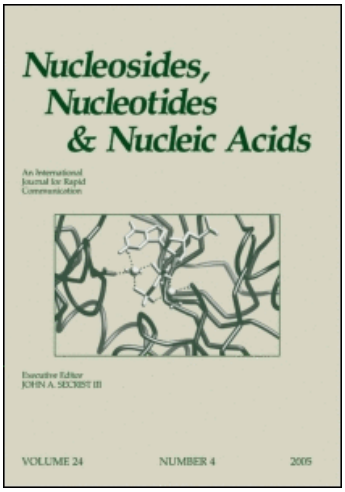

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Synthesis of Novel Isomeric Dideoxydidehydronucleosides

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SYNTHESIS OF NOVEL ISOMERIC DIDEOXYDIDEHYDRONUCLEOSIDES

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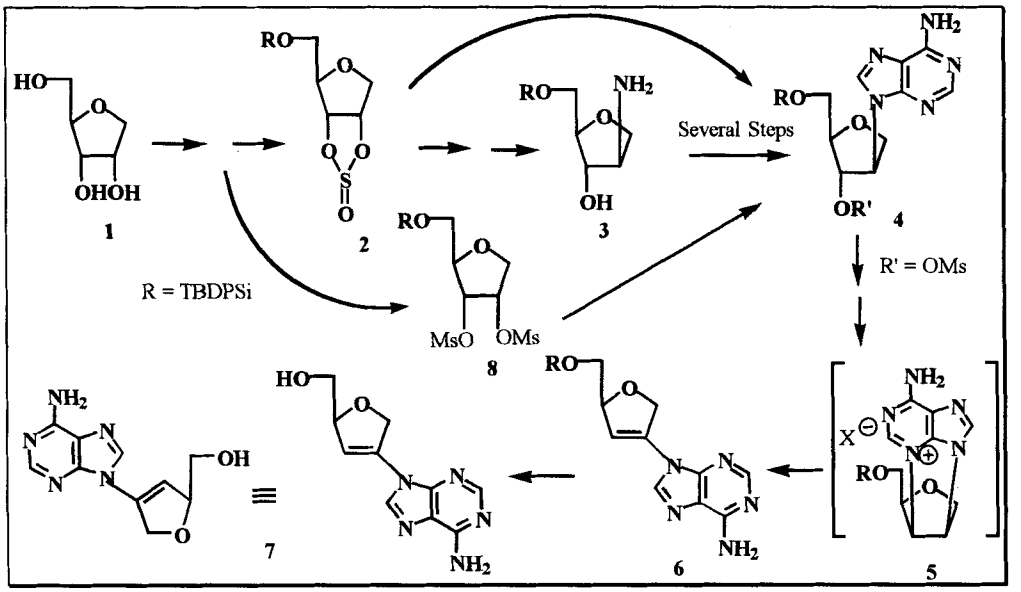
ABSTRACT: Methodologies for the synthesis of novel isomeric dideoxynucleosides with unsaturation in the carbohydrate moiety have been developed. An example of the synthesis (Isod4A) is presented. Antiviral studies are in progress.

For a number of years, we have explored the synthesis, enzymology, and antiviral studies of several classes of isomeric nucleosides. Included in this group are compounds where the base is moved from the natural 1′-position to the isomeric 2′-position or the -CH_2OH is transposed from the 4′- to the 3′-position.[1] For example, (*S,S*)-IsoddA, an isomeric dideoxynucleoside synthesized by us, has anti-HIV activity against HIV-1, HIV-2, and HIV-resistant strains.[2] In the search for new isomeric dideoxynucleosides with anti-HIV activity, we have investigated isomeric nucleosides that have unsaturation in the carbohydrate moiety.

The synthesis is exemplified with the case of Isod4A (**7**). The starting compound was 1,4-anhydro-D-ribitol, **1**.[3] Treatment of protected **1** with $SOCl_2$ in pyridine,[4] produced quantitatively the cyclic sulfite **2.** Coupling of **2** with adenine (K_2CO_3,18-crown-6, DMF) gave IsodA, **4**.[3,5] The latter was also obtained by construction of the adenine base onto the β-amino group of compound **3**.[6] Treatment of the mesylate of **4** with K_2CO_3 in DMF (Δ) gave the protected Isod4A **6**, presumably through the intermediacy of the cycloadenosine **5**. Purine cyclonucleosides, such as 3,5′-anhydroadenosine and 3,3′-anhydroadenosine, have been invoked as intermediates in other studies.[7] Compound **6** was also obtained from **8** (K_2CO_3, DMF, Δ). Deprotection of **6** with NH_4F gave **7.**



The quantitative UV data of **7** confirmed the extended conjugation and the ^{13}C NMR spectrum showed the presence of unsaturated carbons on the sugar moiety at 111 ppm and 132 ppm. The single crystal X-ray data of **7** provided final confirmation of structure and stereochemistry. The C, G, and T analogs were also synthesized. Antiviral studies of these compounds are in progress.

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REFERENCES

1. Nair, V.; Jahnke, T. S. *Antimicrob. Agents and Chemother.* **1995**, *39*, 1017-1029. Bolon, P. J.; Sells, T. B.; Nuesca, Z. M.; Purdy, D. F.; Nair, V. *Tetrahedron* **1994**, *50*, 7747-7764. Nair, V.; Nuesca, Z. M. *J. Am. Chem. Soc.* **1992**, *114*, 7951-7953. Nair, V.; Sells, T. B. *Tetrahedron Lett.* **1992**, *33*, 7639-7642.
2. Nair, V.; St. Clair, M.; Reardon, J. E.; Krasny, H. C.; Hazen, R. J.; Paff, M. T.; Boone, L. R.; Tisdale, M.; Najera, I.; Dornsife, R. E.; Everett, D. R.; Borroto-Esoda, K.; Yale, J. L.; Zimmerman, T. P.; Rideout, J. L. *Antimicrob. Agents and Chemother.* **1995**, *39*, 1993-1999.
3. Purdy, D. F.; Zintek, L. B.; Nair, V. *Nucleosides & Nucleotides* **1994**, *13*, 109-126.
4. Sowa, T.; Tsunoda, K. *Bull. Chem. Soc. Jpn.* **1975**, *48*, 505-507. Gao, Y,; Sharpless, K. B. *J. Am. Chem. Soc.* **1988**, *110*, 7538-7539.

5. Montgomery, J. A.; Thomas, H. J. *J. Org. Chem.* **1978**, *43*, 541-544.

6. Shealy, Y. F.; Clayton, J. D. *J. Pharm. Sci.* **1973**, *62*, 1432-1434. Kasperson, F. M.; Pandit, U. K. *J. Chem. Soc., Perkin Trans.* I **1975**, 1617-1622. Pickering, L.; Nair, V. *Nucleosides & Nucleotides*, **1996**, *15*, 1751-1769.

7. Srivastava, P. C.; Robins, R. K.; Meyer, Jr.; R. B. In *Chemistry of Nucleosides and Nucleotides*, Townsend, L. B., Ed.; Plenum Press: New York, 1988, Vol.1, pp 113-281.