

TABLE OF CONTENTS

ACKNOWLEDGEMENTS	I
ABSTRACT	II
ABSTRAK	IV
TABLE OF CONTENTS.....	VI
LIST OF SCHEMES.....	XIII
LIST OF FIGURES	XVII
LIST OF TABLES.....	XIX
LIST OF APPENDICES	XX
ABBREVIATIONS	XXIII
CHAPTER 1. INTRODUCTION	1
1.1. Background.....	1
1.2. Problems to be addressed/and or hypothesis	2
1.3. General objectives	3
1.4. Specific objectives	3
1.5. Scope and limitations	3
1.6. Expected outputs.....	4
1.7. Thesis content	4
CHAPTER 2. STILBENE SYNTHESIS.....	5
2.1. Brief overview of stilbene monomer syntheses	5
2.1.1. Palladium-catalysed syntheses of stilbenes	5
2.1.1.1. Heck reaction.....	6
2.1.1.2. Decarbonylative Heck reaction	8
2.1.1.3. Heck-type decarboxylative coupling	8
2.1.1.4. Suzuki-Miyaura reaction.....	9
2.1.1.5. Stille reaction.....	10
2.1.1.6. Negishi cross-coupling	11
2.1.1.7. Tandem cross-metathesis (or silylative coupling) and Hiyama coupling.....	12
2.1.2. Non-palladium-catalysed syntheses of stilbenes.....	13

2.1.2.1. Ni(0) or Cu(I) salts-catalysed vinylation	13
2.1.2.2. McMurry coupling.....	13
2.1.2.3. Ruthenium-catalysed cross-metathesis.....	14
2.1.2.4. Cobalt-catalysed Diels-Alder/Wittig olefination.....	15
2.1.2.5. Modified Perkin reaction	15
2.1.2.6. Horner-Wadsworth-Emmons olefination.....	16
2.1.2.7. Knoevenagel condensation	17
2.1.2.8. Lithium-mediated cross coupling	17
2.2. Results and discussion.....	18
2.2.1. Synthesis of stilbene building blocks 2.1, 2.38, 2.39, 2.40, 2.41, 2.42, and 2.43	19
2.2.2. Synthesis of stilbenes possessing resorcinol (3,5-disubstitution) and the 3-substitution pattern (resveratrol analogues)	20
2.2.3. Spectroscopic evidence of stilbene analogues 1.2, 2.46-2.47, 2.48- 2.49, 2.50-2.58 and 2.8.	24
2.3. Experimental section	25
2.3.1. Synthesis of protected iodophenol	26
2.3.1.1. Preparation of 4-iodophenylacetate 2.1	26
2.3.1.2. Preparation of 3-iodophenylacetate 2.38	27
2.3.2. Synthesis of protected 3,5-dihydroxybenzaldehyde.....	27
2.3.2.1. Preparation of 3,5-dibenzoyloxybenzaldehyde 2.39	27
2.3.2.2. Preparation of 3,5-bis(<i>tert</i> -butyldimethylsilyloxy)benzalde- hyde 2.40	28
2.3.3. Synthesis of protected styrenes	29
2.3.3.1. Preparation of 3,5-bis(<i>tert</i> -butyldimethylsilyloxy)styrene 2.41.....	29
2.3.3.2. Preparation of 3,5-dimethoxy styrene 2.42.....	30
2.3.3.3. Preparation of 3,5-dibenzoyloxy styrene 2.43	30
2.3.4. Synthesis of substituted stilbenes	31
2.3.4.1. Preparation of 2.46 & 1.2.....	31
2.3.4.2. Preparation of 2.47 & 2.49.....	32
2.3.4.3. Preparation of 2.8	33
2.3.4.4. Preparation of 2.51	34
2.3.4.5. Preparation of 2.48 & 2.50.....	34
2.3.4.6. Preparation of 2.52	35

2.3.4.7. Preparation of 2.56 & 2.53.....	36
2.3.4.8. Preparation of 2.58 & 2.54.....	37
2.3.4.9. Preparation of 2.57 & 2.55.....	38
2.4. References.....	40
CHAPTER 3. ELECTROCHEMICAL OXIDATIONS ON SOME STILBENE ANALOGUES	
3.1. Introduction to stilbene oxidation and electrochemistry	43
3.1.1. Generalities on phenolic oxidation.....	44
3.1.2. Concepts on phenol electrochemical oxidation	47
3.2. Previous work on stilbene electrochemistry.....	50
3.3. Results and discussion.....	55
3.3.1. Measurement of oxidation potentials of stilbene derivatives	55
3.3.2. Anodic oxidation of <i>para</i> -hydroxy and- acetate stilbenes in CH ₂ Cl ₂ /MeOH	59
3.3.3. Constant current electrolysis of <i>para</i> hydroxy 2.56 and acetate 2.46 stilbenes in pure CH ₂ Cl ₂	61
3.3.4. Spectroscopic evidence of stilbene adducts 3.41, 3.42, 3.44, 3.45, 3.48 together with mixtures of 3.43a & 3.43b and 3.46a & 3.46b.....	62
3.3.5. Mechanistic discussion.....	63
3.4. Experimental section	68
3.4.1. Measurement of oxidation potentials of stilbene derivatives	68
3.4.2. Constant current electrolysis of stilbene derivatives	69
3.5. References.....	74
CHAPTER 4. SYNTHESIS OF NATURAL OLIGOMERIC STILBENOIDS AND ANALOGUES.....	
4.1. Oligostilbenoid biomimetic syntheses.....	76
4.1.1. Biosynthesis of oligostilbenoids	77
4.1.2. Biotransformation and enzymatic coupling.....	79
4.1.2.1. Resveratrol, pterostilbene and their analogues.....	80
4.1.2.2. Oligostilbenoid/stilbene dimers.....	87
4.1.3. Oxidative coupling with Fe ³⁺	90
4.1.3.1. Resveratrol	90
4.1.3.2. Isorhapontigenin	91
4.1.3.3. Other stilbenes	92

