Tetrahedron Letters,Vol.30,No.17,pp 2269-2270,1989 0040-4039/89 $3.00 + .00
Printed in Great Britain Pergamon Press plc

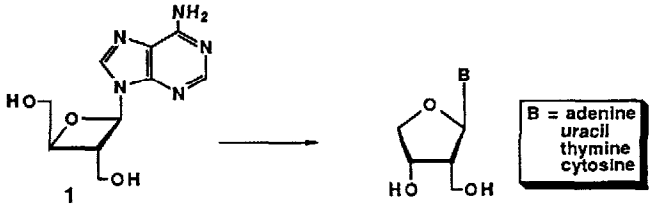
A FACILE SYNTHESIS OF 2-DEOXY-2-HYDROXYMETHYL-β-D-ERYTHROFURANOSYL NUCLEOSIDES FROM 9-(2-DEOXY-2-HYDROXYMETHYL-β-D-ERYTHROOXETANOSYL)ADENINE BY A NOVEL RING EXPANSION ACCOMPANYING TRANSGLYCOSIDATION

Kuniki Kato,[a]* Takae Minami[a], Tomohisa Takita,[a] Shigeru Nishiyama,[b] Shosuke Yamamura,[b] and Hiroshi Naganawa[c]

a Research Laboratories, Pharmaceuticals Group, Nippon Kayaku Co. Ltd., 3-31-12 Shimo, Kita-ku, Tokyo 115, Japan
b Department of Chemistry, Faculty of Science and Technology, Keio University, Hiyoshi, Yokohama 223, Japan
c Institute of Microbial Chemistry, Kamioosaki, Shinagawa-ku, Tokyo 141, Japan

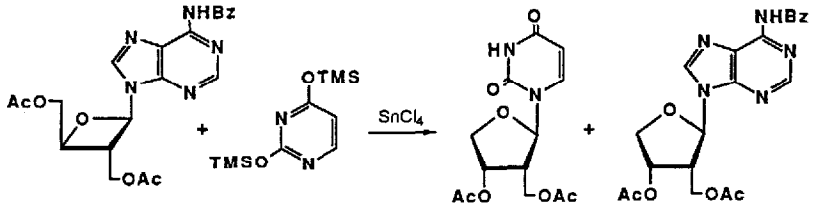
Summary: Reaction of N-benzoyl oxetanocin diacetate with trimethylsilyl pyrimidine in the presence of $SnCl_4$ gives both erythrofuranosyl pyrimidine and purine nucleosides.

The replacement or substitution of the 5'-hydroxyl of adenosine or removal of the 4'-hydroxymethyl group invariably leads to loss of substrate activity toward adenosine deaminase.[1] In addition, 2'- and 3'-methyladenosines show cytotoxicity against KB cells in culture.[2] For the investigation of biological properties of other nucleosides having branched chain sugar, Reist et al. reported rather tedious synthesis of adenine nucleosides carrying 2-deoxy-2-hydroxymethyl-D-threofuranose as a sugar moiety.[3] In the course of our study concerning chemical modification of oxetanocin (**1**),[4] we examined the ring expansion of oxetanosyl nucleosides into biologically interesting nucleosides having a branched chain erythrofuranose. We describe herein a novel and facile synthesis of 2-deoxy-2-hydroxymethyl-β-D-erythrofuranosyl nucleosides from 2-deoxy-2-hydroxymethyl-β-D-erythrooxetanosyl adenine [oxetanocin (**1**)] by a ring expansion accompanying transglycosidation.



When N-benzoyl oxetanocin diacetate (**2**) (1mmol) was treated with bis(trimethylsilyl)-uracil (**3**) (15mmol) in the presence of $SnCl_4$ (15mmol) in CH_3CN - $Cl(CH_2)_2Cl$ at room temp. for 20 min, 1-(2-acetoxymethyl-3-O-acetyl-2-deoxy-β-D-erythrofuranosyl)uracil (**4**)[5] and N^6-benzoyl-9-(2-acetoxymethyl-3-O-acetyl-2-deoxy-β-D-erythrofuranosyl)adenine (**5**)[5] were isolated as a 1:1 mixture in 68% yield (Scheme 1).[6,7]

(Scheme 1)



2 3 4 5

To the best of our knowledge, this is the first example of the ring expansion accompanying transglycosidation and provides a convenient method for the synthesis of 2-deoxy-2-hydroxymethyl-β-D-erythrofuranosyl purine and pyrimidine nucleosides.

