)	1.525(9)	C(1') -C(10')	1.504(10)
C(2) -O(1C)	1.209(10)	C(2') -O(1C')	1.184(14)
C(2) - C(3)	1.507(12)	C(2') -C(3')	1.517(16)
C(3) - C(4)	1.522(12)	C(3') -C(4')	1.531(15)
C(4) - C(5)	1.548(12)	C(4') -C(5')	1.528(16)
C(4) - C(7)	1.551(11)	C(4') -C(7')	1.524(12)
C(5) - C(6)	1.556(12)	C(5') -C(6')	1.552(17)
C(7) - C(8)	1.504(12)	C(7') -C(8')	1.526(16)
C(7) - C(9)	1.545(12)	C(7') -C(9')	1.510(15)
C(10) - S(1)	1.783(7)	C(10')-S(1')	1.768(8)
S(1) -O(1S)	1.467(6)	S(1') -O(1S')	1.422(10)
S(1) -O(2S)	1.467(6)	S(1') -O(2S')	1.477(8)
S(1) -O(3S)	1.464(6)	S(1') -O(3S')	1.463(8)

C(2) - C(1) - C(6)	103.9(6)	C(2') -C(1') -C(6')	104.0(7)
C(2) - C(1) - C(7)	98.2(5)	C(2') -C(1') -C(7')	99.4(6)
C(2) - C(1) -C(10)	113.8(5)	C(2') -C(1') -C(10')	113.1(6)
C(6) - C(1) - C(7)	102.5(6)	C(6') -C(1') -C(7')	101.7(6)
C(6) - C(1) -C(10)	120.1(6)	C(6') -C(1') -C(10')	118.4(7)
C(7) - C(1) -C(10)	115.4(6)	C(7') -C(1') -C(10')	117.7(6)
C(1) - C(2) -O(1C)	126.0(7)	C(1') -C(2') -O(1C')	126.7(10)
C(1) - C(2) - C(3)	106.5(6)	C(1') -C(2') -C(3')	105.9(8)
O(1C) - C(2) - C(3)	127.5(7)	O(1C')-C(2') -C(3')	127.4(11)
C(2) - C(3) - C(4)	102.5(7)	C(2') -C(3') -C(4')	102.5(9)
C(3) - C(4) - C(5)	105.8(7)	C(3') -C(4') -C(5')	105.9(9)
C(3) - C(4) - C(7)	103.2(6)	C(3') -C(4') -C(7')	102.9(8)
C(5) - C(4) - C(7)	102.7(6)	C(5') -C(4') -C(7')	102.1(8)
C(4) - C(5) - C(6)	102.6(7)	C(4') -C(5') -C(6')	103.4(9)
C(1) - C(6) - C(5)	104.4(6)	C(1') -C(6') -C(5')	103.8(8)
C(1) - C(7) - C(4)	94.3(6)	C(1') -C(7') -C(4')	95.2(6)
C(1) - C(7) - C(8)	114.3(6)	C(1') -C(7') -C(8')	112.1(8)
C(1) - C(7) - C(9)	112.9(6)	C(1') -C(7') -C(9')	113.8(8)
C(4) - C(7) - C(8)	115.2(7)	C(4') -C(7') -C(8')	113.6(8)
C(4) - C(7) - C(9)	112.7(6)	C(4') -C(7') -C(9')	113.7(8)
C(8) - C(7) - C(9)	107.3(7)	C(8') -C(7') -C(9')	108.1(9)
C(1) -C(10) - S(1)	116.9(5)	C(1') -C(10')-S(1')	118.9(6)
C(10) - S(1) -O(1S)	102.8(3)	C(10')-S(1') -O(1S')	104.2(5)
C(10) - S(1) -O(2S)	107.7(3)	C(10')-S(1') -O(2S')	106.1(4)
C(10) - S(1) -O(3S)	108.1(3)	C(10')-S(1') -O(3S')	108.4(4)
O(1S) - S(1) -O(2S)	110.7(3)	O(1S')-S(1') -O(2S')	110.1(5)
O(1S) - S(1) -O(3S)	113.2(3)	O(1S')-S(1') -O(3S')	117.9(5)
O(2S) - S(1) -O(3S)	113.6(3)	O(2S')-S(1') -O(3S')	109.4(4)

C(6)	C(1)	C(2)	O(1C)	-113.6(8)	C(6')	C(1')	C(2')	O(1C')	-111.0(12)
C(6)	C(1)	C(2)	C(3)	68.2(7)	C(6')	C(1')	C(2')	C(3')	70.3(9)
C(7)	C(1)	C(2)	O(1C)	141.3(8)	C(7')	C(1')	C(2')	O(1C')	144.3(11)
C(7)	C(1)	C(2)	C(3)	-36.9(7)	C(7')	C(1')	C(2')	C(3')	-34.4(9)
C(10)	C(1)	C(2)	O(1C)	18.8(10)	C(10')	C(1')	C(2')	O(1C')	18.7(14)
C(10)	C(1)	C(2)	C(3)	-159.4(6)	C(10')	C(1')	C(2')	C(3')	-160.0(8)
C(2)	C(1)	C(6)	C(5)	-70.2(7)	C(2')	C(1')	C(6')	C(5')	-70.7(9)
C(7)	C(1)	C(6)	C(5)	31.7(7)	C(7')	C(1')	C(6')	C(5')	32.2(9)
C(10)	C(1)	C(6)	C(5)	161.2(6)	C(10')	C(1')	C(6')	C(5')	162.9(8)
C(2)	C(1)	C(7)	C(4)	54.0(6)	C(2')	C(1')	C(7')	C(4')	53.3(7)
C(2)	C(1)	C(7)	C(8)	-66.2(7)	C(2')	C(1')	C(7')	C(8')	-64.8(9)
C(2)	C(1)	C(7)	C(9)	170.8(6)	C(2')	C(1')	C(7')	C(9')	172.1(8)
C(6)	C(1)	C(7)	C(4)	-52.3(6)	C(6')	C(1')	C(7')	C(4')	-53.2(7)
C(6)	C(1)	C(7)	C(8)	-172.5(7)	C(6')	C(1')	C(7')	C(8')	-171.3(8)
C(6)	C(1)	C(7)	C(9)	64.5(8)	C(6')	C(1')	C(7')	C(9')	65.5(9)
C(10)	C(1)	C(7)	C(4)	175.2(6)	C(10')	C(1')	C(7')	C(4')	175.6(6)
C(10)	C(1)	C(7)	C(8)	55.1(8)	C(10')	C(1')	C(7')	C(8')	57.5(10)
C(10)	C(1)	C(7)	C(9)	-67.9(8)	C(10')	C(1')	C(7')	C(9')	-65.6(10)
C(2)	C(1)	C(10)	S(1)	-91.3(6)	C(2')	C(1')	C(10')	S(1')	-92.7(8)
C(6)	C(1)	C(10)	S(1)	32.7(8)	C(6')	C(1')	C(10')	S(1')	29.2(10)
C(7)	C(1)	C(10)	S(1)	156.3(5)	C(7')	C(1')	C(10')	S(1')	152.2(6)
C(1)	C(2)	C(3)	C(4)	2.9(8)	C(1')	C(2')	C(3')	C(4')	0.8(10)
O(1C)	C(2)	C(3)	C(4)	-175.2(8)	O(1C')	C(2')	C(3')	C(4')	-177.9(11)
C(2)	C(3)	C(4)	C(5)	-74.5(8)	C(2')	C(3')	C(4')	C(5')	-72.6(10)
C(2)	C(3)	C(4)	C(7)	33.0(8)	C(2')	C(3')	C(4')	C(7')	34.2(10)
C(3)	C(4)	C(5)	C(6)	71.2(8)	C(3')	C(4')	C(5')	C(6')	71.3(11)
C(7)	C(4)	C(5)	C(6)	-36.7(8)	C(7')	C(4')	C(5')	C(6')	-36.0(10)
C(3)	C(4)	C(7)	C(1)	-55.2(7)	C(3')	C(4')	C(7')	C(1')	-54.9(8)
C(3)	C(4)	C(7)	C(8)	64.3(8)	C(3')	C(4')	C(7')	C(8')	62.0(10)
C(3)	C(4)	C(7)	C(9)	-172.2(7)	C(3')	C(4')	C(7')	C(9')	-173.8(9)
C(5)	C(4)	C(7)	C(1)	54.7(7)	C(5')	C(4')	C(7')	C(1')	54.8(8)
C(5)	C(4)	C(7)	C(8)	174.1(7)	C(5')	C(4')	C(7')	C(8')	171.7(9)
C(5)	C(4)	C(7)	C(9)	-62.3(8)	C(5')	C(4')	C(7')	C(9')	-64.1(10)
C(4)	C(5)	C(6)	C(1)	2.8(8)	C(4')	C(5')	C(6')	C(1')	1.8(11)
C(1)	C(10)	S(1)	O(1S)	172.0(5)	C(1')	C(10')	S(1')	O(1S')	173.5(7)
C(1)	C(10)	S(1)	O(2S)	-71.1(6)	C(1')	C(10')	S(1')	O(2S')	-70.2(7)
C(1)	C(10)	S(1)	O(3S)	52.1(6)	C(1')	C(10')	S(1')	O(3S')	47.2(7)

6.5.4 Bonds, angles and torsion angles in Potassium 1S-4R-camphor-10-sulphonate

C(1) - C(2)	1.522(19)	C(1') -C(2')	1.506(21)
C(1) - C(6)	1.563(20)	C(1') -C(6')	1.562(22)
C(1) - C(7)	1.558(19)	C(1') -C(7')	1.568(20)
C(1) -C(10)	1.533(19)	C(1') -C(10')	1.522(21)
C(2) -O(1C)	1.218(17)	C(2') -O(1C')	1.189(20)
C(2) - C(3)	1.509(21)	C(2') -C(3')	1.491(25)
C(3) - C(4)	1.516(21)	C(3') -C(4')	1.514(24)
C(4) - C(5)	1.525(21)	C(4') -C(5')	1.54(3)
C(4) - C(7)	1.553(20)	C(4') -C(7')	1.532(21)
C(5) - C(6)	1.523(22)	C(5') -C(6')	1.55(3)
C(7) - C(8)	1.511(22)	C(7') -C(8')	1.486(24)
C(7) - C(9)	1.540(22)	C(7') -C(9')	1.58(3)
C(10) - S(1)	1.807(14)	C(10')-S(1')	1.795(16)
S(1) -O(1S)	1.450(12)	S(1') -O(1S')	1.403(23)
S(1) -O(2S)	1.461(12)	S(1') -O(2S')	1.480(14)
S(1) -O(3S)	1.440(12)	S(1') -O(3S')	1.425(15)