4.1.3.4. Summary	94
4.1.4. Oxidative coupling with silver derivatives	95
4.1.4.1. Resveratrol	95
4.1.4.2. Isorhapontigenin.....	95
4.1.4.3. Piceatannol	96
4.1.4.4. Other stilbenoids.....	96
4.1.4.5. Viniferins	97
4.1.4.6. Summary	97
4.1.5. Dimerisation with other oxidants	98
4.1.5.1. Resveratrol	98
4.1.5.2. Summary	99
4.1.6. Chemical transformation of ϵ -viniferin and its derivatives	100
4.1.7. Stilbenes that fail to dimerise under oxidative conditions	101
4.1.8. Acid-catalysed dimerisation.....	102
4.1.8.1. Resveratrol and isorhapontigenin.....	102
4.1.8.2. Unnatural stilbenes	105
4.1.9. Acid catalysed cyclisation of stilbene oligomers	108
4.1.10. Stilbene photooxidation.....	109
4.2. Non biomimetic syntheses.....	111
4.3. Results and discussion.....	124
4.3.1. Oxidative coupling with Fe^{3+}	127
4.3.2. Oxidative coupling with Ag^+	129
4.3.3. Dimerization with other oxidants	130
4.3.4. Spectroscopic analysis.....	131
4.3.4.1. δ -Viniferin analogue 4.14	131
4.3.4.2. δ -Viniferin analogue 4.184	136
4.3.4.3. Tricuspidatol A analogue 3.47	138
4.3.4.4. Tetrahydronaphthalene 4.183.....	142
4.3.4.5. Trimeric compound 4.185.....	146
4.3.5. Mechanistic considerations	149
4.3.5.1. HSAB Principle	150
4.3.5.2. Oxidative coupling with soft acids	153
4.3.5.3. Oxidative coupling with hard acid single electron oxidants	154
4.3.5.4. Oxidative coupling with borderline acids	155

4.3.5.5. Effect of solvents and ligands on oxidants (metal ions) properties.....	156
4.3.5.6. δ -Viniferin analogues formation via AgOAc promoted oxidative coupling	159
4.3.5.7. δ -Viniferin analogues formation via FeCl ₃ oxidative coupling	160
4.3.5.8. Tricuspidatol-A like formation via FeCl ₃ oxidative coupling.....	162
4.3.5.9. Pallidol and ampelopsin F analogues formation via FeCl ₃ oxidative coupling	164
4.3.5.10.Tetralin analogues formation via FeCl ₃ oxidative coupling	173
4.3.5.11.Trimer with tetralin scaffold formation via PbO ₂ oxidative coupling.....	178
4.3.5.12.Tetralin and indane scaffolds formation catalysed by Brönsted acids	183
4.3.5.13.Comparison of anodic vs FeCl ₃ .6H ₂ O oxidation of stilbenes.....	185
4.4. Conclusion	188
4.5. Experimental section	189
4.5.1. Oligomerisation of 12- hydroxy-3,5-dimethoxystilbene 1.2	189
4.5.1.1. Preparation of 4.14/4.185.....	189
4.5.1.2. Preparation of 4.180	192
4.5.1.3. Preparation of 4.181 & 4.182.....	192
4.5.2. Oligomerisation of 12-hydroxy-3-methoxystilbene 2.56	194
4.5.2.1. Preparation of 3.47	194
4.5.2.2. Preparation of 4.183/4.184.....	195
4.5.3. Oligomerisation of 2.52.....	199
4.5.3.1. Preparation of 1.4 and 1.0.....	199
4.5.4. Oligomerisation of 2.58.....	200
4.5.4.1. Preparation of 4.186	200
References.....	202
CHAPTER 5. MOLECULAR MODELING	207
5.1. Reminders on some general notions in physical chemistry.....	208
5.1.1. Enthalpy.....	208
5.1.2. Entropy	208
5.1.3. Gibbs free energy	208
5.2. Quantum mechanics	209

5.2.1. The Schrödinger equation.....	210
5.2.2. Calculation methods - Solving the Schrödinger equation for complex systems	211
5.2.2.1. Born-Oppenheimer ϕ approximation and methods of calculation	211
5.2.3. Electron spin and molecular orbitals	212
5.2.4. The Pauli exclusion principle.....	212
5.2.5. HartreeóFock method	213
5.2.5.1. Self-consistent field (SCF) theory	213
5.2.6. Basis sets.....	214
5.2.6.1. Polarized basis sets	214
5.2.6.2. Diffuse basis sets	215
5.2.7. Post-Hartree-Fock methods	216
5.2.8. Density functional theory (DFT).....	217
5.2.9. Programs	217
5.2.9.1. Calculation of molecular properties from approximate molecular wave functions	218
5.3. General presentation of chemical interactions.....	219
5.3.1. Cation- π interactions	220
5.3.2. Polar- π interactions	221
5.3.3. Aromatic stacking interactions.....	222
5.3.3.1. A Set of rules.....	223
5.3.3.2. Effects of polarization between π -systems polarized by heteroatoms	225
5.4. Methods and results: modeling of stilbenoids and their oxidized forms.....	231
5.4.1. Definition and calculation method of the bond dissociation energy.....	232
5.4.1.1. Bond dissociation energy calculation method.....	233
5.4.2. Definition and calculation method of the ionization potential.....	234
5.4.2.1. Ionization energy calculation method.....	234
5.4.3. Results and discussion.....	235
5.4.3.1. H atom transfer (HAT) mechanism and BDE calculations	236
5.4.3.2. Electron transfer mechanism and IP calculations.....	237
5.4.3.3. Conformational studies	238
5.4.3.4. Spin density.....	239

