Available online at www.sciencedirect.com
SCIENCE DIRECT®
Carbohydrate Research 338 (2003) 673–680
CARBOHYDRATE RESEARCH
www.elsevier.com/locate/carres

Note

Synthesis of new branched-chain amino sugars

João R. de Freitas Filho,[a] Rajendra M. Srivastava,[a,*] Waldenberg J.P. da Silva,[a] Louis Cottier,[b] Denis Sinou[b]

[a]*Departamento de Química Fundamental, Universidade Federal de Pernambuco Cidade Universitária, CCEN, 50.740-540, Recife, PE, Brazil*
[b]*Laboratoire de Synthèse Asymetrique, associe au CNRS, CPE Lyon, Université Claude Bernard Lyon 1, 43, boulevard du 11 novembre 1918, F-69622 Villeurbanne, France*

Received 27 December 2001; received in revised form 6 November 2002; accepted 10 December 2002

Abstract

1,3-Dipolar cycloaddition of methylideneaniline *N*-oxide to sugar enones is described. The addition occurred exclusively from the side opposite to the aglycone affording the corresponding alkyl α-D-*lyxo*-hexopyranosid-(2,3:5′,4′)-phenylisoxazolidin-4-uloses. Hydrogenation of these compounds readily yielded the corresponding alkyl 3-deoxy-3-*N*-phenylaminomethyl-α-D-talopyranoside, that were readily transformed to the acetates. The structure and conformation of the bicyclic compounds were determined by ^{1}H NMR studies and semi-empirical molecular orbital calculations employing the AM1 method.

Keywords: Amino sugars; Cycloaddition; Nitrone

1. Introduction

Amino sugars are constituents of many biologically active compounds, such as antibiotics,[1,2] and biopolymers.[3] It is known that the relative stereochemistry of the functional groups in natural and unnatural amino sugars plays an important role on the activity profile of the anthracycline.[4] So there has been a great interest in the development of efficient syntheses of these target molecules.

We then focused our attention to the synthesis of amino sugars in a rather simple manner. It has been shown that carbohydrate molecules possessing the enone functionality are the preferred precursors for the synthesis of branched-chain and rare sugars.[5–10]

As 1,3-dipolar cycloaddition of nitrones has been used as a route to amino sugars,[11–13] the addition of methylideneaniline *N*-oxide (or simply referred as a nitrone) to α,β-unsaturated carbonyl compounds derived from sugars has been examined to a limited extent and therefore opens a new way for the functionalization of sugar molecules.[14] In fact, N–O bond in this bicyclic system can readily be cleaved to yield the branched-chain amino sugars. We describe herein a novel and potentially adaptable methodology for the synthesis of isoxazolidino–pyranosidulose system which can readily be transformed to branched-chain amino sugars.

2. Results and discussion

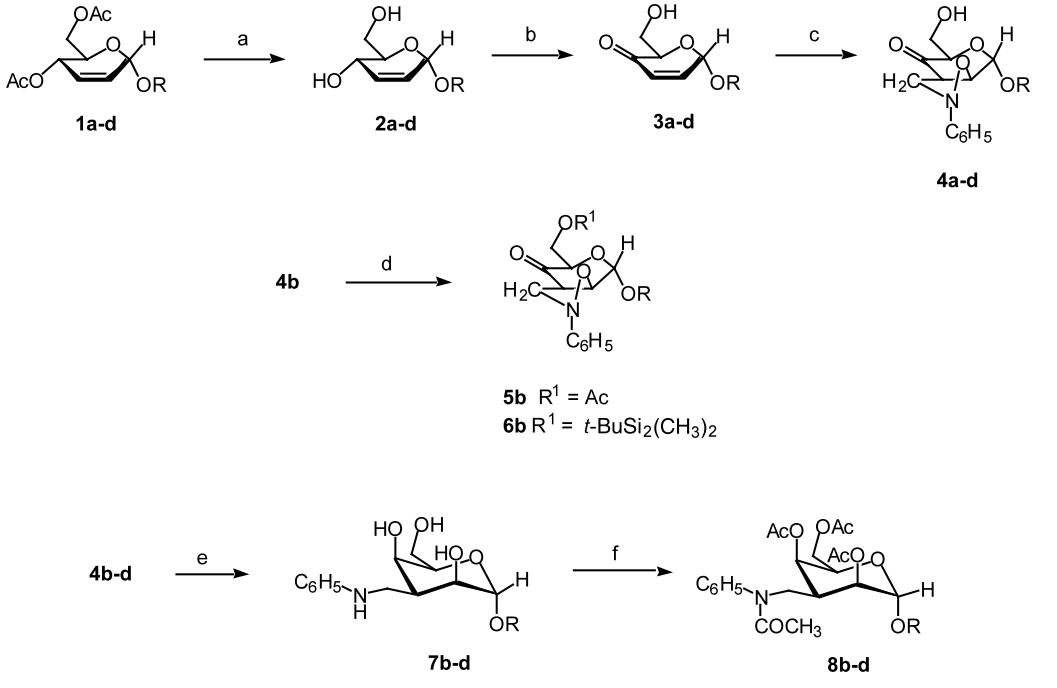
The synthetic route to these amino sugars is described in Scheme 1. The starting unsaturated glycosides **1a**–**d** were prepared by allowing 3,4,6-tri-*O*-acetyl-1,5-anhydro-2-deoxy-D-*arabino*-hex-1-enitol(tri-*O*-acetyl-D-glucal) to react with an appropriate alcohol in the presence of montmorillonite K-10 catalyst.[15,16] This simple procedure provided only α anomers of **1a**–**d**. Deacetylation of alkyl 4,6-di-*O*-acetyl-2,3-dideoxy-α-D-*erythro*-hex-2-enopyranosides (**1a**–**d**), according to the method of Fraser-Reid et al.[5] furnished compounds **2a**–**d**, which in turn were subjected to allylic oxidation at C-4 with activated MnO_2 to afford enones **3a**–**d**. The enones are important precursors for amino and other sugars. Addition of methylideneaniline *N*-oxide[17] to **3a**–**d** gave a

* Corresponding author. Tel.: +55-81-32718440; fax: +55-81-32718442
E-mail address: rms@npd.ufpe.br (R.M. Srivastava).

