tonolysis of 3 that gives cyclohexanone, 4 reacts with HCl to give Cp_2ZrCl_2 and cyclohexene (GC/MS; ^1H NMR), demonstrating that the O-atom has not been transferred to a Zr-C bond in this complex.

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Supplementary Material Available: Experimental details and tables of atomic coordinates, bond angles and distances, anisotropic thermal parameters, and hydrogen atom coordinates (9 pages); table of observed and calculated structure factors (13 pages). Ordering information is given on any current masthead page.

Synthesis of (-)-Oxetanocin

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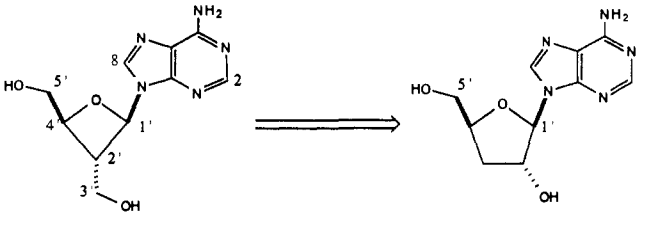
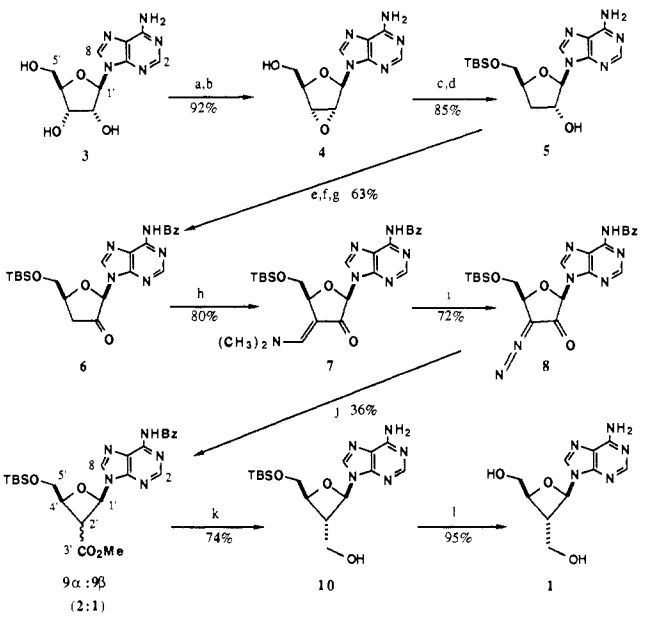
Oxetanocin inhibits the in vitro replication of human immunodeficiency virus (HIV), the causative agent of AIDS.[1,2] X-ray crystallographic analysis[3] of material produced by a strain of *Bacillus megaterium*[4] has established oxetanocin's structure as compound **1**. This unprecedented oxetanosyl-*N*-glycoside presents



1 **2**

new challenges in the synthesis of nucleosides[5] and branched chain carbohydrates.[6] These difficulties are evident in the 19-step Nippon Kayaku synthesis,[7,8] which produces oxetanocin in an overall yield of 0.008%. We report here an alternative synthesis of oxetanocin which should supply sufficient material for the elaboration and biological testing of derivatives.

Scheme I. Synthesis of (-)-Oxetanocin[a]



[a] (a) 2-Acetoxyisobutyryl bromide, CH_3CN; (b) resin$^+OH^-$, MeOH; (c) TBSCl, C_6H_5N; (d) $LiEt_3BH$, THF; (e) BzCl, C_6H_5N; (f) 1 N aqueous NaOH, 1,4-dioxane; (g) $CH_3CH_2NCN(CH_2)_3N(CH_3)_2HCl$, Cl_2CHCO_2H, DMSO, C_6H_6; (h) $(CH_3O)_2CHN(CH_3)_2$; (i) $CF_3SO_2N_3$; (j) $h\nu$, >280 nm, MeOH; (k) $NaBH_4$, EtOH; (l) TMSCl, MeOH.

Recognition of oxetanocin as a structural isomer of cordycepin (**2**)[9,10] suggested ring contraction as the pivotal synthetic transformation.

Although treatment of cordycepin with *tert*-butyldimethylsilyl chloride[11] in pyridine provided the nucleoside **5** directly, a more economical route utilized (-)-adenosine as the starting material. Thus, addition of 4.0 equiv of α-acetoxyisobutyryl bromide to a suspension of (-)-adenosine in acetonitrile containing 1.1 equiv of H_2O at room temperature followed by treatment of the ethyl acetate extract with BioRad AG-1-X8 (OH^-) resin in methanol afforded a 92% yield of crystalline 2',3'-anhydroadenosine (**4**) in the manner described by Robins.[12] Silylation of the 5'-hydroxyl group prior to reduction of the epoxide[13] with 4.0 equiv of $LiEt_3BH$ in THF at room temperature facilitated isolation of the required 3'-deoxynucleoside **5** in an overall yield of 85%. The corresponding 2'-deoxynucleoside was not detected. Treatment of compound **5** with 4.0 equiv of benzoyl chloride in pyridine for 3 h at room temperature gave a mixture of di- and tribenzoates, which, without purification, was selectively O-deacylated by aqueous 1 N NaOH in dioxane.[14] Moffatt oxidation[15] of the resulting N-protected alcohol was carried out in 1 h by adding 0.2 equiv of dichloroacetic acid every 15 min to 5.0 equiv of 1-ethyl-3-(3-(dimethylamino)propyl)carbodiimide hydrochloride dissolved in a 1:1 mixture of DMSO and benzene. After dilution with dichloromethane, the excess carbodiimide was easily removed by washing with water acidified to pH 3. Chromatography of the organic residue on silica gel with ethyl acetate/hexane afforded the ketone **6** in 63% overall yield from the alcohol **5**.

