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CYANO AND ETHYNYL-PYRANONUCLEOSIDES: SYNTHESIS AND EVALUATION OF THEIR ANTIVIRAL AND ANTICANCER ACTIVITY

ABSTRACT

Nucleoside analogues have attracted much scientific attention in recent years as a result of their promising therapeutical applications. The present doctoral dissertation is mainly focused on the synthesis of novel branched-chain *C*-cyano or *C*-ethynyl nucleosides bearing six-membered carbohydrate moieties.

Taking into consideration the recent findings on several branched *C*-cyano and *C*-ethynyl furanonucleosides as antiviral agents and based on the fact that a number of these analogues have been reported to exhibit potent and broad spectrum anti-cancer activities, it was of interest to prepare new series of pyranonucleosides having a cyano and ethynyl group at the branching point of the carbohydrate ring.

The synthesis of a new class of nucleoside analogues possessing an ethynyl in the 3´-position of the sugar moiety is first reported. The presence of the triple bond of *C*-ethynyl-pyranonucleosides, provided an excellent opportunity to further synthesize new double-headed nucleosides. In addition, 3´-*C*-cyano-pyranonucleosides were prepared following a similar sequence of reactions used for the synthesis of *C*-ethynyl derivatives. The synthesis of their corresponding 3´-*C*-cyano-3´-deoxy nucleosides is also presented. In an effort to explore the structure-activity relationships of branched-chain *C*-cyano pyranonucleosides, the synthesis of 4´-*C*-cyano and 4´-*C*-cyano-4´-deoxy analogues was also performed. Last, a simple and efficient protocol for the synthesis of 2´-*C*-cyano and 2´-*C*-cyano-2´-deoxy was also developed. The

novel 2´-substituted derivatives were further converted to pyranosyl analogues bearing a spiro ring at position-2' of the sugar moiety.

The target nucleosides were evaluated for their antiviral and cytostatic properties using several virus strains and cancer cell lines. It is interesting to note that some of the *C*-cyano nucleoside derivatives, showed a similar cytostatic activity spectrum to the free base, 5-fluorouracil.