C(2) - C(1) - C(6)	104.5(11)	C(2') -C(1') -C(6')	106.5(12)
C(2) - C(1) - C(7)	99.6(10)	C(2') -C(1') -C(7')	99.6(11)
C(2) - C(1) -C(10)	114.9(11)	C(2') -C(1') -C(10')	114.6(12)
C(6) - C(1) - C(7)	101.4(11)	C(6') -C(1') -C(7')	102.1(11)
C(6) - C(1) -C(10)	119.3(11)	C(6') -C(1') -C(10')	116.4(12)
C(7) - C(1) -C(10)	114.5(11)	C(7') -C(1') -C(10')	115.6(12)
C(1) - C(2) -O(1C)	126.6(13)	C(1') -C(2') -O(1C')	127.8(14)
C(1) - C(2) - C(3)	106.0(11)	C(1') -C(2') -C(3')	104.3(13)
O(1C) - C(2) - C(3)	127.4(13)	O(1C')-C(2') -C(3')	127.9(15)
C(2) - C(3) - C(4)	103.2(12)	C(2') -C(3') -C(4')	105.7(14)
C(3) - C(4) - C(5)	104.9(12)	C(3') -C(4') -C(5')	105.1(14)
C(3) - C(4) - C(7)	102.1(11)	C(3') -C(4') -C(7')	100.3(13)
C(5) - C(4) - C(7)	102.9(11)	C(5') -C(4') -C(7')	102.3(13)
C(4) - C(5) - C(6)	104.2(12)	C(4') -C(5') -C(6')	104.6(15)
C(1) - C(6) - C(5)	104.0(12)	C(1') -C(6') -C(5')	102.6(14)
C(1) - C(7) - C(4)	94.0(11)	C(1') -C(7') -C(4')	94.4(11)
C(1) - C(7) - C(8)	114.2(12)	C(1') -C(7') -C(8')	114.7(13)
C(1) - C(7) - C(9)	112.6(12)	C(1') -C(7') -C(9')	113.7(13)
C(4) - C(7) - C(8)	112.5(12)	C(4') -C(7') -C(8')	115.2(13)
C(4) - C(7) - C(9)	114.6(12)	C(4') -C(7') -C(9')	112.0(13)
C(8) - C(7) - C(9)	108.6(13)	C(8') -C(7') -C(9')	106.7(14)
C(1) -C(10) - S(1)	117.3(10)	C(1') -C(10')-S(1')	118.3(11)
C(10) - S(1) -O(1S)	107.6(7)	C(10')-S(1') -O(1S')	103.4(11)
C(10) - S(1) -O(2S)	103.0(7)	C(10')-S(1') -O(2S')	108.6(8)
C(10) - S(1) -O(3S)	107.5(7)	C(10')-S(1') -O(3S')	107.7(8)
O(1S) - S(1) -O(2S)	112.4(7)	O(1S')-S(1') -O(2S')	118.1(11)
O(1S) - S(1) -O(3S)	113.4(7)	O(1S')-S(1') -O(3S')	110.9(11)
O(2S) - S(1) -O(3S)	112.2(7)	O(2S')-S(1') -O(3S')	107.7(8)

C(6)	C(1)	C(2)	O(1C)	-112.0(16)	C(6')	C(1')	C(2')	O(1C')	-111.7(18)
C(6)	C(1)	C(2)	C(3)	68.5(13)	C(6')	C(1')	C(2')	C(3')	68.9(15)
C(7)	C(1)	C(2)	O(1C)	143.4(15)	C(7')	C(1')	C(2')	O(1C')	142.5(17)
C(7)	C(1)	C(2)	C(3)	-36.0(13)	C(7')	C(1')	C(2')	C(3')	-36.9(14)
C(10)	C(1)	C(2)	O(1C)	20.6(20)	C(10')	C(1')	C(2')	O(1C')	18.4(23)
C(10)	C(1)	C(2)	C(3)	-158.8(12)	C(10')	C(1')	C(2')	C(3')	-160.9(13)
C(2)	C(1)	C(6)	C(5)	-69.1(13)	C(2')	C(1')	C(6')	C(5')	-71.2(16)
C(7)	C(1)	C(6)	C(5)	34.1(14)	C(7')	C(1')	C(6')	C(5')	32.8(15)
C(10)	C(1)	C(6)	C(5)	160.8(12)	C(10')	C(1')	C(6')	C(5')	159.7(14)
C(2)	C(1)	C(7)	C(4)	54.2(11)	C(2')	C(1')	C(7')	C(4')	55.8(12)
C(2)	C(1)	C(7)	C(8)	171.0(12)	C(2')	C(1')	C(7')	C(8')	-64.6(15)
C(2)	C(1)	C(7)	C(9)	-64.6(14)	C(2')	C(1')	C(7')	C(9')	172.2(13)
C(6)	C(1)	C(7)	C(4)	-52.9(12)	C(6')	C(1')	C(7')	C(4')	-53.5(13)
C(6)	C(1)	C(7)	C(8)	64.0(14)	C(6')	C(1')	C(7')	C(8')	-173.9(14)
C(6)	C(1)	C(7)	C(9)	-171.7(12)	C(6')	C(1')	C(7')	C(9')	62.9(16)
C(10)	C(1)	C(7)	C(4)	177.2(11)	C(10')	C(1')	C(7')	C(4')	179.1(12)
C(10)	C(1)	C(7)	C(8)	-65.9(16)	C(10')	C(1')	C(7')	C(8')	58.8(17)
C(10)	C(1)	C(7)	C(9)	58.5(16)	C(10')	C(1')	C(7')	C(9')	-64.4(17)
C(2)	C(1)	C(10)	S(1)	-91.3(13)	C(2')	C(1')	C(10')	S(1')	-87.0(14)
C(6)	C(1)	C(10)	S(1)	34.0(16)	C(6')	C(1')	C(10')	S(1')	38.1(17)
C(7)	C(1)	C(10)	S(1)	154.3(10)	C(7')	C(1')	C(10')	S(1')	158.0(11)
C(1)	C(2)	C(3)	C(4)	1.5(14)	C(1')	C(2')	C(3')	C(4')	2.9(17)
O(1C)	C(2)	C(3)	C(4)	-177.9(14)	O(1C')	C(2')	C(3')	C(4')	-176.4(16)
C(2)	C(3)	C(4)	C(5)	-73.1(13)	C(2')	C(3')	C(4')	C(5')	-72.7(17)
C(2)	C(3)	C(4)	C(7)	34.0(14)	C(2')	C(3')	C(4')	C(7')	33.1(16)
C(3)	C(4)	C(5)	C(6)	71.7(14)	C(3')	C(4')	C(5')	C(6')	68.3(17)
C(7)	C(4)	C(5)	C(6)	-34.7(14)	C(7')	C(4')	C(5')	C(6')	-36.1(17)
C(3)	C(4)	C(7)	C(1)	-54.6(12)	C(3')	C(4')	C(7')	C(1')	-53.7(13)
C(3)	C(4)	C(7)	C(8)	-172.9(12)	C(3')	C(4')	C(7')	C(8')	66.3(17)
C(3)	C(4)	C(7)	C(9)	62.4(15)	C(3')	C(4')	C(7')	C(9')	-171.5(14)
C(5)	C(4)	C(7)	C(1)	54.0(12)	C(5')	C(4')	C(7')	C(1')	54.5(14)
C(5)	C(4)	C(7)	C(8)	-64.3(15)	C(5')	C(4')	C(7')	C(8')	174.4(15)
C(5)	C(4)	C(7)	C(9)	171.1(12)	C(5')	C(4')	C(7')	C(9')	-63.4(17)
C(4)	C(5)	C(6)	C(1)	0.2(14)	C(4')	C(5')	C(6')	C(1')	1.4(18)
C(1)	C(10)	S(1)	O(1S)	50.0(12)	C(1')	C(10')	S(1')	O(1S')	165.5(14)
C(1)	C(10)	S(1)	O(2S)	168.9(10)	C(1')	C(10')	S(1')	O(2S')	39.3(14)
C(1)	C(10)	S(1)	O(3S)	-72.5(12)	C(1')	C(10')	S(1')	O(3S')	-77.0(13)

6.5.5 Bonds, angles and torsion angles in Calcium 1S-4R-camphor-10-sulphonate

C(1) - C(2)	1.539(7)	C(10) - S(1)	1.783(5)
C(1) - C(6)	1.559(6)	S(1) -O(1S)	1.463(3)
C(1) - C(7)	1.575(6)	S(1) -O(2S)	1.472(4)
C(1) -C(10)	1.527(6)	S(1) -O(3S)	1.458(4)
C(2) -O(1C)	1.223(8)	O(2S) -Ca(1)	2.319(4)
C(2) - C(3)	1.511(9)	Ca(1) -O(1W)	2.345(4)
C(3) - C(4)	1.540(8)	Ca(1) -O(2W)	2.371(4)
C(4) - C(5)	1.531(8)	O(1W) -H(1W)	0.70(6)
C(4) - C(7)	1.549(7)	O(1W) -H(2W)	0.76(6)
C(5) - C(6)	1.560(8)	O(2W) -H(3W)	0.89(5)
C(7) - C(8)	1.531(8)	O(2W) -H(4W)	0.75(6)
C(7) - C(9)	1.531(8)		

C(2) - C(1) - C(6)	103.8(4)	C(4) - C(7) - C(9)	113.5(4)
C(2) - C(1) - C(7)	100.3(4)	C(8) - C(7) - C(9)	108.5(5)
C(2) - C(1) -C(10)	110.8(4)	C(1) -C(10) - S(1)	121.0(3)
C(6) - C(1) - C(7)	101.1(3)	C(10) - S(1) -O(1S)	102.96(20)
C(6) - C(1) -C(10)	119.7(4)	C(10) - S(1) -O(2S)	106.96(20)
C(7) - C(1) -C(10)	118.5(4)	C(10) - S(1) -O(3S)	108.13(20)
C(1) - C(2) -O(1C)	126.6(5)	O(1S) - S(1) -O(2S)	112.41(20)
C(1) - C(2) - C(3)	106.4(4)	O(1S) - S(1) -O(3S)	113.67(19)
O(1C) - C(2) - C(3)	126.9(5)	O(2S) - S(1) -O(3S)	111.99(20)
C(2) - C(3) - C(4)	102.6(5)	S(1) -O(2S) -Ca(1)	156.18(22)
C(3) - C(4) - C(5)	106.9(5)	O(2S) -Ca(1) -O(1W)	89.45(13)
C(3) - C(4) - C(7)	103.4(4)	O(2S) -Ca(1) -O(2W)	88.86(13)
C(5) - C(4) - C(7)	101.6(4)	O(1W) -Ca(1) -O(2W)	91.87(14)
C(4) - C(5) - C(6)	103.1(4)	Ca(1) -O(1W) -H(1W)	137.0(47)
C(1) - C(6) - C(5)	103.8(4)	Ca(1) -O(1W) -H(2W)	120.0(46)
C(1) - C(7) - C(4)	93.9(4)	H(1W) -O(1W) -H(2W)	101.9(66)
C(1) - C(7) - C(8)	113.3(4)	Ca(1) -O(2W) -H(3W)	115.2(33)
C(1) - C(7) - C(9)	112.0(4)	Ca(1) -O(2W) -H(4W)	130.6(45)
C(4) - C(7) - C(8)	115.2(4)	H(3W) -O(2W) -H(4W)	114.0(56)

C(6) - C(1) - C(2) -O(1C)	-110.4(6)	C(6) - C(1) -C(10) - S(1)	-11.5(5)
C(6) - C(1) - C(2) - C(3)	69.4(5)	C(7) - C(1) -C(10) - S(1)	112.7(4)
C(7) - C(1) - C(2) -O(1C)	145.3(6)	C(1) - C(2) - C(3) - C(4)	1.3(6)
C(7) - C(1) - C(2) - C(3)	-34.9(5)	O(1C) - C(2) - C(3) - C(4)	-178.9(6)
C(10) - C(1) - C(2) -O(1C)	19.3(7)	C(2) - C(3) - C(4) - C(5)	-73.0(5)
C(10) - C(1) - C(2) - C(3)	-160.8(4)	C(2) - C(3) - C(4) - C(7)	33.8(5)
C(2) - C(1) - C(6) - C(5)	-71.9(4)	C(3) - C(4) - C(5) - C(6)	69.1(5)
C(7) - C(1) - C(6) - C(5)	31.8(4)	C(7) - C(4) - C(5) - C(6)	-38.9(5)
C(10) - C(1) - C(6) - C(5)	164.0(4)	C(3) - C(4) - C(7) - C(1)	-53.5(4)
C(2) - C(1) - C(7) - C(4)	52.6(4)	C(3) - C(4) - C(7) - C(8)	-171.6(5)
C(2) - C(1) - C(7) - C(8)	172.3(4)	C(3) - C(4) - C(7) - C(9)	62.5(6)
C(2) - C(1) - C(7) - C(9)	-64.7(5)	C(5) - C(4) - C(7) - C(1)	57.2(4)
C(6) - C(1) - C(7) - C(4)	-53.8(4)	C(5) - C(4) - C(7) - C(8)	-60.9(6)
C(6) - C(1) - C(7) - C(8)	65.8(5)	C(5) - C(4) - C(7) - C(9)	173.2(5)
C(6) - C(1) - C(7) - C(9)	-171.1(4)	C(4) - C(5) - C(6) - C(1)	3.8(5)
C(10) - C(1) - C(7) - C(4)	173.2(4)	C(1) -C(10) - S(1) -O(1S)	-176.3(3)
C(10) - C(1) - C(7) - C(8)	-67.2(5)	C(1) -C(10) - S(1) -O(2S)	-57.7(4)
C(10) - C(1) - C(7) - C(9)	55.9(5)	C(1) -C(10) - S(1) -O(3S)	63.1(4)
C(2) - C(1) -C(10) - S(1)	-132.2(4)		

