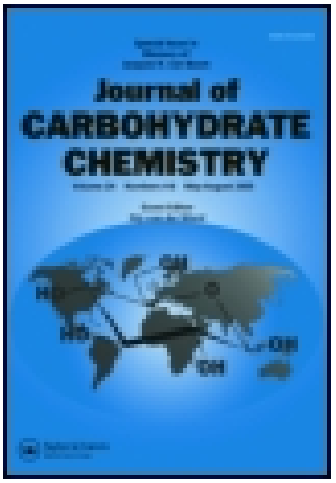

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Beckmann Rearrangement and Baeyer-Villiger Oxidation of N-Benzyl-2-C:1-N-Carbonyl-2-Deoxy-5,6-O-Isopropylidene-3-Keto-α-d-Ribofuranosylamine

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BECKMANN REARRANGEMENT AND BAEYER-VILLIGER OXIDATION OF *N*-BENZYL-2-*C*:1-*N*-CARBONYL-2-DEOXY-5,6-*O*-ISOPROPYLIDENE-3-KETO-α-D-RIBOFURANOSYLAMINE

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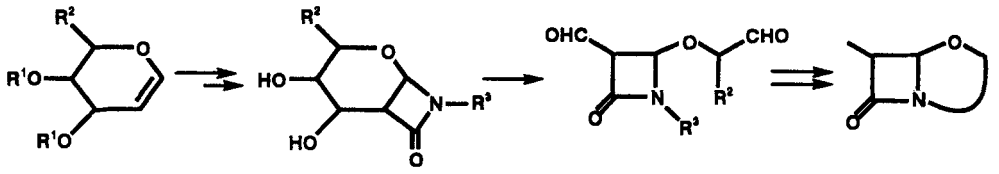
ABSTRACT

N-Benzyl-2-*C*:1-*N*-carbonyl-2-deoxy-5,6-*O*-isopropylidene-3-keto-α-D-ribohexofuranosylamine (**5**), available by [2+2]cycloaddition of trichloroacetyl isocyanate to 1,4-anhydro-3-*O*-benzyl-5,6-*O*-isopropylidene-D-*arabino*-hex-1-enitol (**1**), was subjected to Baeyer-Villiger oxidation, and after transformation into tosyloxyimino compound **14**, for Beckmann rearrangement to afford (1*S*, 3*S*, 6*R*, 4'*R*)- 8-aza-8-benzyl-3-(2',2'-dimethyldioxolanyl-4')-2,4-dioxa-5,7-dioxobicyclo[4.2.0]octane (**12**) and (1*S*, 3*R*, 6*R*, 4'*R*)-8-benzyl-5,8-diaza-3-(2',2'-dimethyldioxolanyl-4')-4-ethoxy-2-oxa-7-oxobicyclo[4.2.0]oct-4-ene(**15**), respectively. Model studies of both reactions were performed using related 3-keto-1,2:5,6-di-*O*-isopropylidene-α-D-ribohexofuranose (**6**).

INTRODUCTION

Ten years ago we initiated a synthetic project leading from glycals to 1-oxabicyclic ß-lactams[1] (Scheme 1). The general idea of the project was to synthesize clavams and 1-oxacephems. Reports from this work have recently been published.[2,3,4]



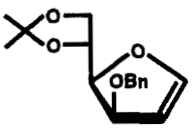
Scheme 1

Stereocontrolled transformations of benzylated galactal into clavam[2] and 1-oxacephem[3] skeletons have been a consequence of the specificity of [2+2]cycloaddition and suitable protection of the terminal hydroxymethyl group. This protection allowed for retainment of chirality at the carbon atom stemming from C-5 of the glycal molecule. In the first two syntheses[2,3] we did not discriminate between the carbon atoms which were split during the glycolic cleavage step. Our attempts at discrimination of the carbon atoms *via* oxidation of the dialdehyde to the dicarboxylic acid failed.[5] Decarboxylation of the group that was in a malonyl array with the ß-lactam carbonyl group was unsuccessful due to ß-elimination.[5] The discrimination of aldehyde groups obtained throughout the course of the glycolic cleavage step has been recently achieved by trapping one of them by an intra-molecular Wittig cyclization.[4]

