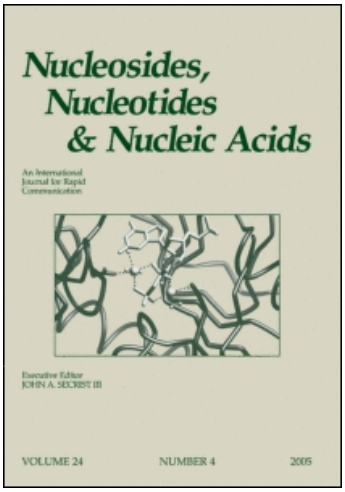


Nucleosides, Nucleotides and Nucleic Acids
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713597286

Synthesis and Antiviral Activities of 1,3-Oxathiolanyl Nucleosides with 5-Hydroxymethyl Substituent

Moon Woo Chun[a]; Sung Pil Choi[a]; Myong Jung Kim[a]; Chol Joon Bae[a]; Hyung Ryong Moon[b]; Hee-Doo Kim[c]; Lak Shin Jeong[b]
[a] College of Pharmacy, Seoul National University, Seoul [b] Laboratory of Medicinal Chemistry, College of Pharmacy, Ewha Womans University, Seoul, Korea [c] College of Pharmacy, Sookmyung Women's University, Seoul, Korea

To cite this Article Chun, Moon Woo , Choi, Sung Pil , Kim, Myong Jung , Bae, Chol Joon , Moon, Hyung Ryong , Kim, Hee-Doo and Jeong, Lak Shin(1999) 'Synthesis and Antiviral Activities of 1,3-Oxathiolanyl Nucleosides with 5-Hydroxymethyl Substituent', Nucleosides, Nucleotides and Nucleic Acids, 18: 4, 615 — 616
To link to this Article: DOI: 10.1080/15257779908041515
URL: http://dx.doi.org/10.1080/15257779908041515

NUCLEOSIDES & NUCLEOTIDES, 18(4&5), 615–616 (1999)

SYNTHESIS AND ANTIVIRAL ACTIVITIES OF 1,3-OXATHIOLANYL NUCLEOSIDES WITH 5-HYDROXYMETHYL SUBSTITUENT

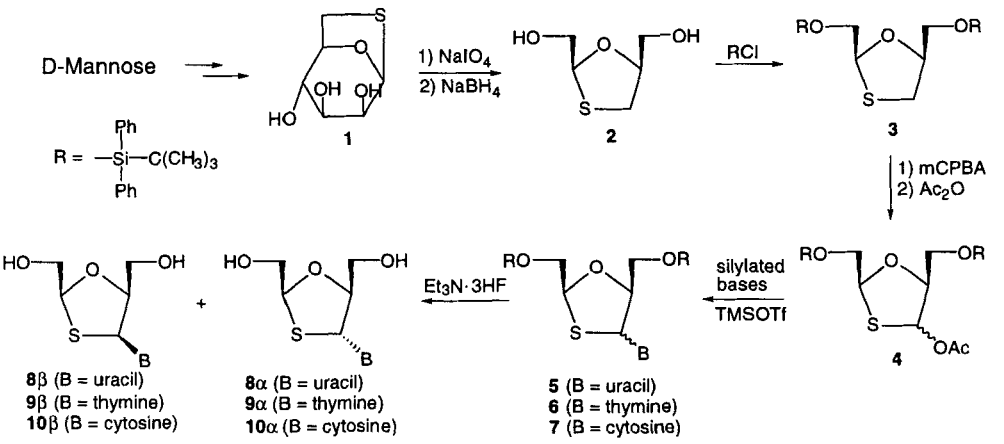
Moon Woo Chun,* Sung Pil Choi, Myong Jung Kim, Chol Joon Bae, Hyung Ryong Moon,[1] Hee-Doo Kim,[2] and Lak Shin Jeong[1]

College of Pharmacy, Seoul National University, Seoul 151-742, [1]Laboratory of Medicinal Chemistry, College of Pharmacy, Ewha Womans University, Seoul 120-750, Korea and [2]College of Pharmacy, Sookmyung Women's University, Seoul 140-742, Korea

Abstract: Novel 1,3-oxathiolanyl pyrimidine nucleosides with 5-hydroxymethyl substituent were synthesized starting from D-mannose and evaluated for antiviral activities against HIV-1, HSV type 1,2 and HCMV.