5.5. Methods and results: Modeling of stilbenes pairs.....	243
5.5.1. Contribution of hydrogen bonding and - interactions in <i>para</i> -hydroxy-substituted stilbenes alignment	244
5.5.2. Comparison of stability between head-to-head and head-to-tail alignments of stilbenes	245
5.5.3. Calculation results on various <i>Re/Si</i> approaches of pterostilbene units	246
5.5.4. Calculation results on various <i>Re/Re</i> approaches of pterostilbene units	251
5.5.5. Calculation results on various <i>Re/Re</i> approaches of demethoxy-pterostilbene units with two methoxy groups aligned <i>syn</i> to each other.....	254
5.5.6. Calculation results on various <i>Re/Re</i> approaches of demethoxy-pterostilbene units with two methoxy groups aligned <i>anti</i> to each other.....	256
5.5.7. Calculation results on various <i>Re/Si</i> approaches of demethoxy-pterostilbene units with two methoxy groups were aligned <i>anti</i> to each other.....	260
5.5.8. Summary.....	262
5.5.9. Study of oxidized stilbene species and their reactivities	264
5.5.9.1. Pterostilbene/pterostilbene radical.....	264
5.5.9.2. Pterostilbene radical/pterostilbene radical	265
5.5.9.3. Demethoxy-pterostilbene/demethoxy-pterostilbene radical	266
5.5.9.4. Demethoxy-pterostilbene radical/demethoxy-pterostilbene radical.....	267
5.6. Ag ⁺ impact on its coordination with stilbene and the alignment of stilbenes	268
5.7. References.....	271
CHAPTER 6. CONCLUSION	274
APPENDICES	277

LIST OF SCHEMES

Scheme 2.1: Palladium acetate catalysed Heck coupling.....	6
Scheme 2.2: Heck coupling catalysed by palladium cross linked polymer.....	6
Scheme 2.3: Stilbene synthesis through two sequential Heck-type reactions.	7
Scheme 2.4: Synthesis of resveratrol <i>via</i> decarbonylative Heck reactions.	8
Scheme 2.5: Stilbene synthesis through Heck-type decarboxylative coupling.	9
Scheme 2.6: Catalytic cycle involved in Suzuki-Miyaura reaction	9
Scheme 2.7: Stilbene synthesis promoted by Suzuki-Miyaura coupling.	10
Scheme 2.8: Catalytic cycle involved in Suzuki-Miyaura reaction.	10
Scheme 2.9: Stilbene synthesis by Stille coupling.....	11
Scheme 2.10: Catalytic cycle involved in Negishi cross-coupling.	11
Scheme 2.11: Stilbene synthesis by Negishi cross-coupling.	12
Scheme 2.12: Stilbene synthesis by Himaya coupling.	12
Scheme 2.13: Cu(I) and Ni(0) catalysed couplings in stilbene synthesis.....	13
Scheme 2.14: Mechanism of the McMurry coupling.	13
Scheme 2.15: McMurry coupled aldehydes to stilbene derivatives.....	14
Scheme 2.16: Synthesis of (<i>E</i>)-hydroxystilbenoids by metathesis.	15
Scheme 2.17: Stilbene synthesis by Co-catalysed Diels-Alder/Wittig olefination.....	15
Scheme 2.18: Hydroxylated stilbene synthesis <i>via</i> a modified Perkin reaction	16
Scheme 2.19: Stilbene synthesis through Horner-Wadsworth-Emmons olefinations between aldehydes and phosphonates.	17
Scheme 2.20: Knoevenagel condensation for preparing stilbenes with electron withdrawing groups.....	17
Scheme 2.21: Preparation of resveratrol through Li-mediated coupling.....	18
Scheme 2.22: Proposed synthetic plan of stilbene derivatives.	18
Scheme 2.23: Heck catalytic cycle.	22
Scheme 2.24: Mechanism of the Heck coupling.	24
Scheme 3.1: Phenol oxidation producing $\text{ArOH}^{\pm\bullet}$, ArO^{\bullet} or ArO^+	45
Scheme 3.2: Electrochemical mechanistic considerations for intermediates ArO^{\bullet} , ArO^+ , or $\text{ArOR}^{\pm\bullet}$ in various conditions	49
Scheme 3.3: Anodic oxidative dimerization of 4,12-dimethoxystilbene in acetate buffer	51
Scheme 3.4: Anodic oxidative dimerization of 4,12-dimethoxystilbene in presence and absence of MeOH.....	52
Scheme 3.5: Anodic oxidation of stilbene derivative at constant potential and its mechanistic consideration.....	53
Scheme 3.6: Electrochemical oxidation of stilbene derivatives in presence of nucleophile.....	53
Scheme 3.7: Possible mechanistic pathways of episulfonium ion intermediate 3.30.....	54
Scheme 3.8: Electro reduction of stilbene	54
Scheme 3.9: Mechanistic consideration of stilbene electrochemical reduction in presence of solvent THF.....	55

