Artificial Ribonucleases: Synthesis and RNA Cleaving Properties of Cationic Conjugates Bearing Imidazole Residues

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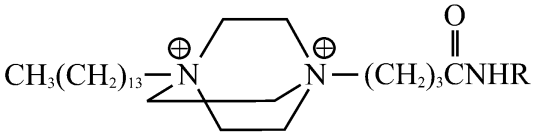
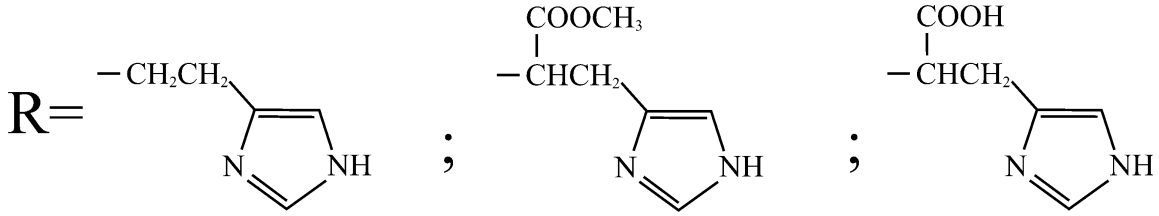
The compounds capable of cleaving phosphodiester bonds in RNA under physiological conditions are needed for development of approaches for investigation of RNA structure in solution and for manipulating RNA nucleases. With such probes, information concerning the state of all phosphodiester bonds and the ribose in entire RNA molecule can be obtained which is important for elucidation of the RNA secondary and tertiary structure. Such RNase mimics can serve as potential agents affecting viral RNA.

This work is devoted to design, synthesis and investigation of RNA hydrolytic activity of artificial ribonucleases, built of a dicationic fragment and the imidazole residue.

The bis-quaternary salts of 1,4-diazabicyclo[2.2.2]octane having a high affinity to phosphate anions served as the RNA binding part of the RNases mimics. 1-Tetradecyl-4-?-(carb-4-nitrophenoxy)-propyl-1,4-diazoniabicyclo[2.2.2]octane dibromide was used as precursor of all final conjugates. Histamine, methyl ester of histidine and histidine served as RNA cleaving groups. The structure of the RNases mimics synthesized was proved by ^{1}H, ^{13}C NMR and the data of elemental analysis or high resolution mass spectra.





All three RNases demonstrate high RNA hydrolytic activity under physiological conditions and cleave phosphodiester bonds preferentially in CpA motifs located in single stranded regions of tRNA.

The first evaluation of the hydrolytic activity of the synthesised RNase mimics showed that all the compounds are promising both as probes for studying the RNA structure and for biomedical applications due to their high specificity and high efficiency in RNA hydrolysis.

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