(-)-L-β-1,3-oxathiolanyl cytosine (3TC, Lamivudine) whose C3 methylene of the furanose was substituted by oxygen atom has shown potent anti-human immunodeficiency virus (HIV) and anti-hepatitis B virus (HBV) activities.[1-2] Another class of nucleosides in which sulfur and oxygen of sugar moiety of 1,3-oxathiolanyl nucleosides were transposed were also reported to show potent antiviral activities.[3] As a part of our ongoing effort to search for new antiviral agent, we decided to put hydroxymethyl substituent into sugar moiety of 1,3-oxathiolanyl nucleosides since ring-enlarged oxetanocin analogues exhibited good anti-HIV activity.[4] Therefore, Novel 1,3-oxathiolanyl nucleosides with 5-hydroxymethyl substituent were synthesized starting from D-mannose and evaluated for antiviral activities against HIV-1, HSV-1,2 and HCMV. Our synthetic plan was to utilize the key intermediate, 1,6-thioanhydro-D-mannose (**1**)[5] which could be easily prepared from D-mannos. Oxidative cleavage of the intermediate **1** with $NaIO_4$ followed by reduction with $NaBH_4$ gave the diol **2**. Two primary hydroxyl groups were protected with TBDPSCl to give **3**. Treatment of **3** with mCPBA followed by refluxing of the resulting sulfoxide with acetic anhydride afforded the acetate **4**. Condensation of the acetate **4** with silylated uracil, thymine and cytosine in the presence of TMSOTf in dichloroethane gave the uracil **5**, thymine **6** and cytosine **7** analogues, respectively. ^1H NMR indicated that the

Scheme 1



α isomer was formed as the major isomer during the condensation due to the steric effects of bulky TBDPS groups. Desilyation of **5-7** with $NEt_3 \cdot 3HF$ yielded the α nucleosides **8α-10α** and β nucleosides **8β-10β**, respectively (Scheme 1).

The antiviral assays of the final nucleosides **8-10** were performed against HIV-1, HSV-1,2, and HCMV. All synthesized compounds did not show significant antiviral activities.

Acknowledgment

This research was supported by the grant from the Good Health R&D project, Ministry of Health and Welfare, Korea.

References

1. Belleau, B.; Dixit, D.; Nguyen-Ba, N.; Kraus, J. L. 5th International Conference on AIDS, Montreal, Canada, June 4-9, **1990**, paper no. T.C.O.I.
2. Jeong, L. S.; Schinazi, R. F.; Beach, J. W.; Kim, H. O.; Nampalli, S.; Shanmuganathan, K.; Alves, A. J.; McMillan, A.; Chu, C. K. *J. Med. Chem.* **1993**, *36*, 181 and references cited therein.
3. Belleau, B.; Brasili, L.; Chan, L.; DiMarco, M. P.; Zacharie, B.; Nguyen-Ba, N.; Jenkinson, H. J.; Coates, J. A. V.; Cameron, J. M. *Bioorg & Med. Chem. Lett.* **1993**, *3*, 1723.
4. Tseng, C. K.-H.; Marquez, V. E.; Milne, G. W. A.; Wysocki, Jr., R. J.; Mitsuya, H.; Shirasaki, T.; Driscoll, J. S. *J. Med. Chem.* **1991**, *10*, 291.
5. Jeong, L. S.; Schinazi, R. F.; Beach, J. W.; Kim, H. O.; Shanmuganathan, K.; Nampalli, S.; Chun, M. W.; Chung, W.-K.; Choi, B. G.; Chu, C. K. *J. Med. Chem.* **1993**, *36*, 2627 and references cited therein.