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Introduction to RNA/DNA Cleavage

Nucleic acids provide exciting and difficult challenges for chemists and biochemists. They are inherently important, yet are highly complex to study. Many aspects of nucleic acid biochemistry are broadly appreciated throughout the scientific community, including the nature of the genetic code, the codon−anticodon relationships between mRNA and tRNA, the importance of radiation damage to DNA,[1] and the need for DNA repair. However, some very important processes are less widely recognized by nonspecialists. For example, controlling the lifetimes of mRNA molecules is one of the means by which Nature governs protein synthesis.[2] The antisense method for controlling gene expression, which has great potential for use in antiviral chemotherapy, uses a similar idea: gene-specific deactivation or destruction of mRNA can inhibit the synthesis of harmful proteins.[3−5]

With recent advances in nucleic acid synthesis, analytical techniques, computational methods, and molecular biology procedures, it is becoming more and more feasible to study chemical reactions of DNA and RNA from a highly detailed molecular perspective. Work at the interface between nucleic acid chemistry and biochemistry dates back many years, and includes the pioneering studies of Dimroth, Eichhorn, Lippard, Sigman, Dervan, and Barton.[6−11] The gold standard for *mechanistic* chemical studies on reactions of DNA is provided by the work of Stubbe and Kozarich.[12,13] The chemical reactions that we focus on in this thematic issue are primarily cleavage reactions that split the biopolymer by attacking its backbone. The comprehensive reviews presented here encompass enzymatic transesterification and hydrolysis of biological phosphodiester bonds, ribozyme-catalyzed reactions that occur in the maturation of RNA, biomimetic hydrolysis and transesterification of RNA by small organic and inorganic molecules, photocleavage of DNA by natural and synthetic reagents, photoprocesses of copper complexes bound to DNA, oxidative cleavage via attack on nucleobases and sugar moieties by either synthetic reagents or natural products, and excision repair of damaged DNA. Both metal-dependent and metal-independent nuclease enzymes are discussed. In such a rapidly advancing area, the forum provided by *Chemical Reviews* provides what we hope will be a timely and comprehensive view of these subjects. Other valuable sources include a recent book on nucleic acid chemistry[14a] and a related article on the metal-dependent cleavage of DNA and RNA.[14b]

My intent has been to assemble a set of articles that will help propel DNA and RNA cleavage studies to the next frontiers, that will serve as a useful reference for some years to come, and that will aid the teaching of courses that address the interface between chemistry and biology. Some important areas of DNA and RNA cleavage were not addressed in this issue, including the enediynes, which have been extensively reviewed in recent years.[15−18] I am grateful to all of the authors for their outstanding contributions and to the Editorial Staff of *Chemical Reviews* and the ACS publications division for all of their help. I acknowledge NSF and the donors of the Petroleum Research Fund, administered by the American Chemical Society, for partial support.

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Guest Editor

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