Acknowledgement: The authors are grateful to Dr. S. Saito for his valuable advice.

References

1. A. Bloch, M. J. Robins, and J. R. McCarthy, Jr., J. Med. Chem., **10**, 908 (1967).

2. E. Walton, S. R. Jenkins, R. F. Nutt, M. Zimmerman, and F. W. Holly, J. Am. Chem. Soc., **88**, 4524 (1966).

3. E. J. Reist, D. F. Calkins, and L. Goodman, J. Am. Chem. Soc., **90**, 3852 (1968).

4. Structure of **1**: H. Nakamura, S. Hasegawa, N. Shimada, A. Fujii, T. Takita, and Y. Iitaka, J. Antibiot., **39**, 1629 (1986); Biological activities: N. Shimada, S. Hasegawa, T. Harada, T. Tomisawa, A. Fujii, and T. Takita, ibid., **39**, 1623 (1986); Total synthesis: S. Niitsuma, Y. Ichikawa, K. Kato, and T. Takita, Tetrahedron Lett., **28**, 1967 (1987); S. Nishiyama, S. Yamamura, K. Kato, and T. Takita, ibid., **29**, 4739, 4743 (1988); D. W. Norbeck and J. D. Kramer, J. Am. Chem. Soc., **110**, 7217 (1988).

5. The spectral data for the new compounds are in accord with the structures assigned, and only selected data are cited: **4**: $C_{13}H_{17}N_2O_7$ [m/z 313 $(M^+ + 1)$]; $[\alpha]_D^{25}$ +39.6° (c 0.23, $CHCl_3$), IR ($CHCl_3$) 3400, 1750, 1720 (sh), and 1700 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.06 (3H, s), 2.11 (3H, s), 2.72 (1H, m), 4.24 (2H, complex), 4.31 (2H, d, J= 6.23 Hz), 5.19 (1H, m), 5.78 (1H, d, J= 8.18 Hz), 5.93 (1H, d, J= 2.93 Hz), 7.49 (1H, d, J= 8.18 Hz), and 9.31 (1H, br. s); ^{13}C NMR ($CDCl_3$) δ 20.65 (q), 20.85 (q), 51.50 (d), 61.74 (t), 74,24 (t), 75.15 (d), 88.37 (d), 101.94 (d), 139.16 (d), 150.31 (s), 163.57 (s), 169.89 (s), and 170.55 (s). **5**: $C_{21}H_{21}N_5O_6$ [m/z 439 (M^+)]; $[\alpha]_D^{25}$ -24.5° (c 0.29, $CHCl_3$); IR ($CHCl_3$) 3400, 1750, 1715, 1615, and 1590 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.06 (3H, s), 2.10 (3H, s), 3.27 (1H, m), 4.26 - 4.50 (4H, complex), 5.28 (1H, m), 6.28 (1H, d, J= 3.26 Hz), 7.48 - 7.66 (3H, complex), 8.05 (2H, d, J= 6.68 Hz), 8.28 (1H, s), 8.78 (1H, s), and 9.23 (1H, s); ^{13}C NMR ($CDCl_3$) δ 20.76 (q), 20.86 (q), 51.05 (d), 61.86 (t), 73.69 (t), 75.11 (d), 87.03 (d), 123.38 (s), 127.88 (2C, d), 128.90 (2C, d), 132.86 (d), 133.51 (s), 140.93 (d), 149.48 (s), 151.68 (s), 152.78 (d), 164.56 (s), 170.19 (s), and 170.59 (s).

6. Similar results were observed with other silylpyrimidine bases such as thymine and cytosine.

7. The reaction mechanism has not been clarified yet.

(Received in Japan 14 February 1989)