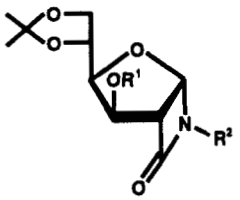
The opening of a sugar ring by other means, such as a retro aldol, Beckmann rearrangement, or Baeyer-Villiger oxidation eliminates the need for discrimination between carbon atoms which are split in the course of glycolic cleavage of the pyranoside ring, and enables opening of the furanoid ring. In the present paper we report on opening of a sugar ring by a Beckmann rearrangement and by a Baeyer-Villiger oxidation.

RESULTS AND DISCUSSION

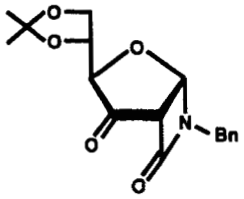
As a model for our studies we selected *N*-benzyl-2-*C*:1-*N*-carbonyl-2-deoxy-5,6-*O*-isopropylidene-α-D-glucofuranosylamine (**4**), readily available from [2+2]cycloadduct of trichloroacetyl isocyanate to furanoid glycal **1**.[6] The standard sequence of *N*-benzylation followed by deprotection of the 3-*O*-benzyl group transformed **2** into **4**. Compound **4** was oxidized to *N*-benzyl-2-*C*:1-*N*-carbonyl-2-deoxy-5,6-*O*-isopropylidene-3-keto-α-D-ribohexofuranosylamine (**5**) using a standard procedure.



1



2 : R^1 = Bn , R^2 = H
3 : R^1 = R^2 = Bn
4 : R^1 = H , R^2 = Bn



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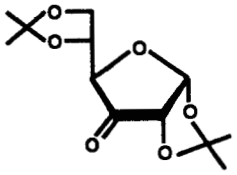
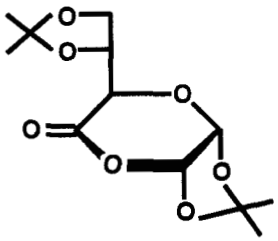


6

Prior to these investigations we decided, however, to examine both reactions using 1,2:5,6-di-*O*-isopropylidene-3-keto-α-D-ribohexofuranose (**6**) derived from 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose.[7] Baeyer-Villiger oxidation of **6** is a known reaction, using *m*-chloroperbenzoic acid[8] or ruthenium tetroxide[8,9] as oxidants to afford the same cyclic ester **7**.



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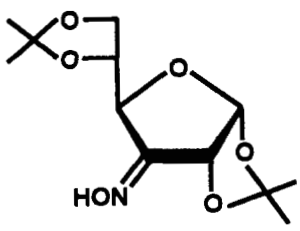
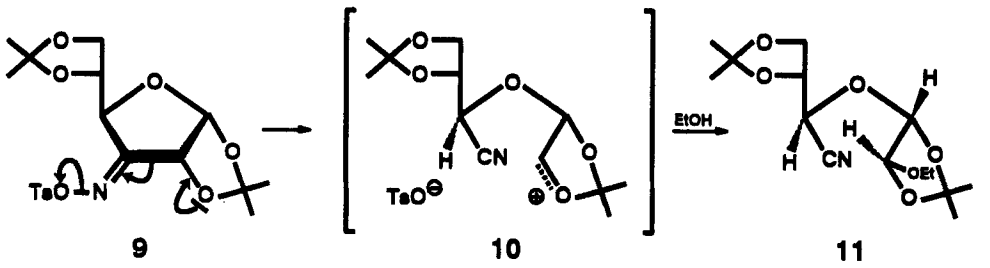


8

Beckmann rearrangement required formation of the known oxime **8** which was subsequently transformed into tosylate **9**. The rearrangement was performed in anhydrous ethanol in the presence of triethylamine. Introduction of water to the reaction mixture caused partial decomposition of the substrate and lowered the yield. Owing to the participation of the unshared electron pair at the O-2 sugar oxygen atom, the base-promoted rearrangement led to formation of (4′*R*, 5′*R*)-3,4-*O*-isopropylidene-2-*O*-(4′-ethoxy-2,2-dimethyldioxolanyl-5)-D-erythrotetrononitrile (**11**) as a single product (Scheme 2). This "abnormal" Beckmann rearrangement has been reported in the past for oximes having an α-heteroatom.[10]

