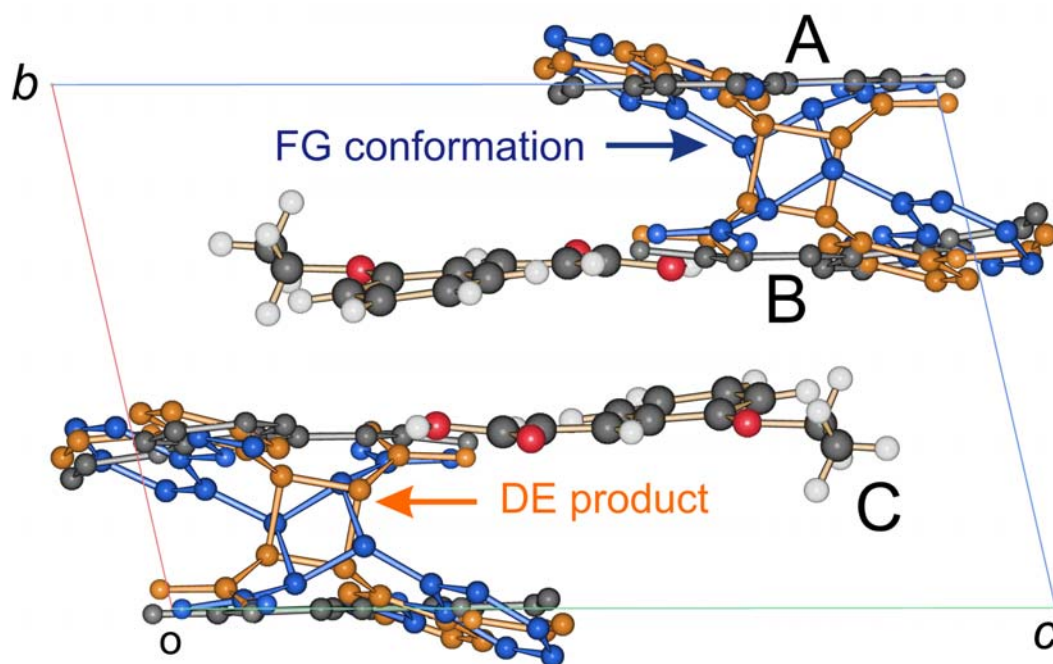


# Solid-State Organic Chemistry of *ortho*-Ethoxy-*trans*-cinnamic acid



**Manuel Antonio Fernandes**

A thesis submitted to the Faculty of Science, University of the Witwatersrand, Johannesburg, in fulfilment of the requirements for the degree of Doctor of Philosophy.

January 2005

## **Declaration**

I declare that this thesis is my own unaided work. It is being submitted for the Degree of Doctor of Philosophy in the University of the Witwatersrand, Johannesburg. It has not been submitted before for any degree or examination in any other University.

---

M.A. Fernandes

14<sup>th</sup> day of January 2005

---

**Abstract**

*ortho*-Ethoxy-*trans*-cinnamic acid (OETCA) has been known to form three polymorphs - the  $\alpha$ -,  $\beta$ - and  $\gamma$ -polymorphs which crystallize in  $P\bar{1}$  ( $Z=2$ ),  $R\bar{3}$  ( $Z=18$ ) and  $C2/c$  ( $Z=8$ ), respectively. These polymorphs have long been of interest from polymorphism and solid-state photoreactivity perspectives but have, until now, never been fully characterized.

In this thesis the complete structures of these polymorphs and their photodimerization products are presented. In addition, a new polymorph, the  $\alpha'$ -polymorph [ $P\bar{1}$  ( $Z=6$ )], which is only obtainable from the  $\alpha$ -polymorph *via* a reversible solid-state phase transformation at 60 °C, has been discovered and characterised.

In all the polymorphs of OETCA, the smallest building component is the hydrogen-bonded carboxylic acid  $R_2^2(8)$  dimers. These dimers further aggregate *via* CH...O interactions to form a ribbon motif in the  $\alpha$ -,  $\alpha'$ - and  $\gamma$ -polymorph structures. Structural and solid-state reactivity differences in these three polymorphs are therefore due to differences in the arrangement of these ribbons.

