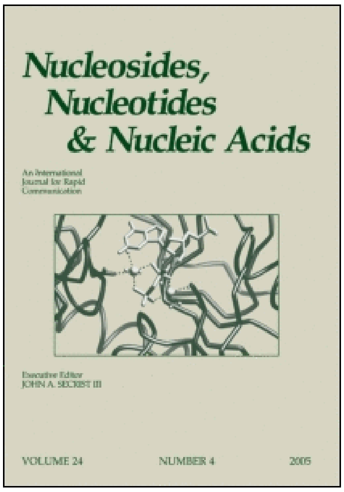


Nucleosides, Nucleotides and Nucleic Acids
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713597286

A New and Convenient Approach for the Synthesis of Ribo- and 2'-Deoxyribo-β-L-Furanonucleosides Starting From β-L-Xylofuranonucleosides

V. Boudou[a]; G. Gosselin[a]; J-L. Imbach[a]
[a] Laboratoire de Chimie Bioorganique, Université des Sciences et Techniques du Languedoc, Montpellier Cedex 5, France

To cite this Article Boudou, V. , Gosselin, G. and Imbach, J-L.(1999) 'A New and Convenient Approach for the Synthesis of Ribo- and 2'-Deoxyribo-β-L-Furanonucleosides Starting From β-L-Xylofuranonucleosides', Nucleosides, Nucleotides and Nucleic Acids, 18: 4, 607 — 609

To link to this Article: DOI: 10.1080/15257779908041512

URL: http://dx.doi.org/10.1080/15257779908041512

NUCLEOSIDES & NUCLEOTIDES, 18(4&5), 607–609 (1999)

A NEW AND CONVENIENT APPROACH FOR THE SYNTHESIS OF RIBO- AND 2'-DEOXYRIBO-β-L-FURANONUCLEOSIDES STARTING FROM β-L-XYLOFURANONUCLEOSIDES

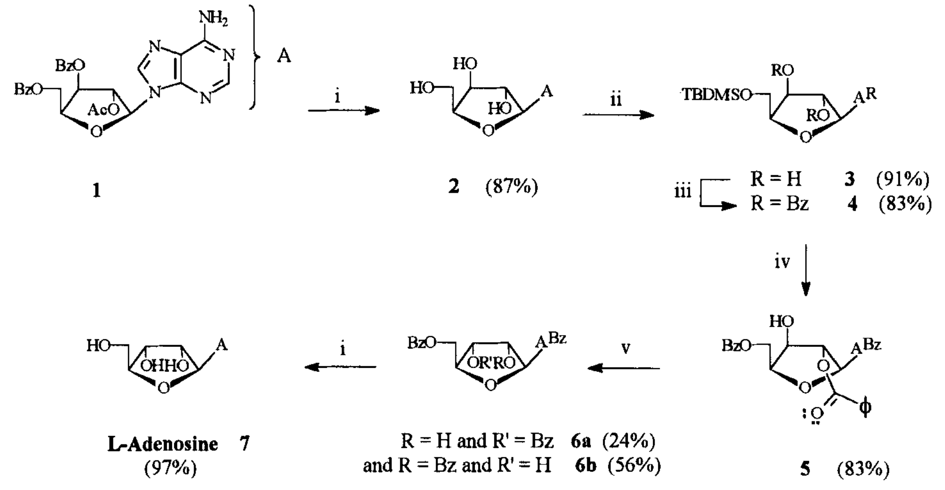
V. Boudou, G. Gosselin* and J.-L. Imbach
UMR CNRS-USTL 5625, Laboratoire de Chimie Bioorganique, Université des Sciences
et Techniques du Languedoc, 34095 Montpellier Cedex 5, France

ABSTRACT : Ribo- and 2'-deoxyribo-β-L-furanosyladenine have been synthesized. Although these compounds have been already reported in the literature, it seemed to us that a more convenient approach for their synthesis deserved to be developed. Intramolecular substitution as well as Mitsunobu reaction were used to invert the configuration of carbon 3' of starting β-L-xylofuranosyl intermediates.

