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Synthesis of 5'-H-Phosphonates of 3'-Substituted Purine Deoxynucleosides

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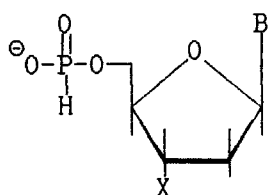
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SYNTHESIS OF 5'-H-PHOSPHONATES OF 3'-SUBSTITUTED PURINE DEOXYNUCLEOSIDES

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Abstract: H-Phosphonates of 3'-azido-2',3'-dideoxyadenosine, 3'-azido-2',3'-dideoxyguanosine and 3'-chloro-2',3'-dideoxyadenosine were synthesized and their antiviral activity in HIV-infected cell cultures was investigated.

As was shown recently 5'-H-phosphonate of AZT 1 blocked reproduction of HIV in MT4 and H9 cell cultures¹. It had nearly the same activity and less toxicity as compared with parental AZT. Here we report the synthesis of H-phosphonates of purine 3'-substituted 2',3'-dideoxynucleosides 2-4, because anti-HIV activity usually decreases for purine 3'-substituted 2',3'-dideoxynucleosides due to poor phosphorylation in cells.



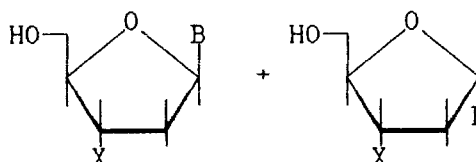
- | | | |
|---|-------|------------------|
| 1 | B=Thy | X=N ₃ |
| 2 | B=Ade | X=N ₃ |
| 3 | B=Gua | X=N ₃ |
| 4 | B=Ade | X=Cl |

3'-Azido- and 3'-chloro derivatives of purine 2',3'-dideoxynucleosides were synthesized by transglycosidation of corresponding thymine derivatives² as well as by direct condensation of heterocyclic bases with 3-chloro- or 3-azido-2,3-dideoxy-5-O-toluy-1-O-methylribosides³. In the case of transglycosidation of 3'-chlorothymidine the

yield of 3'-chloroadenosine was 41%, $\alpha:\beta$ ratio was 2:3.

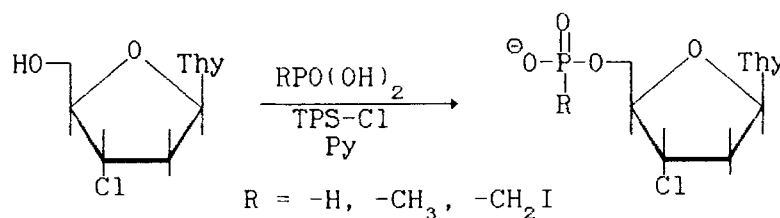
The main results of direct glycosidation were follows:

B	X	Yield	$\alpha:\beta$
Thy	N ₃	52%	5:8
Cyt	N ₃	37%	2:1
Ade	N ₃	34%	0:1
Gua	N ₃	29%	0:1
Thy	Cl	55%	1:1
Ade	Cl	48%	2:1



Phosphitilation was made with H_3PO_3 in the presence of DCC. H-Phosphonates 1-4 were isolated by ion-exchange chromatography on DEAE-Toyopearl with recleaning on LiChroprep RP 18 in water, average yield was 60%. The effectivity of inhibition of HIV-reproduction in MT4 and H9 cells by H-phosphonates 2 and 3 was comparable with that of corresponding nucleosides, whereas their toxicity was lower than that of nucleosides. Antiviral activity of 4 is under investigation.

Some phosphonates of 3'-chloro-2',3'-dideoxythymidine were also prepared by condensation of 3'-chloro-2',3'-dideoxythymidine with phosphorous or corresponding phosphonic acid. These compounds had no anti-HIV activity.



REFERENCES

1. N.B.Tarussova, A.A.Khorlin, A.A.Krayevsky, M.N.Korneyeva, D.N.Nosik, I.V.Kruglov, G.A.Galegov and R.Sh.Beabealashvilli, *Mol.Biol.(Russ)*, **23**, 1716, (1989).
2. M.Imazawa and F.Eckstein, *J.Org.Chem.*, **43**, 3044, (1978).
3. N.B.Dyatkina and A.V.Azhayev, *Synthesis*, 961, (1984).
4. Dr.B.Polsky, unpublished data.