With few exceptions, solid-state [2+2] photodimerization reactions have been found to obey the topochemical principle. Such reactions occur with minimal structural movement in which the contact distance between reacting double bonds is between 3.5 and 4.2 Å. In this respect the solid-state reactivity of both the  $\alpha$ - and  $\alpha'$ -polymorphs is especially interesting and unusual, and indicate that significant movement - both molecular and structural - is possible and necessary for reactions to occur in these polymorphs. Both polymorphs yield the centrosymmetric dimer product - 2,2'-diethoxy- $\alpha$ -truxillic acid. Photodimerization in the layered structure of the  $\alpha$ -polymorph, where the double bond contact distance is at 4.54 Å beyond reasonable photodimerization distance, is probably initially enabled by crystal defects. While the  $\alpha'$ -polymorph is structurally very similar to the  $\alpha$ -polymorph it is instead composed of two reaction sites with double bond contact distances of 3.72 and 4.99 Å, respectively. This

---

polymorph's solid-state reactivity has as a consequence been found to be temperature dependent, with only 66.7% conversion being achieved at 293 K and 100% conversion occurring at 343 K; reaction at 343 K involves both a significant conformation change in a reaction product as well as a heat and reaction driven phase change. In the  $\gamma$ -polymorph the closest distance between the double bonds is 5.26 Å, which together with the structural rigidity imposed by its herring-bone structure ensures that no photodimerization occurs.

The  $\beta$ -polymorph is really a solvate containing either benzene or thiophene within channels in the structure. The interactions between the solvent and OETCA molecules play an important role in maintaining the symmetry and integrity of the structure. The thiophene and benzene forms of the  $\beta$ -polymorph are isomorphous and yield a mirror product (2,2'-diethoxy- $\beta$ -truxinic acid) upon photodimerization - the molecules involved being related by a 4.0 Å translation along the unit cell  $c$  axis.



## Acknowledgements

I would like to thank my supervisor, Prof. D.C. Levendis, for his assistance, guidance and support throughout the course of this project.

I also wish to thank the following:

Prof. F.R.L. Schöning for his constant help, advice and especially inspiration;

Craig Taverner and Johan du Toit whose example and inspiration got me interested in crystallography while I was in honours (4<sup>th</sup> year BSc);

Alexis Apostolidis, Dave Billing, Robert Bogadi, Vimal Ichharam, Tibor Koritsansky, Charles de Koning, Marcus Layh, Jennifer Look, Bernard Omondi, Willem van Otterlo, for their advice, inspiration, support and encouragement over these many years;

Janice Rubin, Andreas Lemmerer, Paul Franklyn and Natalie Thornton, without whose help I might have finished this thesis a whole lot sooner. Actually, the "new" blood has like everybody on this page been a welcome part of my life over the past years.

Lastly, special thanks are due to Leanne Knapton, Jose Oliveira, Chris Perry and Preeti Vashi, for all their help, useful discussions, encouragement and support, for which I am eternally grateful.