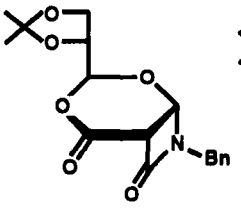


Scheme 2

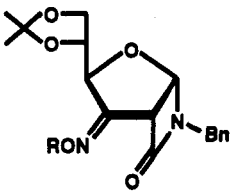
The structure of **11** was proven by X-ray crystallography (*cf* Experimental). Trapping of an ethanol molecule from the solvent and formation of the *trans* substituted dioxolane strongly suggested **10** as an intermediate.

Ketone **5** subjected to Baeyer-Villiger oxidation provided ester **12**. Breaking of the sugar ring took place between C-3 and C-4 carbon atoms, as with glycolic cleavage which is depicted in Scheme 1. This means that after opening of the cyclic ester **12**, the carboxylic function would be placed at C-3 of the azetidin-2-one ring. In order to perform the Beckmann rearrangement ketone **5** was transformed into oxime **13** which in turn was tosylated to give *N*-benzyl-2-*C*:1-*N*-carbonyl-2,3-dideoxy-5,6-*O*-isopropylidene-3-tosyloxyimino-α-D-ribohexofuranosylamine (**14**). In contrast to **9**, tosylate **14** was relatively stable and the rearrangement could be done to give (1*S*, 3*R*, 6*R*, 4′*R*)-8-benzyl-5,8-diaza-3-(2′,2′-dimethyldioxolanyl-4′)-4-ethoxy-2-oxa-7-oxobicyclo[4.2.0]oct-4-ene (**15**) using sodium ethoxide in ethanol solution. Attempts to perform rearrangement in the presence of water or to hydrolyze **15** to the amide **16** failed, causing decomposition of the substrate.

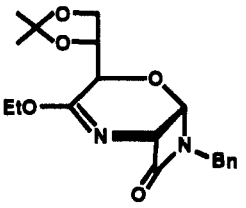
Although Beckmann rearrangement of the tosylate **14** led to the expected regiochemistry and introduced an amino function at the C-3 of the azetidin-2-one ring, the final product **15** was found not to be stable enough to afford an attractive intermediate for synthesis of ß-lactam antibiotics.



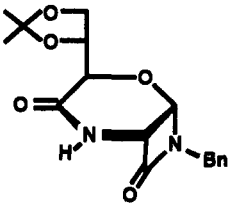
12



13 : R = H
14 : R = Ts



15



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EXPERIMENTAL.

Melting points are uncorrected. Optical rotations were measured with a JASCO DIP-360 digital polarimeter. IR spectra were taken with a Perkin-Elmer FT-IR-1600 spectrophotometer. ^{1}H NMR and ^{13}C NMR spectra were recorded with Varian Gemini 200 and Brucker AM 500 spectrometers. MS, low and high resolution EI and LSIMS mass spectra were performed using AMD 604. Column chromatography was performed on Merck Kieselgel (230-400 mesh).

Compound **2** was obtained from **1**[11] according to the known procedure.[6]

