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Nucleosides, Nucleotides and Nucleic Acids

Publication details, including instructions for authors and subscription information:

<http://www.informaworld.com/smpp/title~content=t713597286>

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To cite this Article Van Aerschot, Arthur , Balzarini, Jan , Pauwels, Rudi , Kerremans, Luk , De Clercq, Erik and Herdewijn, Piet(1989) 'Influence of Fluorination of the Sugar Moiety on the Anti-HIV-1 Activity of 2',3'-Dideoxynucleosides', *Nucleosides, Nucleotides and Nucleic Acids*, 8: 5, 1121 – 1122

To link to this Article: DOI: 10.1080/07328318908054304

URL: <http://dx.doi.org/10.1080/07328318908054304>

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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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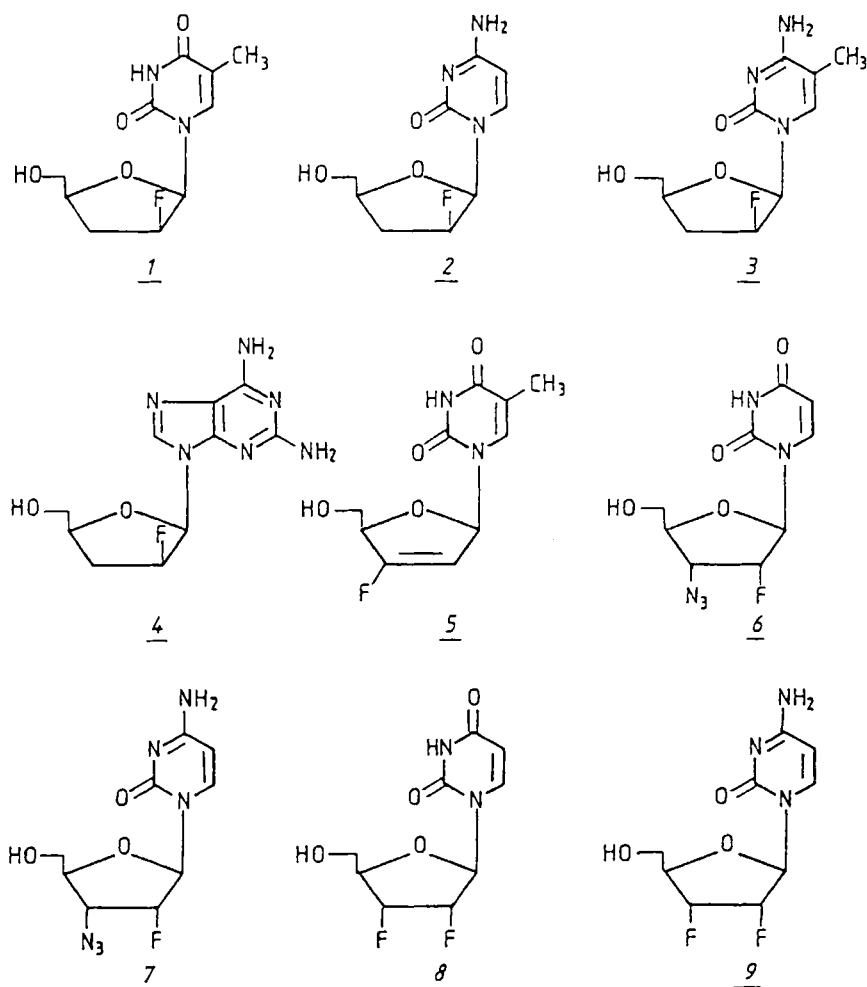
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The advent of AIDS has prompted the search for effective anti-HIV-1 agents, and, in view of the efficacy of azidothymidine in the treatment of AIDS, 2',3'-dideoxynucleosides and analogues thereof have been considered as the most obvious candidates 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	-

ED₅₀ : 50 % effective dose; CD₅₀ : 50 % cytotoxic dose; S.I. : selectivity index (ratio of CD₅₀ to ED₅₀).



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).