Scheme 3.10: Two electron anodic oxidation of stilbenoid under neutral condition.....	56
Scheme 3.11: Anodic oxidation of stilbene derivatives producing stilbene adducts.....	60
Scheme 3.12: Anodic oxidation of 2.56 producing dimerised compound 3.47	61
Scheme 3.13: Anodic oxidation of 2.46 produced halogenated monomer 3.48	61
Scheme 3.14: Anodic oxidation of stilbene derivative in different solvents (pure CH ₂ Cl ₂ and CH ₂ Cl ₂ /MeOH mixture)	65
Scheme 3.15: Electrophilic aromatic substitution of <i>para</i> -acetylated stilbene 2.46 in CH ₂ Cl ₂	66
Scheme 3.16: <i>Para</i> -acetylated stilbene 2.46 undergoes E-C-E-C pathway to produce halogenated product 3.48	67
Scheme 4.1: Synthesis of usnic acid.	77
Scheme 4.2: Sotheeswaran & Pasupathy's proposed biosynthesis of hopeaphenol 1.8	78
Scheme 4.3: Revised proposal for the biosynthesis of hopeaphenol 1.8 through ε -viniferin 1.4	79
Scheme 4.4: Conversion of resveratrol into it dimers by peroxidases from different sources.....	80
Scheme 4.5: Proposed radical intermediates involved in resveratrol oxidative coupling.....	81
Scheme 4.6: Synthesis of quadrangularin A 4.10 from substituted resveratrol 4.8	82
Scheme 4.7: Oxidation of resveratrol 1.0 via COX-1 peroxidase.	83
Scheme 4.8: Dimerisation of pterostilbene 1.2	85
Scheme 4.9: Stilbene dimerisation by laccases from two different fungi <i>T. pubescens</i> and <i>M. thermophyla</i>	85
Scheme 4.10: Stilbene dimerisation by laccase from <i>T. pubescens</i>	87
Scheme 4.11: Biotransformation products of ε -viniferin by HRP/H ₂ O ₂ ; * 1.4 was subjected to AgOAc in dry methanol, see section 3.4.5.....	88
Scheme 4.12: HRP-mediated condensation of stilbenoid dimers with resveratrol 1.0	89
Scheme 4.13: Fe ³⁺ oxidative coupling of resveratrol.	91
Scheme 4.14: Oxidation of isorhapontigenin into its oligomers.	92
Scheme 4.15: Generation of pallidol and ampelopsin F analogues in FeCl ₃ .6H ₂ O/CH ₂ Cl ₂ mixture.....	93
Scheme 4.16: Synthesis of dihydronaphthalene based stilbene dimers in FeCl ₃ .6H ₂ O/CH ₂ Cl ₂ mixture.....	94
Scheme 4.17: Synthesis of cassigarols E and G.	96
Scheme 4.18: Synthesis of (\pm)-maackin.....	97
Scheme 4.19: Synthesis of ε - and δ -viniferins in metallic and organic oxidative conditions.....	99
Scheme 4.20: Oxidation of ε -viniferin pentaacetate 4.52 into amurensin H 4.54 100	100
Scheme 4.21: Protection and isomerisation of ε -viniferin.	100
Scheme 4.22: Cyclization of ε -viniferin derivatives in basic medium.....	101
Scheme 4.23: Intramolecular oxidative coupling of stilbene analogues by VOCl ₃	102
Scheme 4.24: Treatment of resveratrol and isorhapontigenin with formic acid.....	103
Scheme 4.25: Alignment of stilbenes leading to dimerisation.	104
Scheme 4.26: Treatment of resveratrol and piceatannol with NaNO ₂	104

