
Chapter 3: Solvate and Polymorphs of *ortho*-Ethoxy-*trans*-cinnamic acid: The Crystal and Molecular Structures of Schmidt's Polymorphs¹

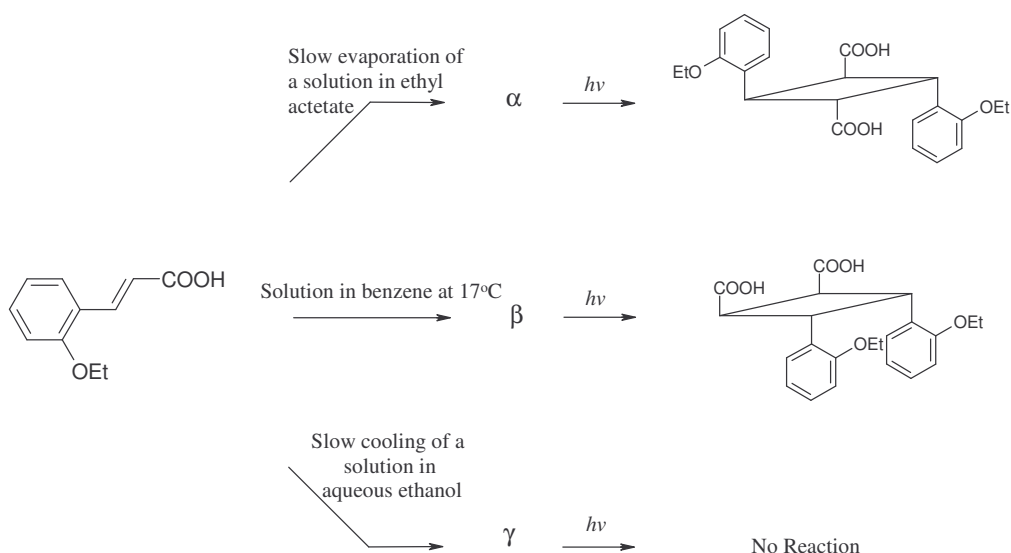
3.1 Introduction

The solid-state intermolecular photodimerization of many *trans*-cinnamic acid derivatives was extensively studied in 1964 by Schmidt and co-workers [Cohen & Schmidt, 1964; Cohen *et al.*, 1964; Schmidt, 1964]. Their innovative work led to the establishment of the topochemical principles and the formulation of Schmidt's criterion for solid-state [2 + 2] photodimerizations which states that in order for such a reaction to occur, the double bonds involved have to be approximately parallel and between 3.5 and 4.2 Å apart [Schmidt, 1971]. This distance was based on experimental observations. However, Schmidt did not seem to regard this range as a hard and fast limit and noted that reactions at slightly larger distances may still be possible. The existence of the three polymorphs of *ortho*-ethoxy-*trans*-cinnamic acid (OETCA) has been known since this time and has been cited in many textbooks as one of the classic examples of solid-state reactions that follow the topochemical principle [Wright, 1987; West, 1984]. Upon exposure to U.V. light, the α - and β -polymorphs produce centrosymmetric and mirror products respectively, while the γ -polymorph is light stable. Scheme 3.1 illustrates the crystallization method needed to grow the various polymorphs as well as their photoproducts obtained on exposure to U.V. light.

Although the complete crystal structures of the OETCA polymorphs had until recently not been reported [Fernandes *et al.*, 2001; Gopalan & Kulkarni, 2001], the distances between the reacting double bonds in these polymorphs are often quoted as being about 4.1 Å for the α -polymorph and 4.0 Å for the β -polymorph. Those in the γ -polymorph are considered

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to be too far apart to allow a photochemical reaction to occur. The quoted distances are based primarily on results obtained from polymorphs of other derivatives of *trans*-cinnamic acid.



Scheme 3.1 [Adapted from Cohen & Green (1973)]

Recently there has been intensification in solid-state organic chemistry research and crystal engineering [Tanaka & Toda, 2000; Garcia-Garibay *et al.*, 2000]. Several groups have investigated the photochemistry and crystal structures of cinnamic acid derivatives [Enkelmann *et al.*, 1993; Hosomi *et al.*, 2000; Iwamoto & Kashino, 1993; Köhler *et al.*, 1993; Sharman *et al.*, 1993]. In this Chapter, the 173K crystal structures of the α -, β - and γ -polymorphs of OETCA are presented with an emphasis on a detailed comparison of the symmetry and interaction between (i) the H-bonded OETCA $R_2^2(8)$ pairs ; (ii) neighboring molecules that could react upon exposure to U.V. light, and (iii) the role of benzene in the β -polymorph.

3.2 Methods for Chapter 3

3.2.1 Crystallization of the Three Phases of OETCA

Crystals of the three phases of OETCA were grown exactly as described in section 2.1-2.3 of Chapter 2. Powder diffraction confirmed that three distinct phases were obtained (Fig. 3.1).

