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Ribonucleosides, Aminoacyl- and Peptidyl-RNA: Synthesis, Thermodynamics, and Structure

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Abstract. Ribonucleosides, RNA and peptides are prepared to study non-covalent interactions of RNA, aminoacyl- and peptidyl-RNA. Techniques used include chemical synthesis in solution and on solid supports, UV- and NM-detected thermal denaturation, X-ray crystallography and $^1\text{H-NMR}$ spectroscopy for conformational studies, assisted by force-field and *ab initio* calculations.



Peter Strazewski studied chemistry at the University of Basel, where he received his Ph.D in 1986 under the guidance of C. Tamm. He was a post-doctoral fellow at the University of Cambridge working with in the group of O. Kennard. He returned to Basel 1990, began his own research project involving ribonucleoside and RNA chemistry, and completed his habilitation in 1995, since when he has been a 'Privatdozent' in the Institute of Organic Chemistry. Further details of his research interests are to be found at <http://www.chemie.unibas.ch/OC/Strazewski/strazewski.html>.

'codon-anticodon' interactions, and how covalently bound amino acids influence the thermodynamics of pairing and conformation of such 'early adaptors'. The biological background of these studies is the messenger-RNA-directed peptidyl-transfer reaction between aminoacylated transfer RNAs, a process involved in ribosomal protein synthesis. The most important techniques used are chemical synthesis in solution and on solid supports, UV- and NMR-detected thermal denaturation for thermodynamic studies, X-ray crystallography, and $^1\text{H-NMR}$ spectroscopy for conformational studies, assisted by force-field and *ab initio* calculations.

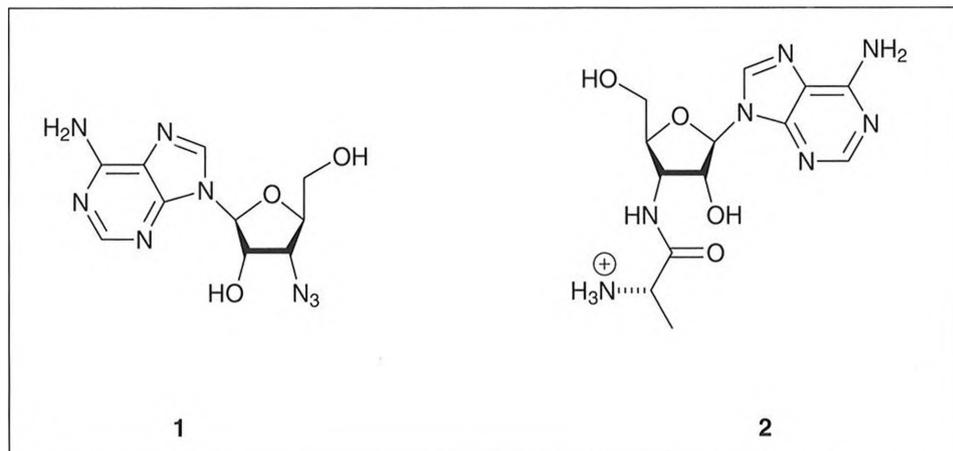
In the earlier periods of our investigations, we were occupied with synthesizing ^{15}N - and ^{17}O -labelled ribonucleosides and with developing a non-linear fitting procedure that could be used to calculate the thermodynamics of base-pairing from heteronuclear NMR signals [1]. We antici-

pate using these methods for the measurements of 'codon-anticodon' interactions between synthetic RNA hairpin molecules and synthetic messenger RNA.

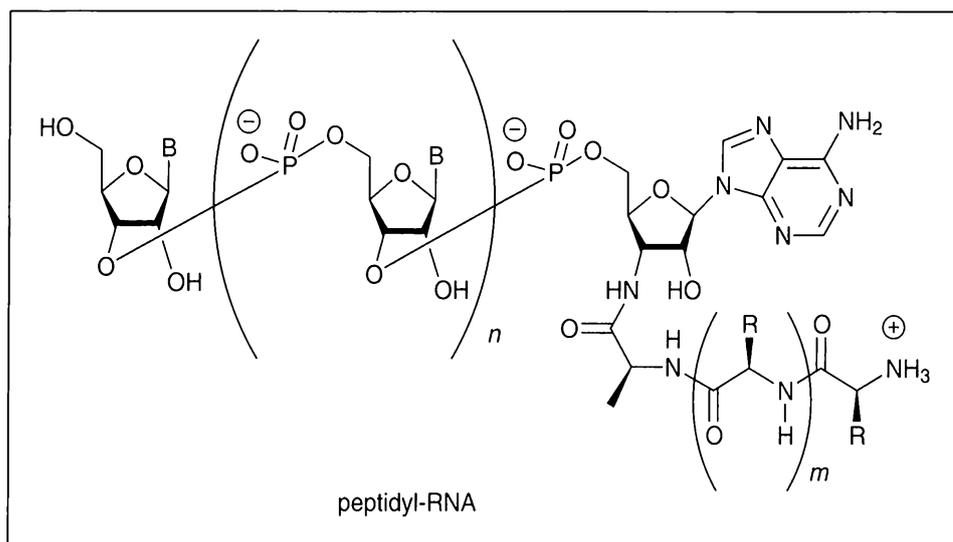
More recently, we have investigated the synthesis of enantiomeric L-ribonucleosides [2] and derivatives, such as **1**, for their use as potential antiviral drugs and of L-RNA for crystallographic purposes as part of a *CHiral2* project [3]. The crystallization of racemic RNA strands may be of use in obtaining crystal-structure data of aminoacyl- or peptidyl-RNA.

Most recently, we synthesized an aminoacylated ribonucleoside derivative, 3'-alanyl-amino-3'-deoxyadenosine **2**. The conformation of this puromycin analog is being studied by $^1\text{H-NMR}$ spectroscopy and calculations [4]. A fully protected derivative thereof is used as the first solid-support-bound nucleoside for the subsequent stepwise synthesis of a peptide and RNA fragment [5]. By means of thermal

We synthesize ribonucleosides, RNA, and peptides for the elucidation of non-covalent interactions of RNA and, most recently, of aminoacyl- and peptidyl-RNA. The goal is to better understand how transfer-RNA-like molecules may be capable of recognizing other RNA strands through



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denaturation, we are examining the pairing thermodynamics of RNA hairpin molecules in the absence and presence of amino acids attached [6].

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