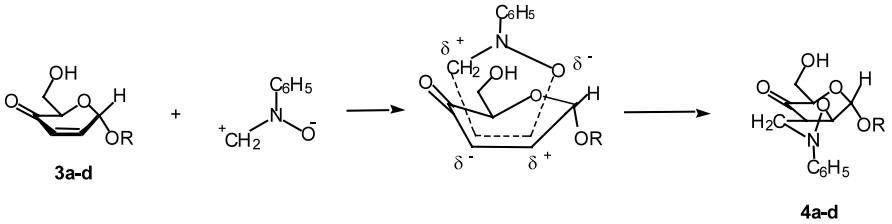
0008-6215/03/$ - see front matter
doi:10.1016/S0008-6215(02)00527-X

cycloadduct **4a**–**d** in moderate yields. The addition of the nitrone to C-2–C-3 double bond in **3a**–**d** occurred from the opposite site of the aglycone to afford isoxazolidines **4a**–**d** exclusively via the transition state shown in Scheme 2.

The structures and configurations of products **4a**–**d** have been deduced through their ^{1}H NMR spectra. Compound **4b** has been chosen for examination by 300 MHz ^{1}H NMR spectroscopy in order to deduce the configuration and conformation of this bicyclic compound. The signal for H-1 appeared as a broad singlet at δ 5.18 ppm. According to the molecular model, the *lyxo* configuration gives a dihedral angle of about 100° between the two hydrogens H-1 and H-2. This means that there should be a small coupling between the two protons referred just now. This fact became apparent when we irradiated H-1, which caused the proton at δ 4.35 ppm to become a sharp doublet (J 8.40 Hz) and there was a loss of ≤ 1.0 Hz or less coupling indicating it to be H-2. This large J value clearly supports a cis relationship between H-2 and H-3. Another interesting feature supporting the *lyxo* configuration is that H-3 appeared at a lower field (δ 3.40 ppm) than expected (approx δ 2.50 Hz); this is demonstrative that the oxygen atom at C-1 and H-3 are axial and this could cause the anisotropic effect and result in a downfield shift for H-3. Alternatively, the molecular model of the *ribo* configuration gives a dihedral angle of $\sim 60°$ or less between H-1 and H-2, giving a $J_{1,2}$ value of about 3.0 Hz or more; this has not been observed. Also, H-3 will not experience the anisotropic effect of the C-1 oxygen atom in the *ribo* configuration. We therefore infer that the configuration was *lyxo* and not *ribo* in **4b**, and the same was true for other compounds **4a**, **c**, and **d** of this series. In spite of our best efforts, it was not possible to detect and isolate the compounds having the *ribo* configuration. Similar results have been observed before in the cycloaddition of nitrones to a α,β-unsaturated sugar lactone.[14]



Scheme 1. Reagents and conditions: (a) MeOH–water–Et_3N, r.t.; (b) MnO_2, $CHCl_2$, r.t.; (c) methylideneaniline *N*-oxide; (d) Ac_2O, C_5H_5N, r.t. for **5b**; $ClSiMe_2t$-Bu, DMF, imidazole, 0 °C for **6b**; (e) H_2 (101 kPa) PtO_2, EtOAc, r.t.; (f) Ac_2O, C_5H_5N, r.t.



Scheme 2. Transition state in the addition of nitrone to **3a**–**d**.

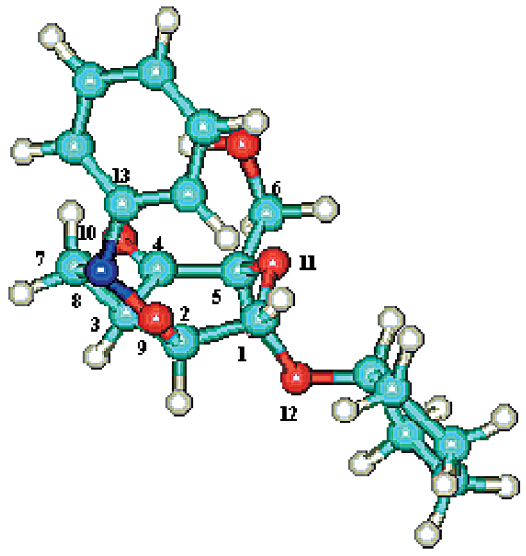


Fig. 1. Structure and more stable conformation of **4b** obtained using the AM1 method.

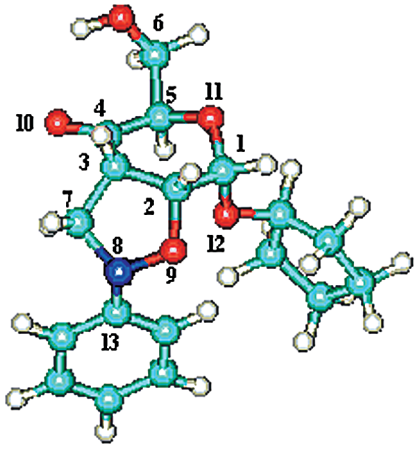


Fig. 2. Structure and more stable conformation of **4b′** obtained using the AM1 method.

Since compounds **4a**–**d** were not crystalline, it was not possible to collect crystallographic data for determining their configurations. So, we prepared the *O*-acetyl and *O*-*tert*-butyldimethylsilyl derivatives **5b** and **6b** from **4b** with the hope to get crystals. Although we got effectively fine crystals, they were not suitable for X-ray analysis.

Hydrogenation of compounds **4b**–**d** using PtO_2 as a catalyst under 1.5 atmosphere of hydrogen resulted in simultaneous cleavage of the N–O bond of the isoxazolidine system and the reduction of the C=O bond to provide **7b**–**d**. The structures of 3-deoxy-*N*-phenylaminomethyl-α-D-talopyranoside (**7b**–**d**) were deduced from the ^{1}H NMR spectra. For example, the anomeric proton of compound **7b** presented a small coupling constant (approx 1.3 Hz) between H-1 and H-2 suggesting an α anomeric configuration. The proton signal of H-4 appeared at δ 3.65 ppm as a broad singlet. Since, the J value between H-4 and H-5 is small (J 3.0 Hz), it is inferred that the OH group at C-4 is axial indicating a *talo* configuration for **7b**–**d**. Moreover, the two-dimensional ^{1}H–^{1}H NMR spectrum clearly showed that H-4 (δ 3.65 ppm) is coupled with H-5 at δ 3.74 and H-3 at δ 2.13 ppm. ^{1}H NMR spectra of **7c**–**d** agreed also with these structures. Acetylation of **7b**–**d** yielded compounds **8b**–**d**; for example the ^{1}H NMR spectrum of compound **8b** exhibited a broad singlet at δ 5.03 ppm for H-2, 4.88 ppm for H-1, and 4.70 ppm for H-4, characteristics of the *talo* configuration.