6.5.6 Bonds, angles and torsion angles in Copper(II) 1S-4R-camphor-10-sulphonate hexahydrate

C(1) - C(2)	1.530(7)	C(5') -C(6')	1.592(7)
C(1) - C(6)	1.549(6)	C(7') -C(8')	1.531(8)
C(1) - C(7)	1.565(6)	C(7') -C(9')	1.538(6)
C(1) -C(10)	1.525(6)	C(10')-S(1')	1.768(4)
C(2) -O(1C)	1.197(7)	S(1') -O(1S')	1.458(4)
C(2) - C(3)	1.520(8)	S(1') -O(2S')	1.456(4)
C(3) - C(4)	1.541(8)	S(1') -O(3S')	1.453(4)
C(4) - C(5)	1.535(7)	Cu(1) -O(1W)	2.028(4)
C(4) - C(7)	1.530(7)	Cu(1) -O(2W)	2.179(5)
C(5) - C(6)	1.571(7)	Cu(1) -O(3W)	1.974(4)
C(7) - C(8)	1.536(7)	Cu(1) -O(4W)	1.968(4)
C(7) - C(9)	1.531(7)	Cu(1) -O(5W)	2.196(5)
C(10) - S(1)	1.777(5)	Cu(1) -O(6W)	2.059(4)
S(1) -O(1S)	1.455(4)	O(1W) -H(11W)	0.78(5)
S(1) -O(2S)	1.454(4)	O(1W) -H(12W)	0.79(5)
S(1) -O(3S)	1.463(4)	O(2W) -H(21W)	0.79(5)
C(1') -C(2')	1.536(6)	O(2W) -H(22W)	0.79(5)
C(1') -C(6')	1.556(6)	O(3W) -H(31W)	0.79(5)
C(1') -C(7')	1.557(6)	O(3W) -H(32W)	0.79(5)
C(1') -C(10')	1.521(6)	O(4W) -H(41W)	0.79(5)
C(2') -O(1C')	1.205(6)	O(4W) -H(42W)	0.79(5)
C(2') -C(3')	1.515(7)	O(5W) -H(51W)	0.79(5)
C(3') -C(4')	1.528(7)	O(5W) -H(52W)	0.79(5)
C(4') -C(5')	1.514(7)	O(6W) -H(61W)	0.79(5)
C(4') -C(7')	1.561(7)	O(6W) -H(62W)	0.79(5)

C(6) - C(1) - C(2) -O(1C)	-109.6(6)	C(6') -C(1') -C(2') -O(1C')	-107.5(5)
C(6) - C(1) - C(2) - C(3)	70.0(5)	C(6') -C(1') -C(2') -C(3')	71.6(4)
C(7) - C(1) - C(2) -O(1C)	144.4(5)	C(7') -C(1') -C(2') -O(1C')	147.8(5)
C(7) - C(1) - C(2) - C(3)	-35.9(5)	C(7') -C(1') -C(2') -C(3')	-33.1(4)
C(10) - C(1) - C(2) -O(1C)	19.0(7)	C(10')-C(1') -C(2') -O(1C')	15.8(6)
C(10) - C(1) - C(2) - C(3)	-161.3(4)	C(10')-C(1') -C(2') -C(3')	-165.1(4)
C(2) - C(1) - C(6) - C(5)	-71.1(4)	C(2') -C(1') -C(6') -C(5')	-70.9(4)
C(7) - C(1) - C(6) - C(5)	31.5(4)	C(7') -C(1') -C(6') -C(5')	32.8(4)
C(10) - C(1) - C(6) - C(5)	166.0(4)	C(10')-C(1') -C(6') -C(5')	171.0(4)
C(2) - C(1) - C(7) - C(4)	54.9(4)	C(2') -C(1') -C(7') -C(4')	51.8(4)
C(2) - C(1) - C(7) - C(8)	-63.7(5)	C(2') -C(1') -C(7') -C(8')	-66.9(5)
C(2) - C(1) - C(7) - C(9)	173.6(4)	C(2') -C(1') -C(7') -C(9')	168.7(4)
C(6) - C(1) - C(7) - C(4)	-51.7(4)	C(6') -C(1') -C(7') -C(4')	-53.0(4)
C(6) - C(1) - C(7) - C(8)	-170.4(4)	C(6') -C(1') -C(7') -C(8')	-171.8(4)
C(6) - C(1) - C(7) - C(9)	67.0(5)	C(6') -C(1') -C(7') -C(9')	63.9(4)
C(10) - C(1) - C(7) - C(4)	173.8(4)	C(10')-C(1') -C(7') -C(4')	173.3(4)
C(10) - C(1) - C(7) - C(8)	55.1(5)	C(10')-C(1') -C(7') -C(8')	54.5(6)
C(10) - C(1) - C(7) - C(9)	-67.5(5)	C(10')-C(1') -C(7') -C(9')	-69.8(5)
C(2) - C(1) -C(10) - S(1)	-142.6(4)	C(2') -C(1') -C(10')-S(1')	175.0(3)
C(6) - C(1) -C(10) - S(1)	-22.8(6)	C(6') -C(1') -C(10')-S(1')	-70.6(4)
C(7) - C(1) -C(10) - S(1)	104.6(4)	C(7') -C(1') -C(10')-S(1')	57.3(5)
C(1) - C(2) - C(3) - C(4)	1.9(5)	C(1') -C(2') -C(3') -C(4')	-1.3(5)
O(1C) - C(2) - C(3) - C(4)	-178.4(5)	O(1C')-C(2') -C(3') -C(4')	177.8(5)
C(2) - C(3) - C(4) - C(5)	-73.8(5)	C(2') -C(3') -C(4') -C(5')	-73.0(5)
C(2) - C(3) - C(4) - C(7)	34.1(5)	C(2') -C(3') -C(4') -C(7')	35.6(5)
C(3) - C(4) - C(5) - C(6)	71.3(5)	C(3') -C(4') -C(5') -C(6')	71.4(4)
C(7) - C(4) - C(5) - C(6)	-35.5(5)	C(7') -C(4') -C(5') -C(6')	-36.7(4)

C(3) - C(4) - C(7) - C(1)	-55.4(4)	C(3') -C(4') -C(7') -C(1')	-54.7(4)
C(3) - C(4) - C(7) - C(8)	63.1(5)	C(3') -C(4') -C(7') -C(8')	61.7(5)
C(3) - C(4) - C(7) - C(9)	-174.2(4)	C(3') -C(4') -C(7') -C(9')	-174.7(4)
C(5) - C(4) - C(7) - C(1)	53.3(4)	C(5') -C(4') -C(7') -C(1')	56.1(4)
C(5) - C(4) - C(7) - C(8)	171.9(4)	C(5') -C(4') -C(7') -C(8')	172.5(4)
C(5) - C(4) - C(7) - C(9)	-65.4(5)	C(5') -C(4') -C(7') -C(9')	-63.9(5)
C(4) - C(5) - C(6) - C(1)	1.7(5)	C(4') -C(5') -C(6') -C(1')	2.3(4)
C(1) -C(10) - S(1) -O(1S)	61.1(4)	C(1') -C(10')-S(1') -O(1S')	165.8(3)
C(1) -C(10) - S(1) -O(2S)	-59.4(4)	C(1') -C(10')-S(1') -O(2S')	-75.9(4)
C(1) -C(10) - S(1) -O(3S)	-179.8(3)	C(1') -C(10')-S(1') -O(3S')	45.8(4)

C(2) - C(1) - C(6)	103.9(4)	C(1') -C(7') -C(9')	115.9(4)
C(2) - C(1) - C(7)	98.8(3)	C(4') -C(7') -C(8')	114.8(4)
C(2) - C(1) -C(10)	110.1(4)	C(4') -C(7') -C(9')	112.0(4)
C(6) - C(1) - C(7)	103.1(3)	C(8') -C(7') -C(9')	108.0(4)
C(6) - C(1) -C(10)	119.1(4)	C(1') -C(10')-S(1')	121.2(3)
C(7) - C(1) -C(10)	119.0(4)	C(10')-S(1') -O(1S')	103.45(20)
C(1) - C(2) -O(1C)	127.1(5)	C(10')-S(1') -O(2S')	106.52(21)
C(1) - C(2) - C(3)	106.4(4)	C(10')-S(1') -O(3S')	108.39(21)
O(1C) - C(2) - C(3)	126.5(5)	O(1S')-S(1') -O(2S')	112.12(21)
C(2) - C(3) - C(4)	102.1(4)	O(1S')-S(1') -O(3S')	112.79(21)
C(3) - C(4) - C(5)	104.8(4)	O(2S')-S(1') -O(3S')	112.86(22)
C(3) - C(4) - C(7)	102.1(4)	O(1W) -Cu(1) -O(2W)	96.71(17)
C(5) - C(4) - C(7)	103.7(4)	O(1W) -Cu(1) -O(3W)	90.26(17)
C(4) - C(5) - C(6)	103.3(4)	O(1W) -Cu(1) -O(4W)	88.65(16)
C(1) - C(6) - C(5)	103.2(4)	O(1W) -Cu(1) -O(5W)	84.46(16)
C(1) - C(7) - C(4)	94.8(3)	O(1W) -Cu(1) -O(6W)	179.49(16)
C(1) - C(7) - C(8)	113.7(4)	O(2W) -Cu(1) -O(3W)	90.51(17)
C(1) - C(7) - C(9)	113.8(4)	O(2W) -Cu(1) -O(4W)	90.03(17)
C(4) - C(7) - C(8)	113.8(4)	O(2W) -Cu(1) -O(5W)	178.83(17)
C(4) - C(7) - C(9)	113.9(4)	O(2W) -Cu(1) -O(6W)	82.79(17)
C(8) - C(7) - C(9)	106.8(4)	O(3W) -Cu(1) -O(4W)	178.84(17)
C(1) -C(10) - S(1)	119.2(3)	O(3W) -Cu(1) -O(5W)	89.33(17)
C(10) - S(1) -O(1S)	107.37(23)	O(3W) -Cu(1) -O(6W)	89.68(16)
C(10) - S(1) -O(2S)	107.24(23)	O(4W) -Cu(1) -O(5W)	90.15(16)
C(10) - S(1) -O(3S)	104.63(22)	O(4W) -Cu(1) -O(6W)	91.40(16)
O(1S) - S(1) -O(2S)	111.99(24)	O(5W) -Cu(1) -O(6W)	96.04(16)
O(1S) - S(1) -O(3S)	111.94(23)	Cu(1) -O(1W) -H(11W)	136.1(36)
O(2S) - S(1) -O(3S)	113.12(22)	Cu(1) -O(1W) -H(12W)	107.6(33)
C(2') -C(1') -C(6')	102.1(3)	H(11W)-O(1W) -H(12W)	113.0(49)
C(2') -C(1') -C(7')	100.5(3)	Cu(1) -O(2W) -H(21W)	126.2(35)
C(2') -C(1') -C(10')	108.7(3)	Cu(1) -O(2W) -H(22W)	122.6(36)
C(6') -C(1') -C(7')	101.9(3)	H(21W)-O(2W) -H(22W)	103.6(50)
C(6') -C(1') -C(10')	116.2(3)	Cu(1) -O(3W) -H(31W)	125.5(33)
C(7') -C(1') -C(10')	124.4(4)	Cu(1) -O(3W) -H(32W)	121.7(33)
C(1') -C(2') -O(1C')	125.5(4)	H(31W)-O(3W) -H(32W)	112.3(47)
C(1') -C(2') -C(3')	107.0(4)	Cu(1) -O(4W) -H(41W)	125.6(33)
O(1C')-C(2') -C(3')	127.5(5)	Cu(1) -O(4W) -H(42W)	122.8(35)
C(2') -C(3') -C(4')	102.0(4)	H(41W)-O(4W) -H(42W)	99.7(48)
C(3') -C(4') -C(5')	106.5(4)	Cu(1) -O(5W) -H(51W)	131.8(36)
C(3') -C(4') -C(7')	103.0(4)	Cu(1) -O(5W) -H(52W)	114.2(34)
C(5') -C(4') -C(7')	103.5(4)	H(51W)-O(5W) -H(52W)	106.0(50)
C(4') -C(5') -C(6')	102.2(4)	Cu(1) -O(6W) -H(61W)	117.1(35)
C(1') -C(6') -C(5')	103.7(4)	Cu(1) -O(6W) -H(62W)	115.4(36)
C(1') -C(7') -C(4')	94.1(3)	H(61W)-O(6W) -H(62W)	102.1(51)
C(1') -C(7') -C(8')	111.9(4)		

