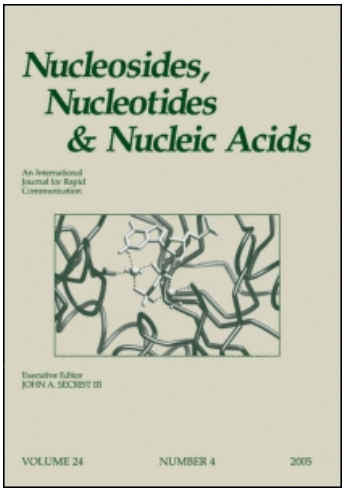

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BRIDGED CYCLIC OLIGORIBONUCLEOTIDES—TOWARDS MODELS FOR CODON-ANTICODON PAIRING

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ABSTRACT

Only three base pairs make up for stable double helices of regular A-type if both helix ends are bridged by flexible non-nucleotide linkers. These cyclic oligoribonucleotides are used as model systems for codon-anticodon pairing in order to reveal base stacking effects arising from structurally relevant bases in the direct neighbourhood of the core triplet duplex.

The interaction between triplet ribonucleotides is of fundamental interest as complexes of this kind reflect codon-anticodon pairing. In aqueous buffer solutions the pairing strength of an oligoribonucleotide duplex that consists of solely three base pairs is too low to be measured with standard UV- and CD-spectroscopic methods. The long-term aim of our work is the development of new model compounds with increased triplet pairing stabilities. In particular, structural features which are assumed to be of significance during codon-anticodon pairing are taken into account.

We have shown that the unfavorable entropic contribution to free enthalpy of pairing is substantially reduced if two short nucleotide sequences are joined on both ends via flexible non-nucleotide linkers (1–3). The pairing of rGAA and the cognate rUUC within the cyclic system is reflected in a typical sigmoid melting profile and a melting temperature of 36°C (1 M NaCl, 10 mM Na_2HPO_4, pH 7.0). The stability of these mini double helices is largely enhanced if dangling unpaired

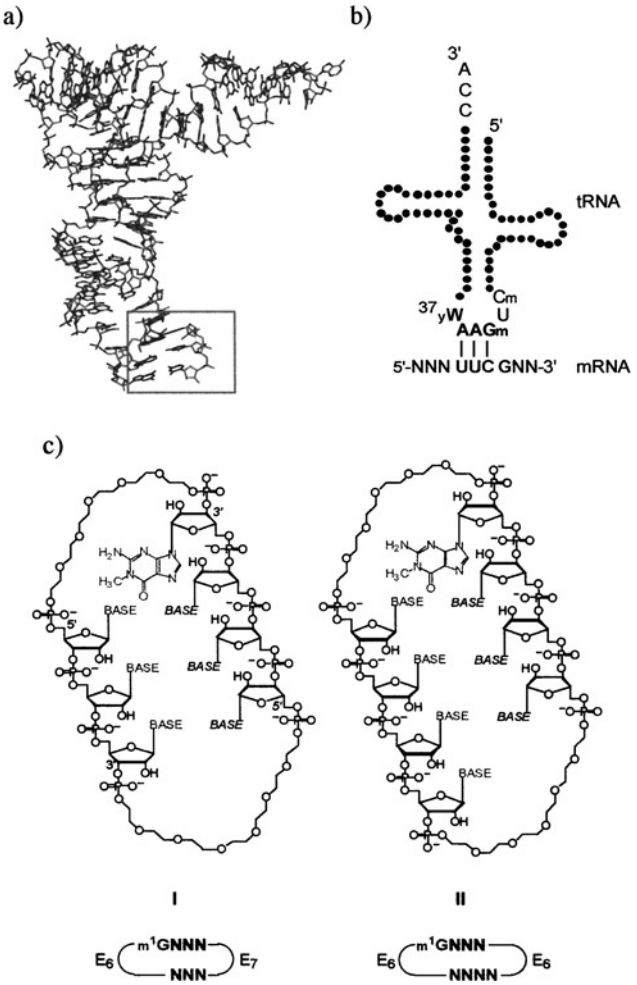

Figure 1. a) Modeling of a codon-anticodon pairing complex. b) Schematic presentation of the structurally relevant bases in direct neighborhood of the core duplex. c) Constitutional types I and II of cyclic model compounds for codon-anticodon pairing.

bases are attached at the 3′-ends (Fig. 1). These bases correspond to the modified tRNA purine bases in position 37 and to the first base of the following mRNA codon.

Furthermore, we have compared the bridged cyclic oligoribonucleotides to their corresponding hairpin counterparts which are, not unexpectedly, of significantly lower stability. Moreover, the conformational type of such a G/C-rich intramolecular duplex with stabilizing dangling bases on both helix ends has been determined at 4.8°C by NMR spectroscopy: the double helix is regular A-type over the full length including the dangling nucleosides and the analysis has also shown that the hexaethylene glycol linker hardly distorts the bridged helix end (4).

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Conclusively, the principle of cyclic bridging offers the availibility of short, but highly stable double helical RNAs. The physico-chemical properties of these compounds are easily ascertained with standard methods used in the field of oligonucleotide chemistry. With respect to codon-anticodon pairing, the presented model compounds provide a reasonable basis for the discussion of base stacking effects that are of importance in biological phenomena concerning the accuracy during translation.

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