In order to confirm the configurations and conformations of **4a**–**d**, we performed the semi-empirical molecular orbital calculations for **4b** and **b′** using the AM1 method. The enthalpy of formation of **4b** and **b′** are −146.17 and −143.85 kcal/mol. The torsion angles H-2–C-2–C-1–H-1 and O-12–C-1–O-11–C-5 in **4b** are −102.2 and 70.1° indicating that the anomeric proton is equatorial and that H-1 and H-2 have a torsion angle of approx 100°. The calculations also show that C-1, C-2, C-3, C-4 and C-5 of the pyranose system are somewhat planar and the ring oxygen atom is above the plane. The isoxazolidine ring has a slight deviation from the planarity since the dihedral angle O-9–N-8–C-7–C-3 is −8.7° only. This is in agreement with the cyclopentyl α-D-*lyxo*-hexopyranosid-(2,3:5′,4′)-2′-phenylisoxazolidin-4-ulose structure assigned to **4b**. The same method was applied to the other isomer **4b′** cyclopentyl α-D-*ribo*-hexopyranosid-(2,3:5′,4′)-2′-phenylisoxazolidin-4-ulose (not isolated). The structures of these two diastereoisomers are given in Figs. 1 and 2, respectively.

In conclusion, we have synthesized three new branched-chain amino sugars in excellent yields by a 1,3-dipolar cycloaddition of methylideneaniline *N*-oxide to enones **3a**–**d**, followed by hydrogenation. The structures as well conformations of these compounds were determined from ^{1}H NMR spectra in conjunction with molecular orbital calculations.

3. Experimental

3.1. General methods

Melting points were determined with a Digital Melting Point Apparatus, series IA-9100, Electrothermal Ltd., England. IR spectra were recorded as KBr films on a Brucker IFFS66 series Fourier transform spectrophotometer. The 300 MHz ^{1}H NMR spectra were recorded with a Varian Unity Plus spectrophotometer or a Brucker DRX 300 using $CDCl_3$ as solvent and Me_4Si as an internal standard. Elemental analyses were performed in our Department. Optical rotations were mea-

sured with a Perkin–Elmer 141 and 241 polarimeters at the Université Claude Bernard Lyon 1, Villeurbanne (France), and at the University of São Carlos, S.P. (Brazil). Thin layer chromatography (TLC) was carried out on plates coated with Silica Gel 60 (E. Merck) and the plates were exposed in a chamber containing iodine vapors which revealed the spots.

3.2. General procedure for the preparation of diols 2a–d

Alkyl 4,6-di-*O*-acetyl-2,3-dideoxy-α-D-*erythro*-hex-2-enopyranosides (**1a**–**d**) were obtained by the method of Toshima et al.[15] The hydrolysis of **1a**–**d** in 9:6:1 MeOH–water–Et_3N (32 mL) required 3 h at room temperature (rt) for deacetylation as determined by TLC. Solvent evaporation under reduced pressure, followed by chromatography on silica (1:1 C_6H_{14}–EtOAc), gave diols **2a**–**d** in almost quantitative yield.

3.2.1. Ethyl 2,3-dideoxy-α-D-*erythro*-hex-2-enopyranoside (2a). Obtained as described above from **1a** (1.25 g, 5.4 mmol) and MeOH–water–Et_3N (32 mL); 1.0 g (86%); R_f 0.12 (9:1 CH_2Cl_2–EtOAc). The ^1H NMR spectrum and the elemental analysis of **2a** were in agreement with the reported data.[5]

3.2.2. Cyclopentyl 2,3-dideoxy-α-D-*erythro*-hex-2-enopyranoside (2b). From **1b** (2.0 g, 9.3 mmol); oil; 1.74 g (93%); R_f 0.16 (9:1 CH_2Cl_2–EtOAc); $[\alpha]_D^{25}$ +54° (*c* 1.0, $CHCl_3$); IR (KBr): 3404 cm^{-1} (*v* OH); ^1H NMR (300 MHz, $CDCl_3$): δ 5.95 (d, 1 H, $J_{3,2}$ 10.2 Hz, H-3), 5.70 (dd, 1 H, $J_{2,3}$ 10.2, $J_{2,4}$ 2.4 Hz, H-2), 5.04 (bs, 1 H, H-1), 4.23 (m, 1 H, OCH), 4.21 (bd, $J_{4,5}$ 9.3 Hz, 1 H, H-4), 3.87 (bd, 2 H, $J_{6,5}$ 3.7 Hz, H-6, H-6′), 3.70 (dt, $J_{5,4}$ 9.4, $J_{6,5}$ 3.7 Hz, 1 H, H-5), 2.33 and 2.22 (bs, exchangeable, 2 H, 2 OH), 1.83–1.51 (m, 8 H, 4 CH_2). Anal. Calcd for $C_{11}H_{18}O_4$ (214.12): C, 61.70; H, 8.47. Found: C, 61.28; H, 8.37.

3.2.3. Cyclohexyl 2,3-dideoxy-α-D-*erythro*-hex-2-enopyranoside (2c). From **1c** (3.0 g, 9.6 mmol); oil; 1.62 g (87%); R_f 0.20 (9:1 CH_2Cl_2–EtOAc); $[\alpha]_D^{25}$ +46° (*c* 3.4, $CHCl_3$); IR: 3100–3600 cm^{-1} (*v* OH) (Nujol); ^1H NMR (300 MHz, $CDCl_3$): δ 5.95 (ddd, 1 H, $J_{3,2}$ 10.2, $J_{3,1}$ 1.3, $J_{3,4}$ 1.3 Hz, H-3), 5.73 (ddd, 1 H, $J_{2,3}$ 10.5, $J_{2,4}$ 2.4, $J_{2,1}$ 2.7 Hz, H-2), 5.13 (m, 1 H, H-1), 4.20 (bd, $J_{4,5}$ 9.0 Hz, H-4), 3.85 (d, 2 H, $J_{6,5}$ 3.9 Hz, H-6, H-6′), 3.75 (dt, 1 H, $J_{5,4}$ 9.0, $J_{5,6}$ 3.9 Hz, H-5), 3.62 (m, 1 H, OCH), 2.63 and 2.37 (bs, exchangeable, 2 H, 2 OH), 2.04–1.10 (m, 10 H, 5 CH_2). Anal. Calcd for $C_{12}H_{20}O_4$ (228.29): C, 63.13; H, 8.83. Found: C, 63.25; H, 9.10.

