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Synthesis and Antiviral Activity of 1,4-Dioxane, 1,4-Oxathiane and 1,4-Morpholine Nucleoside Analogues

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SYNTHESIS AND ANTIVIRAL ACTIVITY OF 1,4-DIOXANE, 1,4-OXATHIANE AND 1,4-MORPHOLINE NUCLEOSIDE ANALOGUES

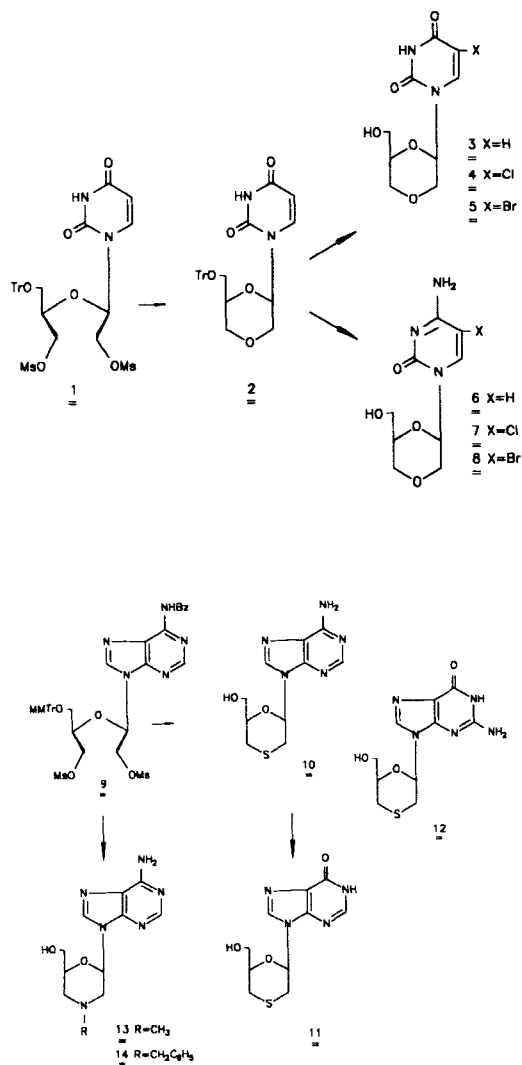
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ABSTRACT. Nucleoside analogues with a 1,4-dioxane, 1,4-oxathiane or 1,4-oxazine ring structure were prepared from the corresponding dimesylated seconucleosides.

Recently, a dideoxycytidine analogue with a 1,3-thioxolane moiety (NGPB-21)¹ and a 1,3-dioxolane analogue of 3'-deoxythymidine (dioxolane-T)² were reported to inhibit the infectivity of HIV-1 *in vitro*. We have now prepared a number of analogues with a six-membered heterocyclic moiety replacing the carbohydrate part. These heterocycles included 1,4-dioxane, 1,4-oxathiane and N-substituted morpholine ring structures. These analogues were prepared from the corresponding 2',3'-seconucleosides by treatment with either sodium hydroxide, sodium sulfide or primary alkylamines. Refluxing 5'-O-trityl-2',3'-di-O-methanesulfonyl-2',3'-secouridine (1) with NaOH in dioxane-water (4:1) for 15 h afforded the dioxanyl derivative 2. Deprotection gave 3, while chlorination or bromination followed by deprotection afforded 4 and 5. The cytidine analogues 6-8 were prepared from their tritylated uridine counterparts by reaction with phosphorus oxychloride and triazole, followed by addition of concentrated ammonia. Detritylation eventually yielded 6-8. Treatment of the dimesylated 2',3'-secoadenosine derivative 9 with sodium sulfide in dioxane-water (4:1) for 6 h at 90°C followed by deprotection gave the oxathiane derivative 10 in excellent yield. Deamination of 10 with adenosine deaminase afforded 11. Likewise, the guanosine analogue 12 was prepared from dimesylated 2',3'-secoguanosine. The morpholine derivatives 13 and 14 were obtained

by reaction of **9** with either methylamine or benzylamine, followed by deprotection. None of these analogues displayed any significant antiviral activity.



REFERENCES

1. M.A. Wainberg, M. Stern, R. Martel, B. Belleau and B. Soudeyns, Vth Intern. Conference on AIDS, Montreal, 1989, Abstracts, p. 552.
2. D.W. Norbeck, S. Spanton, S. Broder and H. Mitsuya, Tetrahedron Lett. 1989, 30, 6263.