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EDITORIAL

M. Vrabel and T. Carell for Cycloadditions in Bioorthogonal Chemistry

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1 Aims and Scope

The series Topics in Current Chemistry presents critical reviews of the present and future trends in modern chemical research. The scope of coverage is all areas of chemical science, including the interfaces with related disciplines, such as biology, medicine and materials science.

The goal of each thematic volume is to give the non-specialist reader, whether in academia or industry, a comprehensive insight into an area where new research is emerging that is of interest to a larger scientific audience.

Each review within the volume critically surveys one aspect of that topic and places it within the context of the volume as a whole. The most significant developments of the last 5–10 years are presented using selected examples to illustrate the principles discussed. The coverage is not intended to be an exhaustive summary of the field or to include large quantities of data, but should rather be conceptual, concentrating on the methodological thinking that will allow the non-specialist reader to understand the information presented. Contributions also offer an outlook on potential future developments in the field.

This article is part of the Topical Collection "Cycloadditions in Bioorthogonal Chemistry"; edited by Milan Vrabel and Thomas Carell.

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Review articles for the individual volumes are invited by the volume editors.

2 Preface

Due to fantastic progress in the art of chemical synthesis, organic chemists today have access to a great arsenal of powerful chemical transformations that enable the synthesis of even the most complex structures and molecules. While some of the most reliable transformation have been known for decades, the repertoire of new, broadly applicable reactions is still expanding, so that even chemical transformations directly on biomolecules have now become routinely possible. Today, high yielding and efficient chemical reactions on biomolecules such as nucleic acids, proteins or oligosaccharides are often summarized under the term bioorthogonal click reactions. In this field, chemists are becoming part of interdisciplinary research groups in which they work hand in hand with biochemists, enzymologists and researchers in the discipline of biophysics.

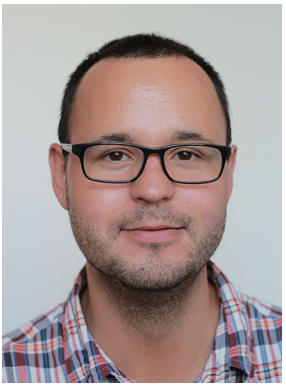
Bioorthogonal chemistry uses chemical transformations that can be performed in the presence of all types of biomolecules and even in living cells, and which occur between two reactive groups that do not react with all the functional groups present on the biomolecules. Given the complexity of living matter, this is a formidable achievement. Once one of the reactive groups is incorporated into the biomolecule of interest, the biomolecule can be selective modified at the given position, even inside a living cell. This would have been impossible 15 years ago.

The development of bioorthogonal chemical transformations goes hand in hand with the invention of new strategies that allow the selective incorporation of bioorthogonal reactive groups into biomolecules. For nucleic acids, this involves the development of phosphoramidite building blocks and special triphosphates. The oligonucleotides are then constructed by solid phase chemistry or enzymatically using the PCR reaction. For proteins, new tools based on the suppression of stop codons are now available, allowing the incorporation of unnatural amino acids into proteins. These amino acids contain bioorthogonal groups at their side chains. For adding bioorthogonal groups into oligosaccharides, one typically uses feeding experiments with modified sugars, which are then inserted into the oligosaccharide using biosynthetic pathways.

This book, in its content, is a unique collection of contributions, compiling the huge progress that has been made in the use of cycloaddition reactions in bioorthogonal chemistry. Among other chemical transformations that are currently routinely used for bioconjugations, the cycloaddition reactions stand out as the most versatile and powerful methods. Based on the pioneering work of chemists such as Rolf Huisgen, Kurt Alder and Otto Diels, who worked out the mechanisms of these transformations decades ago, a new generation of chemists has started to adapt these reactions for manipulation and tagging of biomolecules.

In this setting, this book is therefore also a tribute to these scientific heroes, who until today dominate large parts of our chemistry textbooks and who we all know so well from our studies.

Individual chapters provide overviews on cycloaddition reactions used for biomolecule labeling—the first part of the book deals with dipolar cycloadditions, while the last two chapters are devoted to Diels–Alder-type reactions. The different aspects of the chemistry are outlined and the benefits of each methodology are demonstrated by discussing specific applications and possible future directions in the field. We are deeply indebted to all the authors for their willingness to be a part of this interesting project and for sharing their knowledge and experience in this rapidly growing field. With this book, we hope to invoke interest among students and colleagues in bioorthogonal chemistry, and to encourage and enthuse a new generation of scientists in this exciting scientific area.



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