3.2.4. Cyclopropylmethyl 2,3-dideoxy-α-D-*erythro*-hex-2-enopyranoside (2d). From **1d** (1.34 g, 4.7 mmol); oil; 0.9 g (95%); R_f 0.17 (9:1 CH_2Cl_2–EtOAc); $[\alpha]_D^{25}$ +63° (*c* 0.97, $CHCl_3$); IR (KBr): 3396 cm^{-1} (*v* OH); ^1H NMR (300 MHz, $CDCl_3$): δ 5.95 (d, 1 H, $J_{3,2}$ 9.9 Hz, H-3), 5.79 (dd, 1 H, $J_{2,3}$ 9.9, $J_{2,4}$ 2.1 Hz, H-2), 5.05 (bs, 1 H, H-1), 4.23 (bd, 1 H, $J_{4,5}$ 9.0 Hz, H-4), 3.87 (m, 2 H, H-6, H-6′), 3.75 (dt, 1 H, $J_{5,4}$ 9.0, $J_{5,6}$ 4.2 Hz, H-5), 3.89 (dd, 1 H, *J* 6.9, *J* 10.5 Hz, OCH_2), 3.53 (dd, 1 H, *J* 7.5, *J* 10.5 Hz, OCH_2), 1.90 and 1.75 (2 bs, exchangeable, 2 H, 2 OH), 1.09 (m, 1 H, CH), 0.57–0.23 (m, 4 H, CH_2). Anal. Calcd for $C_{10}H_{16}O_4$ (200.23): C, 59.98; H, 8.05. Found: C, 59.70; H, 7.90.

3.3. General procedure for the preparation of alkyl 2,3-dideoxy-α-D-*glycero*-2-enopyranosid-4-uloses (3a–d)

The appropriate diol **2** (4.67 mmol) was dissolved in CH_2Cl_2 (150 mL), activated MnO_2 (4.61 g, 53 mmol) was added, and the contents stirred at rt until the completion of the reaction. The progress of the reaction was monitored by TLC using 9:1 CH_2Cl_2–EtOAc followed by spot viewing under UV light. Filtration and solvent evaporation gave **3a**–**d** analytically pure after recrystallization from ether–C_6H_{14}.

3.3.1. Ethyl 2,3-dideoxy-α-D-*glycero*-hex-2-enopyranosid-4-ulose (3a). From **2a** (0.82 g, 4.67 mmol); 0.53 g (65%); mp 86–87 °C; R_f 0.36 (4:1 $CHCl_3$–EtOAc); $[\alpha]_D^{25}$ −14.5° (*c* 2.1, $CHCl_3$); IR (KBr): 3457 (*v* OH), 1692 cm^{-1} (*v* C=O); ^1H NMR (300 MHz, $CDCl_3$): δ 6.89 (dd, 1 H, $J_{2,3}$ 10.5, $J_{2,1}$ 3.6 Hz, H-2), 6.10 (d, 1 H, $J_{3,2}$ 10.5 Hz, H-3), 5.28 (d, 1 H, $J_{1,2}$ 3.6 Hz, H-1), 4.50 (t, 1 H, $J_{5,6}$ 4.5 Hz, H-5), 4.00–3.66 (m, 4 H, OCH_2, H-6, H-6′), 2.27 (b, exchangeable, 1 H, OH), 1.28 (t, 3 H, *J* 7.1 Hz, CH_3). Anal. Calcd for $C_8H_{12}O_4$ (172.18): C, 55.81; H, 7.02. Found: C, 55.52; H, 6.86.

3.3.2. Cyclopentyl 2,3-dideoxy-α-D-*glycero*-hex-2-enopyranosid-4-ulose (3b). From **2b** (1.0 g, 4.67 mmol); 0.79 (76%); mp 76.4–77.0 °C; R_f 0.39 (9:1 CH_2Cl_2–EtOAc); $[\alpha]_D^{25}$ −30° (*c* 0.92, $CHCl_3$); IR (KBr): 3457 (*v* OH), 1692 cm^{-1} (*v* C=O); ^1H NMR (300 MHz, $CDCl_3$): δ 6.85 (dd, 1 H, $J_{2,3}$ 10.2, $J_{2,1}$ 3.6 Hz, H-2), 6.09 (d, 1 H, $J_{3,2}$ 10.2 Hz, H-3), 5.32 (d, 1 H, $J_{1,2}$ 3.6 Hz, H-1), 4.49 (dd, 1 H, $J_{5,6}$ 4.5, $J_{5,6'}$ 4.5 Hz, H-5), 4.34 (m, 1 H, OCH), 4.01 (dd, $J_{6,6'}$ 11.7, $J_{6,5}$ 4.5 Hz, H-6), 3.91 (dd, $J_{6',6}$ 11.7, $J_{6',5}$ 4.5 Hz, H-6′), 2.27 (bs, exchangeable, 1 H, OH), 1.87–1.55 (m, 8 H, 4 CH_2). Anal. Calcd for $C_{11}H_{18}O_4$ (212.24): C, 62.25; H, 7.59. Found: C, 62.15; H, 7.39.

3.3.3. Cyclohexyl 2,3-dideoxy-α-D-*glycero*-hex-2-enopyranosid-4-ulose (3c). From **2c** (1.06 g, 4.67 mmol); 0.73 g (69%); mp 99.0–100 °C; R_f 0.42 (9:1 CH_2Cl_2–EtOAc); IR (KBr): 3100–3600 (*v* OH), 1690 cm^{-1} (*v* C=O); ^1H NMR (300 MHz, $CDCl_3$): δ 6.87 (dd, 1 H, $J_{2,3}$ 10.2, $J_{2,1}$ 3.6 Hz, H-2), 6.11 (d, 1 H, $J_{3,2}$ 10.2 Hz, H-3), 5.17 (d, 1 H, $J_{1,2}$ 3.6 Hz, H-1), 4.53 (dd, 1 H, $J_{5,6}$

4.2, $J_{5,6'}$ 4.2 Hz, H-5), 4.02 (dd, $J_{6',6}$ 11.8, $J_{6',5}$ 4.2 Hz, H-6′), 3.92 (dd, 2 H, $J_{6,6'}$ 11.8, $J_{6,5}$ 4.2 Hz, H-6), 3.80–3.62 (m, 1 H, OCH), 2.22 (bs, exchangeable, 1 H, OH), 2.20–0.80 (m, 10 H, 5 CH_2). Anal. Calcd for $C_{12}H_{18}O_4$ (226.26): C, 63.72; H, 7.96. Found: C, 63.42; H, 8.07.

