Poster Session I

Synthesis, In Vitro Evaluation

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Synthesis of Some Uridine and 2'-deoxyUridine 5-N-Alkoxycarbonylcarboxamides. G. Shaw and D.C. Agathocleous, Chemistry and Chemical Technology Department, University of Bradford, Bradford, West Yorkshire, U.K.

Cytotoxic activity found in a 1-alkyluracil-5-N-alkoxycarbonylcarboxamide prompted us to prepare the corresponding ribo- and 2'-deoxyribo-nucleosides as potential anti-viral agents. N,N'-Methoxy (ethoxy and benzyloxy)carbonylmalonamides were prepared by reaction of malonic acid, methyl (ethyl or benzyl) carbamate and acetic anhydride. The malonamides with triethyl orthoformate and acetic anhydride over 40 min gave high yields of ethoxymethylene N,N'-methoxy (ethoxy or benzyloxy)carbonylmalonamides which with methylamine and aniline readily produced 1-methyl (phenyl)uracil-5-N-alkoxycarbonylcarboxamides in high yield. The three ethoxymethylene-N,N'-alkoxycarbonylmalonamides with 2,3-O-β-D-ribofuranosylamine in methanol, triethylamine for 15 min gave on adjustment of the solution to pH 6, a precipitate of the pure 2',3'-O-β-D-isopropylideneuridine 5-N-alkoxycarbonylcarboxamides in yields of 41% (methoxy), 45% (ethoxy) and 57% (benzyloxy). Uridine 5-N-methoxy(ethoxy and benzyloxy)carbonyl carboxamides were obtained in high yield by deblocking the isopropylidene derivatives with trifluoroacetic acid (50% in water). Uridine-5-N-benzyloxycarbonylcarboxamide was converted into 2'-deoxyuridine-5-N-benzyloxycarbonylcarboxamide by successive reaction with tetraisopropyldichloro disiloxane, p-tolyl chlorothioformate and tributyl tin hydride followed by deblocking with tetrabutylammonium fluoride.