---

**Table of Contents**

	<b><u>Page</u></b>
<b>Declaration</b>	ii
<b>Abstract</b>	iii
<b>Dedication</b>	v
<b>Acknowledgements</b>	vi
<b>Table of Contents</b>	vii
<b>List of Abbreviations and Generally used Crystal Codes</b>	xiv
<b>Chapter 1: Introduction</b>	1
<b>1.1 Introduction and Historical Background to Solid-State Organic Chemistry with Emphasis on Solid-State Photochemistry</b>	1
<b>1.2 The phenomenon of polymorphism in molecular crystals.</b>	9
<b>1.3 Nature and Properties of Organic Crystals</b>	15
<b>1.3.1 Forces Keeping Organic Crystals Together</b>	15
<b>1.3.1.1 Interactions between Dipolar Molecules</b>	15
<b>1.3.1.2 Dipole-induced Dipole Interactions</b>	16
<b>1.3.1.3 Dispersion Forces or Induced Dipole-induced Dipole Interactions</b>	17
<b>1.3.1.5 Repulsive Forces</b>	18
<b>1.3.1.6 Atom-atom Potentials, Lattice Energy Calculations and Structure Prediction</b>	19
<b>1.3.2 Examples of Important Intermolecular Interactions</b>	21
<b>1.3.3 Favorable Symmetries Found in Crystals - Trends Followed by Molecules when Forming a Crystal</b>	23
<b>1.3.3.1 Principles of Crystal Packing</b>	23
<b>1.3.3.2 Classification of Symmetries into Favorable and Unfavorable</b>	24
<b>1.3.4 Crystal Habit and the Effects of the Crystallization Solvent</b>	27
<b>1.3.5 Characterization of Hydrogen Bonds in Structures and</b>	28

---

	<b><u>Page</u></b>
Graph Set Notation.	
<b>1.4</b> Frontier Molecular Orbital (FMO) Theory and the Prediction of Photochemical Dimerization Reaction Products	31
<b>1.5</b> Solid Photochemistry of <i>ortho</i> -Ethoxy- <i>trans</i> -cinnamic acid	38
<b>1.6</b> Latest Strategies in Studying Photodimerization Reactions	42
<b>1.7</b> Advanced Concepts in Solid-State Photodimerization Reactions	45
<b>1.7.1</b> The Effect of Irradiation Temperature on Solid-State Photodimerization Reactions	47
<b>1.7.2</b> The Concept of a Reaction Cavity and its Consequences in Predicting Products from Solid-State Photodimerization Reactions	49
<b>1.7.3</b> Dynamical Preformation: The Concept of Photoinduced Lattice Instability	54
<b>1.7.4</b> The Role of Defects in Producing Unexpected Products from Solid-State Photodimerization Reactions	55
<b>1.8</b> The Importance of Solid-State Chemistry - Today	58
<b>1.9</b> The Aims of this Project	60
<b>Chapter 2: General Methods</b>	61
<b>2.1</b> Synthesis of OETCA	61
<b>2.2</b> Crystallization of the Three Crystal Polymorphs of OETCA	62
<b>2.2.1</b> Crystallization of the $\alpha$ -Polymorph of OETCA	63
<b>2.2.2</b> Crystallization of the $\beta$ -Benzene Form of OETCA	63
<b>2.2.2</b> Crystallization of the $\beta$ -Thiophene Form of OETCA	64
<b>2.2.4</b> Crystallization of the $\gamma$ -Polymorph of OETCA	65
<b>2.3</b> Elemental Analysis	65
<b>2.4</b> Melting Point and DSC Measurements	66
<b>2.5</b> Powder XRD Studies of the UV Reaction Processes of all Three Crystal Forms of OETCA	66
<b>2.6</b> Irradiation of Polymorph Crystals	66

---

	<b><u>Page</u></b>
2.7 General Methodology for Single Crystal Analyses	69
<b>Chapter 3: Solvate and Polymorphs of <i>ortho</i>-Ethoxy-<i>trans</i>-cinnamic Acid: The Crystal and Molecular Structures of Schmidt's Polymorphs</b>	71
3.1 Introduction	71
3.2 Methods for Chapter 3	73
3.2.1 Crystallization of the Three Phases of OETCA	73
3.2.2 Data Collection and Crystal Structure Analysis	73
3.3 Results and Discussion	75
3.3.1 The $\alpha$ -Polymorph	78
3.3.2 The $\beta$ -Solvate	80
3.3.3 The $\gamma$ -Polymorph	81
3.4 Conclusion	86
<b>Chapter 4: Photodimerization products of the <math>\alpha</math>- and <math>\beta</math>-Polymorphs of <i>ortho</i>-Ethoxy-<i>trans</i>-cinnamic acid</b>	88
4.1 Introduction	88
4.2 Methods for Chapter 4	89
4.2.1 Crystal Growth	89
4.2.2 X-ray Structural Analysis	90
4.3 Results and Discussion	92
4.3.1 Section 1 - Structure of the $\alpha$ -Photodimer and its Pseudo Polymorph	92
4.3.1.1 Crystal Growth and Molecular Structure	92
4.3.1.2 Hydrogen Bonding, Weak Interactions and Crystal Packing	95
4.3.2 Section 2 - Structure of the $\beta$ -Photodimer and its Calcium Salt	101
4.3.2.1 Molecular Structure	101
4.3.2.2 Hydrogen Bonding, Weak Interactions and	103

