

## TABLE OF CONTENTS

<b>Declaration.....</b>	i
<b>Certificate of the Supervisor.....</b>	ii
<b>Certificate of the External Examiner and ODEC.....</b>	iii
<b>Acknowledgement.....</b>	iv- vi
<b>Abstract.....</b>	vii-xi
<b>Table of contents .....</b>	xii-xvii
<b>List of Tables.....</b>	xviii-xix
<b>List of Figures.....</b>	xx-xxiv
<b>List of Schemes.....</b>	xxv-xxix
<b>List of Abbreviations.....</b>	xxx-xxxii
<b>Chapter 1: Recent Advances in the Stereoselective Synthesis of Chroman Derivatives via Ar–O, ArO–C, and Ar–C Bond-Forming Intramolecular Cyclizations of Epoxides, Aziridines, and Vicinal Diols..</b>	1-22
1.1. Introduction.....	2
1.2. Importance of Heterocycles.....	3
1.3. Benzoxacycles: the 2,3-Dihydrobenzofuran, Chroman, 1,4-Benzodioxane, and 1-Benzoxepane Scaffolds.....	4
1.4. Chroman as a Privileged Scaffold.....	5
1.5. Synthetic Strategies towards Chromans.....	6
1.6. A Brief Introduction to Epoxides, Aziridines and Vicinal Diols....	7
1.6.1. Epoxides.....	7
1.6.2. Aziridines.....	8
1.6.3. Vicinal diols.....	9
1.7. Synthesis of Chroman Derivatives Using Epoxides, Aziridines and Vicinal Diols.....	

1.7.1. Using Epoxides.....	10
1.7.1.1. Intramolecular Friedel-Crafts Epoxide-Arene	10
Cyclization.....	
1.7.1.2 Intramolecular Ring-Opening of Epoxides by Tethered Phenols.....	14
1.7.2. Using Aziridines.....	18
1.7.2.1. Intramolecular Friedel-Crafts Aziridine-Arene	18
Cyclization.....	
1.7.2.2. Intramolecular Ring-Opening of Aziridines by Tethered Phenols.....	19
1.7.3. Using Vicinal 1,2 Diols.....	19
1.8. Conclusions.....	20
1.9. Thesis Overview.....	21
1.10. References.....	22
<b>Chapter 2: Diastereoselective Synthesis of <i>trans</i>-4-Arylchroman-3-ols via Ar-C Bond-Forming Intramolecular Friedel-Crafts Epoxide-Arene Cyclization Reaction and Its Applications in the Synthesis of <i>cis</i>-4-Arylchroman-3-ols and Chroman-Fused 2,3-Dihydrobenzofuran.....</b>	29-96
2.1. Introduction.....	30
2.2. Literature Known Methods to Access 4-Arylchroman-3-ols.....	31
2.3. Background and Objectives.....	32
2.4. Results and Discussion.....	34
2.4.1. Synthesis of <i>trans</i> -2-Aryl-3-(aryloxymethyl)oxirane.....	34
2.4.2. Screening of Reaction Conditions for the IFCEAC Reaction.....	34
2.4.3. TsOH·H <sub>2</sub> O-Catalyzed IFCEAC of <i>trans</i> -2-Aryl-3-(aryloxymethyl)oxiranes leading to the Formation of ( $\pm$ )- <i>trans</i> -4-Phenylchroman-3-ols.....	38
2.4.4. Upscaling of the Reaction: Gram-Scale Synthesis of <i>trans</i> -4-arylchroman-3-ol.....	42
2.4.5. Synthesis of <i>trans</i> -4-Arylchroman-3-ol with Free Phenolic-OH Groups on Ar <sup>1</sup> and Ar <sup>2</sup> Rings.....	42

2.4.6. Asymmetric Version of the Developed Methodology.....	44
2.4.7. Proposed Reaction Mechanism.....	44
2.4.8. Application of <i>trans</i> -4-Arylchroman-3-ols: Synthesis of <i>cis</i> -4-Arylchroman-3-ols from the Corresponding <i>trans</i> -Isomers.....	46
2.4.9. Application of <i>cis</i> -4-Arylchroman-3-ols: Synthesis of a Chroman-Fused 2,3-Dihydrobenzofuran System.....	47
2.5. Conclusions.....	47
2.6. Experimental Section.....	48
2.6.1. General Remarks.....	48
2.6.2. Preparation of Compounds.....	48
2.7. References.....	87
2.8. NMR Spectra of Selected Compounds.....	89
<b>Chapter 3: <i>syn</i>-Diastereoselective Synthesis of Chroman-Fused Tetralins via Ar–C Bond-Forming Intramolecular Friedel–Crafts Epoxide-Arene Cyclization Reaction.....</b>	97-148
3.1. Introduction.....	98
3.2. Background and Objectives.....	99
3.3. Results and Discussion.....	99
3.3.1. Retrosynthetic Analysis and Synthetic Challenges.....	99
3.3.2. Synthesis of Tetralin-Embedded Epoxy Tosylate.....	101
3.3.3. Synthesis of Tetralin-Embedded Glycidyl Ethers.....	101
3.3.4. Screening of Reaction Conditions for IFCEAC Reaction.....	102
3.3.5. IFCEAC of <b>8b-n</b> .....	104
3.3.6. Proposed Reaction Mechanism.....	106
3.4.7. Synthesis of a Chroman-Fused Tetralin with <i>trans</i> -Stereochemistry at the Ring Junction.....	107
3.5. Conclusion.....	108
3.6. Experimental Section.....	108
3.6.1. General Remarks.....	108
3.6.2. Preparation of Compounds.....	108
3.6.3. X-ray crystallography.....	127

