Efficient Synthesis of Oligonucleotide Conjugates on Solid-Support Using an (Aminoethoxycarbonyl)aminohexyl Group for 5'-Terminal Modification.

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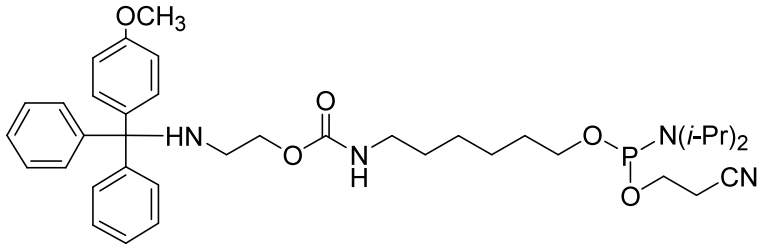
Solid-support conjugation at the 5'-terminal primary amine of oligonucleotides is a convenient and powerful method for introducing various functional groups. However, conventional aliphatic amines do not necessarily provide conjugates with sufficient yields. To improve the modification efficacy, we used the amino-linker (aminoethoxycarbonyl)aminohexyl group (ssH-linker) (1), for solid-support conjugation. In the ssH-linker terminal modification, reactive free amino group could be easily presented onto a solid-support due to rapid removal of the amino-protecting group, and activated amino acids or cholesterol molecules could be covalently connected more efficiently (2) than to typical 6-aminohexyl-linkers. Based on these results, the ssH-linker can be a useful terminal modification for the solid-support conjugation of functional molecules.



1) Y.Komatsu, N.Kojima, M.Sugino, A.Mikami, K.Nonaka, Y.Fujiwara, T. Sugimoto, K.Sato, K.Matsubara and E.Ohtsuka, *Bioorganic & Medicinal. Chem.* **16**, 941-949 (2008)
2) N.Kojima, T.Takebayashi, A.Mikami, E.Ohtsuka, Y.Komatsu, *Bioorganic & Medicinal. Chem. Lett.* **19**, 2144-2147 (2009)