3.3.4. Cyclopropylmethyl 2,3-dideoxy-α-D-*glycero*-hex-2-enopyranosid-4-ulose (3d). From **2d** (0.94 g, 4.67 mmol); 0.64 g (68%); mp 96.4–96.9 °C; R_f 0.32 (9:1 CH_2Cl_2–EtOAc); $[\alpha]_D^{25}$ +18.6° (*c* 1.2, $CHCl_3$); IR (KBr): 3456 (*v* OH), 1692 cm^{-1} (*v* C=O); ^1H NMR (300 MHz, $CDCl_3$): δ 6.92 (dd, 1 H, $J_{2,3}$ 10.5, $J_{2,1}$ 3.7 Hz, H-2), 6.13 (d, 1 H, $J_{3,2}$ 10.5 Hz, H-3), 5.33 (d, 1 H, $J_{1,2}$ 3.7 Hz, H-1), 4.52 (dd, 1 H, $J_{5,6}$ 4.2, $J_{5,6'}$ 4.2 Hz, H-5), 4.03 (dd, $J_{6,6'}$ 11.7, $J_{6,5}$ 4.2 Hz, 1 H, H-6), 3.93 (dd, $J_{6',6}$ 11.7, $J_{6',5}$ 4.2 Hz, 1 H, H-6′), 3.52 (m, 2 H, OCH_2), 1.95 (bs, exchangeable proton, 1 H, OH), 1.18 (m, 1 H, CH), 0.60–0.20 (m, 4 H, 2 CH_2). Anal. Calcd for $C_{10}H_{14}O_4 \cdot 0.25\ H_2O$ (202.72): C, 59.25; H, 7.20. Found: C, 59.34; H, 7.18.

3.4. General method for the preparation of 4a–d

A mixture of the phenylhydroxylamine (3 mmol) and 37% aq formaldehyde (5 mmol) in EtOH (5 mL) was warmed to 50 °C and the appropriate enone **3a**–**d** (3 mmol) was added. The mixture was refluxed for 1.5 h. The progress of the reaction was monitored by TLC. Solvent evaporation and purification of the crude residue on silica gel column using 4:1 C_6H_{14}–AcOEt as eluent provided **4a**–**d**.

3.4.1. Ethyl α-D-*lyxo*-hexopyranosid-4-(2,3:5′,4′)-2′-phenylisoxazolidin-4-ulose (4a). From **3a** (0.52 g, 3 mmol); syrup, 0.26 g (52%); R_f 0.61 (4:1 $CHCl_3$–EtOAc); $[\alpha]_D^{25}$ +54.6° (*c* 1, $CHCl_3$); IR (KBr): 3450 (*v* OH), 1725 cm^{-1} (*v* C=O); ^1H NMR (300 MHz, $CDCl_3$): δ 7.30–7.25 (m, 2 H, H-2′, H-6′, Ph-H), 7.06–6.98 (m, 3 H, H-3′, H-4′, H-5′, Ph–H), 5.13 (s, 1 H, H-1), 4.42 (d, 1 H, $J_{2,3}$ 8.4 Hz, H-2), 4.13 (dd, 1 H, $J_{5,6}$ 3.3, $J_{5,6'}$ 3.3 Hz, H-5), 3.90 (m, 1 H, H-6), 3.79 (m, 1 H, H-6′), 3.80 (d, 2 H, $J_{CH_2N,3}$ 7.8 Hz, CH_2N), 3.70–3.64 (m, 2 H, OCH_2), 3.39 (dt, H, $J_{3,2}$ 8.4, J_{3,CH_2N} 7.8 Hz, H-3), 2.67 (bs, exchangeable, 1 H, OH), 1.25 (t, 3 H, *J* 7.1 Hz, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ 206.7 (C-4), 150.0 (C-1′), 129.4 (C-3′), 123.4 (C-4′), 115.7 (C-2′), 96.9 (C-1), 77.4 (C-5), 77.0 (C-2), 76.1 (O–C), 64.5 (C-6), 62.7 (CH_2N), 56.3 (CH_2, aglycone), 51.0 (C-3), 15.1 (CH_3). Anal. Calcd for $C_{15}H_{19}NO_5$ (293.32): C, 61.42; H, 6.53; N, 4.77. Found: C, 61.78; H, 6.71; N, 4.51.

3.4.2. Cyclopentyl α-D-*lyxo*-hexopyranosid-(2,3:5′,4′)-2′-phenylisoxazolidin-4-ulose (4b). From **3b** (0.64 g, 3 mmol); syrup, 0.68 g (76%); R_f 0.55 (4:1 $CHCl_3$–EtOAc); $[\alpha]_D^{25}$ +134.9° (*c* 0.38, CH_2Cl_2); IR (KBr): 3467 (*v* OH), 1670 cm^{-1} (*v* C=O); ^1H NMR (300 MHz, $CDCl_3$): δ 7.42–7.26 (m, 2 H, H-2′, H-6′, Ph-H), 7.15–7.00 (m, 3 H, H-3′, H-4′, H-5′, Ph–H), 5.18 (s, 1 H, H-1), 4.35 (dd, 1 H, $J_{2,3}$ 8.4, $J_{2,1}$ 1.0 Hz, H-2), 4.32 (m, 1 H, OCH), 4.17 (ddd, $J_{5,6}$ 3.6, $J_{5,6'}$ 3.6, 1 H, J_{5,CH_2N} 3.6 Hz, H-5), 3.89 (m, 2 H, H-6, H-6′), 3.80 (dd, 2 H, $J_{CH_2N,3}$ 7.5, $J_{CH_2N,5}$ 1.2 Hz, CH_2N), 3.40 (dt, 1 H, $J_{3,2}$ 8.4, J_{3,CH_2N} 7.5 Hz, H-3), 2.54 (bs, exchangeable, 1 H, OH), 1.79–1.58 (m, 8 H, 4 CH_2); ^{13}C NMR (75 MHz, $CDCl_3$): δ 206.9 (C-4), 150.1 (C-1′), 129.3 (C-3′, C-5′), 123.3 (C-4′), 116.0 (C-2′, C-6′), 94.9 (C-1), 81.2 (C-5), 79.5 (C-2), 76.5 (OC), 60.7 (C-6), 55.2 (CH_2N), 51.1 (C-3), 33.5 and 23.8 ($2 \times CH_2$). Anal. Calcd for $C_{18}H_{23}NO_5$ (333.17): C, 64.84; H, 6.95; N, 4.20. Found: C, 65.13; H, 6.97; N, 3.95.