***N*-Benzyl-3-*O*-benzyl-2-*C*:1-*N*-carbonyl-2-deoxy-5,6-*O*-isopropylidene-α-D-glucofuranosylamine (3).** Compound **2** (0.1 g, 0.31 mmol) in benzene (10 mL) was treated with anhydrous K_2CO_3 (0.5 g), benzyl bromide (100 μL, 0.144 g, 0.84 mmol) and tetrabutylammonium bromide (0.05 g, 0.15 mmol). The mixture was stirred and refluxed until disapearance of the substrate (1 h). Subsequently, it was filtered, concentrated and purified on a silica gel column using hexane - ethyl acetate 2.5 : 1 $^{v}/_{v}$ as an eluent to afford **3** (0.078 g, 61%); mp 85-86 °C; $[\alpha]_D$ +18° (*c* 1, CH_2Cl_2); IR (nujol) 1745 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.36 (s, 6H, isopr.), 3.66 (dd, 1H, *J* 5.17 and 8.6 Hz, H-6), 3.81 (d, 1H, *J* 2.9 Hz, H-2), 3.86 (dd, 1H, *J* 3.6 and 7.4 Hz, H-4), 4.01 (dd, 1H, *J* 6.4 and 8.6 Hz, H-6'), 4.25 (d, 1H, *J* 3.6 Hz, H-3), 4.31 (s, 2H, NBn), 4.39 (m, 1H, H-5), 4.53, 4.59 (2d, 2H, *J* 11.1 Hz, OBn), 5.55 (d, H, *J* 2.9 Hz, H-1); MS (EI) *m/z* : $(M\text{-}CH_3)^+$, 394.

Anal. Calcd for $C_{24}H_{27}NO_5$: C, 70.40; H, 6.65; N, 3.42. Found: C, 70.2; H, 6.6; N, 3.6.

***N*-Benzyl-2-*C*:1-*N*-carbonyl-2-deoxy-5,6-*O*-isopropylidene-α-D-glucofuranosylamine (4).** Compound **3** (0.028 g, 0.068 mmol) was hydrogenated in methanol (5 mL) over 10% Pd/C for 5 h. The catalyst was filtered off and the solvent was evaporated. The residue was crystallized from ethyl acetate - hexane to give **4** (0.02 g, 92%); mp 129-130 °C; $[\alpha]_D$ +27° (*c* 0.5, CH_2Cl_2); IR (nujol) 3425, 3178, 1750 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.34, 1.38 (2s, 6H, isopr.), 3.63 (dd, 1H, *J* 4.8, 8.6 Hz, H-6), 3.72 (d, 1H, *J* 2.9 Hz, H-2), 3.74 (dd, 1H, *J* 3.3, 8.3 Hz, H-4), 4.05 (dd, 1H, *J* 6.2, 8.6 Hz, H-6'), 4.28 (m, 1H, H-5), 4.30 (s, 2H, NBn), 4.55 (d, 1H, *J* 3.3 Hz, H-3), 5.57 (d, 1H, *J* 2.9 Hz, H-1); MS (EI) *m/z* : $(M+H)^+$, 320.

Anal. Calcd for $C_{31}H_{33}NO_5$: C, 63.94; H, 6.62; N, 4.38. Found: C, 63.7; H, 6.8; N, 4.4.

***N*-Benzyl-2-*C*:1-*N*-carbonyl-2-deoxy-5,6-*O*-isopropylidene-3-keto-α-D-ribohexofuranosylamine (5).** Compound **4** (0.2 g, 0.62 mmol) was dissolved in CH_2Cl_2 (10 mL) and treated with pyridinium chlorochromate (1.0 g, 4.64 mmol) and pulverized molecular sieves A4. The mixture was stirred for 2 h. Subsequently, the solvent was evaporated and the residue was extracted with toluene. The extract was passed through Celite and concentrated The crude residue was purified by chromatography using hexane - ethyl acetate 1 : 1 $^v/_v$ to afford **5** (0.14 g, 72%); mp 82-83 °C; $[\alpha]_D$ + 373° (*c* 0.5, CH_2Cl_2); IR (CCl_4) 1794, 1754 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.34, 1.37 (2s, 6H, isopr.), 3.92 (d, 1H, *J* 2.9 Hz, H-2), 3.95 (m, 2H, H-66'), 4.34, 4.57 (2d, 2H, *J* 15.0 Hz, NBn), 4.35 (m, 2H, H-4,5), 5.71 (d, 1H, *J* 2.9 Hz, H-1); MS (EI, HR) *m/z* : $(M-CH_3)^+$ calcd for $C_{16}H_{16}NO_5$: 302.10284. Found: 302.10287.

Anal. Calcd for $C_{17}H_{19}NO_5$: C, 64.34; H, 6.03; N, 4.41. Found: C, 64,3; H, 6.0; N, 4.4.

