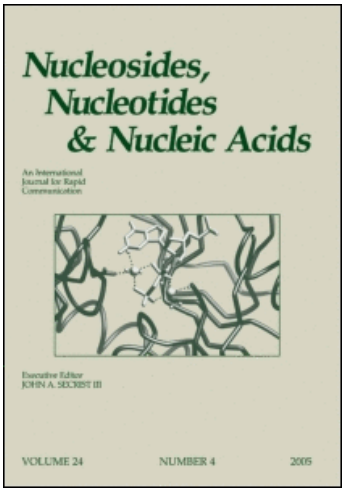

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5-Haloethyl-deoxyuridine Analogues: Synthesis and Antiviral Activity

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5-HALOETHYL-DEOXYURIDINE ANALOGUES: SYNTHESIS AND ANTIVIRAL ACTIVITY

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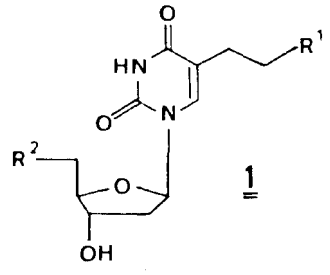
Summary: 5-(2-Chloroethyl)-2'-deoxyuridine (CEDU) possesses antiviral activity against herpes viruses comparable to BVDU; like BVDU it inhibits HSV I and VZV, and, to a lesser extent, HSV II.

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.



1

	R^1	R^2
1a	Cl	OH
1b	Br	OH
1c	I	OH
1d	Cl	Cl
1e	Br	Br
1f	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.

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