# Contents

List of Abbreviations i-iii
Preface iv-viii

**CHAPTER 1: Role of Diversity Oriented Organic Synthesis of Small Molecules in Drug Discovery Research** 1-37

1.1 Introduction 2
1.2 Drug Discovery Research in the Past Time 3
1.3 Modern Drug Discovery Research 3
1.4 Role of Natural Products in Drug Discovery Process 4
1.5 Role of Modern Organic Synthesis in Drug Discovery Research 7

1.5.1 Small Molecules and Chemical Genetics 7
1.5.2 Small Molecules and Chemical Space 8
1.5.3 Small Molecules and Combinatorial Chemistry 9
    1.5.3.1 Combinatorial Synthesis on Solid Phase 10
    1.5.3.2 Combinatorial Synthesis in Solution Phase 12
1.5.4 Diversity Oriented Synthesis (DOS) of Small Molecules and Chemical Space 13
1.5.5 Approaches to DOS 15
    1.5.5.1 Appendage Diversity 15
    1.5.5.2 Stereochemical Diversity 16
    1.5.5.3 Skeletal Diversity 17
1.5.6 Design Strategies for DOS of Natural Product-Like Libraries 19
    1.5.6.1 Libraries Based on Core Scaffolds of Individual Natural Products 19
    1.5.6.2 Libraries Based on Specific Substructures from Classes of Natural Products 20
    1.5.6.3 Libraries with general structural characteristics of Natural Products 21
1.5.7 Recent Examples of DOS 22
1.5.8 Conclusion 33
CHAPTER 2: Synthesis of Unsymmetrical Triarylmethanes and 9-Arylxanthenes
by Friedel-Crafts Diarylmethylation of Electron-Rich Arenes 38-92

SECTION 2A: Synthesis of Unsymmetrical Triarylmethanes by Intermolecular
Friedel-Crafts Diarylmethylation of Electron-Rich Arenes 39-66

SECTION 2B: Synthesis of Unsymmetrical 9-Arylxanthenes by Intramolecular
Friedel-Crafts Diarylmethylation of Electron-Rich Arenes 67-92

CHAPTER 3: Synthesis of [(Aryl)arylsulfanyl]methyl]pyridines (AASMPs) as a New
Class of Antimalarial Agents 93-132

3.1 Introduction 94
3.2 Life Cycle of Malaria Parasite 94
3.3 Antimalarial Drugs 95
3.4 Mechanism of Action Antimalarial Drugs 97
3.5 New Targets and Ligands for Malaria 100
3.6  Basis of Present Work 102
3.7  Results and Discussion 102
3.7.1 Chemistry 102
3.7.2 Biology 106
3.8  Conclusion 112
3.9  Experimental Section 113
3.10 References 124
3.11 Spectra 127

CHAPTER 4: Design, Synthesis and Antitubercular Activity of Diarylmethylnaphthol Derivatives 133-173

4.1  Introduction 134
4.2  Antitubercular Drugs 135
4.3  Small Molecules as Chemical Probes and Drug Lead for TB 137
4.4  Basis of Present Work 139
4.5  Results and Discussion 140
4.6  Structure-Activity Relationships 144
4.7  Conclusion 144
4.8  Experimental Section 145
4.9  References 164
4.10 Spectra 168

CHAPTER 5: Enantioselective Synthesis of Natural Product-Like Benzo-Annulated Oxa-Heterocycles 174-235

SECTION 5A: $\beta$-Hydroxy-$\alpha$-tosyloxy Esters as Chiral Building Blocks for the Enantioselective Synthesis of Benzo-annulated Oxa-Heterocycles: Scope and Limitations 175-215

5.1.1 Introduction 176
5.1.2 Basis of Present Work 177
5.1.3 Results and Discussion 178
5.1.4 Conclusion 183
5.1.5 Experimental Section 184
5.1.6 References 203
SECTION 5B: Enantioselective Synthesis of a 2,3-Disubstituted 1-Benzoxepine Derivative

5.2.1 Introduction
5.2.2 Basis of Present Work
5.2.3 Results and Discussion
5.2.4 Conclusion
5.2.5 Experimental Section
5.2.6 References
5.2.7 Spectra

SECTION 6: Total Synthesis of Spisulosine: A Potent Anticancer Agent from Marine Calm Spisula Polynim

6.1 Introduction
6.2 Basis of Present Work
6.3 Results and Discussion
6.4 Conclusion
6.5 Experimental Section
6.6 References
6.7 Spectra

About the Author

List of Publications