3-Deoxy-1,2:5,6-di-*O*-isopropylidene-3-tosyloxyimino-α-D-ribohexofuranose (9). Oxime **8** (0.15 g, 0.55 mmol) was dissolved in toluene (7 mL) and treated with pulverized NaOH (1.0 g) and tosyl chloride (0.12 g, 0.63 mmol). The mixture was stirred for 30 min, then filtered through Celite and concentrated. The residue was washed with hexane to give unstable **9** (0.195 g, 83%); ^1H NMR (C_6D_6) δ 1.16, 1.18, 1.20, 1.24 (4s, 12H, isopr.), 1.79 (s, 3H, Ts), 3.53 (dd, 1H, *J* 6.9, 8.4 Hz, H-6), 3.67 (dd, 1H, *J* 7.3, 8.4 Hz, H-6'), 4.00 (dt, 1H, *J* 2.4, 6.9, 7.3 Hz, H-5), 4.36 (dd, 1H, *J* 1.3, 2.4 Hz, H-4), 4.80 (dd, 1H, *J* 1.3, 4.2 Hz, H-2), 5.67 (d, 1H, *J* 4.2 Hz, H-1), 6.69, 7.91 (2d, 4H, Ts).

(4'*R*, 5'*R*) 3,4-*O*-isopropylidene-2-*O*-(4'-ethoxy-2,2-dimethyldioxolanyl-5)-D-erythrotetrononitrile (11). Compound **9** (0.195 g, 0.45 mmol) in anhydrous ethanol (10 mL) and triethylamine (3 mL) was stirred and refluxed for 2 h. Subsequently the solvent was carefully evaporated. The residue was extracted with toluene and the solvent was evaporated to afford 0.16 g of crude product. Crystallization using toluene - ethyl acetate 100 : 5 $^{v}/_{v}$ gave **11** (0.07 g, 51%); mp 74-76 °C; $[\alpha]_D$ -78° (*c* 5, CH_2Cl_2), Raman shift 2243 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.21 (t, 3H, Et), 1.37, 1.46, 1.51, 1.58 (4s, 12H, isopr.), 3.49, 3.77 (2dq, 2H, Et), 3.99 (dd, 1H, *J* 4.3, 9.2 Hz, H-4), 4.12 (dd, 1H, *J* 6.2, 9.1 Hz, H-4'), 4.26 (d, 1H, *J* 6.2 Hz, H-2), 4.33 (dt, 1H, H-3), 5.13 (s, 1H, H-2), 5.22 (s, 1H, H-1); MS (EI, HR) *m/z* : $(M\text{-}CH_3)^+$ calcd for $C_{13}H_{20}NO_6$: 286.12906. Found: 286.12897.

Anal. Calcd for $C_{14}H_{23}NO_6$: C, 55.80; H, 7.69; N, 4.64. Found: C, 55.9; H, 7.9; N, 4.6.

X-Ray Structure determination of compound 11. Unit cell parameters obtained by the least-squares fit of 25 reflections on a four-circle CAD4 diffractometer are: a = 5.552(1), b = 12.112.(2), c = 24.409(3) Å, α = β = γ = 90 °, V = 1641.3(4) $Å^3$. Orthorhombic $P2_12_12_1$ space group with 4 molecules in the unit cell was assigned on the basis of systematic extinctions; d_{calc} = 1.219 Mg m^{-3}. 1699 independent reflections have been collected in the θ range 3.62 - 74.76 °, using monochromatized CuK_α radiation and θ/2θ scanning mode.

The structure was solved by direct methods with the use of SHELXS86 program[12] and refined by the full-matrix least squares procedure of the SHELXL93 program.[13] Hydrogen atoms were found from the difference maps and their positions and B_{iso} parameters were refined. The absolute configuration has been assigned on the basis of the known asymmetric centres. The substituents at the C1-C2 bond have the *trans* configuration (O1-C1-C2-O4 torsion angle is 153.8(2) °).