Scheme 4.27: Formation of indane and tetralin skeletons via EPP oxidative coupling.....	105
Scheme 4.28: Synthesis of tetralin skeleton by BBr ₃	106
Scheme 4.29: Formation of tetralin and indane skeletons via MPA/S and TPA/S oxidative coupling.....	107
Scheme 4.30: Acid catalysed cyclisation of ε -viniferin.....	108
Scheme 4.31: Acid catalysed cyclisation of vitisin A and B.....	109
Scheme 4.32: Photooxidation of ε -viniferin.....	110
Scheme 4.33: Photooxidation of stilbene dimers and trimers.....	111
Scheme 4.34: Construction of epoxide 4.124 and hexacyclic intermediate 4.126	113
Scheme 4.35: Total synthesis of tetramethyl hopeahainol A 4.129 , hopeahainol A 4.131 , and hopeanol 4.132	114
Scheme 4.36: Total synthesis of three dimeric resveratrol-based natural products (4.107 , 4.140 and 4.108) from key building block 4.133	116
Scheme 4.37: Total synthesis of three dimeric resveratrol-based natural products (4.6 and 4.142) from key building block 4.141	117
Scheme 4.38: Sequential, cascade-based halogenation to access pallidol 1.6	117
Scheme 4.39: Sequential, cascade-based halogenation to access ampelopsin F 1.5	118
Scheme 4.40: Alternate use of key intermediate 4.147 to access the unique architectures of related nonnatural products (such as 4.152)	119
Scheme 4.41: Synthesis of potential precursors for natural products.....	120
Scheme 4.42: Synthesis of malibatol A analogue 4.164	121
Scheme 4.43: Synthesis of amurensin H	122
Scheme 4.44: Synthesis of viniferifuran analogue 4.169	123
Scheme 4.45: Synthesis of malibatol A 4.179 and shoreaphenol 4.178 analogues	124
Scheme 4.46: Summary of synthesized oligostilbenoids via chemical oxidation	126
Scheme 4.47: Synthesis of tricuspidatol A analogues in FeCl ₃ .6H ₂ O/CH ₂ Cl ₂ /MeOH mixture.....	127
Scheme 4.48: Generation of pallidol and ampelopsin F analogues in FeCl ₃ .6H ₂ O/CH ₂ Cl ₂ mixture.....	128
Scheme 4.49: Synthesis of tetrahydronaphthalene and dihydronaphthalene based stilbene dimers in FeCl ₃ .6H ₂ O/CH ₂ Cl ₂ mixture.....	128
Scheme 4.50: Synthesis of γ -viniferin via FeCl ₃ .6H ₂ O oxidation	129
Scheme 4.51: Synthesis of δ -viniferin analogues by AgOAc oxidative coupling.....	129
Scheme 4.52: Oxidative coupling by PbO ₂ of stilbenes 1.2 , 2.58 and 2.56	130
Scheme 4.53: Tetralin and tricuspidatol A analogues as oxidative coupling products from stilbene 2.56	131
Scheme 4.54: Acid base complex formation	150
Scheme 4.55: Single electron oxidation with soft acid treatment stilbene incorporating a C12-OH group.....	154
Scheme 4.56: Stilbene dimer skeletons produced by hard acid treatment of various stilbene starting materials.....	155
Scheme 4.57: Stilbene dimer skeletons produced by treatment of stilbenes with borderline acids.....	156
Scheme 4.58: Treatment of resveratrol and isorhapontigenin by FeCl ₃ .6H ₂ O and K ₃ [Fe(CN) ₆] in various solvents	157
Scheme 4.59: Acetone/water exchange in Fe ³⁺ complexes	158
Scheme 4.60: Oxidation of 12-OH-stilbenes and alignment of the reacting species leading to δ -viniferin type dimers.....	160
Scheme 4.61: Oxidation of <i>para</i> oxygenated stilbenes by FeCl ₃ .6H ₂ O.....	161

Scheme 4.62: Mechanism of the formation of ε -viniferin 1.4 from resveratrol 1.0	162
Scheme 4.63: Proposed mechanism of the formation of tricuspidatol A analogues 3.47 and 4.180	164
Scheme 4.64: Proposed transient species upon single electron oxidation of stilbenes.....	165
Scheme 4.65: <i>Re/Si</i> and <i>Re/Re</i> (or <i>Si/Si</i>) approaches of reacting stilbenes leading to pallidol and ampelopsin F analogues respectively in one-pot reaction	168
Scheme 4.66: Obtention of pallidol and ampelopsin F analogues from 4,12-dioxygenated stilbene 4.40	170
Scheme 4.67: Radical cation intermediates en route to pallidol analogue 4.181 from pterostilbene 1.2	171
Scheme 4.68: equilibrium between stable 4.213 and unstable 4.214 radical cations.....	171
Scheme 4.69: Formation of ampelopsin F analogue 4.182 from pterostilbene 1.2 through the addition of radical cations 4.213 and 4.214	172
Scheme 4.70: Mechanism of the formation of tetralin 4.183 from demethoxypterostilbene 2.56	174
Scheme 4.71: Tetralin 4.183 formation via Diels Alder cycloaddition.....	175
Scheme 4.72: Revised mechanism for the formation of a stilbene tetramer via a Diels-Alder cycloaddition of isorhapontigenin 1.1 (modified from reference 24).	176
Scheme 4.73: Mechanism of formation of restrytisol C analogues 4.44 and 4.45 (adapted from reference 26).....	177
Scheme 4.74: Alternative mechanism of formation of restrytisol C analogue 4.44	178
Scheme 4.75: Formation of δ -viniferin skeleton via PbO_2 oxidative coupling	179
Scheme 4.76: Formation of tetralin skeleton via PbO_2 oxidative coupling.....	182
Scheme 4.77: Acid catalysed stilbene dimerisation products (adapted from references 33, 35-37).....	183
Scheme 4.78: Various pathways leading to indane and tetralin skeletons through acid-catalysed dimerisation of 3,4-dimethoxystilbenes (adapted from reference 35).....	185
Scheme 4.79: Comparison of stilbene derivatives electrochemical oxidation with $\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$ oxidation in a mixture of $\text{CH}_2\text{Cl}_2/\text{MeOH}$	186
Scheme 4.80: Comparison of stilbene derivatives electrochemical oxidation with $\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$ oxidation in CH_2Cl_2	187
Scheme 5.1: H atom transfer mechanism of stilbenoid.....	236
Scheme 5.2: Electron transfer mechanism for stilbenoid	237

