Inhibition of α-glucosidase by dna-based nojirimycin analogs

Ryu MAYUMI, Akihiko HATANO
Graduate School of Applied Chemistry, Shibaura Institute of Technology
Fukasaku 307, Minuma-ku, Saitama City, 337-8570 Japan
Ryu MAYUMI : mc21037@shibaura-it.ac.jp

EXTENDED ABSTRACT

Glucose is the only source of energy for humans and has also been linked to diabetes and dieting. As one of the drugs for the treatment of diabetes, deoxynojirimycin (DNJ), which is a type of amino sugar and is similar in structure to glucose, is known. DNJ has the property of specifically binding to the enzyme active site of α-glucosidase, an enzyme present in small intestinal epithelial cells that converts disaccharides to monosaccharides. This means that DNJ inhibits the breakdown of disaccharides and reduces the amount of sugar absorbed into the cells, thereby balancing blood sugar levels.

In recent years, research on polyvalent DNJ inhibitors utilizing the properties of DNJ has been actively conducted. Since α-glucosidase is a membrane enzyme, it has been reported that the inhibitory effect of DNJ is improved by using a unique compound as a scaffold.

Therefore, in this study, we sought the same or higher inhibitory efficiency as these polyvalent iminosaccharides and designed a polyvalent DNJ inhibitor based on DNA. DNA is a double helix molecule consisting of four bases, with a base-to-base distance of 3.6 Å and a right-handed turn of about 10 bases. By utilizing these properties, it is possible to control and cluster the base sequence, and it is expected that the local concentration effect will be higher than that of conventional polyvalent DNJ inhibitors, and that it will exhibit different functions from conventional inhibitors and become an efficient inhibitor.

KEYWORDS

diabetes, deoxynojirimycin (DNJ), α-glucosidase, DNA, polyvalent iminosaccharides, polyvalent DNJ inhibitor

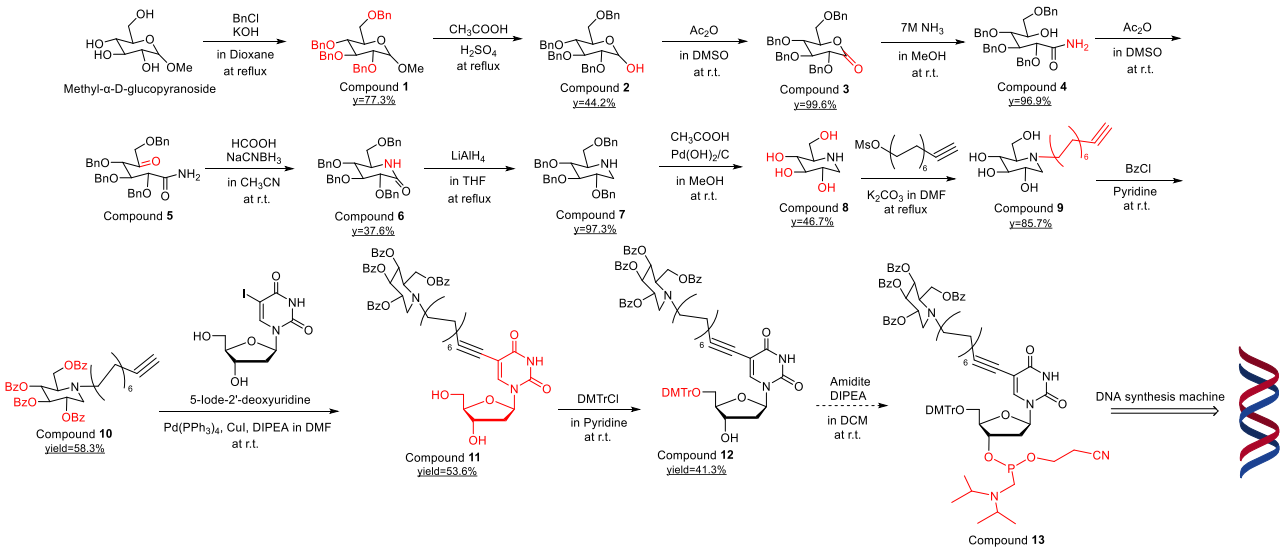

Figure.1 Synthesis scheme of DNA-type polyvalent DNJ inhibitors