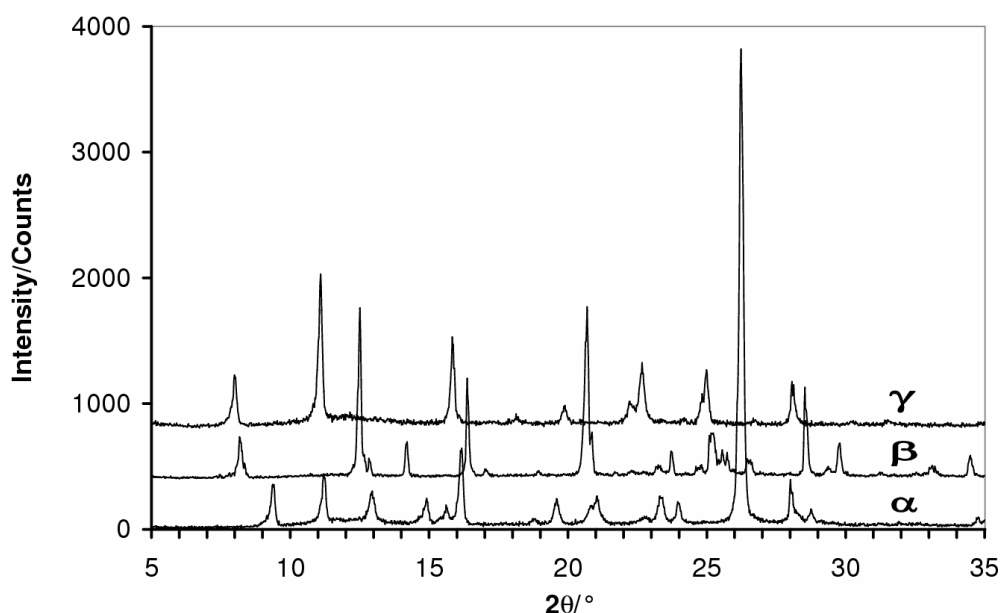


Figure 3.1: Powder XRD of the three phases of OETCA.

3.2.2 Data Collection and Crystal Structure Analysis

Low temperature (173 K) intensity data for the different polymorphs were collected on a Bruker SMART 1K CCD area detector diffractometer with graphite monochromated Mo K_α radiation (50kV, 30mA). The collection method involved ω -scans of width 0.3° . Data reduction was carried out using the program *SAINT+* [Bruker, 1999a]. Crystallographic data for the three polymorphs are listed in Table 3.1.

The crystal structures of the α - and γ -polymorphs were solved using direct methods and standard full-matrix refinement with all non-hydrogen

atoms refined anisotropically using the *SHELXTL* [Bruker, 1999b] structure solution package. Although all of the hydrogen atoms could be found from the difference Fourier maps, they were placed geometrically for the final refinements, with isotropic thermal parameters. The placement of the carboxylic hydrogen atoms is described in more detail below.

The β -phase, commonly referred to as the ' β -polymorph' in the literature [Schmidt, 1964; Wright, 1987; West, 1984], is really a solvate, or host-guest complex. Crystals of the β -phase are trigonal with unit cell parameters given in Table 3.1. These are in approximate agreement with the unit cell parameters first published by Schmidt [Schmidt, 1964: CSD Refcode ZZZNOS02: $a = 37.7$, $b=37.7$, $c = 4.08\text{\AA}$; see also Fig. 1.2 in Chapter 1]. An analysis of the diffraction data using programs LAUE [Farrugia, 1997], XPREP [Bruker, 1999] and PLATON [Spek, 2003] showed that the Laue class is -3 (hexagonal axes) with space group $R\bar{3}$. However, several weak but significant systematic absence violations were observed, particularly those related to the Rhombohedral centering. Furthermore, the anisotropic parameters for the benzene molecule are large and suggested possible disorder. In view of this, extensive tests were performed using several disorder models for the benzene including constrained refinements in lower space group symmetries $P3$, $P\bar{3}$, $P3_1$, $P3_2$, $R3$ and even the triclinic space group $P\bar{1}$. However, there was no significant improvement in the refinement of the crystallographic data (R -factors, goodness-of-fit, parameter shifts, e.s.d.'s of parameters) or in the description of the benzene solvate molecule. Therefore the final structure and refinement of the β -phase is reported with the highest possible symmetry for this structure, $R\bar{3}$, in line with recommendations made by Marsh (1995).

TABLE 3.1
Crystallographic Data

Polymorph	α	β	γ
Chemical formula	$C_{11}H_{12}O_3$	$C_{11}H_{12}O_3$, 0.132(C_6H_6)	$C_{11}H_{12}O_3$
Formula weight	192.21	202.49	192.21
Crystal system	Triclinic	Rhombohedral	Monoclinic
Space group	$P\bar{1}$	$R\bar{3}$	$C2/c$
T, K	173(2)	173(2)	173(2)
a , Å	6.6992(6)	37.5134(14)	16.997(3)
b , Å	8.6807(8)	37.5134(14)	5.4611(8)
c , Å	10.0151(9)	3.9370(2)	23.217(4)
α , deg	72.019(2)	90	90
β , deg	71.464(2)	90	110.850(3)
γ , deg	67.867(2)	120	90
V , Å ³	499.54(8)	4798.1(4)	2013.9(6)
Z	2	18	8
ρ_{calcd} , g cm ⁻³	1.278	1.260	1.268
R	0.0578	0.0655	0.0414
R_w	0.1680	0.1734	0.1186
S	1.057	1.122	1.016

3.3 Results and Discussion

There is a significant similarity in the OETCA molecular geometry in all three phases in that they show almost identical orientations of the ethoxy group in each crystal form. The ORTEP diagrams for the OETCA molecule in the α -, β - and γ -polymorphs are compared in Fig. 3.2. The OETCA molecule in all three polymorphs is almost planar. The main difference

between the three molecules is the position of the carboxylic hydrogen atom.

