and 2,6-diaminopurine), owing to their proton donating/accepting capacity. Any other substitutions at C-2 or C-6 of the purine moiety led to the decrease or annihilation of the biological activity. While extensive data regarding the effect of the C-2 and C-6 substituents on the antiviral and cytostatic activity of purine ANPs were obtained, data relating to the effect of the C-8 substitution are rather scarce. Thus, various 8-substituted purine ANPs were synthesized by nucleophilic aromatic substitution reactions or various cross-couplings, starting from the corresponding 8-bromopurine derivatives. The antiviral properties of these analogues will be reported.

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Acyclic Nucleoside Phosphonates: Past, Present, and Future

Withdrawn

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Design, Synthesis, and Anti-HCV Activity of 2′-Modified-4′-selenonucleosides

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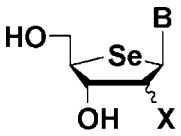
Hepatitis C virus (HCV) has a positive sense single strand RNA genome which is replicated to a negative strand RNA by RNA dependent RNA polymerase of NS5B. Since the inhibition of RNA dependent RNA polymerase leads to no replication of HCV, this enzyme serves as an attractive target for the development of new anti-HCV agents. Many classes of nucleoside and non-nucleoside derivatives have been synthesized as anti-RNA dependent RNA polymerase inhibitors. Among those, 2′-fluoro- and 2′-azidonucleosides have been shown to be good templates for antiviral and antitumor agents. On the basis of a bioisosteric rationale, their 2′-fluoro- and 2′-azido-4′-thio analogues were also reported to show potent anticancer and antiviral activities. Recently, we have reported the synthesis of 4′-selenonucleosides and their unusual conformations. Thus, on the basis of bioisosteric rationale, it would be of great interest to synthesize the 2′-modified-4′-selenonucleosides (X = OH, F, or N_3) and to compare their biological activity with that of 4′-oxo- or 4′-thionucleosides. In the synthesis of 2′-fluoro-4′-selenonucleosides, it was first revealed that selenium atom participated in the DAST fluorination of 4′-selenonucleosides and that conformational bias induced by bulky selenium acted as a decisive factor in the DAST fluorination. Among compounds synthesized, 2′-"UP"-fluoro-thymine analogue showed significant anti-HCV activity in a cell-based replicon assay. Asymmetric synthesis, conformational study, and antiviral activity of novel 2′-modified-4′-selenonucleosides will be presented in detail.



X = OH, F, or N_3

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Genome Specific Diagnosis of Influenza Virus Strains by Hairpin-type Peptide Nucleic Acid

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Influenza A virus is a negative-strand RNA virus that possesses 8 genome segments in the virion. The virus conserved essential genome sequences to retain the infectivity, while it mutates the other sequence parts to obtain versatility. Here we identified the highly conserved 15 base sequences on the nonstructural protein (NS) genome by CONSERV software. We designed a hairpin-type peptide nucleic acid (PNA), of which the sequence is complementary to the NS genome conserved sequence of swine-origin influenza virus A/Osaka/53/H1N1. The hairpin-type PNA effectively recognized the viral genome of the swine-origin influenza virus and inhibited the reverse-transcription in a sequence specific manner. We immobilized the hairpin-type PNA on a plate to examine if the PNA could capture and diagnose the swine-origin influenza virus. As a result, the hairpin-type PNA selectively captured the swine-origin influenza virus (pdm-H1N1) from other seasonal viruses (Fig. 1). Further, we developed a method to visualize the virus genome on the plate by naked eyes even the virus concentration was 10–100 fold lower than that of clinical samples (Fig. 2). Our method can be utilized for the diagnosis of drug-resistant or highly pathogenic viruses based on their genome sequences without PCR and fluorescence detection system.

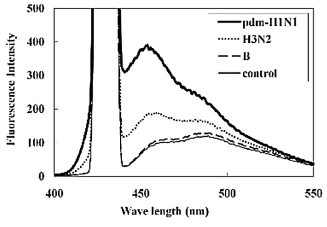

Fig.1. Genome sequence specific detection of swine-origin influenza virus by a hairpin-type PNA.

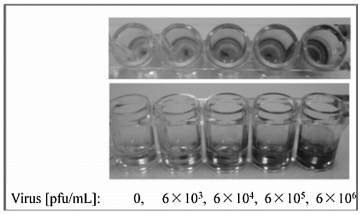

Fig.2. Detection of swine-origin influenza virus genome by naked eyes.

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