3.4.3. Cyclohexyl α-D-*lyxo*-hexopyranosid-(2,3:5′,4′)-2′-phenylisoxazolidin-4-ulose (4c). From **3c** (0.68 g, 3 mmol); syrup, 0.53 g (62%); R_f 0.63 (9:1 CH_2Cl_2–EtOAc); $[\alpha]_D^{25}$ +104.6° (*c* 0.4, $CHCl_3$); IR (KBr): 3312 (*v* OH), 1693 cm^{-1} (*v* C=O); ^1H NMR (300 MHz, $CDCl_3$): δ 7.31–7.28 (m, 2 H, H-2′, H-6′, Ph-H), 7.07–7.01 (m, 3 H, H-3′, H-4′, H-5′, Ph-H), 5.29 (s, 1 H, H-1), 4.38 (dd, 1 H, $J_{2,3}$ 8.7, $J_{2,1}$ 1.2 Hz, H-2), 4.20 (bdd, 1 H, $J_{5,6}$ 3.6, $J_{5,6'}$ 3.6 Hz, H-5), 3.90 (m, 2 H, H-6, H-6′), 3.79 (dd, 2 H, $J_{CH_2N,3}$ 7.5, $J_{CH_2N,5}$ 1.5 Hz, CH_2N), 3.69 (m, 1 H, OCH), 3.38 (dt, 1 H, $J_{3,2}$ 8.7, $J_{3,7}$ 7.5 Hz, H-3), 2.52 (bs, exchangeable, 1 H, OH), 1.95–1.54 (m, 10 H, 5 CH_2); ^{13}C NMR (75 MHz, $CDCl_3$): δ 207.1 (C-4), 150.0 (C-1′), 129.4 (C-3′, C-5′), 123.4 (C-4′), 115.0 (C-2′, C-6′), 94.0 (C-1), 78.2 (C-5), 76.3 (C-2), 75.9 (OC), 62.6 (C-6), 56.5 (CH_2N), 49.8 (C-3), 36.5, 25.8 and 24.3 ($3 \times CH_2$). Anal. Calcd for $C_{19}H_{25}NO_5$ (347.40): C, 65.68; H, 7.25; N, 4.03. Found: C, 66.02; H, 7.32; N, 4.04.

3.4.4. Cyclopropylmethyl α-D-*lyxo*-hexopyranosid-(2,3:5′,4′)-2′-phenylisoxazolidin-4-ulose (4d). From **3d** (0.59 g, 3 mmol); syrup, 0.34 g (52%); R_f 0.52 (4:1 $CHCl_3$–EtOAc); $[\alpha]_D^{25}$ +53.2° (*c* 0.4, $CHCl_3$); IR (KBr): 3385 (*v* OH), 1725 cm^{-1} (*v* C=O); ^1H NMR (300 MHz, $CDCl_3$): δ 7.31–7.25 (m, 2 H, H-2′, H-6′, Ph-H), 7.08–7.01 (m, 3 H, H-3′, H-4′, H-5′, Ph-H), 5.21 (s, 1 H, H-1), 4.46 (d, 1 H, $J_{2,3}$ 8.4 Hz, H-2), 4.15 (dd, 1 H, $J_{5,6}$ 3.6, $J_{5,6'}$ 3.6 Hz, H-5), 3.90–3.40 (m, 2 H, H-6, H-6′), 3.81 (d, 2 H, $J_{CH_2N,3}$ 7.2 Hz, CH_2N), 3.43 (m, 2 H, OCH_2), 3.12 (dt, 1 H, $J_{3,2}$ 8.4, J_{3,CH_2N} 7.2 Hz, H-3), 2.05 (bs, s, exchangeable, 1 H, OH), 0.90 (m, 1 H, CH), 0.60 (m, 2 H, CH_2), 0.20 (m, 2 H, CH_2); ^{13}C NMR (75 MHz, $CDCl_3$): δ 205.9 (C-4), 150.3 (C-1′), 128.3 (C-3′, C-5′), 124.3 (C-4′), 115.1 (C-2′, C-6′), 94.3 (C-1), 79.5 (C-5), 75.5 (C-2), 67.0 (C-6), 64.2 (CH_2, aglycone), 63.3 (C-3), 57.4 (CH_2N), 11.2 (CH), 10.9 (CH_2). Anal. Calcd for $C_{17}H_{21}NO_5$ (319.36): C, 63.93; H, 6.63; N, 4.39. Found: C, 64.13; H, 6.97; N, 3.95.

3.5. General procedure for the synthesis of 7b–d

The appropriate isoxazolidine **4b–d** (0.75 mmol) in EtOAc (10 mL) containing 20 mg of PtO_2 was hydrogenated at 152 kPa for 4 h. Filtration of the catalyst followed by removal of the solvent under diminished pressure gave a product that was promptly chromatographed over a silica gel column using 1:1 C_6H_{14}–EtOAc as the eluent.

3.5.1. Cyclopentyl 3-deoxy-3-*N*-phenylaminomethyl-α-D-talopyranoside (7b). From **4b** (0.25 g, 0.75 mmol); syrup, 0.21 g (86%); R_f 0.42 (8.5:1:0.5 CH_2Cl_2–EtOAc–MeOH); $[\alpha]_D^{25}$ +84° (*c* 0.3, CH_2Cl_2); IR (KBr): 3467 (*v* OH), 1603 cm^{-1} (bend N–H); ^1H NMR (300 MHz, $CDCl_3$): δ 7.42–7.26 (m, 2 H, H-2′, H-6′, Ph-H), 7.15–7.00 (m, 3 H, H-3′, H-4′, H-5′, Ph-H), 4.95 (d, 1 H, $J_{1,2}$ 1.3 Hz, H-1), 4.22 (m, 1 H, OCH), 4.12 (bs, 1 H, H-2), 3.96 (d, $J_{6,5}$ 3.3 Hz, 2 H, H-6, H-6′), 3.74 (t, 1 H, $J_{5.6}$ 3.0 Hz, H-5), 3.65 (bs, 1 H, H-4), 3.44 (dd, 1 H, $J_{H,H}$ 13.5, $J_{CH_2N',3}$ 6.3 Hz, CH_2N), 3.42 (dd, 1 H, $J_{H,H}$ 13.5, $J_{CH_2N,3}$ 8.1 Hz, CH_2N), 2.13 (m, 1 H, H-3), 2.13 (bs, 1 H, OH), 1.77–1.52 (m, 8 H, 4 CH_2); ^{13}C NMR (75 MHz, $CDCl_3$): δ 148.5 (C-1′), 129.7 (C-3′, C-5′), 117.9 (C-4′), 113.4 (C-2′, C-6′), 99.7 (C-1), 79.2 (C-5), 70.4 (OCH), 70.3 (C-2), 69.9 (C-4), 65.3 (C-6), 42.8 (CH_2N), 37.4 (C-3), 33.5 and 23.9 (CH_2, aglycone). Anal. Calcd for $C_{18}H_{27}NO_5$ (337.41): C, 64.07; H, 8.06; N, 4.15. Found: C, 63.83; H, 8.42; N, 3.86.