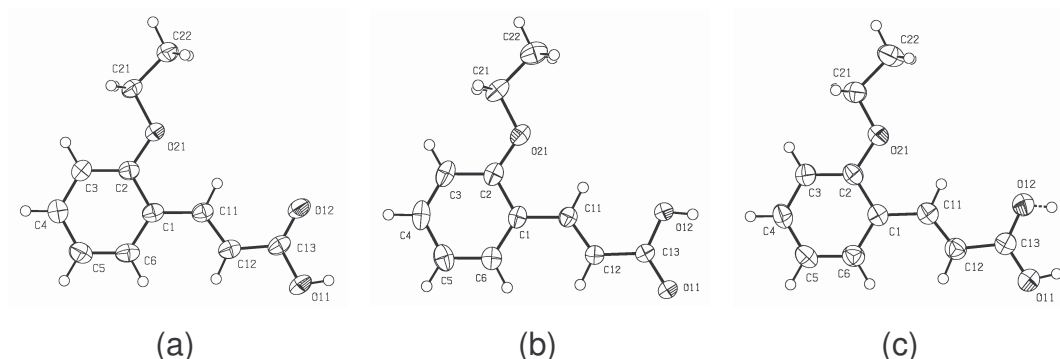


Figure 3.2: OETCA molecules from the (a) α -, (b) β -(benzene)- and (c) γ -polymorphs.

The position of the carboxylic hydrogen was calculated geometrically using the position indicated by the difference Fourier maps. These are illustrated in Fig. 3.3 for the three polymorphs. In the α -polymorph the carboxylic hydrogen atom is connected to O11 while in the β -polymorph it is connected to O12. In the γ -polymorph this hydrogen atom is disordered over the two carboxylic atom sites in an almost 1:1 ratio. This hydrogen atom was placed geometrically over the two positions and its site occupancy factor allowed to refine for each position. The H-positions inferred from the difference Fourier maps (Fig 3.3) are quite convincing. However, Herbstein *et al.* (1999) have noted that temperatures lower than 20 K may be essential for the accurate placement of hydrogen atoms. Hydrogen positions have however also been shown to be temperature dependent in benzoic acids [Wilson *et al.*, 1996a,b].

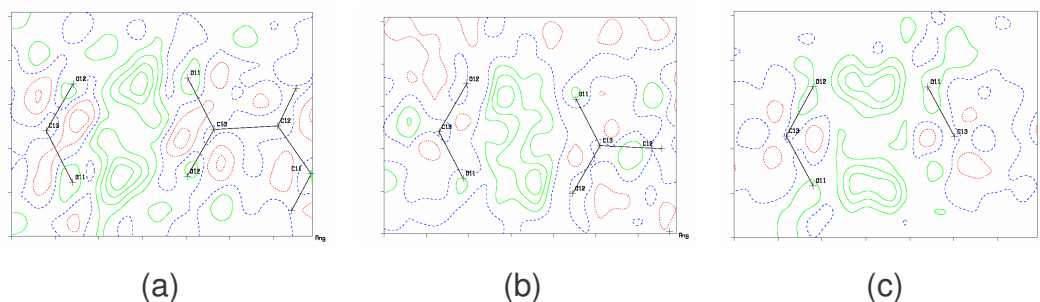


Figure 3.3: Difference Fourier maps indicating the position of the carboxylic hydrogen atom in the (a) α -, (b) β -(benzene)- and (c) γ -polymorphs.

The β -solvate has benzene filled channels along the c axis. The benzene molecule is centered at $(0,0,\frac{1}{2})$. The stacking of the benzene along the c -axis is illustrated by the Fourier maps in Fig. 3.4. The closest distance between benzene molecules in this model therefore approximately corresponds to the dimension of the c axis, 3.94 Å. The site occupancy of the benzene in the final refinements was adjusted to 0.79 corresponding to the value determined from elemental analysis.

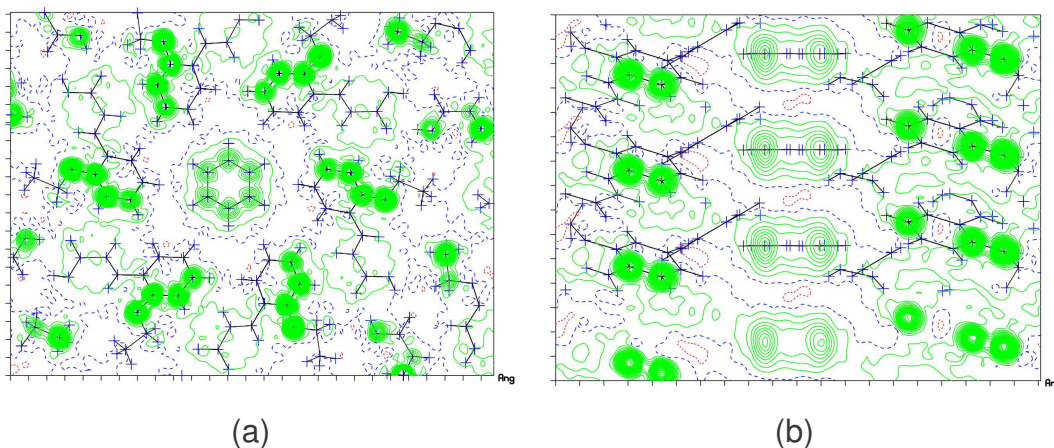


Figure 3.4: Fourier maps showing the benzene host molecules in the β -polymorph of *o*-ethoxy-*trans*-cinnamic acid; (a) Projection down the c axis; (b) Projection down the a axis.

3.3.1 The α -Polymorph

The unit cell consists of two molecules, which are related to each other through a center of symmetry in $P\bar{1}$. A stereoscopic representation of the unit cell is given in Fig. 3.5.

