

Contents

1	Introduction	1
1.1	Historical Background of MALDI-MS	1
1.2	Principle of MALDI-MS	2
1.2.1	Ion Sources for LDI and MALDI	3
1.2.2	Ionisation of Molecules	4
1.2.3	Ion Yield and Laser Fluence	4
1.2.4	Primary Ionisation	5
1.2.4.1	The ‘Lucky Survivor’ Model of Primary Ionisation ..	5
1.2.4.2	The Photoionisation/Pooling Model of Primary Ionisation	5
1.2.5	Secondary Ionisation	5
1.2.5.1	Matrix Suppression Effect	7
1.2.5.2	Analyte Suppression Effect	7
1.2.5.3	Other Secondary Reactions	7
1.2.6	Sample Preparation	8
1.2.7	The Rate of the Matrix Crystal Growth	8
1.2.7.1	Moderately Fast Crystallisation	8
1.2.7.2	Slow Crystallisation	8
1.2.7.3	Rapid Crystallisation	9
1.3	MALDI-MS-Imaging (MSI)	9
1.3.1	Choice and Application of the Matrix	11
1.4	Lipids and Their Analysis	12
1.4.1	Types of Brain Lipids	12
1.4.2	Analysis of Lipids	13
1.4.3	Developing New Matrices	15

CONTENTS

1.5 Outline of the Thesis	16
2 Literature Overview	17
2.1 Introduction	17
2.2 Synthesis of Matrices	19
2.2.1 HCCA As a Basic Scaffold for the Synthesis of New Matrices	19
2.2.2 Synthetic Ways To <i>E</i> -Cinnamic Acid Derivatives	19
2.2.2.1 The Perkin Condensation Reaction	19
2.2.2.2 The Knoevenagel Condensation	20
2.2.2.3 The Heck Coupling	21
2.2.3 Synthetic Ways to <i>Z</i> -Cinnamic Acid Derivatives	22
2.2.3.1 Photoinduced Isomerisation of <i>E</i> -Cinnamic Acids	22
2.2.3.2 <i>Z</i> -selective Catalytic Hydrogenation of Alkynes	23
2.2.3.3 The Horner-Wadsworth-Emmons (HWE) Olefination .	23
2.3 Multivariate Analysis	24
2.3.1 Principal Component Analysis	24
2.3.1.1 Theory of Principal Component Analysis	24
2.3.1.2 Algorithm of PCA	25
2.3.1.3 Interpretation of PCA	26
3 Goals and Objectives	27
4 Results and Discussion	29
4.1 Development of New MALDI Matrices	30
4.1.1 Factors Affecting the Quality of MALDI Spectrum	30
4.1.1.1 Instrumental Factors	30
4.1.1.2 Experimental Factors	31
4.1.1.3 Matrix Properties	31
4.2 Design and Synthesis of Compound Library	31
4.3 The Overview of MALDI-MS Performance of Synthesised Compounds.	32
4.3.1 Phenylcinnamic Acid Derivatives	32
4.3.2 HCCA Derivatives	38
4.3.3 Diene Derivatives	39
4.3.4 Heterocyclic Derivatives	42
4.4 New Matrices For Small and Large Proteins	45
4.4.1 Protein Calibration Standard-I using 337 nm (N_2) Laser	45

CONTENTS

4.4.2 Protein Calibration Standard-II using 337 nm (N ₂) Laser	47
4.4.3 Protein Calibration Standard-I using 355 nm (Nd:YAG) Laser	48
4.4.4 Protein Calibration Standard-II using 355 nm (Nd:YAG)Laser	48
4.5 p-PhCCAA a New Matrix for Lipid Classes in Negative Mode	48
4.5.1 p-PhCCAA and Matrix Suppression Effect	48
4.5.2 p-PhCCAA and MALDI-Imaging	52
4.6 Structure-Performance Relationship of Phenylcinnamic Acid Derivatives	53
4.6.1 Performance Dependence on the Molar Extinction Coefficient.	54
4.6.2 Performance Dependence on the Substitution Position	58
4.6.3 Performance Dependence on the Functional Group at Carboxy Carbon	60
4.6.4 Selectivity and Performance Dependence on the Hydrophobicity of the Solvent System	61
4.7 X-ray Crystal Structure Analysis of Selected MALDI-Matrices	63
4.8 Principal Component Analysis	66
4.9 Summary Of the Chapter	71
5 Conclusion	75
6 Experimental Section	79
6.1 Experimental Section	79
6.1.1 General Information	79
6.1.2 Characterisation:	83
6.1.2.1 Phenylcinnamic Acid Derivatives	83
6.1.2.2 HCCA Derivatives	108
6.1.2.3 Diene Derivatives	123
6.1.2.4 Pyrrole derivatives	130
7 Appendix 1	141
8 Appendix 2	148
References	157