LIST OF FIGURES

Figure 2.1:	Synthesised building blocks of stilbenoids.....	20
Figure 2.2:	Synthesised fully and partially protected resveratrol analogues with 3,5-substitution pattern.....	21
Figure 2.3:	Synthesised fully and partially protected resveratrol analogues with 3-substitution pattern.....	22
Figure 3.1(a-h):	Cyclic voltammograms (CV) of various substituted stilbene derivatives.....	57
Figure 3.2:	Possible enantiomeric and diastereomeric pairs.....	62
Figure 4.1:	(Z)- δ -viniferin 1.3b	81
Figure 4.2:	Structures of restyrtisol A 4.11, restyrtisol B 4.12 and restyrtisol C 4.13.....	84
Figure 4.3:	Main HMBC correlations for 4.14	133
Figure 4.4:	AM1 calculation for 4.14	134
Figure 4.5:	Main HMBC correlations for 4.184	136
Figure 4.6:	Main HMBC correlations for 3.47	139
Figure 4.7:	AM1 calculation of tricuspidatol A analogue 3.47	140
Figure 4.8:	Main HMBC and long range COSY correlations for 4.183	143
Figure 4.9:	Computational model of 4.183.....	145
Figure 4.10:	Main HMBC correlations for 4.185	147
Figure 4.11:	Metal-olefin bonding model.....	159
Figure 4.12:	Four different <i>Re/Re</i> (or <i>Si/Si</i>) alignments for 2.56	175
Figure 5.1:	Simplified diagram of the linear combination of s and p orbitals.....	215
Figure 5.2:	Mathematical representation of a (a) $\ddot{\text{o}}$ classical Gaussian function and (b) a diffuse Gaussian function	216
Figure 5.3:	Binding energies for simple cations to benzene in gas phase.....	221
Figure 5.4:	π Hydrogen bonds	221
Figure 5.5:	An sp ² hybridised atom in a π -system.....	222
Figure 5.6:	Model for an atom which contributes one electron to the molecular π -system; projection parallel to the plane of the π -system.....	223
Figure 5.7:	Interaction between two idealized π -atoms as a function of orientation: two attractive geometries and the repulsive face-to-face geometry are illustrated. (y-axis: angle of anti-clockwise rotation about the central positive charge of the upper π -atom; x-axis: offset toward the right-hand side of the diagram)	224
Figure 5.8:	Edge-on or T-shaped geometry.....	225
Figure 5.9:	Face-to-face π -stacked geometry	226
Figure 5.10:	Orientations for the π - π interactions between polarized π -systems. R ₁ and R ₂ are the polarizing groups.....	229
Figure 5.11:	Limit structures possible for edge-to-face aromatic interactions: a) T-shaped, b) edge-tilted-T, and c) face-tilted-T	230

Figure 5.12: Schematic representation of the angle θ and distances d_1-d_4 used for describing edge-to-face interactions	230
Figure 5.13: Optimised geometries of stilbene derivatives after calculations.....	236
Figure 5.14: SOMO (singlet Occupied Molecular Orbital) of resveratrol radical.	239
Figure 5.15: Spin densities of stilbenoid radicals and radical cations.	241
Figure 5.15 (cont'd): Spin densities of stilbenoid radicals and radical cations.	242
Figure 5.15 (cont'd): Spin densities of stilbenoid radicals and radical cations.	243
Figure 5.16: Influence of the hydroxyls on the stacking of a stilbene pair	245
Figure 5.17: Influence of geometry type on stilbene alignment.....	245
Figure 5.18: Calculation results on <i>Re/Si</i> approaches of pterostilbene-pterostilbene radical.	265
Figure 5.19: Calculation result on <i>Re/Re</i> approaches of pterostilbene radical-pterostilbene radical.	266
Figure 5.20: Calculation result on <i>Re/Re</i> approaches of demethoxypterostilbene- demethoxypterostilbene radical.	267
Figure 5.21: Calculation result on <i>Re/Re</i> approaches of demethoxypterostilbene radical- demethoxypterostilbene radical.....	268
Figure 5.22: Stilbene- Ag^+ model.	268
Figure 5.23: LUMO, HOMO, HOMO-1 and HOMO-2 of stilbene- Ag^+ complex.	269
Figure 5.24: Calculated distance between stack of stilbenoids with and without Ag^+	270

LIST OF TABLES

Table 3.1: Oxidation potentials of various substituted stilbene derivatives	59
Table 4.1: ^1H -(300 MHz) and ^{13}C -(75 MHz) NMR data 4.14	135
Table 4.2: ^1H -(500 MHz) and ^{13}C -(125 MHz) NMR data of 4.184	137
Table 4.3: ^1H -(300 MHz) and ^{13}C -(75 MHz) NMR data of 3.47	141
Table 4.4: ^1H -(500 MHz) and ^{13}C -(125 MHz) NMR data of 4.183	144
Table 4.5: Computed dihedral angles and measured coupling constants for protons of the central ring of 4.183	145
Table 4.6: ^1H -(400 MHz) and ^{13}C -(125 MHz) NMR data of 4.185	148
Table 4.7: Hard, borderline and soft acids and bases. ⁵²	152
Table 5.0: Electrostatic contribution to π -stacking interactions between polarised π -systems (in kJ/mol). ⁹	227
Table 5.1: Calculated BDE for some of the stilbenoids.....	237
Table 5.2: IP values of stilbenoids	238
Table 5.3: Torsion angles values for stilbenoids.	239
Table 5.4: Calculation results on various <i>Re/Si</i> approaches of pterostilbene units.	249
Table 5.6 (cont'd): Calculation results on various <i>Re/Re</i> approaches of pterostilbene units.....	250
Table 5.5: Measured distances between selected atoms from alignment 5.1-5.5.....	250
Table 5.6: Calculation results on various <i>Re/Re</i> approaches of pterostilbene units.	252
Table 5.6: Calculation results on various <i>Re/Re</i> approaches of pterostilbene units.	253
Table 5.7: Calculation results on various <i>Re/Re</i> approaches of demethoxy- pterostilbene units with two methoxy groups aligned <i>syn</i> to each other.....	255
Table 5.7 (cont'd): Calculation results on various <i>Re/Re</i> approaches of deme- thoxypterostilbene units with two methoxy groups aligned <i>syn</i> to each other.....	256
Table 5.8: Calculation results on various <i>Re/Re</i> approaches of demethoxy- pterostilbene units with two methoxy groups aligned <i>anti</i> to each other.....	258
Table 5.8: Calculation results on various <i>Re/Re</i> approaches of demethoxy- pterostilbene units with two methoxy groups aligned <i>anti</i> to each other.....	259
Table 5.9: Calculation results on various <i>Re/Si</i> approaches of demethoxy- pterostilbene units with two methoxy groups aligned <i>anti</i> to each other.....	261
Table 5.9 (cont'd): Calculation results on various <i>Re/Si</i> approaches of deme- thoxypterostilbene units with two methoxy groups aligned <i>anti</i> to each other.....	262