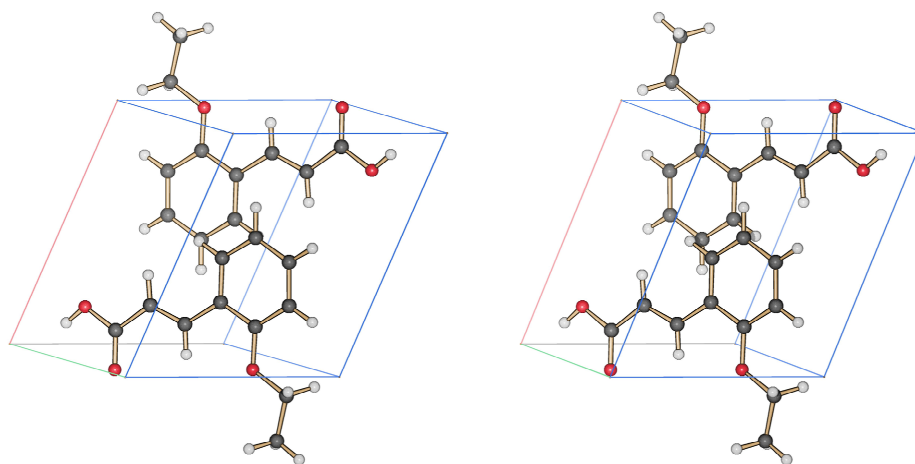


Figure 3.5: Stereo view of the unit cell of the α -polymorph of OETCA.

Like the other three polymorphs the basic building block for this structure consists of conventional O-H...O (O...O, 2.637(2) Å) centrosymmetric hydrogen bonded $R_2^2(8)$ dimer pairs with the carboxylic hydrogen bound to O11 in this case. These dimers are further hydrogen bonded through two C-H...O interactions (C6-H6...O11: 2.552Å, 150.69°; C6...O11: 3.413Å and C5-H5...O12: 2.760Å, 155.28°; C5...O12: 3.645Å) to other OETCA dimer pairs to form a ribbon aggregate of molecules (Fig. 3.6). These distances are within the generally accepted limits for C-H...O interactions [C...O 3.00-4.00Å Desiraju; 1996] and resemble those of *p*-toluic acid [Bernstein *et al.*, 1994; Takwale & Paul, 1971]. The lengths and angles of these interactions are quite long and hence weak when compared to previously reported cinnamic acid derivative structures [see for example Sharma *et al.*, 1993]. This is most probably due to the arene hydrogen atoms not being very acidic [Desiraju, 1991]. The structure is also held together by a C-H... π interaction [Nishio, 2004]: the hydrogen to benzene centroid distance being 2.798 Å (H22C... π). This leads to a

centrosymmetric C-H... π stabilized arrangement of OETCA molecules (Fig. 3.7b), which reinforces the α -polymorph structure. The shortest centroid to centroid distance representing a π ... π interaction is about 5.26 Å suggesting that these interactions are not important in this structure.

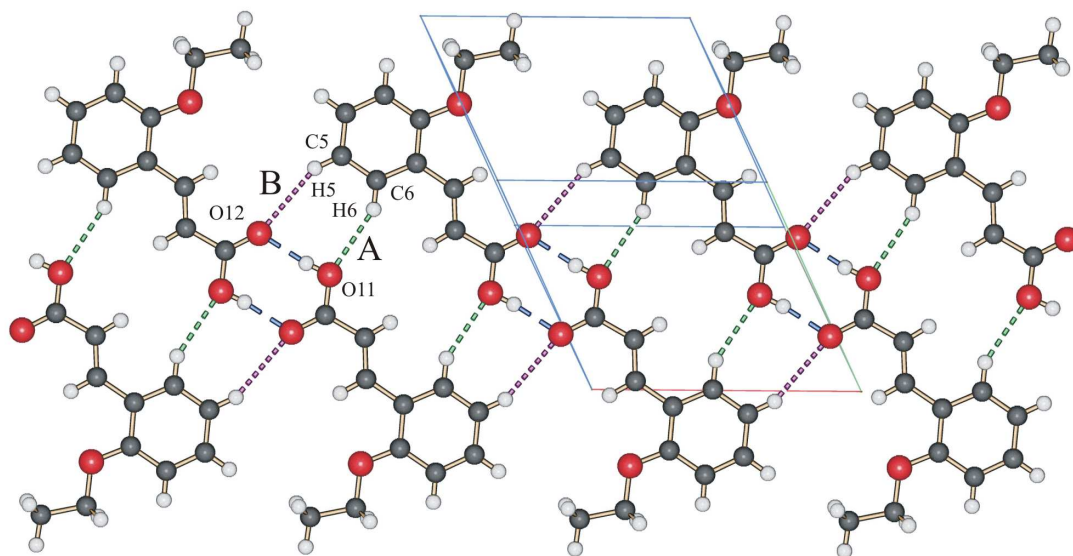


Figure 3.6: The C-H...O interaction (A: O11...C6, 3.413 Å and B: O12...C5, 3.645 Å) and O-H...O hydrogen bond stabilized ribbon motif of the α -polymorph.

Upon translation of the unit cell and this ribbon aggregate in all three dimensions, a layered structure is created with alternating layers formed from these two molecules (Fig. 3.7). These layers are composed of the ribbon aggregates, which are connected to each other by the ethoxy groups of the OETCA.