6.5.7 Bonds, angles and torsion angles in R-phenylglycinium 1S-4R-camphor-10-sulphonate

C(1) - C(2)	1.524(7)
C(1) - C(6)	1.560(7)
C(1) - C(7)	1.566(7)
C(1) -C(10)	1.517(8)
C(2) -O(1C)	1.217(7)
C(2) - C(3)	1.515(8)
C(3) - C(4)	1.533(8)
C(4) - C(5)	1.523(8)
C(4) - C(7)	1.560(8)
C(5) - C(6)	1.539(8)
C(7) - C(8)	1.524(8)
C(7) - C(9)	1.523(9)
C(10) - S(1)	1.751(6)
S(1) -O(1S)	1.441(5)
S(1) -O(2S)	1.425(7)
S(1) -O(3S)	1.447(5)

C(1A) -N(1A)	1.491(8)
C(1A) -C(3A)	1.528(8)
C(1A) -C(21A)	1.509(8)
N(1A) -H(1NA)	0.79(6)
N(1A) -H(2NA)	1.16(6)
N(1A) -H(3NA)	0.78(6)
C(3A) -O(31A)	1.322(8)
C(3A) -O(32A)	1.167(8)
O(31A)-H(31A)	0.86(6)
C(21A)-C(22A)	1.377(8)
C(21A)-C(26A)	1.388(8)
C(22A)-C(23A)	1.383(8)
C(23A)-C(24A)	1.371(9)
C(24A)-C(25A)	1.384(9)
C(25A)-C(26A)	1.370(8)

C(2) - C(1) - C(6)	102.5(4)
C(2) - C(1) - C(7)	98.7(4)
C(2) - C(1) -C(10)	114.6(4)
C(6) - C(1) - C(7)	102.2(4)
C(6) - C(1) -C(10)	120.0(4)
C(7) - C(1) -C(10)	115.8(4)
C(1) - C(2) -O(1C)	126.8(5)
C(1) - C(2) - C(3)	107.7(4)
O(1C) - C(2) - C(3)	125.5(5)
C(2) - C(3) - C(4)	101.5(5)
C(3) - C(4) - C(5)	106.5(5)
C(3) - C(4) - C(7)	102.1(4)
C(5) - C(4) - C(7)	103.5(4)
C(4) - C(5) - C(6)	103.1(5)
C(1) - C(6) - C(5)	104.8(4)
C(1) - C(7) - C(4)	93.9(4)
C(1) - C(7) - C(8)	112.6(5)
C(1) - C(7) - C(9)	113.2(5)
C(4) - C(7) - C(8)	115.6(5)
C(4) - C(7) - C(9)	112.8(5)
C(8) - C(7) - C(9)	108.4(5)
C(1) -C(10) - S(1)	121.5(4)
C(10) - S(1) -O(1S)	105.4(3)
C(10) - S(1) -O(2S)	109.1(4)
C(10) - S(1) -O(3S)	107.2(3)

O(1S) - S(1) -O(2S)	116.0(3)
O(1S) - S(1) -O(3S)	111.1(3)
O(2S) - S(1) -O(3S)	107.6(4)
N(1A) -C(1A) -C(3A)	106.9(4)
N(1A) -C(1A) -C(21A)	111.7(4)
C(3A) -C(1A) -C(21A)	111.9(4)
C(1A) -N(1A) -H(1NA)	109.9(46)
C(1A) -N(1A) -H(2NA)	114.0(28)
C(1A) -N(1A) -H(3NA)	106.7(46)
H(1NA)-N(1A) -H(2NA)	103.6(53)
H(1NA)-N(1A) -H(3NA)	110.0(65)
H(2NA)-N(1A) -H(3NA)	112.6(54)
C(1A) -C(3A) -O(31A)	109.4(5)
C(1A) -C(3A) -O(32A)	125.1(6)
O(31A)-C(3A) -O(32A)	125.5(6)
C(3A) -O(31A)-H(31A)	113.3(41)
C(1A) -C(21A)-C(22A)	119.3(5)
C(1A) -C(21A)-C(26A)	120.9(5)
C(22A)-C(21A)-C(26A)	119.8(5)
C(21A)-C(22A)-C(23A)	119.6(5)
C(22A)-C(23A)-C(24A)	121.1(6)
C(23A)-C(24A)-C(25A)	118.8(6)
C(24A)-C(25A)-C(26A)	121.0(6)
C(21A)-C(26A)-C(25A)	119.7(5)

C(6)	C(1)	C(2)	O(1C)	-114.0(6)	C(5)	C(4)	C(7)	C(8)	171.8(5)
C(6)	C(1)	C(2)	C(3)	68.9(5)	C(5)	C(4)	C(7)	C(9)	-62.7(6)
C(7)	C(1)	C(2)	O(1C)	141.3(6)	C(4)	C(5)	C(6)	C(1)	3.8(5)
C(7)	C(1)	C(2)	C(3)	-35.8(5)	C(1)	C(10)	S(1)	O(1S)	179.7(4)
C(10)	C(1)	C(2)	O(1C)	17.7(8)	C(1)	C(10)	S(1)	O(2S)	-55.0(6)
C(10)	C(1)	C(2)	C(3)	-159.4(5)	C(1)	C(10)	S(1)	O(3S)	61.3(5)
C(2)	C(1)	C(6)	C(5)	-71.3(5)	C(3A)	C(1A)	N(1A)	H(1NA)	65.5(49)
C(7)	C(1)	C(6)	C(5)	30.6(5)	C(3A)	C(1A)	N(1A)	H(2NA)	-50.3(31)
C(10)	C(1)	C(6)	C(5)	160.4(5)	C(3A)	C(1A)	N(1A)	H(3NA)	-175.3(48)
C(2)	C(1)	C(7)	C(4)	54.3(4)	C(21A)	C(1A)	N(1A)	H(1NA)	-171.8(49)
C(2)	C(1)	C(7)	C(8)	-65.5(5)	C(21A)	C(1A)	N(1A)	H(2NA)	72.4(31)
C(2)	C(1)	C(7)	C(9)	171.1(5)	C(21A)	C(1A)	N(1A)	H(3NA)	-52.6(48)
C(6)	C(1)	C(7)	C(4)	-50.6(4)	N(1A)	C(1A)	C(3A)	O(31A)	-169.9(5)
C(6)	C(1)	C(7)	C(8)	-170.4(4)	N(1A)	C(1A)	C(3A)	O(32A)	11.1(8)
C(6)	C(1)	C(7)	C(9)	66.2(5)	C(21A)	C(1A)	C(3A)	O(31A)	67.6(6)
C(10)	C(1)	C(7)	C(4)	177.1(4)	C(21A)	C(1A)	C(3A)	O(32A)	-111.4(7)
C(10)	C(1)	C(7)	C(8)	57.3(6)	N(1A)	C(1A)	C(21A)	C(22A)	128.2(5)
C(10)	C(1)	C(7)	C(9)	-66.1(6)	N(1A)	C(1A)	C(21A)	C(26A)	-53.5(7)
C(2)	C(1)	C(10)	S(1)	-100.6(5)	C(3A)	C(1A)	C(21A)	C(22A)	-112.0(6)
C(6)	C(1)	C(10)	S(1)	22.0(7)	C(3A)	C(1A)	C(21A)	C(26A)	66.3(7)
C(7)	C(1)	C(10)	S(1)	145.5(4)	C(1A)	C(3A)	O(31A)	H(31A)	-171.3(44)
C(1)	C(2)	C(3)	C(4)	0.8(6)	O(32A)	C(3A)	O(31A)	H(31A)	7.7(45)
O(1C)	C(2)	C(3)	C(4)	-176.4(5)	C(1A)	C(21A)	C(22A)	C(23A)	177.4(5)
C(2)	C(3)	C(4)	C(5)	-73.1(5)	C(26A)	C(21A)	C(22A)	C(23A)	-0.9(8)
C(2)	C(3)	C(4)	C(7)	35.0(5)	C(1A)	C(21A)	C(26A)	C(25A)	-178.0(5)
C(3)	C(4)	C(5)	C(6)	69.9(5)	C(22A)	C(21A)	C(26A)	C(25A)	0.3(8)
C(7)	C(4)	C(5)	C(6)	-37.3(5)	C(21A)	C(22A)	C(23A)	C(24A)	1.1(9)
C(3)	C(4)	C(7)	C(1)	-56.0(5)	C(22A)	C(23A)	C(24A)	C(25A)	-0.7(9)
C(3)	C(4)	C(7)	C(8)	61.3(6)	C(23A)	C(24A)	C(25A)	C(26A)	0.1(9)
C(3)	C(4)	C(7)	C(9)	-173.3(5)	C(24A)	C(25A)	C(26A)	C(21A)	0.2(9)
C(5)	C(4)	C(7)	C(1)	54.5(5)					

6.5.8 Bonds, angles and torsion angles in S-methioninium 1S-4R-camphor-10-sulphonate

C(1) - C(2)	1.534(8)	S(1) -O(2S)	1.470(6)
C(1) - C(6)	1.571(8)	S(1) -O(3S)	1.431(8)
C(1) - C(7)	1.560(8)	C(1') -N(1')	1.499(8)
C(1) -C(10)	1.503(8)	C(1') -C(3')	1.491(8)
C(2) -O(1C)	1.215(9)	C(1') -C(2')	1.542(8)
C(2) - C(3)	1.486(10)	N(1') -H(1N')	1.08(6)
C(3) - C(4)	1.532(10)	N(1') -H(2N')	1.08(5)
C(4) - C(5)	1.549(10)	N(1') -H(3N')	1.08(6)
C(4) - C(7)	1.553(9)	C(3') -O(31')	1.306(8)
C(5) - C(6)	1.529(10)	C(3') -O(32')	1.212(8)
C(7) - C(8)	1.538(9)	O(31')-H(31')	0.78(8)
C(7) - C(9)	1.519(11)	C(2') -C(21')	1.523(9)
C(10) - S(1)	1.779(6)	C(21')-S(1')	1.813(6)
S(1) -O(1S)	1.460(5)	S(1') -C(1S')	1.789(9)