3.5.2. Cyclohexyl 3-deoxy-3-*N*-phenylaminomethyl-α-D-talopyranoside (7c). From **4c** (0.26 g, 0.75 mmol); syrup, 0.2 g (78%); R_f 0.47 (8.5:1:0.5 CH_2Cl_2–EtOAc–MeOH); $[\alpha]_D^{25}$ +82.1° (*c* 0.79, CH_2Cl_2); IR (KBr): 3407 (*v* OH), 1603 cm^{-1} (bend N–H); ^1H NMR (300 MHz, $CDCl_3$): δ 7.21–7.15 (m, 2 H, H-2′, H-6′, Ph-H), 6.73–6.66 (m, 3 H, H-3′, H-4′, H-5′, Ph-H), 5.03 (bs, 1 H, $J_{1,2}$ 1.5 Hz, H-1), 4.11 (bs, 1 H, H-2), 3.93 (d, 2 H, $J_{5,6}$ 3.6 Hz, H-6, H-6′), 3.78 (t, 1 H, $J_{5,6}$ 3.6 Hz, H-5), 3.67 (bs, 1 H, H-4), 3.60 (m, 1 H, OCH), 3.55 (dd, 1 H, $J_{H,H}$ 13.5, $J_{CH_2N,3}$ 6.3 Hz, CH_2N), 3.42 (dd, 1 H, $J_{H,H}$ 13.5, $J_{CH_2N,3}$ 8.1 Hz, CH_2N), 2.29 (bs, 1 H, OH), 2.16 (m, 1 H, H-3), 1.88–1.20 (m, 10 H, 5 CH_2); ^{13}C NMR (75 MHz, $CDCl_3$): δ 152.7 (C-1′), 129.3 (C-3′, C-5′), 122.1 (C-4′), 114.2 (C-2′, C-6′), 98.8 (C-1), 75.5 (C-5), 70.4 (OCH), 69.8 (C-2), 69.6 (C-4), 64.8 (C-6), 42.6 (CH_2N), 37.3 (C-3), 31.9, 24.3 and 21.4 (CH_2, aglycone). Anal. Calcd for $C_{19}H_{29}NO_5$ (351.44): C, 64.93; H, 8.32; N, 3.98. Found: C, 64.84; H, 8.34; N, 3.64.

3.5.3. Cyclopropylmethyl 3-deoxy-3-phenylaminomethyl-α-D-talopyranoside (7d). From **4d** (0.24g, 0.75 mmol); syrup, 0.18 g (75%); R_f 0.44 (8.5:1:0.5 CH_2Cl_2–EtOAc–MeOH); $[\alpha]_D^{25}$ +70.2° (*c* 0.9, $CHCl_3$); IR (KBr): 3383 (*v* OH), 1603 cm^{-1} (bend N–H); ^1H NMR (300 MHz, $CDCl_3$): δ 7.31–7.25 (m, 2 H, H-2′, H-6′, Ph-H), 7.08–7.01 (m, 3 H, H-3′, H-4′, H-5′, Ph-H), 4.95 (bs, 1 H, H-1), 4.14 (bs, 1 H, H-2), 3.94 (d, 2 H, $J_{5,6}$ 3.6 Hz, H-6, H-6′), 3.78 (bs, 1 H, H-4), 3.76 (m, 1 H, H-5), 3.62 (dd, 1 H, $J_{H,H}$ 13.5, $J_{CH_2N,3}$ 6.3 Hz, CH_2N), 3.48 (dd, 1 H, $J_{H,H}$ 13.5, $J_{CH_2N,3}$ 8.1 Hz, CH_2N), 3.36 (dd, 2 H, *J* 11.1, *J* 6.6 Hz, OCH_2), 2.23 (m, 1 H, H-3), 2.23 (bs, 1 H, OH), 1.05 (m, 1 H, CH), 0.51 (m, 2 H, CH_2), 0.20 (m, 2 H, CH_2); ^{13}C NMR (75 MHz, $CDCl_3$): δ 149.3 (C-1′), 128.7 (C-3′, C-5′), 117.3 (C-4′), 114.1 (C-2′, C-6′), 98.7 (C-1), 79.5 (C-5), 75.5 (C-2), 67.4 (C-6), 64.5 (CH_2, aglycone), 62.8 (C-3), 46.2 (CH_2N), 12.1 (CH), 10.1 (CH_2). Anal. Calcd for $C_{17}H_{25}NO_5$ (323.38): C, 63.14; H, 7.79; N, 4.33. Found: C, 63.60; H, 7.97; N, 4.32.

3.6. General procedure for the preparation of 3-deoxy-3-(*N*-acetyl-*N*-phenylaminomethyl)-2,4,6-tri-*O*-acetyl-α-D-talopyranosides (8b–d)

The appropriate compound **7b–d** (0.42 mmol) was dissolved in dry Py (2 mL) and the solution cooled to 0 °C. Acetic anhydride (1.5 mL) was added and the contents left under stirring overnight. A single spot was observed on the TLC plate as detected under UV light. Evaporation of the solvent left a syrup that was quickly passed through a silica gel column using 7:3 C_6H_{14}–EtOAc as the eluent in order to purify the material.

