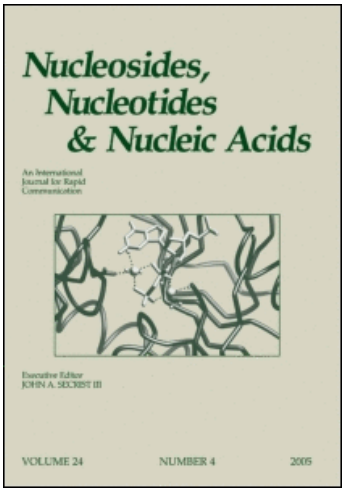

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INFLUENCE OF FLUORINATION OF THE SUGAR MOIETY ON THE ANTI-HIV-1 ACTIVITY OF 2',3'-DIDEOXYNUCLEOSIDES

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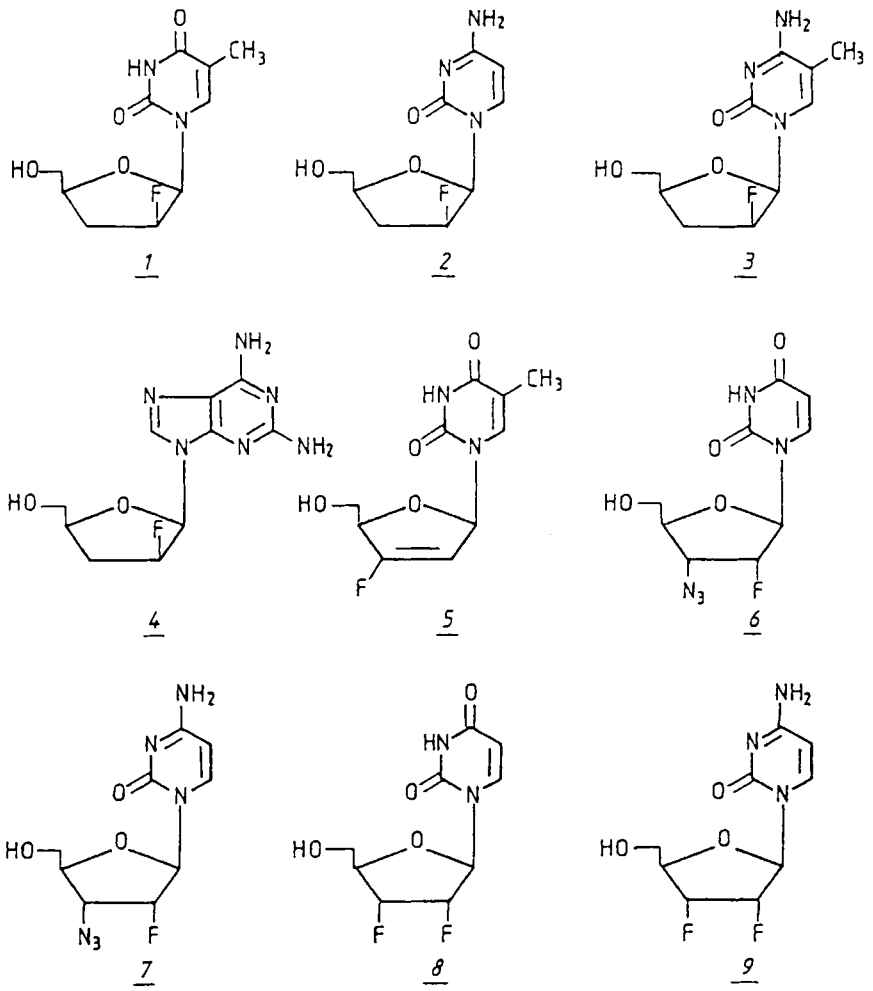
The advent of AIDS has prompted the search for effective anti-HIV-1 agents, and, in view of the efficacy of azidothymidine in the treatment of AIDS, 2',3'-dideoxynucleosides and analogues thereof have been considered as the most obvious candidates for AIDS chemotherapy. Various substituents have been introduced at the 3'-position, but only the 3'-azido and 3'-fluoro derivatives were found active against HIV-1. Introduction of a fluorine in organic compounds frequently causes a dramatic change in their biological activity. The stability of the carbon-fluorine bond and the strong electronegative character of fluorine, altering the electronic properties of the substituted molecule, led us to synthesize dideoxynucleosides with a fluorine substituent at different positions. The synthe-

TABLE 1. ANTI-HIV-1 ACTIVITY IN MT-4 CELLS

Compound	ED_{50} (μM)	CD_{50} (μM)	S.I.
1	> 500	> 500	-
2	9.8	117	12
3	> 500	> 500	-
4	> 100	> 100	-
5	10-50	232 ± 38	4.5-23
6	8.4 ± 2	46 ± 5	12
7	> 500	243 ± 28	-
8	> 500	> 500	-
9	> 500	> 500	-

ED_{50} : 50 % effective dose; CD_{50} : 50 % cytotoxic dose; S.I. : selectivity index (ratio of CD_{50} to ED_{50}).



sis and anti-HIV-1 activity of four 2'-fluoro-2',3'-dideoxy-aranucleosides, 3'-fluoro-2',3'-didehydro-2',3'-dideoxythymidine, two 3'-azido-2'-fluoro-2',3'-dideoxynucleosides and two 2',3'-difluoro-2',3'-dideoxynucleosides are presented. Three compounds (2, 5 and 6) exhibited a selective inhibitory effect on the replication of HIV-1 in MT-4 cells (Table 1).