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The series *Topics in Heterocyclic Chemistry* presents critical reviews on "Heterocyclic Compounds" within topic-related volumes dealing with all aspects such as synthesis, reaction mechanisms, structure complexity, properties, reactivity, stability, fundamental and theoretical studies, biology, biomedical studies, pharmacological aspects, applications in material sciences, etc. Metabolism will also be included which will provide information useful in designing pharmacologically active agents. Pathways involving destruction of heterocyclic rings will also be dealt with so that synthesis of specifically functionalized non-heterocyclic molecules can be designed.

The overall scope is to cover topics dealing with most of the areas of current trends in heterocyclic chemistry which will suit to a larger heterocyclic community.

As a rule, contributions are specially commissioned. The editors and publishers will, however, always be pleased to receive suggestions and supplementary information. Papers are accepted for *Topics in Heterocyclic Chemistry* in English.

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Aims and Scope

The series *Topics in Heterocyclic Chemistry* presents critical reviews on "Heterocyclic Compounds" within topic related volumes dealing with all aspects such as synthesis, reaction mechanisms, structure complexity, properties, reactivity, stability, fundamental and theoretical studies, biology, biomedical studies, pharmacological aspects, applications in material sciences etc. Metabolism is also included which provides information useful in designing pharmacologically active agents. Pathways involving destruction of heterocyclic ring are also dealt with so that synthesis of specifically functionalized non-heterocyclic molecules can be designed.

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*Dedicated to the memory of my devoted parents, Waldron and Jane,
who with their love, inspiration, and guidance sparked my interest
at a young age in both science and chemistry*

Preface

This volume consists of 11 chapters covering the chemistry and applications of indole and indole derivatives. Often considered to be the pre-eminent heterocycle and the molecular scaffold of greatest medicinal importance, indole continues to captivate chemists and biologists alike.

In Chap. 1, Wu concisely summarizes of “New Indole-Containing Medicinal Compounds”, including both existing indole and oxindole drugs, such as sumatriptan, ondansetron, and fluvastatin, and those in current clinical trials, such as cediranib, bravanib, and vilazodone.

In Chap. 2, “Indoles: Industrial, Agricultural and Over-the-Counter Uses”, Barden continues the theme of indole applications from the first chapter by illustrating the role of indoles as agricultural compounds, dyes, pigments, dietary supplements, nutraceuticals, perfumes, and flavoring agents.

In Chap. 3, Sundberg, an indole pioneer and the author of the 1970 classic monograph “The Chemistry of Indoles”, covers thoroughly “Electrophilic Substitution Reactions of Indoles”, which is probably the most ubiquitous reaction of indole and one that continues to be extraordinarily useful in synthesis.

In Chap. 4, Kishbaugh reviews the less well known but emerging “Reactions of Indole with Nucleophiles”, with a rich collection of both nucleophilic additions to electron-deficient indoles and nucleophilic substitution reactions of indole.

In Chap. 5, “Metalation of Indole”, Pelkey comprehensively reviews the enormous literature of direct and directed metalation and halogen-metal exchange, reaction protocols that have assumed incredible utility in indole chemistry.

In Chap. 6, a companion to the preceding chapter, Li and Gribble document “Metal-Catalyzed Cross-Coupling Reactions for Indoles”, which covers palladium, copper, rhodium, iron, and nickel cross-couplings of indole – a suite of reactions that has assumed great importance in indole synthesis and chemistry.

In Chap. 7, Badenock reviews the relatively new area of “Radical Reactions of Indole”, with extensive coverage of both intermolecular reactions and intramolecular cyclizations, including application to the facile construction of medium-size rings.

In two complementary reviews, Chaps. 8 and 9, Berthel, Firooznia, and Kester discuss in great depth the enormously flexible cycloaddition reactions of indoles. Chapter 8 is an array of “[2+2], [3+2], and [2+2+2] Cycloaddition Reactions of Indole Derivatives”, while Chap. 9 covers “[4+2] Cycloaddition Reactions of

Indole Derivatives”, wherein the versatile indole double bond can serve as either dienophile or part of a diene.

In Chap. 10, Russel presents “Oxindoles and Spirocyclic Variations: Strategies for C3 Functionalization” of indoles and the role this emerging strategy plays both in the asymmetric introduction of C3 quaternary centers and in the synthesis of oxindoles and myriad-related natural products, including oxaspirocycles and azaspirocycles.

In Chap. 11, Fu continues the theme of indole-containing natural products with an exhaustive treatment of the “Advances in the Total Syntheses of Complex Indole Natural Products”, with a focus on indole alkaloids of recent interest such as diazepam, chartelline, penitrem, yatakemycin, welwitindolinone, and several others.

I am indebted to my authors for their truly outstanding contributions to what I believe is a long overdue and important addition to the literature of indoles. I particularly thank my former students (Barden, Kishbaugh, Pelkey, Badenock, Berthel, and Fu) for their willingness to participate in this endeavor, and my heterocyclic colleagues and friends (Wu, Sundberg, Li, and Russel) for their equally hard work. I especially thank my series editor Bert Maes for the opportunity to be the editor of this volume.

Hanover, New Hampshire
2010

Gordon W. Gribble

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