---

	<b><u>Page</u></b>
Crystal Packing	
<b>4.3.2.3</b> Molecular Structure of a Ca Salt of the $\beta$ - Photodimer	106
<b>4.3.2.4</b> Hydrogen Bonding, Weak Interactions and Crystal Packing	109
<b>4.4</b> Conclusion	111
<b>Chapter 5: New Crystal Forms of the <math>\beta</math>-Polymorph and their Solid-State Behavior and Photoreactivity</b>	112
<b>5.1</b> Introduction	112
<b>5.2</b> Methods for Chapter 5	112
<b>5.2.1</b> Crystal Growth	112
<b>5.2.2</b> Photodimerization	113
<b>5.2.3</b> X-ray Structural Analysis	113
<b>5.3</b> Results and Discussion	115
<b>5.3.1</b> Attempts at Creating New Versions of the $\beta$ -Benzene Solvate Structure	115
<b>5.3.2</b> Molecular Structure	116
<b>5.3.3</b> Hydrogen Bonding	118
<b>5.3.4</b> Crystal Packing	118
<b>5.3.5</b> Thermal Analysis Studies	122
<b>5.3.6</b> Temperature Dependent Phase Transition Properties of the $\beta$ -Polymorph	124
<b>5.3.7</b> Solid-State Photodimerization Information from X-ray Powder Diffraction	126
<b>5.3.8</b> Solid-State Kinetics as Monitored with NMR spectroscopy	128
<b>5.4</b> Conclusion	129

---

	<u>Page</u>
<b>Chapter 6: A New Polymorph of OETCA: Single-to-Single-Crystal Phase Transformation and Mechanism</b>	131
6.1 Introduction	131
6.2 Methods for Chapter 6	133
6.2.1 Crystal Growth	133
6.2.2 DSC Measurements	133
6.2.3 High Temperature $\alpha'$ -OETCA Polymorph Single-Crystal Analysis	133
6.2.4 Stabilized $\alpha'$ -Polymorph Single-Crystal Analysis	135
6.3 Results and Discussion	136
6.3.1 Thermal Analysis Studies	136
6.3.2 The Naming of this New Polymorph	139
6.3.3 Molecular Structure	140
6.3.4 Classical Hydrogen Bonding	143
6.3.5 Crystal Packing	146
6.3.6 Closest Distances between the Reactive Double Bonds in the $\alpha'$ -Polymorph	148
6.3.7 Stabilizing the $\alpha'$ -Polymorph	150
6.3.8 Phase Change Mechanism: Comparing the $\alpha$ and $\alpha'$ -Polymorphs	152
6.3.9 Relationships between the Various OETCA Polymorphs	160
6.4 Conclusions	162
<b>Chapter 7: Photodimerization of the <math>\alpha'</math>-Polymorph of <i>ortho</i>-Ethoxy-<i>trans</i>-cinnamic acid in the Solid-State. Part1: Monitoring the Reaction at 293 K</b>	164
7.1 Introduction	164
7.2 Methods for Chapter 7	166
7.2.1 Crystal Growth	166
7.2.2 Photodimerization	166

