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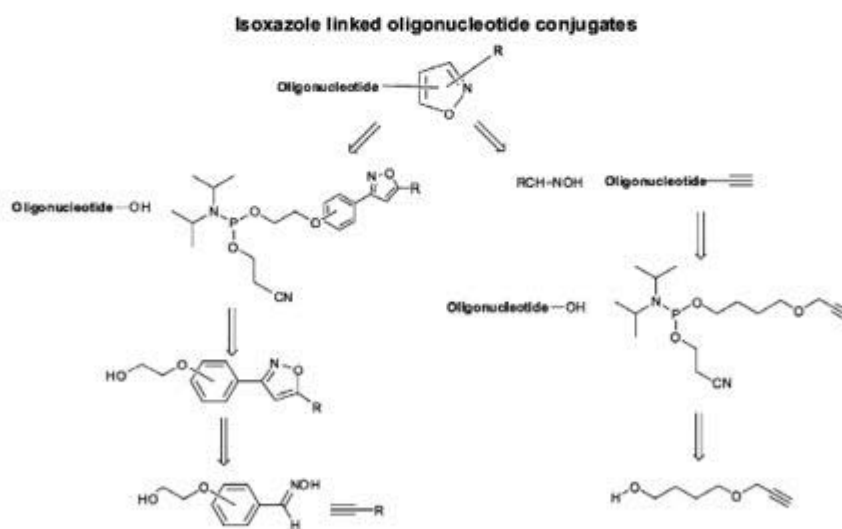
First page

ISOXAZOLE LINKED OLIGONUCLEOTIDE CONJUGATES BY ON RESIN AND PREVIOUSLY CLICKED NITRILE OXIDE ALKYNE CYCLOADDITIONS

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Bioconjugation protocols in environments free from residual copper or other catalytic components are important for therapeutic and biomedical applications as well as in living systems. In this communication we discuss the versatility of the catalyst free, isoxazole generating nitrile oxide alkyne Huisgen cycloaddition for provision of chemically modified oligonucleotide conjugates. Two distinct approaches will be demonstrated. In the first we discuss on resin cycloaddition between *in situ* generated nitrile oxides and oligonucleotides bearing alkyne functionalities at the either, or both, the 3'- or the 5'-termini¹⁻³. In the second we discuss the construction of oligonucleotide conjugates by phosphoramidite chemistry of previously-clicked isoxazole derivatives. Examples of conjugates prepared each approach and the merits of the previously clicked and on resin click approaches will be discussed.



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