The centrosymmetric relationship between the two OETCA molecules and the layered nature of the structure play a large role in the solid-state photochemical properties of this polymorph which is discussed in detail in Chapter 9.

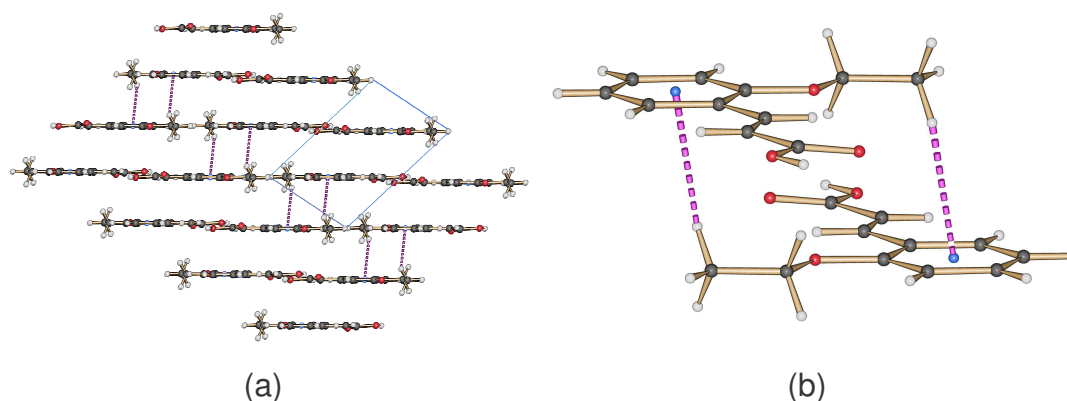


Figure 3.7: Crystal packing in the α -polymorph of OETCA; (a) illustration showing the layered structure; (b) centrosymmetric C-H... π interaction unique to the α -polymorph. The C-H... π interaction reinforcing the layered structure is shown using purple dotted lines in both diagrams.

3.3.2 The β -Solvate

The positions of the benzene molecules in the channels of the β -polymorph, made up by the OETCA host structure, are illustrated in the $\langle 001 \rangle$ projection of the $R\bar{3}$ unit cell (Fig. 3.8).

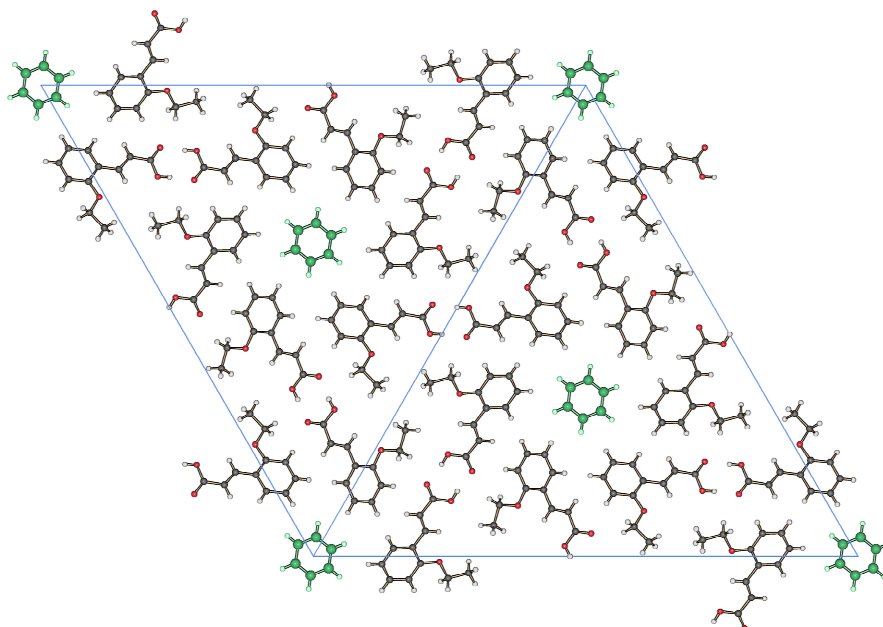


Figure 3.8: Illustration of the unit cell of the β -(benzene)-polymorph of OETCA. The positions of benzene molecules (green) have been emphasized by using slightly larger C-radii.

Benzene seems to be a template around which the OETCA molecules arrange in a spiral and is required in order to form this solvate. Similar observations of the role of benzene were made for cyclohexanedione- and cyclophane-benzene complexes [Etter *et al.*, 1986; Klebe & Diederich, 1993]. In addition, if the benzene is allowed to escape, the structure collapses converting to the α -polymorph in the process (an observation previously noted by Schmidt and his co-workers [Cohen & Schmidt, 1964; Cohen *et al.*, 1964; Schmidt, 1964]). There are no strong interactions between the benzene guest and its host. Instead, the benzene molecules are stacked approximately parallel to each other through π - π interactions and interact with the surrounding OETCA molecules through van der Waals interactions. The OETCA molecules form conventional O-H $\cdots$ O (O $\cdots$ O, 2.618(2) Å) centrosymmetric hydrogen bonded $R_2^2(8)$ dimer pairs with the carboxylic hydrogen bound to O12. There is no further hydrogen bonding in this structure. The structure is instead kept together by π - π interactions of the overlapping phenyl and alkene groups of the stacked OETCA molecules – the stacking being caused by translation along the *c* axis yielding a centroid to centroid (or $\pi\cdots\pi$) separation of 3.9370 (2) Å. The stacked OETCA molecules are also slightly staggered relative to each other - an arrangement which minimizes like-like interactions between the molecules.

