Development of the drug release system in hole transfer reaction through DNA

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ABSTRACT

DNA is known as a good hole carrier, and the application for a molecular wire has been studied. The efficiency of hole transfer was estimated as band intensity of phosphorimagery after electrophoresis in polyacrylamide gel. For the application of long-range hole transport through DNA to gene diagnosis and electrochemical technology, the hole transport without complicated and unwieldy analyzing processes is strongly desired. Herein, we developed novel nucleosides, which release various function units by oxidation. We synthesized novel nucleosides, which were designed based on the chemistry of an efficient hole trapping nucleoside 8-methoxy G.

Introduction

In recent year, DNA has attracted much attention as a conductive polymer. In these studies, the quantification of guanine damage by the radioisotopes or the photodynamics analysis such as fluorescence decay and transient absorption are often used for the detection of hole transport, although they are very troublesome and time-consuming. For the application of long-range hole transport through DNA to gene diagnosis and electrochemical technology, the hole transport without complicated and unwieldy analyzing processes is strongly desired.

Result and Discussion

Guanine (G) base is a major target for oxidative DNA damage because it has the lowest oxidation potential among DNA bases. The damage is the consequence of oxidation of G to a guanine radical cation that reacts further with water or molecular oxygen. It has long been known that 2-aminomimidazolone (dlz) is one of the prominent 2'-deoxyguanosine (dG) decomposition products. More recently, we have demonstrated that dlz is actually a major isolable product from a guanine radical cation in the photooxidation of duplex oligodeoxynucleotides (ODNs). Efficient formation of dlz has also been reported in the oxidation of 8-methoxydeoxyguanosine (8-OMe-dG) by riboflavin, and it was suggested that 8-OMe-dG released methyl carbamate, simultaneously (Scheme 1). By the incorporation of another functionalized leaving group instead of methoxy group of 8-OMe-dG, we can design a new nucleoside. We synthesized novel nucleosides, which were designed based on the chemistry of an efficient hole trapping nucleoside 8-OMe-dG.
Scheme 1. Proposed mechanism for the photooxidation of 8-OMe-dG giving dlz

\[ \text{8-OMe-dG} \xrightarrow{\text{H}^+} \text{MeNHz} \rightarrow \text{Rib} \rightarrow \text{Rib} \]

\[ \text{MeNHz} \rightarrow \text{H}_{2}\text{O} \]

\[ \text{Hole Injected in DNA} \]

\[ \text{Hole Trapping} \]

\[ \text{Releasing Functional Molecule} \]

Figure 1. The nucleotide X in a duplex DNA releases various functional molecules.

The hole injected into DNA was trapped at the location of these nucleobases, and modified nucleobases quickly released various functional units by oxidation (Figure 1).

In conclusion, we developed novel nucleosides, which efficiently released various function units by oxidation.

REFERENCES