LIST OF APPENDICES

Appendix 1: ^1H NMR (300 MHz, CDCl_3) spectrum of 4-iodophenyl acetate 2.1	277
Appendix 2: ^1H NMR (300 MHz, CDCl_3) spectrum of 3-iodophenyl acetate 2.38	278
Appendix 2b: ^1H NMR (300 MHz, CDCl_3) enlargement (7.0-7.6 ppm) spectrum of 3-iodophenyl acetate 2.38	279
Appendix 3: ^1H NMR (300 MHz, CDCl_3) spectrum of 3,5-bis(benzyloxy)benzaldehyde 2.39	280
Appendix 4: ^1H NMR (300 MHz, CDCl_3) spectrum of 3,5-bis(tert-butyldimethylsilyloxy)benzaldehyde 2.40	281
Appendix 5: ^1H NMR (400 MHz, CDCl_3) spectrum of (5-vinyl-1,3-phenylene)bis(oxy)bis(tert-butyldimethylsilane) 2.41	282
Appendix 6: ^1H NMR (300 MHz, CDCl_3) spectrum of 3,5-dimethoxystyrene 2.42	283
Appendix 7: ^1H NMR (300 MHz, CDCl_3) spectrum of 3,5-dibenzyloxyxystyrene 2.43	284
Appendix 8: ^1H NMR (400 MHz, CDCl_3) spectrum of 12-acetoxy-3,5-dimethoxystilbene 2.46	285
Appendix 9: ^1H NMR (500 MHz, CDCl_3) spectrum of 12-acetoxy-3,5-dimethoxystilbene 2.47	286
Appendix 9: ^1H NMR (500 MHz, CDCl_3) enlargement (6.9-7.6 ppm) spectrum of 12-acetoxy-3,5-dimethoxystilbene 2.47	287
Appendix 10: ^1H NMR (300 MHz, CDCl_3) spectrum of 12-methoxy-3,5-dimethoxystilbene 2.8	288
Appendix 11: ^1H NMR (400 MHz, CDCl_3) spectrum of 12-methoxy-3,5-ditert-butydimethoxyxylanestilbene 2.48	289
Appendix 12: ^1H NMR (500 MHz, CDCl_3) spectrum of 12-hydroxy-3,5-dibenzyoxystilbene 2.49	290
Appendix 13: ^1H NMR (500 MHz, CDCl_3) spectrum of pterostilbene 1.2	291
Appendix 14: ^1H NMR (400 MHz, CDCl_3) spectrum of 12-methoxy-3-hydroxy-5-butydimethoxyxilanestilbene 2.5	292
Appendix 15: ^1H NMR (400 MHz, deuterated acetone) spectrum of 12-methoxy-3,5-dihydroxystilbene 2.51	293
Appendix 16: ^1H NMR (500 MHz, deuterated acetone) spectrum of 12-acetoxy-3,5-dihydroxystilbene 2.52	294
Appendix 17: ^1H NMR (400 MHz, CDCl_3) spectrum of 12-acetoxy-3,5-dihydroxystilbene 2.53	295
Appendix 18: ^1H NMR (500 MHz, CDCl_3) spectrum of 12-acetoxy-3-acethoxystilbene 2.54	296
Appendix 19: ^1H NMR (400 MHz, CDCl_3) spectrum of 12-methoxy-3-acetoxy-5-stilbene 2.55	297
Appendix 20: ^1H NMR (500 MHz, CDCl_3) spectrum of 12-hydroxy-3-methoxystilbene 2.56	298

