Synthesis of L-2-Deoxythreose Nucleosides as Potential Antiviral Agents

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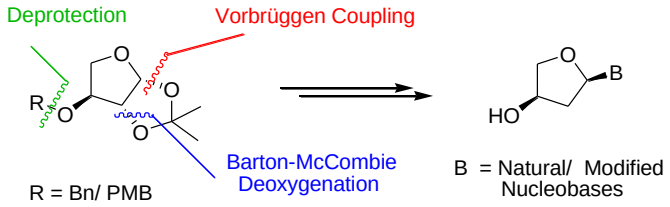
L-2-deoxythreose nucleoside phosphonates are known to selectively inhibit HIV without affecting human DNA synthesis.[1] These nucleoside analogues require two additional phosphorylation steps by cellular kinases before they are incorporated in the viral genome and lead to chain termination. It is believed that a *cis* orientation of the base and the 3'-substituent is a structural requirement for optimal conversion to the diphosphate. Inspired by these findings, we decided to explore the antiviral properties of the threose-based nucleoside analogues, which are anticipated to have superior bioavailability compared to the parent phosphonates.

The synthesis of analogs involving a Vorbrüggen coupling and a Barton-McCombie deoxygenation, will be described.



Reference:
1. Wu *et al*. J. Am. Chem. Soc. (2005), **127**, 5056-5065.