(1*S*, 3*S*, 6*R*, 4'*R*)- 8-Aza-8-benzyl-3-(2',2'-dimethyldioxolanyl-4')-2,4-dioxa-5,7-dioxobicyclo[4.2.0]octane (12). Compound **5** (0.034 g, 0.11 mmol) in acid and ethanol-free chloroform (5 mL) was treated with sodium bicarbonate (0.3 g) and 55% *m*-chloroperbenzoic acid (0.12 g, 0.38 mmol). The reaction mixture was stirred for 1 h. Subsequently, it was filtered and the precipitate was washed with chloroform. The chloroform solution was washed with sodium bisulfite and sodium bicarbonate, dried and

Table 1. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$ x 10^3) for **11**. U_{eq} is defined as one third of the trace of the orthogonalized U_{ij} tensor.

	x	y	z	U_{eq}
O(1)	8058(3)	6933(2)	7609(1)	51(1)
O(2)	7850(4)	5826(2)	8392(1)	59(1)
O(3)	4169(4)	6647(2)	8394(1)	53(1)
O(4)	6451(4)	7891(2)	8914(1)	64(1)
O(5)	12673(4)	7091(3)	6029(1)	74(1)
O(6)	9042(3)	7107(2)	6460(1)	60(1)
C(1)	8117(5)	6891(3)	8186(1)	50(1)
C(2)	5909(5)	7495(2)	8390(1)	51(1)
N(3)	9013(9)	4401(2)	7067(1)	85(1)
C(4)	9464(6)	5279(3)	7193(1)	59(1)
C(5)	10061(5)	6432(2)	7357(1)	49(1)
C(6)	10843(5)	7119(3)	6868(1)	51(1)
C(7)	13052(6)	6695(3)	6567(2)	64(1)
C(8)	10149(6)	7065(3)	5931(1)	59(1)
C(9)	9476(10)	8080(5)	5615(2)	86(1)
C(10)	9372(14)	6016(5)	5654(2)	90(1)
C(11)	5345(5)	5631(3)	8514(1)	58(1)
C(12)	5157(9)	5366(5)	9128(2)	83(1)
C(13)	4350(8)	4750(3)	8152(2)	76(1)
C(14)	4533(10)	8514(4)	9156(2)	81(1)
C(15)	5257(15)	8796(6)	9725(2)	100(2)