Appendix 21: ^1H NMR (400 MHz, CDCl_3) spectrum of 12-methoxy-3-hydroxystilbene 2.57	299
Appendix 22: ^1H NMR (500 MHz, deuterated acetone) spectrum of 12-hydroxy-3-hydroxystilbene 2.58	300
Appendix 23: ^{13}C NMR (125 MHz, CDCl_3) spectrum of pterostilbene 1.2	301
Appendix 24: ^{13}C NMR (125 MHz, CDCl_3) spectrum of 12-hydroxy-3-methoxystilbene 2.56	302
Appendix 25: ESI-TOF-MS (-) spectrum of pterostilbene 1.2	303
Appendix 26: ESI-TOF-MS (-) spectrum of pterostilbene 2.56	304
Appendix 27: ^1H NMR (400 MHz, CDCl_3) spectrum of (<i>E</i>)-4-(2,6-dichloro-3,5-dimethoxystyryl)phenyl acetate 3.48	305
Appendix 28: ^{13}C NMR (75 MHz, CDCl_3) spectrum of (<i>E</i>)-4-(2,6-dichloro-3,5-dimethoxystyryl)phenyl acetate 3.48	306
Appendix 29: ORTEP of (<i>E</i>)-4-(2,6-dichloro-3,5-dimethoxystyryl)phenyl acetate 3.48	307
Appendix 30: ES-TOF-MS (+) spectrum of 3.48	308
Appendix 31: ^1H NMR (400 MHz, CDCl_3) spectrum of diastereoisomer 3.41	309
Appendix 32: ^1H NMR (400 MHz, CDCl_3) spectrum of diastereoisomer 3.42	310
Appendix 33: ^1H NMR (400 MHz, CDCl_3) spectrum of diastereoisomer 3.44	311
Appendix 34: ^1H NMR (400 MHz, CDCl_3) spectrum of diastereoisomer 3.45	312
Appendix 35: ^1H NMR (400 MHz, CDCl_3) spectrum of diastereoisomers 3.43a & 3.43b	313
Appendix 36: ^1H NMR (400 MHz, CDCl_3) spectrum of diastereoisomers 3.46a & 3.46b	314
Appendix 37: ESI-TOF-MS (+) spectrum of 3.44	315
Appendix 38: ES-TOF-MS (+) spectrum of 3.41	316
Appendix 39: ES-TOF-MS (+) spectrum of diastereoisomers 3.43a & 3.43b	317
Appendix 40: ES-TOF-MS (+) spectrum of diastereoisomers 3.46a & 3.46b	318
Appendix 41: ^1H NMR (500 MHz, CDCl_3) spectrum of δ -viniferin analogue 4.14	319
Appendix 42: ^{13}C NMR (125 MHz, CDCl_3) spectrum of δ -viniferin analogue 4.14	320
Appendix 43: ESI-TOF-MS (-) spectrum of δ -viniferin analogue 4.14	321
Appendix 44: ^1H NMR (500 MHz, CDCl_3) spectrum of δ -viniferin analogue 4.184	322
Appendix 45: ^{13}C NMR (125 MHz, CDCl_3) spectrum of δ -viniferin analogue 4.184	323
Appendix 46: ESI-TOF-MS (-) spectrum of δ -viniferin analogue 4.184	324
Appendix 47: ^1H NMR (500 MHz, CDCl_3) spectrum of tricuspidatol 3.47	325
Appendix 47: ^1H NMR (500 MHz, CDCl_3) enlargement (3.6-7.2 ppm) spectrum of tricuspidatol 3.47	326
Appendix 48: ^{13}C NMR (125 MHz, CDCl_3) spectrum of tricuspidatol 3.47	326
Appendix 49: ESI-TOF-MS (-) spectrum of tricuspidatol 3.47	327
Appendix 50: ^1H NMR (500 MHz, CDCl_3) spectrum of tetralin 4.183	328
Appendix 50: ^1H NMR (500 MHz, CDCl_3) enlargement spectrum (3.0-4.5 ppm and 6.3-7.2 ppm) of tetralin 4.183	329
Appendix 51: ^{13}C NMR (125 MHz, CDCl_3) spectrum of tetralin 4.183	330
Appendix 52: ESI-TOF-MS (-) spectrum of tetralin 4.183	331
Appendix 53: ^1H NMR (400 MHz, CDCl_3) spectrum of trimer 4.185	332

Appendix 53: ^1H NMR (400 MHz, CDCl_3) enlargement (6.0-7.3 ppm) spectrum of trimer 4.185	333
Appendix 54: ^{13}C NMR (400 MHz, CDCl_3) spectrum of trimer 4.185	334
Appendix 55: ESI-TOF-MS (+) spectrum of trimer 4.185	335
Appendix 56: ^1H NMR (400 MHz, CDCl_3) spectrum of tricuspidatol A analogue 4.180	336
Appendix 57: ^1H NMR (400 MHz, CDCl_3) enlargement (3.4-4.6 ppm and 6.0- 7.2 ppm) spectrum of 4.182a and 4.181a mixture	338
Appendix 58: ^1H NMR (500 MHz, deuterated acetone) spectrum of ε -viniferin 1.4	339
Appendix 59: ^1H NMR (500 MHz, deuterated acetone) spectrum of resveratrol 1.0	340
Appendix 60: ^1H NMR (500 MHz, deuterated acetone) spectrum of δ -viniferin analogue 4.186	341
Appendix 60: ^1H NMR (500 MHz, deuterated acetone) spectrum of δ -viniferin analogue 4.186	342
Appendix 61: ESI-TOF-MS (+) spectrum of δ -viniferin analogue 4.186	343

ABBREVIATIONS

AIBN = 2,2 ϕ -azobisisobutyronitrile

BDE = bond dissociation energy

CCE = constant current electrolysis

CV = cyclic voltammogram

*m*CPBA = *meta*-chloroperoxybenzoic acid

DCC = *N,N* ϕ dicyclohexylcarbodiimide

DFT = density functional theory

DMAP = 4-dimethylaminopyridine

DMSO = dimethyl sulfoxide

Ep = electrode potential

9-I-BBN = 9-iodo-9-borabicyclo[3.3.1]nonane

IBX = 2-iodoxybenzoic acid

IP = ionization potential

mA = milli Ampere

TBAF = tetra-n-butylammonium fluoride

TFA = trifluoroacetic acid

THF = tetrahydrofuran

TMS = trimethylsilyl

*p*TsOH = *para*-toluenesulfonic acid

V = volt