DNA-Catalyzed Hydrolysis of Esters and Aromatic Amides

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Deoxyribozymes are single-stranded DNA oligonucleotides that catalyze various chemical reactions, analogous to protein enzymes as polymers of amino acids and to ribozymes as polymers of ribonucleotides. We previously reported DNA catalysts that can hydrolyze DNA phosphodiester linkages. These deoxryboymes were identified during selection experiments seeking peptide bond hydrolysis. Identification of DNA-hydrolyzing DNA enzymes was especially surprising, considering the much longer uncatalyzed half-life for hydrolysis of a DNA phospohdiester bond (~30 million years) compared to that of a peptide bond (~200 years). Here, we have used in vitro selection to identify DNA catalysts that hydrolyze ester linkages as well as DNA catalysts that hydrolyze aromatic amides, for which the leaving group is an aniline moiety. The aromatic amide-hydrolyzing deoxyribozymes were examined using linear free energy relationship analysis. The hydrolysis reaction is essentially unaffected by substituents on the aromatic ring ($\rho \approx 0$), suggesting general acid-catalyzed elimination as the rate-determining step of the addition-elimination hydrolysis mechanism. These findings establish that DNA has the catalytic ability to achieve hydrolysis of esters and aromatic amides as carbonyl-based substrates. The results also suggest a mechanism-based approach to achieve DNA-catalyzed aliphatic amide hydrolysis.