

# Preface

The study of heterocyclic compounds covers a broad area of chemistry. Their structures contain at least two different atoms as members of a saturated, unsaturated or aromatic ring, which forms either a simple monocyclic compound or a part of a larger structure of fused rings. Equally, halogenation is a similarly broad field and both topics are interwoven within these chapters. Research on both fields is ongoing and broad, and a comprehensive overview is not possible but rather, this book is oriented towards current research involving representative transformations and strategies for the synthesis of halogenated heterocycles and their use.

The subject of Chap. 1 is the recent developments in nucleophilic aromatic substitutions, using the example of perfluoroheteroaromatic compounds as precursors for the synthesis of highly functionalized heterocycles, macrocycles, ring-fused systems and glycosyl donors. Chapter 2 presents the chemistry of a single fluorine atom in the heterocyclic molecule and describes the latest methods of synthesizing monofluoro-substituted heterocycles via nucleophilic and electrophilic fluorination. Chapter 3 goes further and describes halogenation and halocyclization reactions resulting in  $\beta$ -halofurans discussed according to the halogen atom, i.e. iodination, bromination, chlorination and fluorination, and their synthesis from the halo-substituted starting compounds. Chapter 4 explores the synthesis of halogenated five- and six-membered sulphur containing heterocycles. Electrophilic halogenation often requires reagents having a heterocyclic structure with an N-halo bond, and Chap. 5 focuses on representative reaction patterns in which N–X heterocyclic reagents are used as halogenating reagents and in other transformations such as oxidation, substitution, addition, cyclization and asymmetric reactions. Chapter 6 shows how “halogen dance” reactions became an important tool for synthesizing halogenated heterocycles substituted at specific positions. Chapter 7 looks at the application of halogenated heterocycles and discusses the chemistry and structure–activity relationships, mechanisms of action and the clinical use of halogenated heterocyclic pharmaceuticals. Chapter 8 reviews the occurrence and fate of three model halogenated heterocyclic pharmaceuticals belonging to different pharmaceutical classes in the environment. Finally, Chapter 9 reviews recent research into the direct halogenation of heterocyclic compounds with the aim of providing “greener” alternatives. Each of the methods discussed, electrophilic, nucleophilic and radical, was approached from the perspective of alternative strategies, reagents, solvents and activation.

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