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Synthesis of New Pseudonucleosides Containing Sulfamylated Derivatives of Natural Amino Acids as Aglycone

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SYNTHESIS OF NEW PSEUDONUCLEOSIDES CONTAINING SULFAMYLATED DERIVATIVES OF NATURAL AMINO ACIDS AS AGLYCONE

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ABSTRACT: New chiral sulfahydantoins have been synthesized via alkaline cyclisation, starting from symetric sulfamide derivatives of natural amino acids. Tetraacetyl ribofuranose was used in the glycosylation step in order to obtain the pseudonucleosides in β -anomeric configuration.

Introduction: In the course of our investigations of modified nucleosides, our interest was focused on the development of synthetic ways for pseudonucleosides containing modified aglycone¹. The modification of the heterocyclic aglycone is important for the preparation of new nucleosidic analogues used in antiviral and/or antitumoral chemotherapy. In order to interfere with biological process, pseudonucleoside has to be able to inhibit nucleoside biogenesis enzymes, or to selectively hybridize with natural nucleotides. Recently, we have reported the synthesis of new pseudonucleosides containing chiral sulfahydantoin². We have extended our studies in the series pseudonucleosidic derivatives of symetric sulfamides.

Synthesis: Chiral sulfahydantoins have been synthesized via alkaline cyclisation, starting from amino esters. The symetric sulfamides were prepared using K. Danek et al.method³ in 71-85% yield by treatment of the amino esters with sulfuryl chloride in pentane. Cyclisation was obtained by refluxing the sulfamides with sodium methoxide in methanol for one hour.

Then, the Vorbrüggen⁴ method of glycosylation was applied. This route, requiring preliminary silylation of the aglycone, proved to be a method of choice for the

glycosylation of sulfahydantoins. The heterocycle was first treated by hexamethyldisilazane (HMDS) containing catalytic quantities of ammonium sulfate.

The condensation with tetraacetyl- β -D-ribofuranose was carried out in acetonitrile, in the presence of tin tetrachloride. Finally, the ester groups were removed by treatment with mathanolic-ammonia.

All of these compounds were caracterized by usual spectroscopic methods, i.e. ¹H and ¹³C NMR, mass spectrometry and elemental analyses.

The β -anomeric configuration of the pseudonucleosides was confirmed by ¹H NMR studies ($J_{H^1H^2} = 7.2 - 7.8 \text{ Hz}$)

Conclusion: We described here the preparation of new pseudonucleosides containing sulfamylated derivate of natural amino acids as aglycones. The pharmacological evaluation of these compounds is in progress.

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