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The Synthesis and Evaluation of Hypericin and Analogs of Hypericin

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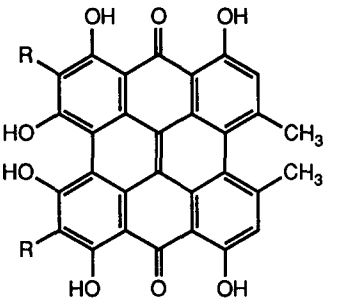
Hypericin (**1**, R = H) has been shown to effectively inhibit the



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infectivity of retroviruses such as HIV, EIAV and BLV. The mode of action of this novel antiviral agent is not known, but studies in our laboratory indicate that antiviral activity requires light. We will present both a versatile synthetic approach to analogs of hypericin and the biological evaluation of these analogs.

26 A Convenient Method for the Synthesis of 2', 3'-Dideoxynucleosides

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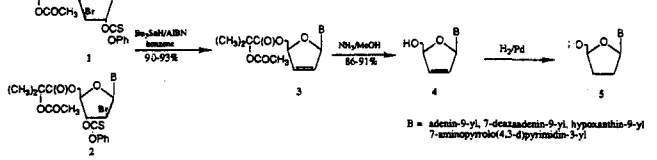
2', 3'-Didehydro-2', 3'-dideoxynucleosides and 2', 3'-dideoxynucleosides displayed potent activity against HIV [De Clercg, E., Aerschott Van, A., Herdevijn, P., Baba, H., Pauwels, R., Balzirini, J. (1989), *Nucleosides*, 659] and two reprensentatives of this class of compounds 3'-azido-3'-deoxythymidine and 2', 3'-dideoxyinosine are the only drugs against AIDS available so far.

In this study we present a new general approach to the synthesis of 2', 3'-dideoxynucleosides based on a free radical β-elimination of bromo and phenoxythiocarbonyl groups [Serafinowski, P. (1990) *Synthesis*, 411] and the use of 2-acetoxyisobutyryl bromide [Greenberg, S.; Moffat, J. (1973) *J. Am. Chem. Soc.* 4016, Dorland, E.; Serafinowski, P. (1992) *Synthesis*, in press]



Compounds **1** and **2** - key precursors for the free radical β-elimination with tributyltin hydride - were prepared in high yields via the reaction of the appropriate nucleosides with 2-acetoxyisobutyryl bromide. The reaction was conducted in a manner which ensured introduction of the 5'-O-(2-acetoxyisobutyryl) and 3'(2')-bromo groups in one step, without formation of undesired, unstable 5'-O-dioxolano derivatives, so that the 5'-O-(2-acetoxyisobutyryl) group could serve as a transient protection during subsequent transformations of the carbohydrate moiety [Dorland, E.; Serafinowski, P. (1992), *Synthesis*, in press].

The use of 5'-O-(2-acetoxyisobutyryl) group, coupled with almost quantitative free radical β-elimination of bromo and phenoxythiocarbonyl leaving groups resulted in a convenient general method for the synthesis of 2', 3'-dideoxynucleosides and proved particularly useful for 2', 3'-dideoxyinosine which was obtained in 43% overall yield.