

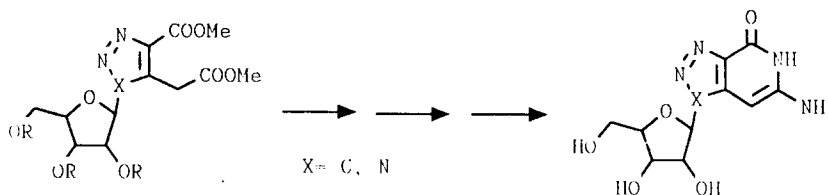
28

Synthesis of C- and N-Nucleosides and Use of Distance Geometry Approach for the Evaluation of *In Vitro* Antiviral Activity

J. Glöse¹, B. Kobe², M. Prhac¹, A. Štimac¹ and T. Šolmajer³

1. Boris Kidrič Institute of Chemistry, 61115 Ljubljana and Krka, Pharmaceutical and Chemical Works, 68000 Novo mesto; 2. Dept. of Chemistry, University of Ljubljana, 3. Lek, Chemical and Pharmaceutical Works, Ljubljana, Slovenia, Yugoslavia

1,3-Dipolar cycloaddition reactions of 2,3,5-tri-O-benzoyl- β -D-ribofuranosyl azide and protected 5-(β -D-ribofuranosyl)-2H-tetrazoles with allenes and acetylenes were utilized for a synthesis of appropriately substituted pyrazolo and triazolo intermediates. These were further transformed into 3-deaza guanosine analogs. A three dimensional receptor model of parainfluenza virus type 3 developed by Ghose *et al.*, J.Med.Chem.32,746(1989), using a distance geometry approach to analyze the *in vitro* antiviral activity of several novel ribonucleosides, was used. On the basis of atomic physicochemical properties *i.e.* hydrophobicity, molar refractivity and charge density, the interaction energy of minimum energy conformations of 22 compounds with hypothetical virus active site were evaluated.

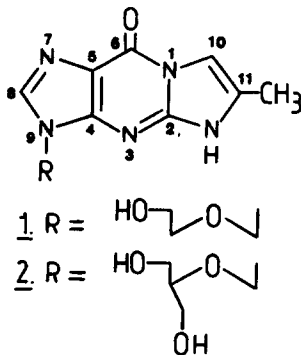


29

Synthesis and Properties of Novel Derivatives of 1,N-2-Bridged Acyclovir and DHPG. B. Golankiewicz and T. Ostrowski. Institute of Bioorganic Chemistry of the Polish Academy of Sciences, 61-704 Poznań, Poland.

It has been found recently that the modification of two potent antivirals, acyclovir and DHPG, with 1,N-2 isopropeno bridge results in the compounds (1,2) of enhanced selectivity.^{1a}

Methyl group at the position 11 of 1 and 2 is important for their antiviral activity. Corresponding unsubstituted compounds are 10-100 times less active.^{1b} In connection to the above, a series of novel 1,N-2-bridged analogues bearing various substituents at the 8, 10 and 11 position of 1 is now synthesized and characterized. The compounds substituted with *i.e.* Br, F, CH₃, C(CH₃)₃, C₆H₅, *p*-BrC₆H₄, *p*-C₆H₄C₆H₅ are aimed³ to yield i) further improvement of the selectivity, ii) fluorescent antivirals. The susceptibility of the appended ring towards oxidation is found to be dependent upon the substitution.



1. Boryski, J; Golankiewicz, B; De Clercq, E. a. J.Med.Chem. 1988 31, 1351. b. unpublished.