C(2) - C(1) - C(6)	101.6(5)	C(10) - S(1) -O(1S)	108.6(3)
C(2) - C(1) - C(7)	99.5(4)	C(10) - S(1) -O(2S)	107.2(3)
C(2) - C(1) -C(10)	109.4(5)	C(10) - S(1) -O(3S)	104.8(4)
C(6) - C(1) - C(7)	101.9(4)	O(1S) - S(1) -O(2S)	111.8(3)
C(6) - C(1) -C(10)	116.2(5)	O(1S) - S(1) -O(3S)	111.3(4)
C(7) - C(1) -C(10)	124.8(5)	O(2S) - S(1) -O(3S)	112.8(4)
C(1) - C(2) -O(1C)	125.0(6)	N(1') -C(1') -C(3')	108.7(5)
C(1) - C(2) - C(3)	108.0(5)	N(1') -C(1') -C(2')	111.9(5)
O(1C) - C(2) - C(3)	127.0(6)	C(3') -C(1') -C(2')	112.5(5)
C(2) - C(3) - C(4)	102.3(6)	C(1') -N(1') -H(1N')	99.2(31)
C(3) - C(4) - C(5)	105.1(5)	C(1') -N(1') -H(2N')	102.7(29)
C(3) - C(4) - C(7)	102.1(5)	C(1') -N(1') -H(3N')	124.9(31)
C(5) - C(4) - C(7)	102.1(5)	H(1N')-N(1') -H(2N')	123.9(42)
C(4) - C(5) - C(6)	104.3(5)	H(1N')-N(1') -H(3N')	102.1(43)
C(1) - C(6) - C(5)	103.9(5)	H(2N')-N(1') -H(3N')	106.0(42)
C(1) - C(7) - C(4)	94.7(4)	C(1') -C(3') -O(31')	111.9(5)
C(1) - C(7) - C(8)	115.5(5)	C(1') -C(3') -O(32')	123.4(6)
C(1) - C(7) - C(9)	112.9(5)	O(31')-C(3') -O(32')	124.7(6)
C(4) - C(7) - C(8)	110.8(5)	C(3') -O(31')-H(31')	115.7(58)
C(4) - C(7) - C(9)	115.1(6)	C(1') -C(2') -C(21')	113.0(5)
C(8) - C(7) - C(9)	107.6(6)	C(2') -C(21')-S(1')	114.0(4)
C(1) -C(10) - S(1)	120.8(4)	C(21')-S(1') -C(1S')	101.1(4)

C(6) - C(1) - C(2) -O(1C)	-106.4(7)	C(3) - C(4) - C(7) - C(1)	-54.7(5)
C(6) - C(1) - C(2) - C(3)	72.0(6)	C(3) - C(4) - C(7) - C(8)	-174.3(5)
C(7) - C(1) - C(2) -O(1C)	149.3(7)	C(3) - C(4) - C(7) - C(9)	63.3(7)
C(7) - C(1) - C(2) - C(3)	-32.3(6)	C(5) - C(4) - C(7) - C(1)	53.8(5)
C(10) - C(1) - C(2) -O(1C)	17.0(9)	C(5) - C(4) - C(7) - C(8)	-65.7(6)
C(10) - C(1) - C(2) - C(3)	-164.5(5)	C(5) - C(4) - C(7) - C(9)	171.9(6)
C(2) - C(1) - C(6) - C(5)	-69.7(6)	C(4) - C(5) - C(6) - C(1)	1.4(6)
C(7) - C(1) - C(6) - C(5)	32.7(6)	C(1) -C(10) - S(1) -O(1S)	46.8(6)
C(10) - C(1) - C(6) - C(5)	171.7(5)	C(1) -C(10) - S(1) -O(2S)	-74.1(5)
C(2) - C(1) - C(7) - C(4)	51.5(5)	C(1) -C(10) - S(1) -O(3S)	165.8(5)
C(2) - C(1) - C(7) - C(8)	167.2(5)	C(3') -C(1') -N(1') -H(1N')	-121.2(31)
C(2) - C(1) - C(7) - C(9)	-68.3(6)	C(3') -C(1') -N(1') -H(2N')	6.8(30)
C(6) - C(1) - C(7) - C(4)	-52.6(5)	C(3') -C(1') -N(1') -H(3N')	127.0(38)
C(6) - C(1) - C(7) - C(8)	63.2(6)	C(2') -C(1') -N(1') -H(1N')	114.0(31)
C(6) - C(1) - C(7) - C(9)	-172.3(6)	C(2') -C(1') -N(1') -H(2N')	-118.0(29)
C(10) - C(1) - C(7) - C(4)	173.2(5)	C(2') -C(1') -N(1') -H(3N')	2.2(38)
C(10) - C(1) - C(7) - C(8)	-71.0(7)	N(1') -C(1') -C(3') -O(31')	179.1(5)
C(10) - C(1) - C(7) - C(9)	53.5(8)	N(1') -C(1') -C(3') -O(32')	0.6(8)
C(2) - C(1) -C(10) - S(1)	172.7(4)	C(2') -C(1') -C(3') -O(31')	-56.5(7)
C(6) - C(1) -C(10) - S(1)	-73.0(6)	C(2') -C(1') -C(3') -O(32')	125.1(6)
C(7) - C(1) -C(10) - S(1)	55.5(7)	N(1') -C(1') -C(2') -C(21')	71.9(6)
C(1) - C(2) - C(3) - C(4)	-1.9(7)	C(3') -C(1') -C(2') -C(21')	-50.7(7)
O(1C) - C(2) - C(3) - C(4)	176.5(7)	C(1') -C(3') -O(31') -H(31')	168.2(64)
C(2) - C(3) - C(4) - C(5)	-70.3(6)	O(32') -C(3') -O(31') -H(31')	-13.4(65)
C(2) - C(3) - C(4) - C(7)	36.0(6)	C(1') -C(2') -C(21') -S(1')	179.0(4)
C(3) - C(4) - C(5) - C(6)	70.9(6)	C(2') -C(21') -S(1') -C(1S')	73.4(5)
C(7) - C(4) - C(5) - C(6)	-35.3(6)		

6.5.9 Bonds, angles and torsion angles in S-methioninium 1R-4S-camphor-10-sulphonate

C(1) - C(2)	1.512(5)
C(1) - C(6)	1.573(5)
C(1) - C(7)	1.581(5)
C(1) -C(10)	1.525(5)
C(2) -O(1C)	1.221(4)
C(2) - C(3)	1.525(5)
C(3) - C(4)	1.541(6)
C(4) - C(5)	1.536(6)
C(4) - C(7)	1.547(5)
C(5) - C(6)	1.556(6)
C(7) - C(8)	1.513(6)
C(7) - C(9)	1.541(6)
C(10)- S(1)	1.787(3)
S(1) -O(1S)	1.457(3)
S(1) -O(2S)	1.478(3)
S(1) -O(3S)	1.450(3)
C(1A) -N(1A)	1.490(5)
C(1A) -C(3A)	1.531(5)
C(1A) -C(2A)	1.530(6)
N(1A) -H(1NA)	0.73(5)
N(1A) -H(2NA)	0.97(4)
N(1A) -H(3NA)	0.95(5)
C(3A) -O(31A)	1.317(4)
C(3A) -O(32A)	1.203(4)
O(31A)-H(31A)	0.91(5)
C(2A) -C(21A)	1.530(8)
C(21A)-S(1A)	1.971(7)
C(21A)-S(1B)	1.806(6)
S(1A) -C(1SA)	1.787(21)
S(1B) -C(1SB)	1.842(10)

C(2) - C(1) - C(6)	104.1(3)
C(2) - C(1) - C(7)	99.2(3)
C(2) - C(1) -C(10)	116.0(3)
C(6) - C(1) - C(7)	101.2(3)
C(6) - C(1) -C(10)	118.7(3)
C(7) - C(1) -C(10)	114.8(3)
C(1) - C(2) -O(1C)	127.3(3)
C(1) - C(2) - C(3)	107.7(3)
O(1C)- C(2) - C(3)	125.0(3)
C(2) - C(3) - C(4)	101.1(3)
C(3) - C(4) - C(5)	107.0(3)
C(3) - C(4) - C(7)	102.8(3)
C(5) - C(4) - C(7)	103.5(3)
C(4) - C(5) - C(6)	102.5(4)
C(1) - C(6) - C(5)	104.5(3)
C(1) - C(7) - C(4)	93.7(3)
C(1) - C(7) - C(8)	112.8(3)
C(1) - C(7) - C(9)	113.2(3)
C(4) - C(7) - C(8)	114.6(3)
C(4) - C(7) - C(9)	113.5(3)
C(8) - C(7) - C(9)	108.5(3)
C(1) -C(10) - S(1)	118.76(23)
C(10)- S(1) -O(1S)	104.72(15)
C(10) - S(1) -O(2S)	107.05(15)
C(10) - S(1) -O(3S)	107.31(15)
O(1S) - S(1) -O(2S)	112.53(15)
O(1S) - S(1) -O(3S)	113.86(15)
O(2S) - S(1) -O(3S)	110.81(15)
N(1A) -C(1A) -C(3A)	108.1(3)
N(1A) -C(1A) -C(2A)	112.0(3)
C(3A) -C(1A) -C(2A)	111.5(3)
C(1A) -N(1A) -H(1NA)	95.8(39)
C(1A) -N(1A) -H(2NA)	110.5(25)
C(1A) -N(1A) -H(3NA)	111.7(28)
H(1NA)-N(1A) -H(2NA)	120.5(46)
H(1NA)-N(1A) -H(3NA)	113.4(48)
H(2NA)-N(1A) -H(3NA)	104.9(37)
C(1A) -C(3A) -O(31A)	110.7(3)
C(1A) -C(3A) -O(32A)	123.7(3)
O(31A)-C(3A) -O(32A)	125.6(3)
C(3A) -O(31A)-H(31A)	105.5(29)
C(1A) -C(2A) -C(21A)	113.7(4)
C(2A) -C(21A)-S(1A)	90.8(3)
C(2A) -C(21A)-S(1B)	121.0(4)
C(21A)-S(1A) -C(1SA)	98.0(7)
C(21A)-S(1B) -C(1SB)	96.8(4)

C(6)	C(1)	C(2)	-O(1C)	114.7(4)
C(6)	C(1)	C(2)	C(3)	-68.4(3)
C(7)	C(1)	C(2)	-O(1C)	-141.2(4)
C(7)	C(1)	C(2)	C(3)	35.7(3)
C(10)	C(1)	C(2)	-O(1C)	-17.7(5)
C(10)	C(1)	C(2)	C(3)	159.2(3)
C(2)	C(1)	C(6)	C(5)	70.8(3)
C(7)	C(1)	C(6)	C(5)	-31.8(4)
C(10)	C(1)	C(6)	C(5)	-158.4(3)
C(2)	C(1)	C(7)	C(4)	-54.1(3)
C(2)	C(1)	C(7)	C(8)	64.7(4)
C(2)	C(1)	C(7)	C(9)	-171.7(3)
C(6)	C(1)	C(7)	C(4)	52.4(3)
C(6)	C(1)	C(7)	C(8)	171.2(3)
C(6)	C(1)	C(7)	C(9)	-65.2(4)
C(10)	C(1)	C(7)	C(4)	-178.4(3)
C(10)	C(1)	C(7)	C(8)	-59.7(4)
C(10)	C(1)	C(7)	C(9)	64.0(4)
C(2)	C(1)	-C(10)	S(1)	86.5(3)
C(6)	C(1)	-C(10)	S(1)	-38.8(4)
C(7)	C(1)	-C(10)	S(1)	-158.60(24)
C(1)	C(2)	C(3)	C(4)	-1.4(4)
O(1C)	C(2)	C(3)	C(4)	175.6(4)
C(2)	C(3)	C(4)	C(5)	73.9(4)
C(2)	C(3)	C(4)	C(7)	-34.7(4)
C(3)	C(4)	C(5)	C(6)	-70.4(4)
C(7)	C(4)	C(5)	C(6)	37.8(4)
C(3)	C(4)	C(7)	C(1)	55.3(3)
C(3)	C(4)	C(7)	C(8)	-62.0(4)
C(3)	C(4)	C(7)	C(9)	172.6(3)
C(5)	C(4)	C(7)	C(1)	-56.1(3)
C(5)	C(4)	C(7)	C(8)	-173.3(4)
C(5)	C(4)	C(7)	C(9)	61.3(4)
C(4)	C(5)	C(6)	C(1)	-2.8(4)
C(1)	-C(10)	S(1)	-O(1S)	-176.4(3)
C(1)	-C(10)	S(1)	-O(2S)	-63.9(3)
C(1)	-C(10)	S(1)	-O(3S)	55.1(3)
C(3A)	-C(1A)	-N(1A)	-H(1NA)	172.4(39)
C(3A)	-C(1A)	-N(1A)	-H(2NA)	-61.9(27)
C(3A)	-C(1A)	-N(1A)	-H(3NA)	54.4(30)
C(2A)	-C(1A)	-N(1A)	-H(1NA)	49.2(39)
C(2A)	-C(1A)	-N(1A)	-H(2NA)	174.8(27)
C(2A)	-C(1A)	-N(1A)	-H(3NA)	-68.8(30)
N(1A)	-C(1A)	-C(3A)	-O(31A)	165.1(3)
N(1A)	-C(1A)	-C(3A)	-O(32A)	-17.7(5)
C(2A)	-C(1A)	-C(3A)	-O(31A)	-71.3(4)
C(2A)	-C(1A)	-C(3A)	-O(32A)	105.9(4)
N(1A)	-C(1A)	-C(2A)	-C(21A)	67.2(5)
C(3A)	-C(1A)	-C(2A)	-C(21A)	-54.1(5)
C(1A)	-C(3A)	-O(31A)	-H(31A)	178.9(30)
O(32A)	-C(3A)	-O(31A)	-H(31A)	1.8(30)
C(1A)	-C(2A)	-C(21A)	-S(1A)	-175.7(3)
C(1A)	-C(2A)	-C(21A)	-S(1B)	178.9(4)
C(2A)	-C(21A)	-S(1A)	-C(1SA)	142.4(7)
C(2A)	-C(21A)	-S(1B)	-C(1SB)	85.2(5)

