

Preface

Nucleosides and nucleotides are key endogenous molecules engaged in many biological events such as RNA and DNA synthesis, metabolism, enzyme regulation, etc. Nucleosides and nucleotides are the major components of nucleic acids. Synthetic nucleos(t)ides have been extensively modified either by chemical or enzymatic procedures to mimic their physiological counterparts and show important antiviral or antiproliferative activities, among others.

The chemical or enzymatic synthesis and modification of nucleos(t)ides is a major research topic in organic, medicinal, and bioorganic chemistry. This book contains a selection of different chapters prepared by highly reputed scientists involved in the field of nucleosides and nucleotides, covering different aspects of their synthesis and/or their applications that provide valuable information to all the scientists working in this field. Each chapter in this volume reflects the own work performed by the respective contributors in the laboratories.

The first seven chapters are involved with the enzymatic or chemoenzymatic synthesis of nucleic acid derivatives. Nowadays, the application of bioprocesses catalyzed by whole cells or enzymes in industrial settings is gaining momentum as compared to traditional chemical synthetic processes. In this context, the enzymatic synthesis of active pharmaceutical ingredients (APIs) shows many advantages, such as one-pot reactions under mild conditions, high stereo- and regioselectivity, and an environmentally friendly technology.

In this context, many different authors are working together to publish a special issue that will focus on the development of new enzymatic or chemoenzymatic strategies for the synthesis of nucleic acid derivatives catalyzed either by whole cells or enzymes, showing the advantages and drawbacks of this methodology versus traditional chemical methods

In the first chapter, Kamel et al. have performed an exhaustive revision about the potential of nucleoside phosphorylases (NPs) as biocatalysts for industrial synthesis of nucleoside analogues, providing detailed information about their substrate specificity and structural properties that influence their activity. Additionally, they describe the potential of mutagenic approaches to widen the substrate spectrum of nucleoside phosphorylases, showing an overview about the upscaling approaches for the production of nucleoside analogues

In Chapter 2, Dr. Daniela Ubiali and Prof. Giovanna Speranza present an overview of the recent work on enzymatic phosphorylation of nucleosides to nucleoside 5'-monophosphate (NMPs) by nonspecific acid phosphatases

(NSAPs) or 2'-deoxyribonucleoside kinases (dNKs). In Chapter 3, Dr. Lewkowicz and Dr. Iribarren summarize the available information regarding the biocatalyzed whole cell synthesis of nucleosides and their analogues referring to relevant examples and recent researches. Furthermore, Dr. Trelles et al. performed an interesting revision about the different cell-immobilization techniques applied to the development of active biocatalysts for the synthesis of nucleic acid derivatives by immobilized cells (Chapter 4). In a similar way, Dr. Arroyo analyzes recent literature concerning the development of novel enzymatic production of nucleic acid derivatives using immobilized enzymes (Chapter 5), including detailed examples and procedures. In Chapter 6, Dr. Ding illustrates the most current relevant examples of *in vivo* and *in vitro* multienzymatic systems as an efficient alternative to traditional multistep chemical procedures used for the synthesis of nucleic acid derivatives.

In a different way, Dr. Eremeeva and Dr. Herdewijn, in Chapter 7, present an exhaustive revision about the enzymatic synthesis of redesigned nucleic acids (xeno-nucleic acids, XNA) using polymerases. In this sense, the enzymatic production of several XNAs, such as base-modified XNAs, sugar-modified XNAs, or the phosphodiester backbone-XNA, is reported.

The last five chapters concentrate on the chemical synthesis and/or applications of these unique molecules. Particularly, Chapters 8–12 deal with the chemical synthesis of nucleosides and oligonucleotides. Thus, in Chapter 8, Dr. Seley-Radke reports a historic perspective of the synthetic approaches followed for the preparation of a unique class of nucleosides, the fleximer nucleosides, designed to understand better how the flexibility in the nucleobase affects the receptor-ligand recognition and function and their potential to overcome the challenges of binding site mutations. Fleximers are flexible nucleosides with several key advantages over natural purine nucleosides.

Chapter 9 by Dr. Eritja et al. focuses on the synthesis of oligonucleotides bearing nucleic acid derivatives of biomedical and structural interest. In this chapter, an overview of valuable and versatile nucleic acid derivatives developed by the group during the past decade is presented together with their emerging applications as well as a highlight of the important recent progress made in the field.

In Chapter 10, Dr. Morales describes the synthesis and applications of carbohydrate-oligonucleotide conjugates. The interest in such conjugates is to take advantage by integrating the properties of both kinds of molecules (carbohydrates and oligonucleotides) in a single molecule. This type of conjugates have attracted a lot of attention to explore their application as potential therapeutic agents, aptamers, ribozymes, biosensors, biochips, diagnostic tools, etc.

Chapter 11 focuses on microarrays; Dr. Damha and colleagues detail the advances in light-directed synthesis of high-density microarrays. This interesting chapter gathers the phosphoramidite chemistry applied to the photolithographic synthesis of microarrays; the recent improvements in the synthesis of DNA microarrays; the synthesis of RNA microarrays; the enzymatic approaches to RNA array synthesis; and the synthesis of 2'-F-ANA microarrays.

Finally, in Chapter 12, Dr. Schinazi and coworkers describe how SAMHD1 (a dNTP triphosphohydrolase that degrades dNTPs into 2'-deoxynucleosides and triphosphates) mediates the negative regulation of cellular dNTP levels.

We hope that the readers will find the contents of this book interesting and instructive and challenging enough to be involved in the fantastic field of nucleos(t)ides and nucleic acids. Finally, last but not the least, the editors sincerely thank all the authors who have contributed to this book with very interesting chapters.

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Enzymatic Synthesis of

Nucleoside Phosphates

Sarah Sampaio, et al.

Technique for the synthesis of

the 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