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A FACILE AND PRACTICAL SYNTHESIS OF THE DERIVATIVES OF 1-O-ACETYL-2-DEOXY-2-HYDROXYMETHYL-D-ERYTHROOXETANOSE, A KEY SUGAR MOIETY FOR THE SYNTHESIS OF OXETANOSYL-N-GLYCOSIDE

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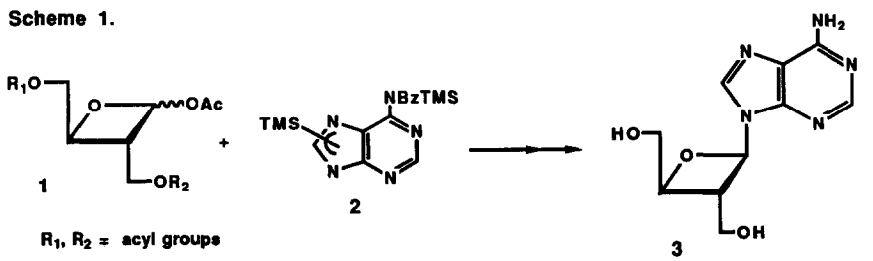
Summary: Intramolecular cyclization of the epoxy-alcohol (**6**) with KOH in aq. DMSO gave predominantly the oxetane compound (**7**), which could be transformed into some 1-O-acetyl-D-oxetanoses.

Recently, we have reported the total synthesis of oxetanocin (**3**),[1] a novel oxetanosyl N-glycoside, by an N-glycosidation reaction between an 1-O-acetyl-D-oxetanose (**1**) and a silylated adenine (**2**) with the aid of Lewis acid (Scheme 1).[2] However, being so tedious to get the diester (**1**) by the method reported in the previous paper [17 steps from **4**, 1.8% overall yield], more convenient synthetic route was needed in order to make analogues of **3**. We now describe a facile and practical synthesis of 1-O-acetyl-2-deoxy-2-hydroxymethyl-D-erythrooxetanose derivatives.

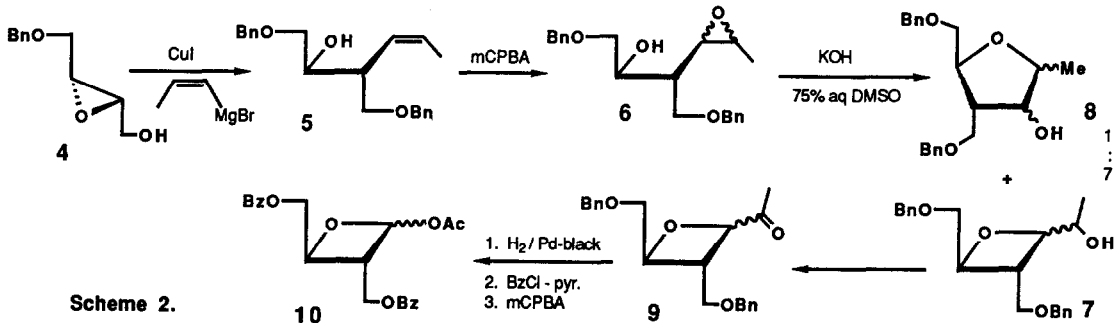
The known optically active epoxide (**4**)[3] was readily converted into the olefin-alcohol (**5**) (the geometry of the double bond was assigned as Z form from the values of J = 11Hz) in 3 steps [1) CH_3CH=$CHMgBr$(4eq), CuI(0.4eq) in THF-ether, -30°C, 5 h;[4] 2) $PhCH(OMe)_2$ (1.5eq), TsOH in toluene, reflux, 3 h; 3) DIBAL-H(5eq) in toluene, -60°C, 12 h: 68% overall yield], which was oxidized to the epoxy-alcohol (**6**)[5,6] [mCPBA(2eq) in CH_2Cl_2, 0°C, 2 h, 95%]. The crucial oxetane ring formation via intramolecular cyclization was performed in the following reaction conditions;[7] a mixture of **6** and KOH (10eq) in 75% aq. DMSO was heated at 150°C for 1 h to give the oxetane-alcohol (**7**)[6] in 62% yield along with the furan-alcohol (**8**) in 9% yield.[8] Then, **7** was oxidized to give a 5 : 4 mixture of 3,5-anhydro-D-arabino and D-ribo-hexitols (**9**) [SO_3-pyr(6eq), Et_3N(20eq) in DMSO, room temp., 2 h, 87%]. Finally, each stereoisomer of **9** was converted to the corresponding dibenzoates (**10**) in 3 steps [1) H_2/

Scheme 1.



R_1, R_2 = acyl groups

Pd-black in THF, room temp., 5 h; 2) BzCl(3eq) in pyr., 0°C, 3 h; 3) mCPBA in CH_2Cl_2, 0°C, 8 h: 73% overall yield]. Both stereoisomers so far obtained were identical with those of authentic samples[2] in all respects of spectral and chromatographical data. Thus, 1-O-acetyl-α and β-D-oxetanoses could be synthesized in 9 steps from **4** in 25% overall yield (Scheme 2).[9]

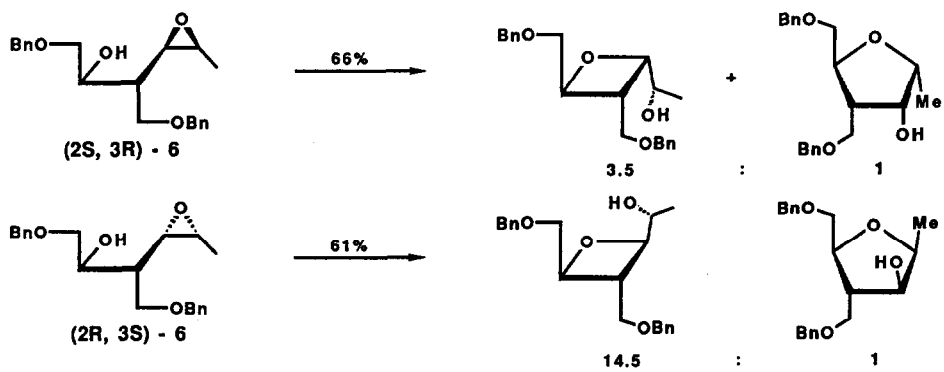


Scheme 2.

In conclusion, we believe that the route described herein can be of practical utility in the preparation of various oxetanocin analogues.

References

1. H. Nakamura, S. Hasegawa, N. Shimada, A. Fujii, T. Takita, and Y. Iitaka, J. Antibiot., **39**, 1629 (1986).
2. S. Nishiyama, S. Yamamura, K. Kato, and T. Takita, Tetrahedron Lett., **29**, 4739, 4743 (1988).
3. T. Katsuki, A. W. M. Lee, P. Ma, V. S. Martin, S. Masamune, K. B. Sharpless, D. Tuddenham, and F. J. Walker, J. Org. Chem., **47**, 1373 (1983).
4. M. A. Tius and H. Fauq, J. Org. Chem., **48**, 4132 (1983).
5. The ratio of (2S, 3R)-**6** to (2R, 3S)-**6** was 3 : 2.
6. Used to the next reaction without separation of the stereoisomers.
7. A. Murai, M. Ono, and T. Masamune, J. Chem. Soc. Chem. Commun., **1976**, 864.
8. Each stereoisomer of **6** was subjected to the same reaction conditions. It was found that the stereochemistry of the epoxide had a great effect on a cyclization mode.



The details of mechanistic aspects of these cyclization reactions will be reported in due course.

9. Both isomers could be available for the N-glycosidation. See ref. 2.

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