6.5.10 Bonds, angles and torsion angles in S-valinium 1R-4S-camphor-10-sulphonate

C(1) - C(2)	1.534(8)	S(1) -O(2S)	1.451(5)
C(1) - C(6)	1.570(7)	S(1) -O(3S)	1.449(4)
C(1) - C(7)	1.555(7)	C(1A) -N(1A)	1.509(7)
C(1) -C(10)	1.519(7)	C(1A) -C(3A)	1.507(7)
C(2) -O(1C)	1.210(8)	C(1A) -C(2A)	1.528(7)
C(2) - C(3)	1.510(9)	N(1A) -H(1NA)	0.94(5)
C(3) - C(4)	1.540(9)	N(1A) -H(2NA)	0.81(6)
C(4) - C(5)	1.527(8)	N(1A) -H(3NA)	0.89(6)
C(4) - C(7)	1.568(8)	C(3A) -O(31A)	1.337(7)
C(5) - C(6)	1.548(8)	C(3A) -O(32A)	1.196(7)
C(7) - C(8)	1.521(9)	O(31A)-H(31A)	0.87(5)
C(7) - C(9)	1.528(8)	C(2A) -C(21A)	1.530(10)
C(10)- S(1)	1.783(5)	C(2A) -C(22A)	1.523(9)
		S(1) -O(1S)	1.456(5)

C(2) - C(1) - C(6)	101.0(4)	C(10) - S(1) -O(1S)	104.13(25)
C(2) - C(1) - C(7)	100.6(4)	C(10) - S(1) -O(2S)	107.9(3)
C(2) - C(1) -C(10)	109.4(4)	C(10) - S(1) -O(3S)	107.29(24)
C(6) - C(1) - C(7)	101.9(4)	O(1S) - S(1) -O(2S)	114.7(3)
C(6) - C(1) -C(10)	116.8(4)	O(1S) - S(1) -O(3S)	110.0(3)
C(7) - C(1) -C(10)	123.7(4)	O(2S) - S(1) -O(3S)	112.1(3)
C(1) - C(2) -O(1C)	125.1(5)	N(1A) -C(1A) -C(3A)	107.6(4)
C(1) - C(2) - C(3)	108.3(5)	N(1A) -C(1A) -C(2A)	112.1(4)
O(1C)- C(2) - C(3)	126.6(6)	C(3A) -C(1A) -C(2A)	115.2(4)
C(2) - C(3) - C(4)	100.7(5)	C(1A) -N(1A) -H(1NA)	110.6(33)
C(3) - C(4) - C(5)	105.9(5)	C(1A) -N(1A) -H(2NA)	112.0(42)
C(3) - C(4) - C(7)	103.6(4)	C(1A) -N(1A) -H(3NA)	110.0(40)
C(5) - C(4) - C(7)	102.6(4)	H(1NA)-N(1A) -H(2NA)	105.8(53)
C(4) - C(5) - C(6)	103.5(5)	H(1NA)-N(1A) -H(3NA)	114.9(52)
C(1) - C(6) - C(5)	103.8(4)	H(2NA)-N(1A) -H(3NA)	103.3(58)
C(1) - C(7) - C(4)	93.8(4)	C(1A) -C(3A) -O(31A)	111.8(4)
C(1) - C(7) - C(8)	112.8(5)	C(1A) -C(3A) -O(32A)	123.2(5)
C(1) - C(7) - C(9)	115.1(4)	O(31A)-C(3A) -O(32A)	125.0(5)
C(4) - C(7) - C(8)	114.7(5)	C(3A) -O(31A)-H(31A)	99.9(35)
C(4) - C(7) - C(9)	111.1(4)	C(1A) -C(2A) -C(21A)	111.2(5)
C(8) - C(7) - C(9)	108.9(5)	C(1A) -C(2A) -C(22A)	112.9(5)
C(1) -C(10) - S(1)	121.4(4)	C(21A)-C(2A) -C(22A)	109.8(5)

C(6) - C(1) - C(2) -O(1C)	107.0(6)	C(3) - C(4) - C(7) - C(1)	54.5(5)
C(6) - C(1) - C(2) - C(3)	-71.8(5)	C(3) - C(4) - C(7) - C(8)	-62.7(6)
C(7) - C(1) - C(2) -O(1C)	-148.5(6)	C(3) - C(4) - C(7) - C(9)	173.3(5)
C(7) - C(1) - C(2) - C(3)	32.7(5)	C(5) - C(4) - C(7) - C(1)	-55.5(5)
C(10) - C(1) - C(2) -O(1C)	-16.8(8)	C(5) - C(4) - C(7) - C(8)	-172.7(5)
C(10) - C(1) - C(2) - C(3)	164.4(4)	C(5) - C(4) - C(7) - C(9)	63.3(5)
C(2) - C(1) - C(6) - C(5)	70.8(5)	C(4) - C(5) - C(6) - C(1)	-2.6(5)
C(7) - C(1) - C(6) - C(5)	-32.6(5)	C(1) -C(10) - S(1) -O(1S)	-173.5(4)
C(10) - C(1) - C(6) - C(5)	-170.6(4)	C(1) -C(10) - S(1) -O(2S)	-51.1(5)
C(2) - C(1) - C(7) - C(4)	-51.0(4)	C(1) -C(10) - S(1) -O(3S)	69.9(4)
C(2) - C(1) - C(7) - C(8)	67.8(5)	C(3A) -C(1A) -N(1A) -H(1NA)	-32.4(36)
C(2) - C(1) - C(7) - C(9)	-166.4(4)	C(3A) -C(1A) -N(1A) -H(2NA)	-150.2(45)
C(6) - C(1) - C(7) - C(4)	52.8(4)	C(3A) -C(1A) -N(1A) -H(3NA)	95.5(42)
C(6) - C(1) - C(7) - C(8)	171.6(5)	C(2A) -C(1A) -N(1A) -H(1NA)	-160.1(36)
C(6) - C(1) - C(7) - C(9)	-62.6(5)	C(2A) -C(1A) -N(1A) -H(2NA)	82.1(45)
C(10) - C(1) - C(7) - C(4)	-173.2(4)	C(2A) -C(1A) -N(1A) -H(3NA)	-32.2(42)
C(10) - C(1) - C(7) - C(8)	-54.3(7)	N(1A) -C(1A) -C(3A) -O(31A)	-174.8(4)
C(10) - C(1) - C(7) - C(9)	71.4(6)	N(1A) -C(1A) -C(3A) -O(32A)	5.9(7)
C(2) - C(1) -C(10) - S(1)	-173.4(4)	C(2A) -C(1A) -C(3A) -O(31A)	-49.0(6)
C(6) - C(1) -C(10) - S(1)	72.6(5)	C(2A) -C(1A) -C(3A) -O(32A)	131.8(6)
C(7) - C(1) -C(10) - S(1)	-55.4(6)	N(1A) -C(1A) -C(2A) -C(21A)	-59.5(6)
C(1) - C(2) - C(3) - C(4)	1.6(6)	N(1A) -C(1A) -C(2A) -C(22A)	64.5(6)
O(1C) - C(2) - C(3) - C(4)	-177.1(6)	C(3A) -C(1A) -C(2A) -C(21A)	177.0(5)
C(2) - C(3) - C(4) - C(5)	71.9(6)	C(3A) -C(1A) -C(2A) -C(22A)	-59.0(6)
C(2) - C(3) - C(4) - C(7)	-35.6(5)	C(1A) -C(3A) -O(31A)-H(31A)	-179.7(36)
C(3) - C(4) - C(5) - C(6)	-71.5(5)	O(32A)-C(3A) -O(31A)-H(31A)	-0.4(36)
C(7) - C(4) - C(5) - C(6)	36.9(5)		

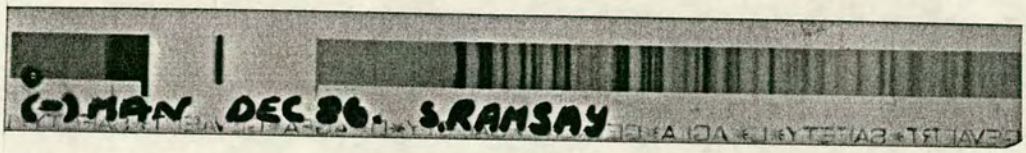
CHAPTER 7

RESOLUTION OF RACEMIC MIXTURES

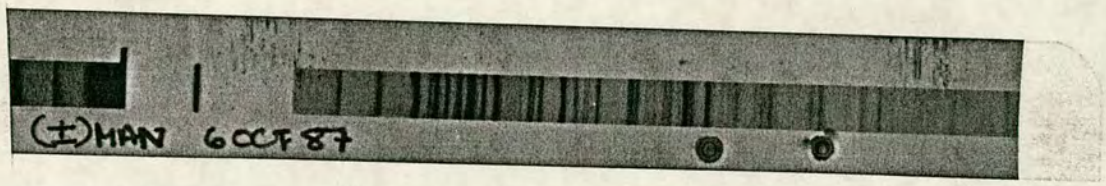
7.1 Resolution of amino acids and mandelic acid

A study of the resolution of racemic mixtures of some of the amino acids was carried out. 1:1 mixtures of the three distinguishable combinations of compounds, listed below, were prepared. The mixtures were dissolved in water and the first crop of crystals collected. Powder diffraction photographs of samples of the crystals deposited were compared to identify the products of these resolutions of racemic mixtures. Several 'standards' were first prepared:- R-MAN, RS-MAN, S-PHE, S-MET, S-ALA-R-MAN, S-ALA-S-MAN, S-PHE-R-MAN, S-PHE-S-MAN, S-MET-R-MAN, S-MET-S-MAN. Copies of the Hägg-Guinier powder photographs ($CuK_{\alpha 1}$ radiation, 1mm≡0.57° in 2θ, see section 2.7) are shown and an interpretation given below.