3.3.3 The γ -Polymorph

A stereoscopic representation of the γ -polymorph unit cell is shown as Fig. 3.9. The γ -polymorph structure can be classed as being herringbone in nature in that the structure is built up of a zigzag arrangement of layers of OETCA molecules (Fig. 3.10).

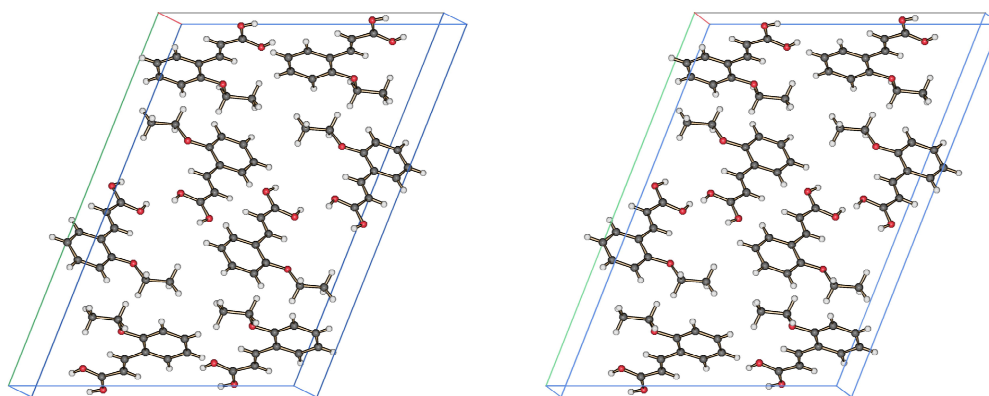


Figure 3.9: Stereo view of the unit cell of the γ -polymorph of OETCA.

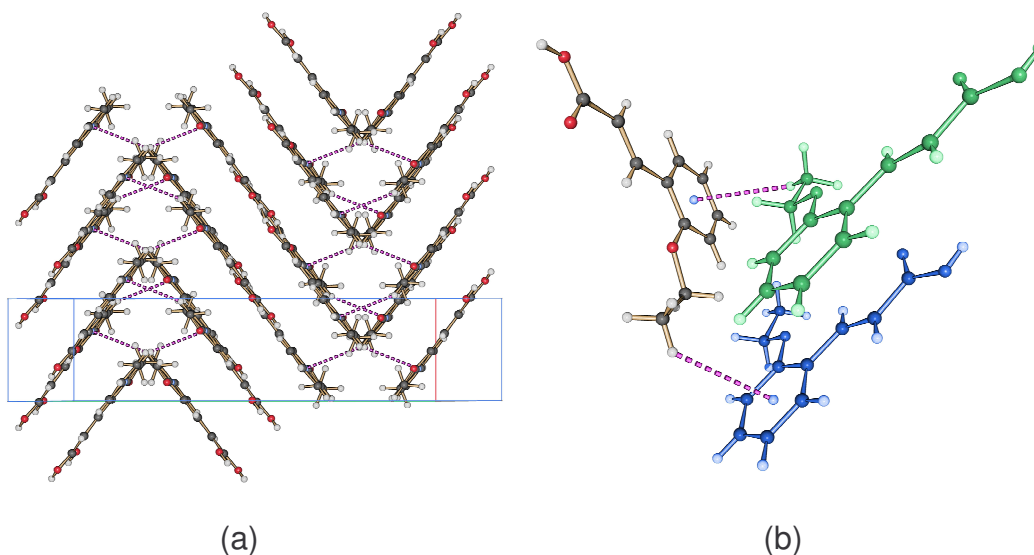


Figure 3.10: The herring bone structure of the γ -polymorph of OETCA (a). C-H... π interactions have been emphasized with dotted purple lines. The source of the C-H...O interactions is shown in (b), where each OETCA molecule acts as a proton donor to a neighboring OETCA ribbon and as an acceptor to another.

The structure is composed of conventional O-H...O (O...O, 2.6241(17) Å) centrosymmetric hydrogen bonded $R_2^2(8)$ dimer pairs with the carboxylic hydrogen being disordered over both of the carboxylic oxygen atoms. As in the α -polymorph these OETCA dimer pairs aggregate further through two C-H...O interactions (C6-H6...O11: 2.595 Å, 143.05°; C6...O11: 3.403 Å and C5-H5...O12: 2.757 Å, 160.42°; C5...O12, 3.667 Å)

to other OETCA dimer pairs to form a ribbon of molecules (Fig. 3.11). With the exception of the disordered carboxylic hydrogen, the 2-D ribbon motif is almost identical to that of the α -polymorph with the C-H...O distances being within 0.05 Å of each other. No significant π ... π interactions exist in this structure as measured by short inter ring centroid distances. However, two short C-H... π interactions exist with H... π distances of 3.379 Å (H12... π) and 3.258 Å (H22B... π), respectively. These are almost 0.5 Å longer than the equivalent type of interaction in the α -polymorph (all three structures have C-H distances set at 0.95 Å), suggesting that the α -polymorph is more stable than the γ -polymorph at lower temperatures (see Chapter 6). The geometry of the C22-H22B... π contact suggests that C-H... π interactions are important in stabilizing the herringbone structure of the γ -polymorph as shown in Fig. 3.10. Each OETCA molecule acts as a proton donor to a neighboring OETCA ribbon and as an acceptor to another.

