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5-Haloethyl-deoxyuridine Analogues: Synthesis and Antiviral Activity

Herfried Griengl^a; Walter Hayden^a; Erich H'aneck^b

^a Institute of Organic Chemistry, Technical University Graz, Graz, Austria ^b Brigitte Rosemsrth, Sandoz Forschungsinstitut, Vienna, Austria

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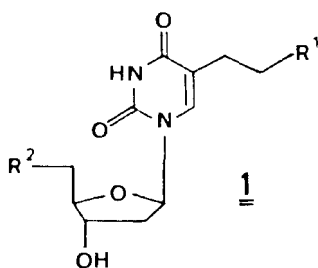
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5-HALOETHYL-DEOXYURIDINE ANALOGUES: SYNTHESIS AND ANTIVIRAL ACTIVITY

Herfried Griengl, Walter Hayden and Erich Wanek, Institute of Organic Chemistry, Technical University Graz, A-8010 Graz, Austria, and Brigitte Rosenwirth, Sandoz Forschungsinstitut, A-1235 Vienna, Austria.

Summary: 5-(2-Chloroethyl)-2'-deoxyuridine (CEDU) possesses antiviral activity against herpes viruses comparable to BVDU; like BVDU it inhibits HSV I and VZV, and, to a lesser extent, HSV II.

Among the many 5-substituted pyrimidine nucleoside analogues that have been synthesized and evaluated for antiviral activity, 5-(2-bromovinyl)-2'-deoxyuridine (BVDU) is one of the most potent and selective antiherpes compounds. From the study of structure-activity relationships it was concluded that a double bond in the side chain is essential for biological efficacy. We have synthesized and evaluated several 5-haloethyl derivatives of 2'-deoxyuridine to get further information on the structural requirements for antiviral activity.



| | R ¹ | R ² |
|-----------|----------------|----------------|
| <u>1a</u> | Cl | OH |
| <u>1b</u> | Br | OH |
| <u>1c</u> | I | OH |
| <u>1d</u> | Cl | Cl |
| <u>1e</u> | Br | Br |
| <u>1f</u> | I | I |

While the bromoethyl (1b) and the iodoethyl (1c) analogues inhibited various HSV I strains only at 100-1000 fold higher concentrations than BVDU, 5-(2-chloroethyl)-2'-deoxyuridine (1a, CEDU) showed MIC values similar to BVDU in HEP2 cells and 3-10 fold higher MIC values than BVDU in Vero cells. Thus, this compound having an alkyl side chain in 5 possesses antiviral activity comparable to BVDU. Interestingly, the virus spectrum of CEDU is the same as that of BVDU: our compound is very effective against HSV I and VZV, whereas HSV II is only inhibited at rather high concentrations.