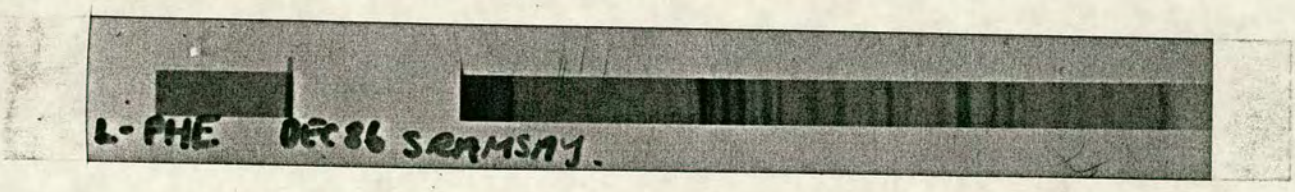
7.1.1 Standard reference compounds:



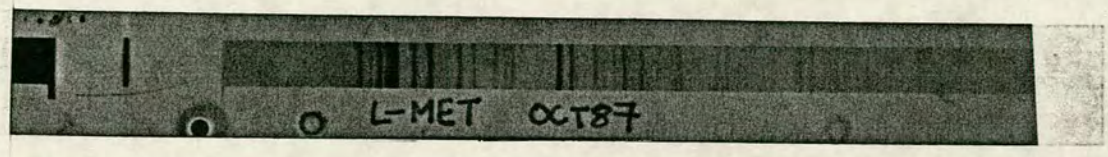
R-Mandelic Acid



RS-Mandelic Acid

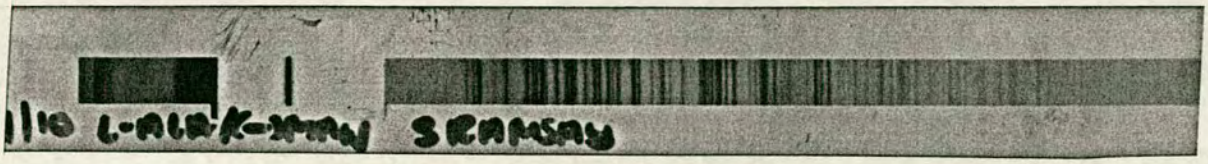


S-Phenylalanine

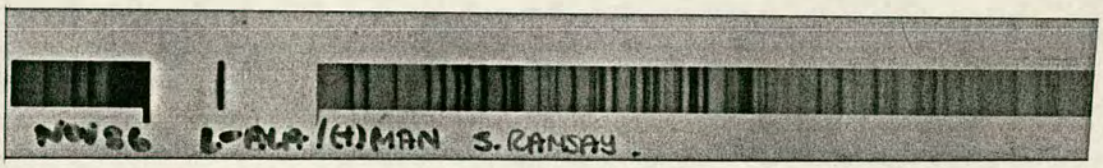


S-Methionine

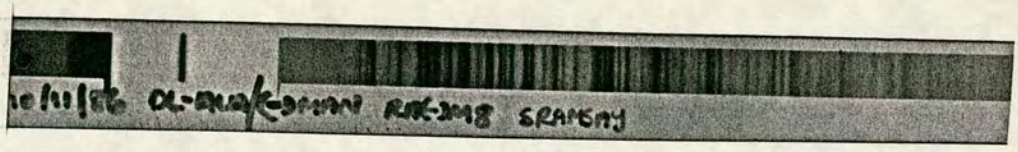
7.1.2 Alanine-Mandelic Acid Mixtures:



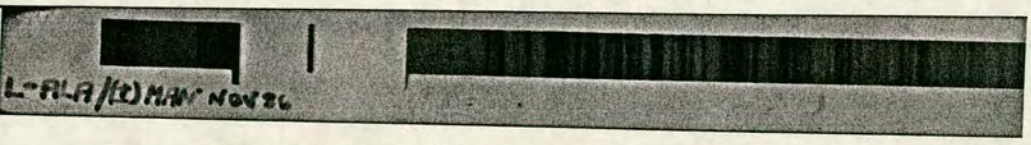
S-alanine / R-mandelic acid



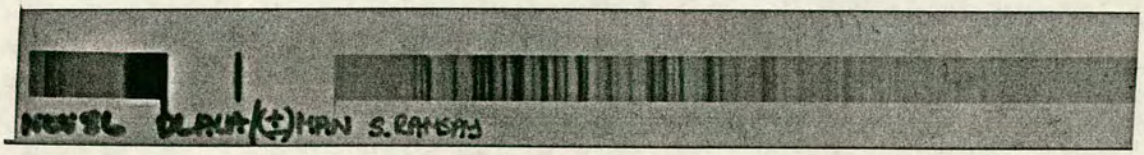
S-alanine / S-mandelic acid



RS-alanine / R-mandelic acid

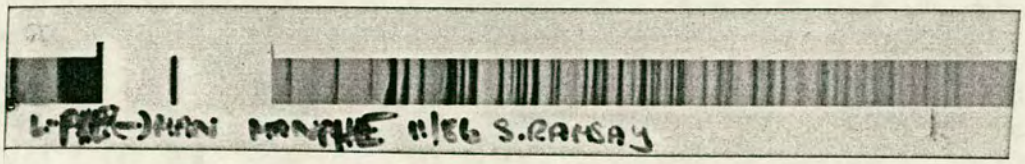


S-alanine / RS-mandelic acid

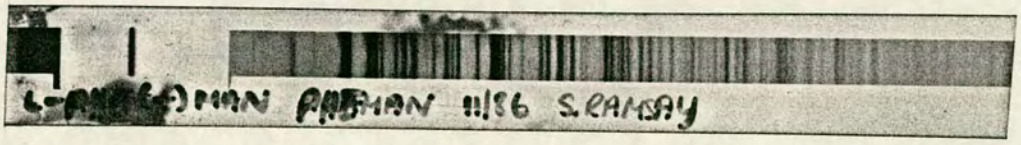


RS-alanine / RS-mandelic acid

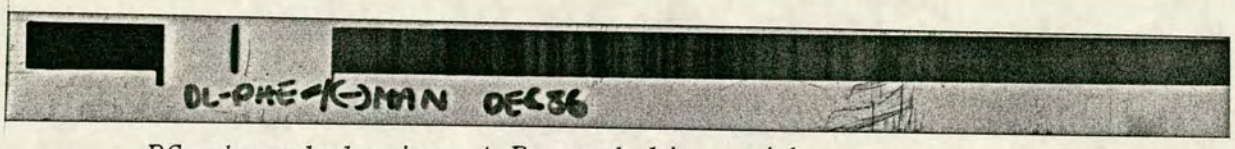
7.1.3 Phenylalanine-Mandelic Acid Mixtures:



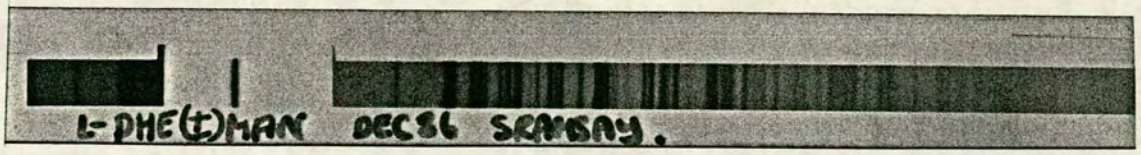
S-phenylalanine / R-mandelic acid



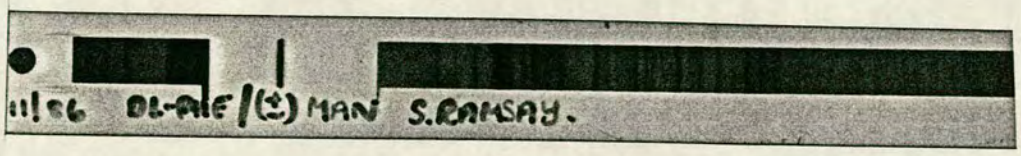
S-phenylalanine / S-mandelic acid



RS-phenylalanine / R-mandelic acid

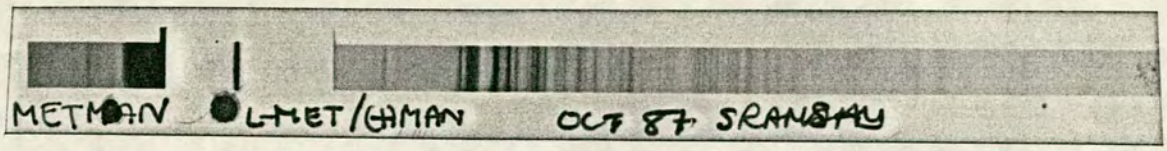


S-phenylalanine / RS-mandelic acid

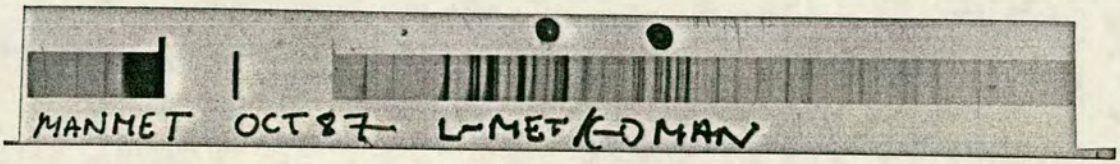


RS-phenylalanine / RS-mandelic acid

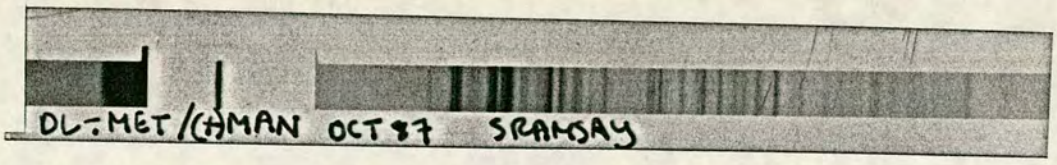
7.1.4 Methionine-Mandelic Acid Mixtures:



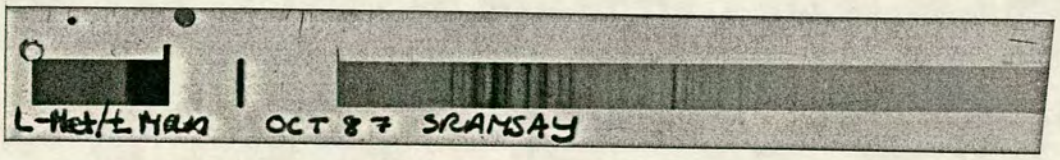
S-methionine / R-mandelic acid



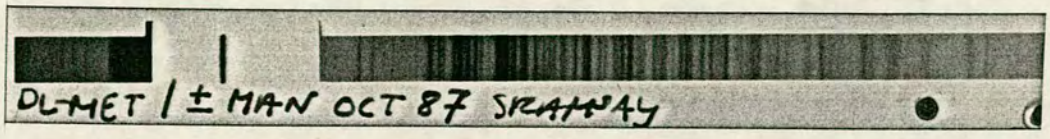
S-methionine / S-mandelic acid



RS-methionine / R-mandelic acid



S-methionine / RS-mandelic acid



RS-methionine / RS-mandelic acid

7.1.5 Interpretation of photographs:

1:1 resolution mixture	standard photograph most like that of the product	identity of product
RS-ALA/RS-MAN	S-ALA-R-MAN	S-ALA-R-MAN*
RS-ALA/R-MAN	S-ALA-R-MAN	S-ALA-R-MAN
S-ALA/RS-MAN	S-ALA-R-MAN	S-ALA-R-MAN
RS-PHE/RS-MAN	none	new product
RS-PHE/R-MAN	S-PHE-S-MAN	R-PHE-R-MAN
S-PHE/RS-MAN	S-PHE-S-MAN	S-PHE-S-MAN
RS-MET/RS-MAN	S-MET-R-MAN**	S-MET-R-MAN*
RS-MET/R-MAN	S-MET-R-MAN**	S-MET-R-MAN
S-MET/RS-MAN	S-MET-R-MAN	S-MET-R-MAN

* = this product and/or its enantiomer
**= possibly like this photograph. many lines match, but relative intensities vary, perhaps because of preferred orientation

S-ALA-R-MAN is clearly preferred over its diastereomer, S-ALA-S-MAN. There is some preference shown for S-PHE-S-MAN and S-MET-R-MAN over their diastereomers, S-PHE-R-MAN and S-MET-S-MAN.