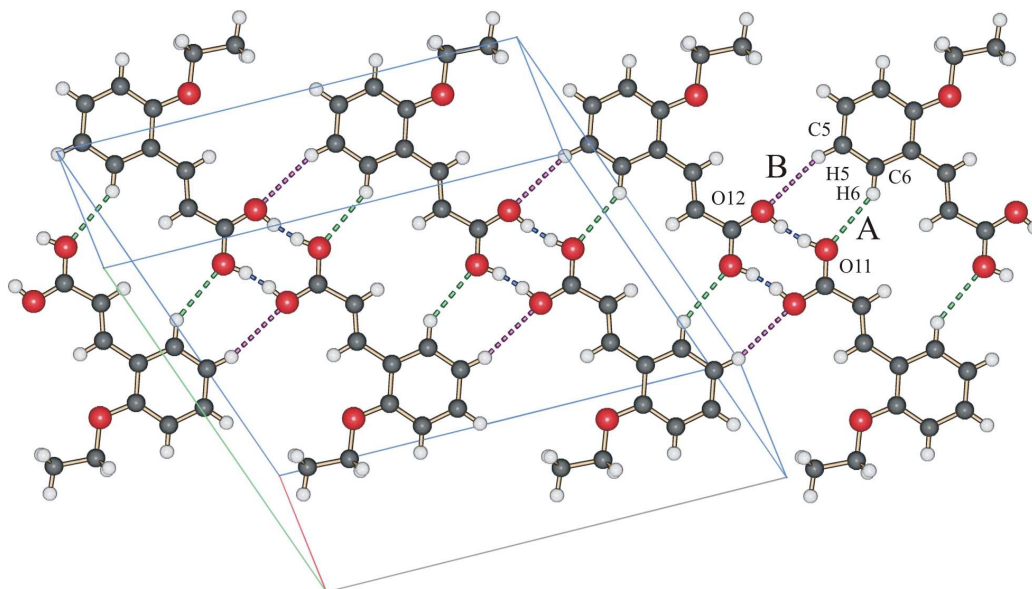


Figure 3.11: The C-H...O interaction (A: O11...C6, 3.403 Å and B: O12...C5, 3.665 Å) and O-H...O hydrogen bond stabilized ribbon motif of the γ -polymorph.

As mentioned in the introduction these phases have long been used as examples of “polymorphs” that obey the topochemical principle. However, the distances involved in the reaction processes were not reported. Figs. 3.12a and 3.12b show the closest pair of OETCA molecules in the α - and β -polymorphs, respectively, with the broken lines between them indicating where the new bonds would form in the photochemical process.

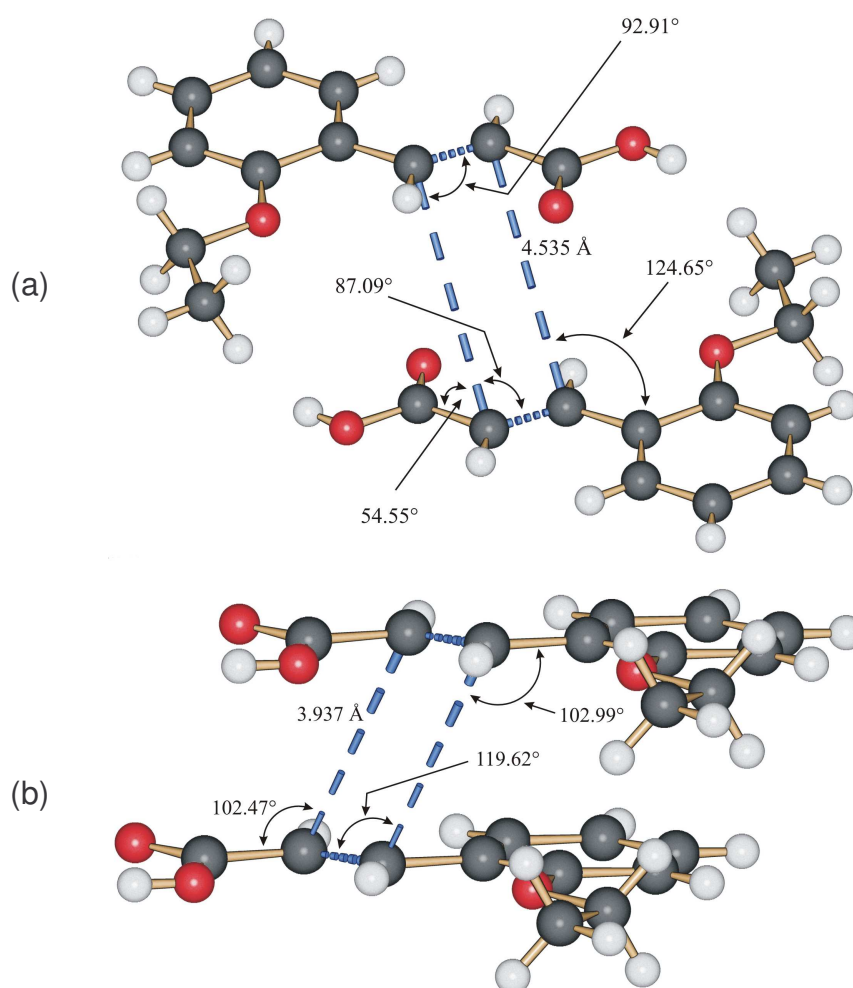


Figure 3.12: The predimer OETCA molecules in (a) the α - and (b) the β -polymorph.