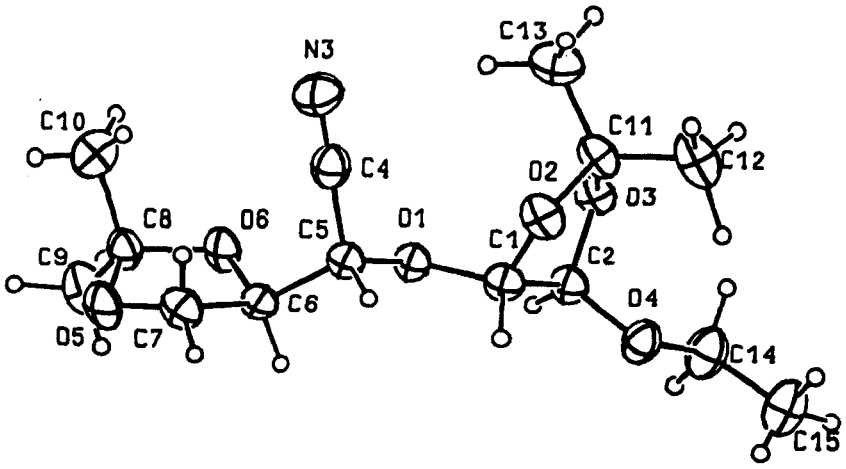

Fig. 1. ORTEP diagram of compound **11.**

concentrated. The crude product was crystallized from a chloroform-hexane mixture to afford **12** (0.03 g, 84%), mp 167-168 °C; $[\alpha]_D$ + 139° (*c* 0.5, CH_2Cl_2); IR ($CHCl_3$) 1791, 1761 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.35, 1.39 (2s, 6H, isopr.) 3.61 (dd, 1H, *J* 5.5, 9.0 Hz, H-5'a), 3.95 (dd, 1H, *J* 6.9, 9.0 Hz, H-5'b), 4.16 (dd, 1H, *J* 4.3, 5.5, 6.9 Hz, H-4'), 4.20 (d, 1H, *J* 3.8 Hz, H-6), 4.40, 4.45 (2d, 2H, *J* 14.8 Hz, NBn), 5.30 (dd, 1H, *J* 0.4, 4.3 Hz, H-3), 5.55 (dd, 1H, *J* 0.4, 3.8 Hz, H-1); ^{13}C NMR ($CDCl_3$), 25.08, 26.15 (2Me), 45.74 (Bn), 55.25 (C-6), 64.25 (C-5'), 74.76 (C-4'), 78.38 (C-1), 92.95 (C-3), 110.81 (C-2'), 128.62, 128.72, 129.27, 134.07 (Bn), 156.95 (C-7), 160.16 (C-5); MS (EI, HR) *m/z*, $(M-CH_3)^+$ calcd for $C_{16}H_{16}NO_6$: 318.09776. Found: 318.09792; $M^{+\cdot}$ calcd for $C_{17}H_{19}NO_6$: 333.12123. Found 333.12101.

Anal. Calcd for $C_{17}H_{19}NO_6$: C, 61.25; H, 5.74; N, 4.20. Found: C, 61.2; H, 5.8; N, 4.2.

***N*-Benzyl-2-*C*:1-*N*-carbonyl-2,3-dideoxy-3-hydroxyimino-5,6-*O*-isopropylidene-α-D-ribohexofuranosylamine (13).** Compound **5** (0.045 g, 014 mmol) was dissolved in ethanol (3 mL) and pyridine (1 mL) and treated with hydroxylamine hydrochloride (0.25 g, 3.6 mmol). The mixture was stirred for 3 h. Subsequently, the solvent was evaporated and the residue was extracted with toluene. The extract was filtered through Celite and concentrated. The crude product was dissolved in ethyl acetate, treated with hexane to

become cloudy and left overnight. The product was separated to afford **13** (0.032 g, 68%), mp 112-113 °C; $[\alpha]_D$ + 362° (*c* 0.5, CH_2Cl_2); IR (CCl_4) 1778, 1758 cm^{-1}; ^1H NMR ($CDCl_3$) major isomer (87%), δ 1.36, 1.41 (2s, 6H, isopr.), 3.83 (dd, 1H, *J* 5.8, 8.5 Hz, H-6), 4.00 (dd, 1H, *J* 6.7, 8.5 Hz, H-6'), 4.30, 4.51 (2d, 2H, *J* 15.0 Hz, NBn), 4.35 (m, 1H, H-5), 4.62 (dd, 1H, *J* 1.3, 4.9 Hz, H-4), 4.67 (dd, 1H, *J* 1.3, 3.0 Hz, H-2), 5.56 (d, 1H, *J* 3.0 Hz, H-1), 8.12 (s, 1H, OH); minor isomer (13%), δ 1.35, 1.42 (2s, 6H, isopr.), 3.78 (dd, 1H, *J* 6.6, 8.3 Hz, H-6), 3.97 (dd, 1H, *J* 6.9, 8.3 Hz, H-6'), 4.19, 4.62 (2d, 2H, *J* 14.9 Hz, NBn), 4.18 (dd, 1H, *J* 1.4, 3.4 Hz, H-2), 4.84 (dt, 1H, *J* 2.8, 6.6, 6.9 Hz, H-5), 5.27 (dd, 1H, *J* 1.4, 2.8 Hz, H-4), 5.61 (d, 1H, *J* 3.4 Hz, H-1); MS (EI, HR) *m/z*, $(M\text{-}CH_3)^+$ calcd for $C_{16}H_{17}NO_5$ 317.11374. Found: 317.1140.

Anal. Calcd for $C_{17}H_{20}N_2O_5$: C, 61.43; H, 6.06; N, 8.42. Found: C, 61.4; H, 6.0; N, 8.3.

