
Preface

Heterocyclic molecules play a significant role in life processes and have played a major role in industrial developments of the last century, for instance in the field of dyes, pharmaceuticals, pesticides, polymers etc. They comprise not only some of the most interesting and biologically important natural products like alkaloids, carbohydrates, nucleic acids, and antibiotics but include many practical drugs and a large segment of known synthetic organic compounds. Hence scientists have devoted a great amount of effort to find optimal synthetic approaches to a variety of heterocyclic compounds.

Among the most successful and selective synthetic processes are cycloaddition reactions, since they involve simultaneous or sequential formation of two or more bonds often with a high degree of stereoselectivity and regioselectivity. For instance, 1,3 dipolar cycloadditions are electronically equivalent to Diels–Alder reactions and are among the most common 5-membered ring-forming systems. In addition they usually proceed with a high degree of stereo- and regio-control. It is therefore, not surprising that synthesis of many important classes of heterocycles, including those of useful biologically active molecules, have utilized cycloaddition steps in their formation. Furthermore, many heterocycles serve as intermediates in the synthesis of polyfunctional molecules.

In this volume we present five selected contributions by well-known authors, each an authority in his field. The first chapter deals with construction of isoxazolines (dihydroisoxazoles) via 1,3-dipolar cycloadditions of nitronates or of nitrile oxides generated from nitroalkanes. This includes inter- as well as intramolecular processes. Many of these heterocycles possess important synthetic and biological properties and are shown to lead to stereo- and regioselective introduction of multifunctional molecules such as amino alcohols, β -amino acids, aldols, nitriles, and others.

The second chapter is devoted to cycloadditions of azides, which comprise a highly versatile functional group. The chapter discusses both catalyzed and non-catalyzed (thermal) cycloadditions of azides to multiple bonds leading to many interesting classes of N-heterocycles. Both inter- and intramolecular azide cycloaddition reactions are featured. Furthermore, bioconjugation involving azides and their use in tagging of proteins, DNA as well as of living systems are highlighted.

Enantioselective 1,3-dipolar cycloadditions employing azomethine ylides and asymmetric catalysis are discussed in the next chapter. The formation of chiral non-racemic pyrrolidine derivatives via dipolar cycloadditions presents an important challenge that has been successfully overcome. The role of catalysis involving different metals is also highlighted.

Chapter 4 concerns the cycloaddition of carbonyl ylides generated from diazo carbonyl compounds and rhodium or copper catalysts. In this framework chemoselective and enantioselective transformations leading to the formation of various heterocycles such as tetrahydrofurans, oxazolidines, mesoionic and bicyclic compounds, alkaloids, and other natural products are described.

The final chapter deals with phosphorus ylides, in particular of phosphacumulenes, and their utilization in the synthesis of a number of heterocyclic ring systems including butenolides, tetramates, and macrolides. I want to thank all authors for their excellent presentations and their splendid cooperation.

This volume is dedicated with love to my children Lilly and Lawrence and their families.

Ramat Gan, February 2008

Alfred Hassner

Synthesis of Heterocycles via Cycloadditions I

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