In the α -polymorph the molecules are related through a center of inversion and upon exposure to ultraviolet light a centrosymmetric cyclobutane product is obtained. The distance between the alkene atoms involved in this case is 4.535 Å at 173 K. This value changes slightly according to the experimental conditions used to collect the diffraction data with the crystal contracting as the temperature is lowered. This distance falls outside the observed range demarcated by Schmidt's criterion. However, the photochemical reaction does happen and it is thought that it is assisted by defects in the crystal structure involving the $\bar{1}02$ (the miller index of the molecular layer itself - see Chapter 9). In the β -polymorph, the two molecules are related by a translation along the c axis and separated by 3.937 Å. The double bonds are parallel to each other in the predimer pairs of both α - and β -structures. Upon examining the γ -structure, the closest distances between double bonds of two molecules of OETCA related by a center of symmetry is 5.258 Å (Fig. 3.13a). The closest double bond distance between a pair of OETCA molecules potentially forming a mirror product is 5.460 Å (Fig. 3.13b). Clearly these distances are too far for the photodimerization reaction to occur, confirming observations by Schmidt and co-workers [Cohen & Schmidt, 1964; Cohen *et al.*, 1964; Schmidt, 1964]. Interestingly, the almost equidistant separation between the mirror related and inversion related molecules strongly resembles the schematic representation given in Fig. 1.14 (Chapter 1).

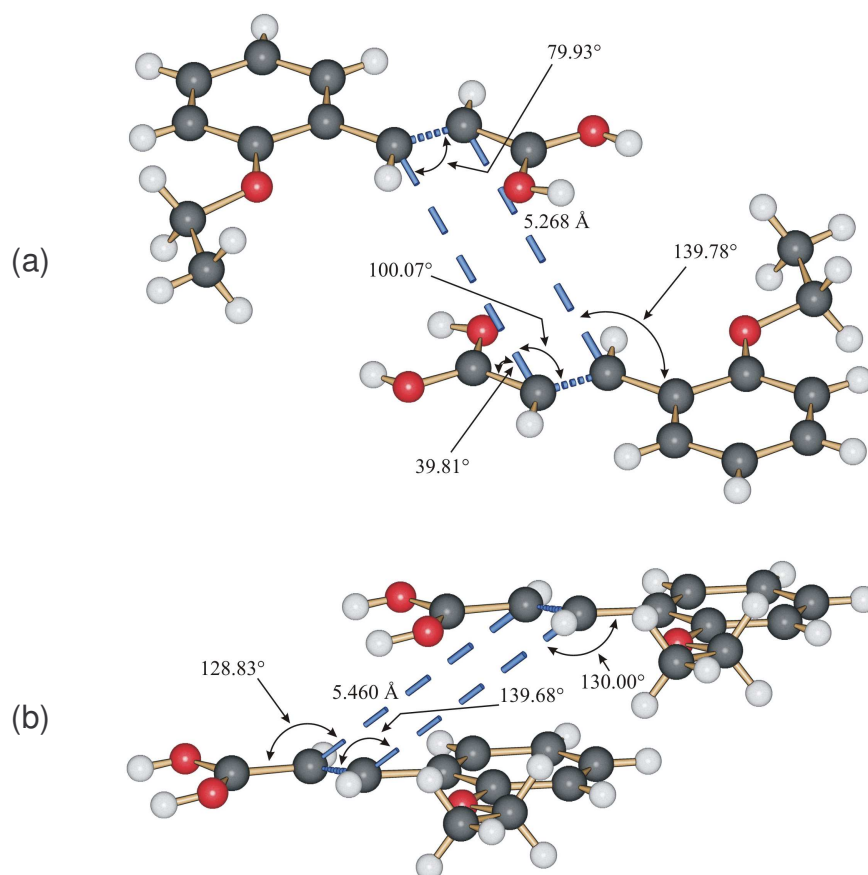


Figure 3.13: The geometry of the predimer OETCA molecules in the γ -polymorph; (a) the closest centrosymmetrically related pair of molecules; (b) the closest translation related or "mirror" related pair of molecules.

3.4 Conclusion

The space groups and unit cell parameters found in this work agree with those first published by Cohen and Schmidt [Cohen & Schmidt, 1964; Cohen *et al.*, 1964; Schmidt, 1964]. However, analysis of the complete 3-dimensional 173 K structures has revealed several important features of the polymorphs of OETCA. Firstly, the β -polymorph is actually a 0.79:6 benzene:OETCA solvate. Benzene molecules, stacked in the channel and held by weak interactions with the aromatic C-H groups of the OETCA molecules, play a decisive role in maintaining the symmetry and intermolecular spacing of the β -predimers (neighbouring OETCA

molecules that potentially undergo [2+2] photodimerization). Loss of the host molecules results in a β - to α -phase transition at room temperature. Other solvate molecules, such as thiophene, yield crystals isomorphous to the β -form (see Chapter 5), suggesting that a range of new solvates of *trans*-cinnamic acids and cinnamides could be designed to give specific photodimerization products. The importance of intermolecular C-H...O interactions between synthons (H-bonded OETCA pairs) common to the α - and γ -polymorphs has also been confirmed. Differences in the geometry of C-H... π in these two polymorphs have also been highlighted. Accurate geometries of the α -, β - and γ -predimers have been quantified. The closest distances between double bonds in the α -, β - and γ -polymorphs are 4.535, 3.937 and 5.258 Å, at 173 K, respectively. Lastly, the calculated density value determined in the present study for the α -, β - and γ -polymorphs are strictly comparable. Therefore, the very low value reported by Schmidt [see Fig. 1.2; Schmidt, 1964] seems to be an artifact, probably due to the fact that the benzene molecules were not accounted for in the density calculation.