Additionally, crystals suitable for single crystal x-ray diffraction were deposited as a result of some of the trial resolutions, from a mixture containing S-ALA/RS-MAN in a 1:1 ratio. The unit cell and space group were determined from oscillation and Weissenberg photographs. The cell was triclinic and the volume very similar to that of S-ALA-R-MAN. This led to the conclusion that this crystal had the same structure as S-ALA-R-MAN. However, single crystal structure determination

does not necessarily reveal the nature of the bulk of the deposited crystals. Nmr revealed that there was indeed a 1:1 ratio between the two components in these deposited single crystals, as indeed there was for the reverse resolution of RS-ALA- by R-MAN from a 1:1 mixture. No single crystals were found in the latter resolution attempt. Nmr is limited in that it can reveal the ratio of the components, but unlike x-ray diffraction techniques it can give no information about the structure. These results are not included in the main table of nmr data, the results of attempts to prepare the diastereomeric compounds from pure components. They were analysed in precisely the same way.

7.2 Preferred products of resolutions:

Single crystals of one diastereomer for x-ray structure determination were often more easily produced from pure components than the other diastereomer. S-ALA-R-MAN was easier than S-ALA-S-MAN and S-ALA-R-MAN is also the preferred product in resolution, as noted above.

It was easier to produce single crystals of S-PHE-R-MAN than its diastereomer, although for the same concentration of components, crystals of S-PHE-S-MAN tended to be bigger, but not single. This indicates that S-PHE-S-MAN is faster growing and is consistent with it being the slightly preferred product of resolution, as noted above.

Both diastereomers containing MET grew crystals equally fast, but while S-MET-R-MAN yielded single crystals readily, S-MET-S-MAN did not, and the crystal structure was not determined. This is consistent with there being some preference for S-MET-R-MAN in resolutions, as noted above.

S-ABA-S-MAN also crystallised as readily as S-ABA-R-MAN, but the crystals tended to be far thinner and unsuitable for X-ray structure determination. It is likely that S-ABA-R-MAN would be preferred over S-ABA-S-MAN in a resolution.

An explanation for the preference of one diastereomer over another may lie in the number and strength of hydrogen bonds in the structure. See section 4.5 for the hydrogen bonding patterns.

Number of hydrogen bonds per MAN-amino acid unit:

S-ALA-R-MAN:	6.5	S-ALA-S-MAN:	5
S-PHE-R-MAN:	6 or 5	S-PHE-S-MAN:	5

S-ALA-R-MAN has more hydrogen bonds than its diastereomer because of the inclusion of a water molecule in the structure, which adds one hydrogen bond per unit. The extra half comes from the contribution made by a bifurcated hydrogen bond in S-ALA-R-MAN. The hydrogen bonds in the preferred diastereomer do not appear to be stronger, in that they are no shorter that those in S-ALA-S-MAN. Thus it is the increase in the number of hydrogen bonds brought about by the water molecule which favours one diastereomer over the other.

S-PHE-R-MAN, the less favoured diastereomer has more hydrogen bonds if the bifurcated ones are given full weight, but they have equal numbers otherwise. However, corresponding hydrogen bonds in S-PHE-S-MAN are shorter, which may account for the slight preference of S-PHE-S-MAN over S-PHE-S-MAN.

S-MET-R-MAN and S-ABA-R-MAN did not have diastereomeric compounds, so no analysis can be made.

7.3 Camphor-10-sulphonic acid in resolution of racemic mixtures

7.3.1 Camphor-10-sulphonic acid and Phenylglycine:

Resolutions to find the preferred diastereomeric salt were not attempted because it had become apparent which diastereomer was preferred during attempts to prepare the diastereomers from pure components. Solutions of 1:1 mixtures of R-PHG and 1S-4R-(+)-CSA deposited equant crystals, 1-2 mm in size along with a small amount of fine needles. 1:1 mixtures of R-PHG and 1R-4S-(-)-CSA, however, deposited only a small amount of fine needles. This occurred both for aqueous and aqueous ethanol solutions. NMR revealed that the equant crystals were 1:1 complexes, whereas the needles were recrystallised PHG. Thus it was shown that 1S-4R-(+)-CSA cocrystallises readily with R-PHG, but not at all with S-PHG. This confirmed the preference recorded in the literature, and showed it to be absolute. The conformations of PHG asnd CSA in the successful co-crystallisation product allowed for an extended network of hydrogen bonds, details of which are given in section 6.3.6.

Such a complementarity in the two molecules must be impossible with the hand of either inverted, since no crystallisation at all took place. Unfortunately, PHE, which has an extra (β-) carbon atom not found in PHG, did not recrystallise with either hand of CSA, so no comparison of these two related amino acids was possible.

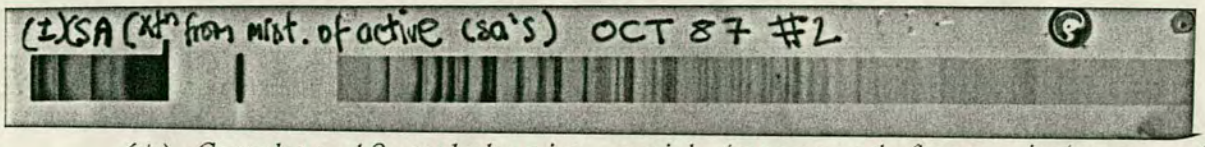
It was possible to make comparison with the less closely related amino acids MET and VAL because they did crystallise, and it became apparent that the packing arrangement had moved over to the familiar bilayer structure, in which H-bonds link the structure in two dimensions, not all three as in the PHG salt. Indeed, it was

much more difficult to grow these crystals, and many other combinations of neutral amino acids with CSA were entirely unsuccessful.

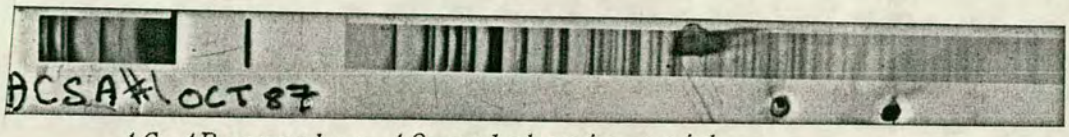
The PHG structure was most similar to the hydronium salt, with localised ribbons in which hydrogen bonding takes place, with the creation of "extra" hydrogen bonds between the hydrophilic end of the amino acid and the carbonyl oxygen of the CSA molecule. This "extra" hydrogen bond would be unable to form in the diastereomer; instead, the phenyl ring might be presented to the carbonyl group with no possibility of the formation of a hydrogen bond, and making molecular packing of the two molecules impossible.

X-ray powder photographs were made to find the powder patterns of bulk samples and these are photocopied below. The samples were:- racemic CSA, 1S-4R-CSA, racemic PHG, the products of the attempted cocrystallisations of R-PHG with 1R-4S-CSA and with 1S-4R-CSA.

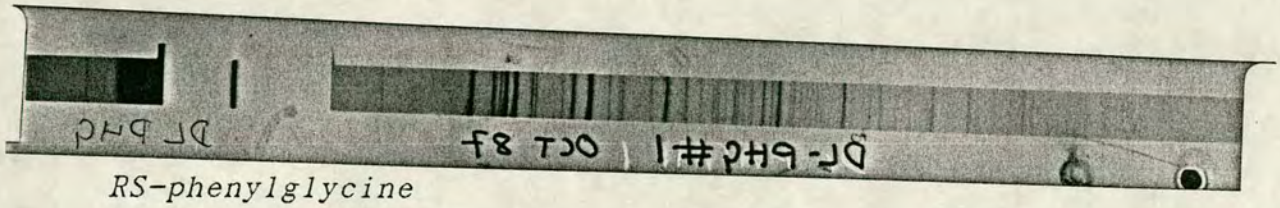
7.3.2. Camphor-10-sulphonic acid / methionine mixtures:



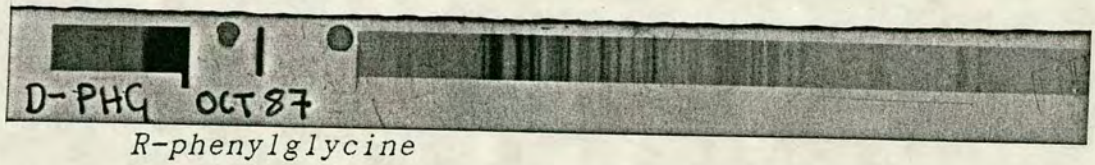
(±)-Camphor-10-sulphonic acid (prepared from mixture of enantiomers)



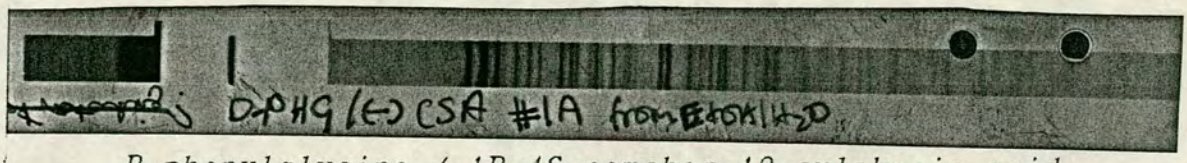
1S-4R-camphor-10-sulphonic acid



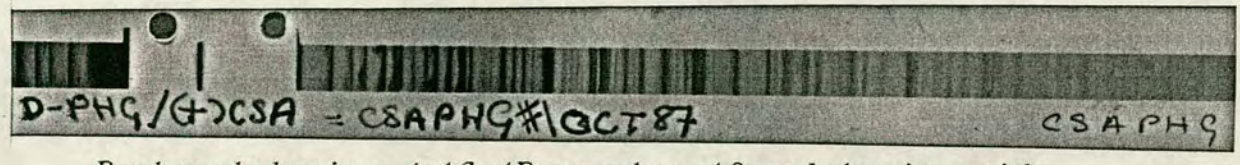
RS-phenylglycine



R-phenylglycine



R-phenylglycine / 1R-4S-camphor-10-sulphonic acid



R-phenylglycine / 1S-4R-camphor-10-sulphonic acid

7.3.3 Interpretation of the photographs:

R-PHG-1S-4R-CSA, the successful cocrystallisation product had a strong pattern from ground up large crystals, which nmr had revealed contained a 1:1 ratio of the two compounds and which crystal structure determination revealed to be a salt of the two components. A sample of the small amount of needles which recrystallised from the opposite cocrystallisation attempt, which nmr had revealed to be solely PHG, gave a very weak pattern, probably because the sample was too small. It is unfortunate that it is impossible to compare intermolecular interactions in the two diastereomers because the R-PHG-1R-4S-CSA diastereomer does not crystallise.

Unexpectedly, the powder pattern of racemic CSA was identical to that of 1S-4R-CSA. Racemic CSA was recrystallised and rephotographed to verify this. Apparently racemic CSA exhibited autoresolution into separate crystals for the two enantiomers, rather than a racemic crystal structure containing both enantiomers. The enantiomeric structure is described in sections 5.1, 6.2, 6.3 and 6.4.

7.3.4 Camphor-10-sulphonic acid and Methionine:

The only amino acid for which both diastereomeric salts were available was methionine. However it was difficult to produce any crystals at all, so trial resolution were not expected to be fruitful and were therefore not attempted. It was not possible, therefore, to identify the preferred diastereomer, if any.

S-MET-1S-4R-CSA has shorter and therefore perhaps stronger hydrogen bonds than S-MET-1R-4S-CSA, although the hydrogen bonds tend to be more linear in S-MET-1R-4S-CSA. S-MET-1S-4R-CSA contains 4 real hydrogen bonds, but

S-MET-1R-4S-CSA has 5, including one pair of bifurcated hydrogen bonds. Both structures have bilayers and in S-MET-1R-4S-CSA the methionine molecules have two fold disorder in their side chains.

7.4 Concluding remark

A major feature of all of the resolutions studied except phenylglycine with camphor-10-sulphonic acid is the formation of bilayers, i.e. alternating hydrophobic and hydrophilic surfaces. Additional hydrogen-bonding capability in amino acid side chains tends to prevent cocrystallisation with both mandelic acid and camphor-10-sulphonic acid (see esp. sections 3.9 and 3.10).

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