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Rapid, base-catalyzed epimerization at C-1′[16] precluded application of the standard formylation-diazo transfer protocol[17,18] to the preparation of diazoketone **8**. However, activation of the 3′-carbon was readily achieved by heating the ketone **6** in neat *N,N*-dimethylformamide dimethyl acetal at 60 °C for 15 min to give the enamino ketone **7** in 80% yield. The observation of NOE's[19] between H-1′ and H-4′ and H-5′ and H-8 verified that the stereochemistry at C-1′ had been preserved in this unusually facile reaction.[20] In contrast, diazo transfer[21a] to the enamine[21b] proved to be unusually difficult. After the enamine failed to react with excess tosyl azide in refluxing toluene, we were delighted to find that diazo transfer from triflyl azide[22] in 1,2-dichloroethane at 60 °C was complete in just 2 h. Application of the reaction mixture to a column of silica gel packed in ethyl acetate/hexane and elution with the same solvents (1:3 to 10:0) yielded the diazoketone **8** as a light yellow solid. Salient spectral features of this compound included a strong IR absorption at 2115 cm^{-1} ($C{=}N^{+}{=}N^{-}$), a doublet of doublets (J = 7.5 Hz, J' = 5.0 Hz) at 5.44 ppm assigned to the 4′ hydrogen, and an $(M + H)^{+}$ = 494.1971 (calcd mass for $C_{23}H_{28}N_7O_4Si$ = 494.1972). In the key step, irradiation of the diazoketone **8** in methanol with a 450-W, Pyrex-filtered, Hanovia lamp for 30 min at room temperature produced the oxetanes **9α** and **9β**, the products of Wolff rearrangement.[23-25] Separation of the diastereomeric oxetanes from each other and from the ketone **6** (12%)[26] and N^6-benzoyladenine (25%)[27] was achieved by chromatography on silica gel. NOE's between the 2′ and 5′ and 2′ and 8 protons established that the major diastereomer (**9α**, 24%, $[\alpha]^{25}_D$ −18.4° (*c* 1.58, $CHCl_3$)) possessed the all-trans stereochemistry of oxetanocin. The absence of these NOE's in the minor, all-cis diastereomer (**9β**, 12%, $[\alpha]^{25}_D$ +27.6° (*c* 1.01, $CHCl_3$)) and the presence of an NOE between the 8 and 5′ protons confirmed that the Wolff rearrangement had proceeded with complete retention of configuration.[28] Treatment of the major epimer with excess $NaBH_4$ in ethanol rapidly reduced the methyl ester and then, more slowly, effected N-debenzoylation to give the monoprotected alcohol **10** (74%), a valuable intermediate for further modification.[29] Addition of 1.7 equiv of trimethylsilyl chloride to a solution of **10** in methanol followed by neutralization with Dowex-SBR (OH^-) resin released oxetanocin (**1**) in nearly quantitative yield. The identity of the synthetic ($[\alpha]^{25}_D$ −41.3° (*c* 0.65, pyridine)) and natural ($[\alpha]^{20}_D$ −44.3° (*c* 0.21, pyridine))[4] material was established by direct comparison (TLC, MS, 300 MHz NMR) with an authentic sample. In particular, the chemical shifts of their ten ^{13}C NMR (125.8 MHz) resonances in D_2O differed by less than $\pm\overline{0.03}$ ppm. In summary, (−)-oxetanocin has been synthesized in 12 steps from adenosine in an overall yield of 5%. Application of this methodology to the preparation of pyrimidine analogues of oxetanocin is in progress.

Acknowledgment. We are grateful to Randal Chen for providing a sample of natural oxetanocin and Patricia Pavlik and David Whittern for assistance in obtaining spectral data.

Supplementary Material Available: Spectral and physical data for compounds **1** and **5–10** (3 pages). Ordering information is given on any current masthead page.

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The Structure of 1,4-Cyclohexadiene at 153 K

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The minimum energy conformation of 1,4-cyclohexadiene (1,4-dihydrobenzene)[1-8] has become a subject of renewed interest because of recent research on the structure of its cis and trans substituted and condensed ring derivatives.[9-14]

There are conflicting conclusions concerning the structure of the parent molecule in the gas phase. One electron diffraction study concluded that the molecule was planar or nearly planar,[3] but a later study[6] favored a nonplanar molecule with C_{2h} symmetry and a dihedral angle of 159° between the ethylene planes. The boat conformation was apparently favored,[9] although the vibration, rotational Raman, and NMR spectra were best interpreted as

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