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DESIGN AND SYNTHESIS OF LNA-BASED MERCAPTOACETAMIDO-LINKED NUCLEOSIDE DIMERS

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□ *Three LNA-based mercaptoacetamido-linked nonionic nucleoside dimers* $\boldsymbol{T^L}$***-S-T***, ***T-S-*** $\boldsymbol{T^L}$, *and* $\boldsymbol{T^L}$***-S-*** $\boldsymbol{T^L}$ *have been synthesized by HOBT and HBTU catalyzed condensation of silyl-protected 2-S-(thymidin-5′-yl)mercaptoacetic acid or 2-S-(2′-O,4′-C-methylenethymidin-5′-yl)mercaptoacetic acid with 3′-amino-3′-deoxy-5′-O-DMT-2′-O,4′-C-methylenethymidine or with 3′-amino-3′-deoxy-5′-O-DMT-β-thymidine followed by desilylation of the protected dimers. The 3′-O-phosphoramidite derivative of one of the nucleoside dimers was successfully prepared by condensation with [P(-Cl)(-*OCH_2CH_2CN*){-*$N(iPr)_2$*}] in DCM in the presence of* N,N*-diisopropylethylamine (DIPEA), which is a building block for the preparation of mercaptoacetamido-linked oligonucleotides of therapeutic applications.*

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Keywords Locked nucleic acid; phosphate backbone modification; mercaptoacetamido-linkage; phosphoramidite-derivative

INTRODUCTION

The recent development in antisense, antigene, and RNA interference technologies by using chemically modified oligonucleotides (ONs) has attracted a great deal of both chemists and biologists.[1–5] The modified

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