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DESIGN AND SYNTHESIS OF TRIAZOLE-LINKED *XYLO*-NUCLEOSIDE DIMERS

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□ *Three triazole-linked nonionic xylo-nucleoside dimers* T^{L}-t-T^{xL}, T^{L}-t-A^{BzxL} *and* T^{L}-t-C^{BzxL} *have been synthesized for the first time by Cu(I) catalyzed azide-alkyne [3 + 2] cycloaddition reaction (CuAAC) of 1-(3′-azido-3′-deoxy-2′-O,4′-C-methylene-β-D-ribo-furanosyl)thymine with different alkynes,* i.e., *1-(5′-deoxy-5′-C-ethynyl-2′-O,4′-C-methylene-β-D-xylofuranosyl)thymine, 9-(5′-deoxy-5′-C-ethynyl-2′-O,4′-C-methylene-β-D-xylo-furanosyl)-N6-benzoyladenine and 1-(5′-deoxy-5′-C-ethynyl-2′-O,4′-C-methylene-β-D-xylofuranosyl)-N4-benzoylcytosine in 90%–92% yields. Among the two Cu(I) reagents, $CuSO_4.5H_2O$-sodium ascorbate in THF:^{t}BuOH:H_2O (1:1:1) and $CuBr.SMe_2$ in THF used for cycloaddition (click) reaction, the former one was found to be better yielding than the latter one.*

Keywords Click chemistry; Huisgen-Sharpless-Meldal [3+2] cycloaddition; locked nucleic acid; phosphate backbone modification

INTRODUCTION

Inhibition of gene expression by antisense oligonucleotides has gained much attention as a promising drug design concept, since its inception in 1978.[1–3] Successful drug development based on this technique requires the synthesis and use of chemically modified oligonucleotides that render stability to nucleolytic digestion, enhance cellular uptake, hybridise with high affinity, and specificity toward the targeted mRNA/DNA.[4] Among the sugar-modified nucleosides, 2′-*O*,4′-*C* methylene bridge containing oligonucleotides such as β-D-ribo-LNA and β-D-*xylo*-LNA hybridize to both DNA

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