---

	<b><u>Page</u></b>
<b>7.2.3</b> X-ray Structural Analysis	167
<b>7.3</b> Results and Discussion	169
<b>7.3.1</b> Reaction by UV Radiation	169
<b>7.3.2</b> Molecular Structure	174
<b>7.3.3</b> Hydrogen Bonding	178
<b>7.3.4</b> Crystal Packing	182
<b>7.4</b> Conclusions	184
<b>Chapter 8: Photodimerization of the <math>\alpha'</math>-polymorph of <i>ortho</i>-Ethoxy-<i>trans</i>-cinnamic acid in the Solid-State. Part2: Monitoring the Reaction at 343 K</b>	185
<b>8.1</b> Introduction	185
<b>8.2</b> Methods for Chapter 8	186
<b>8.2.1</b> Crystal Growth	186
<b>8.2.2</b> Photodimerization	186
<b>8.2.3</b> X-ray Structural Analysis	186
<b>8.2.4</b> Powder Diffraction Studies	189
<b>8.3</b> Results and Discussion	189
<b>8.3.1</b> Reaction by UV Radiation	189
<b>8.3.2</b> Stage One	190
<b>8.3.2.1</b> Rate of Conversion, Unit Cell Parameter and Selected Intermolecular Distance Changes as Determined by Single-Crystal X-ray Diffraction	190
<b>8.3.2.2</b> Molecular Structure	199
<b>8.3.2.3</b> Hydrogen Bonding	206
<b>8.3.2.4</b> Crystal Packing	211
<b>8.3.3</b> Stage Two	216
<b>8.3.4</b> Final Comments on the DE to FG Conformation Change	220
<b>8.4</b> Conclusion	225

---

	<b><u>Page</u></b>
<b>Chapter 9: Photodimerization of the <math>\alpha</math>-Polymorph of OETCA in the Solid-State: Reaction and Proposed Mechanism</b>	227
<b>9.1</b> Introduction	227
<b>9.2</b> Methods for Chapter 9	228
<b>9.2.1</b> Photodimerization Study	228
<b>9.3</b> Results and Discussion	228
<b>9.3.1</b> NMR Spectroscopic Data	232
<b>9.3.2</b> Single-Crystal X-ray Diffraction	233
<b>9.3.3</b> Powder X-ray Diffraction	244
<b>9.4</b> Conclusion	248
<b>Chapter 10: Conclusions</b>	249
<b>Chapter 11: References</b>	255
<b>Appendices</b>	
<b>Appendix A: Full Crystallographic Details for all Structures Reported in this Thesis Organized by Chapter</b>	A1
<b>Appendix B: CCD Snapshots of the <math>20\bar{4}</math> Reflection</b>	B1
<b>Appendix C: NMR Spectra</b>	C1
<b>Appendix D: Full Crystallographic Data Sets of each Crystal Structure Reported in this Thesis as well as PDF Versions of each Chapter. Data Sorted by Chapter.</b>	CD

---

**List of Abbreviations and Generally used Crystal Codes**

$\alpha$ -dimer $\alpha$ -photodimer $\alpha$ -photoproduct	The photodimerization product from the $\alpha$ - and $\alpha'$ -polymorphs - 2,2'-diethoxy- $\alpha$ -truxillic acid
$\beta$ -dimer $\beta$ -photodimer $\beta$ -photoproduct	The photodimerization product from the $\beta$ -polymorph - 2,2'-diethoxy- $\beta$ -truxinic acid
BRX	The crystal structure of the $\beta$ -photodimer
CCDC	Cambridge Crystallographic Data Centre
CSD	Cambridge Structural Database
DMF	<i>N,N</i> -Dimethylformamide
DMSO	Dimethyl sulfoxide
DSC	Differential Scanning Calorimetry
GK	The crystal structure of the $\alpha$ -photodimer published by Gopalan & Kulkarni (2001)
OETCA	<i>ortho</i> -ethoxy- <i>trans</i> -cinnamic acid
PXRD	Powder X-ray Diffraction
RTD	Crystal structure of the final product crystal from the photodimerization of the $\alpha'$ -polymorph at 293 K

RX	The crystal structure of the $\alpha$ -photodimer
RXS	The crystal structure of the $\alpha$ -photodimer and DMSO-d6 solvate
SCSC	Single-crystal-to-single-crystal