Recently, nucleoside analogues with the unnatural β-L-configuration have emerged as a new class of sugar-modified derivatives with potential antiviral and / or antitumoral activity. For instance, β-L(-)-2',3'-dideoxy-3'-thiacytidine (3TC, Lamivudine) was approved as an anti-immunodeficiency (HIV) agent and β-L-2',3'-dideoxy-5-fluorocytidine has been found to exhibit activity against HIV as well as hepatitis B virus (HBV), both *in vitro* and *in vivo*. Other β-L-dideoxynucleoside enantiomers are currently the subject of intensive research works.[1]

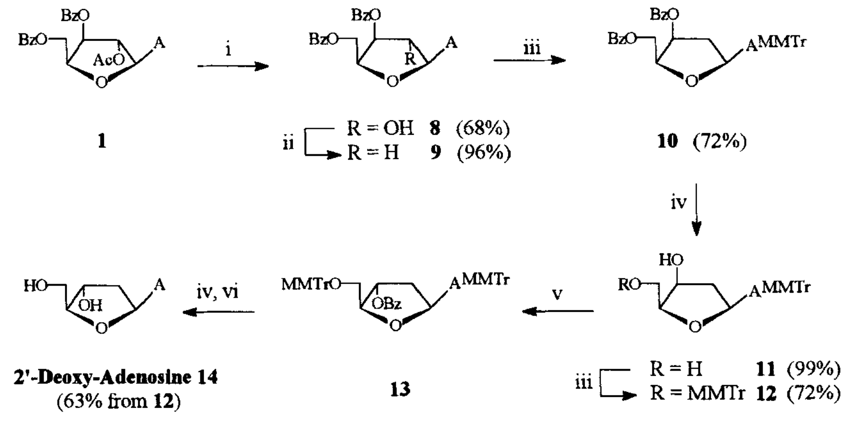
In continuation of our research program on L-sugar modified nucleoside analogues, we now describe the stereospecific synthesis of 9-(β-L-ribofuranosyl)adenine (7) and 9-(2-deoxy-β-L-ribofuranosyl)adenine (14) starting from a suitably protected and easily accessible 9-(β-L-xylofuranosyl)adenine derivative (1).

9-(β-L-Ribofuranosyl)adenine 7 : From a synthetic viewpoint (Scheme 1), the starting compound 1 was obtained according to a method previously described by our group[2] in 44% yield in 6 steps from L-xylose. Then 2' and 5'-OH as well as 6-NH_2



i : NH_3, MeOH; ii : TBDMSCl/C_5H_5N; iii : BzCl, DMAP/C_5H_5N; iv : TBAF 1M, AcOH/THF; v : Tf_2O, DMAP/C_5H_5N-CH_2Cl_2 then H_2O.

SCHEME 1



i : $NH_2NH_2.H_2O$/AcOH-C_5H_5N; ii : $C_6H_5OC(S)Cl$, DMAP/CH_3CN then $[(CH_3)_3Si]_3SiH$, AIBN/Dioxane; iii : MMTrCl/C_5H_5N; iv : NH_3, MeOH; v : DEAD, PPh_3, BzOH/THF; vi : AcOH 80%.

SCHEME 2

functions were protected by benzoyl groups (4 steps) to afford the intermediate 5. The 3'-OH was activated as a triflate ester which was immediately removed under an intramolecular Sn2 mechanism induced by the oxygen doublet of the benzoyl group in position 2'.[3] The reaction led to the formation of an acyloxonium ion between the positions 2' and 3' on the sugar α face. Hydrolysis of this intermediate gave two regioisomers, benzoylated in the 3' position (6a) or in the 2' (6b). Finally, aminolysis of the benzoyl groups afforded the desired 9-(β-L-ribofuranosyl)adenine 7.

9-(2-Deoxy-β-L-ribofuranosyl)adenine 14 : (Scheme 2). Selective deacylation of 1 followed by a reductive deoxygenation at C-2' afforded compound 9. The 6-NH_2 and 5'-OH functions were protected by a monomethoxytrityl group to give compound 12. A Mitsunobu reaction[4] was carried out in order to invert the configuration of carbon C-3'. The resulting benzoylated compound 13 was successively treated by methanolic ammonia and aqueous acetic acid 80% to give the desired 9-(2-deoxy-β-L-ribofuranosyl)adenine 14.

Conclusion : During this work we have developed new and convenient approaches for the synthesis of both ribo- and 2'-deoxyribo-β-L-furanonucleosides of adenine. These unnatural L-enantiomers are currently studied for their potential biological activities.

Acknowledgments : This work was in part supported by a grant of the Ministère de la Recherche et de la Technologie (France).

REFERENCES

1. Gosselin, G.; Boudou, V.; Griffon, J.-F.; Pavia, G.;. Pierra, C.; Imbach, J.-L.; Aubertin, A.-M.; Schinazi, R.F. and Sommadossi, J.-P. *Nucleosides, Nucleotides*, **1997**, 16 (7-9), 1389-1398, and references cited therein.

2. Gosselin, G.; Bergogne, M.-C. and Imbach, J.-L. *J. Heterocycl. Chem.*, **1993**, 30, 1229-1233.

3. Herdewijn, P. *Tetrahedron*, 1989, **45**, 6563-6580.

4. Mitsunobu, O. *Synthesis*, 1981, 1-28.