***N*-Benzyl-2-*C*:1-*N*-carbonyl-2,3-dideoxy-5,6-*O*-isopropylidene-3-tosyloxyimino-α-D-ribohexofuranosylamine (14).** Compound **13** (0.04 g, 0.12 mmol) was dissolved in toluene (4 mL) and upon stirring it was treated with pulverized NaOH (0.3 g) and tosyl chloride (0.025 g, 0.13 mmol). After 10 min the mixture was passed through Celite and concentrated. The residue was extracted with hexane to remove an excess of tosyl chloride. The remaining syrup was dissolved in toluene (0.5 mL), treated with hexane to become cloudy and left overnight. Crystals of **14** (0.043 g, 73%) were separated; mp 124-125 °C; $[\alpha]_D$ + 306° (*c* 0.5, CH_2Cl_2); IR ($CHCl_3$) 1775 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.33, 1.34 (2s, 6H, isopr.), 2.45 (s, 3H, Ts), 3.74 (dd, 1H, *J* 6.4, 8.4 Hz, H-6), 3.89 (dd, 1H, *J* 6.8, 8,4 Hz, H-6'), 4.22, 4.49 (2d, 2H, *J* 15.0 Hz, NBn), 4.39 (dt, 1H, *J* 2.9, 6.4, 6.8 Hz, H-5), 4.65 (dd, 1H, *J* 1.1, 2.9 Hz, H-4), 4.76 (dd, 1H, *J* 1.1, 3.0 Hz, H-2), 5.57 (d, 1H, *J* 3.0 Hz, H-1); MS (LSIMS) *m/z*, $(M+H)^+$ 487.

Anal. Calcd for $C_{24}H_{26}N_2O_7S$: C, 59.24; H, 5.39; N, 5.75. Found: C, 59.3; H, 5.4; N, 5.7.

(1*S*, 3*R*, 6*R*, 4'*R*)- 8-Benzyl-5,8-diaza-3-(2',2'-dimethyldioxolanyl-4')-4-ethoxy-2-oxa-7-oxobicyclo[4.2.0]oct-4-ene (15). Compound **14** (0.035 g, 0.072 mmol) was dissolved in anhydrous ethanol, cooled to 0 °C and treated with 6% sodium ethoxide in ethanol (0.5 mL). The mixture was stirred till the substrate was dissolved (about 1 min). Subsequently, toluene (10 mL) was added, the solution was saturated with carbon dioxide,

passed through Celite and concentrated. The residue was extracted with hexane, passed through Celite, and concentrated to afford the crude product **15** (0.023 g, 88%). Further purification on a silica gel column using hexane - ethyl acetate 3 : 2 $^{v}/_{v}$ led to substantial loss of the product (40% yield); $[\alpha]_D$ + 107° (*c* 0.1, CH_2Cl_2); IR (film) 1769, 1708, 1656, 1621 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.26 (t, 3H, Et), 1.36, 1.43 (2s, 6H, isopr.), 3.85 (dd, 1H, *J* 6.1, 8.3 Hz, H-5'a), 4.00 (dd, 1H, *J* 7.1, 8.3 Hz, H-5'b), 4.11 (d, 1H, *J* 3.1 Hz, H-3), 4.18 (m, 2H, Et), 4.24, 4.52 (2d, 2H, *J* 14.7 Hz, Bn), 4.60 (dt, 1H, *J* 3.1, 6.1, 7.1 Hz, H-4'), 4.80 (d, 1H, *J* 3.6 Hz, H-6), 5.21 (d, 1H, *J* 3.6 Hz, H-1); ^{13}C NMR ($CDCl_3$) : 13.94 (Et), 25.21, 26.00 (2Me), 44.39 (Bn), 61.75 (Et), 64.66 (C-6), 64.78 (C-5'), 65.74 (C-3), 74.40 (C-4'), 77.71 (C-7), 109.85 (C-2'); MS (LSIMS, HR) *m/z*, $(M+H)^+$ calcd for $C_{19}H_{25}N_2O_5$: 361.17634. Found: 361.17592.

Anal. Calcd for $C_{19}H_{24}N_2O_5$: C, 63.32; H, 6.71; N, 7.77. Found: C, 63.6; H, 7.0; N, 7.5.

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