3.7. References.....	128
3.8. NMR Spectra of Selected Compounds.....	131
<b>Chapter 4: Studies on the Synthesis of (+)-Nebivolol Intermediates via Ar–O and ArO–C Bond-Forming Reactions of Vicinal Diols.....</b>	<b>149-181</b>
4.1. Introduction.....	150
4.2. Literature Known Methods to Access ( <i>S,R,R,R</i> )-Nebivolol.....	150
4.3. Background and Objectives.....	154
4.4. Results and Discussion.....	156
4.4.1. Attempted Synthesis of Chroman Derivative via $S_NAr$ Reaction.....	156
4.4.2. Attempted Synthesis of Chroman Derivative via Intramolecular Ring-Opening of Cyclic Orthoester.....	158
4.4.3. Synthesis of Chroman Derivative via One-Pot Epoxidation/Epoxyde Ring-Opening/Cyclization.....	160
4.5. Conclusions.....	162
4.6. Experimental Section.....	162
4.6.1. General Remarks.....	162
4.6.2. Preparation of Compounds.....	162
4.7. References.....	173
4.8. NMR Spectra of Selected Compounds.....	176
<b>Chapter 5: Studies on the Synthesis of 2-Amino-2-(chroman-2-yl)ethanols via a Late-Stage Dienone-Phenol Rearrangement of Spirocyclohexadienone Scaffolds.....</b>	<b>182-212</b>
5.1. Introduction.....	183
5.2. Background and Objectives.....	184
5.3. Results and Discussion.....	185
5.3.1. Attempted Synthesis of 2-Amino-2-(chroman-2-yl)ethanols from a Chroman-Bearing $\alpha$ -Hydroxy Ester.....	185
5.3.2. Attempted Synthesis of 2-Amino-2-(chroman-2-yl)ethanols via a Late-Stage Dienone-Phenol Rearrangement.....	186

5.4. Conclusion.....	190
5.5. Experimental Section.....	190
5.5.1. General Remarks.....	190
5.5.2. Preparation of Compounds.....	190
5.6. References.....	201
5.7. NMR Spectra of Selected Compounds.....	205
5.8. HPLC Traces of Diols.....	212
<b>Chapter 6: Diastereoselective Synthesis of 2-(<i>N</i>-Tosylamido)-2-(chroman-2-yl)ethanols and Related Compounds via ArO–C Bond-Forming Intramolecular Aziridine Ring-Opening Cyclization.....</b>	213-264
6.1. Introduction.....	214
6.2. Background and Objectives.....	215
6.3. Results and Discussion.....	216
6.3.1. Preparation of Olefin Substrates.....	216
6.3.2. Aziridination of Olefins to Access <i>N</i> -Tosylaziridines.....	217
6.3.3. Intramolecular Ring-Opening Cyclization of <i>N</i> -Tosylaziridines.....	218
6.4. Conclusions.....	225
6.5. Experimental Section.....	225
6.5.1. General Remarks.....	225
6.5.2. Preparation of Compounds.....	225
6.5.3. X-ray Crystallography Data.....	250
6.6. References.....	252
6.7. NMR Spectra of Selected Compounds.....	256
<b>Chapter 7: Diastereoselective Synthesis of 6,7-Dihydrobenzo[<i>f</i>]benzo[4,5]imidazo[1,2-<i>d</i>][1,4]oxazepines via Sequential ArO–C Bond-Forming Intramolecular Epoxide Ring-Opening and Ar–O Bond-Forming Intramolecular S<sub>N</sub>Ar Reactions.....</b>	265-298
7.1. Introduction.....	266
7.2. Background and Objectives.....	267
7.3. Results and Discussion.....	269

7.3.1. Synthesis of 6,7-Dihydrobenzo[ <i>f</i> ]benzo[4,5]imidazo[1,2- <i>d</i> ][1,4]oxazepines.....	269
7.3.1.1. Preparation of Epoxide Substrates.....	269
7.3.1.2. Ring-Opening — Cyclization of Epoxides with 2-(2-Fluorophenyl)-benzimidazole.....	270
7.3.2. Synthesis of a Chroman-Linked 6,7-Dihydrobenzo[ <i>f</i> ]benzo[4,5]imidazo[1,2- <i>d</i> ][1,4]oxazepine.....	272
7.4. Conclusion.....	274
7.5. Experimental Section.....	275
7.5.1. General Remarks.....	275
7.5.2. Preparation of Compounds.....	275
7.6. References.....	290
7.7. NMR Spectra of Selected Compounds.....	292
<b>Appendices.....</b>	<b>a</b>
A. List of Publications.....	b
B. List of Conference/Symposium/Seminar Attended.....	c
C. Front pages of published research papers.....	d