3.6.1. Cyclopentyl 3-deoxy-2,4,6-tri-*O*-acetyl-3-*N*-acetyl-phenylaminomethyl-α-D-talopyranoside (8b). From **7b** (0.14 g, 0.42 mmol); syrup, 0.12 g (82%); R_f 0.37 (4:1 $CHCl_3$–EtOAc); $[\alpha]_D^{25}$ +42.1° (*c* 0.38, CH_2Cl_2); IR (KBr): 1742 cm^{-1} (*v* OAc); ^1H NMR (300 MHz, $CDCl_3$): δ 7.42–7.26 (m, 2 H, H-2′, H-6′, Ph-H), 7.15–7.00 (m, 3 H, H-3′, H-4′, H-5′, Ph-H), 5.03 (bs, 1 H, H-2), 4.88 (bs, 1 H, H-1), 4.70 (bs, 1 H, H-4), 4.18–3.96 (m, 4 H, H-5, H-6, H-6′, OCH), 4.07 (dd, 1 H, $J_{H,H}$ 13.8, $J_{CH_2N,3}$ 5.7 Hz, CH_2N), 3.52 (dd, 1 H, $J_{H,H}$ 13.8, $J_{CH_2N,3}$ 6.6 Hz, CH_2N), 2.35 (m, 1 H, H-3), 2.13 (s, 3 H, Ac), 2.05 (s, 3 H, Ac), 2.02 (s, 3 H, Ac), 1.78 (s, 3 H, NAc), 1.68–1.53 (m, 8 H, 4 CH_2); ^{13}C NMR (75 MHz, $CDCl_3$): δ 171.3, 171.0, 170.6 (3 C, CO_2), 167.3 (NCO), 148.5 (C-1′), 129.3 (C-3′, C-5′), 123.1 (C-4′), 115.4 (C-2′, C-6′), 89.0 (C-1), 79.2 (C-5), 75.1 (OCH), 73.8 (C-2), 71.0 (C-4), 68.3 (C-6), 42.3 (CH_2N), 32.8 (C-3), 31.1 and 22.3 (CH_2, aglycone), 20.1 (4 × CH_3). Anal. Calcd for $C_{26}H_{35}NO_9$ (505.56): C, 61.77; H, 6.98; N, 2.77. Found: C, 61.81; H, 7.16; N, 2.86.

3.6.2. Cyclohexyl 3-deoxy-2,4,6-tri-*O*-acetyl-3-*N*-acetyl-phenylaminomethyl-α-D-talopyranoside (8c). From **7c** (0.15 g, 0.42 mmol); syrup, 0.12 g (85%); R_f 0.40 (9:1 CH_2Cl_2–EtOAc); $[\alpha]_D^{25}$ +36° (*c* 0.5, CH_2Cl_2); IR (KBr): 1745 cm^{-1} (*v* OAc); ^1H NMR (300 MHz, $CDCl_3$): δ 7.21–7.15 (m, 2 H, H-2′, H-6′, Ph-H), 6.73–6.66 (m, 3 H, H-3′, H-4′, H-5′, Ph-H), 5.03 (bs, 1 H,

H-2), 4.88 (bs, 1 H, H-1), 4.72 (d, 1 H, *J* 2.4 Hz, H-4), 4.18–3.94 (m, 4 H, H-5, H-6, H-6′, OCH, CH_2N), 3.56 (dd, 1 H, $J_{H,H}$ 13.5, $J_{CH_2N,3}$ 5.7 Hz, CH_2N), 2.38 (s, 1 H, H-3), 2.13 (s, 3 H, Ac), 2.05 (s, 3 H, Ac), 2.01 (s, 3 H, Ac) 1.78 (s, 3 H, NAc), 1.83–1.21 (m, 10 H, 5 CH_2); ^{13}C NMR (75 MHz, $CDCl_3$): δ 170.4, 170.2, 169.7 (3 C, CO_2), 166.0 (NAc), 152.7 (C-1′), 129.1 (C-3′), 121.4 (C-4′), 114.3 (C-2′), 96.9 (C-1), 76 (C-2), 74.5 (C-5), 66.4 (OCH), 65.0 (C-6), 63.7 (C-4), 41.3 (CH_2N), 33.7 (C-3), 31.8, 26.0 and 24.6 (CH_2, aglycone), 20.7 (4 × CH_3). Anal. Calcd for $C_{27}H_{37}NO_9$ (519.59): C, 62.41; H, 7.17; N, 2.69. Found: C, 62.50; H, 7.36; N, 2.35.

3.6.3. Cyclopropylmethyl 3-deoxy-2,4,6-tri-*O*-acetyl-*N*-acetyl-*N*-phenylaminomethyl-α-D-talopyranoside (8d). From **7d** (0.14 g, 0.42 mmol); syrup, 0.11 g (83%); R_f 0.39 (4:1 $CHCl_3$–EtOAc); $[\alpha]_D^{25}$ +38.7° (*c* 0.4, $CHCl_3$); IR (KBr): 1740 cm^{-1} (*ν* OAc); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.31–7.25 (m, 2 H, H-2′, H-6′), 7.08–7.01 (m, 3 H, H-3′, H-4′, H-5′), 5.08 (bs, 1 H, H-2), 4.90 (bs, 1H, H-1), 4.80 (d, 1 H, *J* 2.7 Hz, H-4), 4.17 (m, 3 H, H-5, H-6 and H-6′), 3.71 (dd, 2 H, *J* 6.0, *J* 10.8 Hz, CH_2O), 3.52 (dd, 1 H, $J_{H,H}$ 10.8, $J_{CH_2N,3}$ 8.4 Hz, CH_2N), 3.44 (dd, 1 H, $J_{H,H}$ 10.8, $J_{CH_2N,3}$ 7.2 Hz, CH_2N), 2.44 (m, 1 H, H-3), 2.14 (s, 3 H, Ac), 2.04 (s, 3 H, Ac), 2.02 (s, 3 H, Ac), 1.79 (s, 3 H, NAc), 1.02 (m, 1, CH), 0.52 (m, 2 H, CH_2), 0.19 (m, 2 H, CH_2); ^{13}C NMR (75 MHz, $CDCl_3$): δ 170.3, 170.0, 169.6 (3 C, CO_2), 167.1 (NAc), 147.5 (C-1′), 131.3 (C-3′, C-5′), 125.2 (C-4′), 113.4 (C-2′, C-6′), 91.2 (C-1), 79.5 (C-5), 75.5 (C-2), 67.4 (C-6), 63.7 (C-4), 63.5 (CH_2, aglycone), 61.8 (C-3), 41.3 (CH_2N), 16.5 (CH_3), 12.3 (CH), 10.3 (CH_2). Anal. Calcd for $C_{25}H_{33}NO_9 \cdot 0.5\ H_2O$ (500.52): C, 59.98; H, 6.84; N, 2.79. Found: C, 59.69; H, 6.71; N, 3.08.

3.6.4. Cyclopentyl 6-*O*-acetyl-α-D-*lyxo*-hexopyranosid-(2,3:5′,4′)-2′-phenylisoxazolidin-4-ulose (5b). Compound **4b** (0.2 g, 6 mmol) was dissolved in dry Py (10 mL) and the solution cooled to 0 °C. Acetic anhydride (1.5 mL) was added and the contents left under stirring overnight. A single spot was observed by TLC (9:1 CH_2Cl_2–EtOAc) having a R_f value of 0.58. Evaporation of the solvent left a syrup which was quickly passed through a silica gel column using petroleum ether (40–60 °C) as the eluent. Solvent evaporation provided **5b** as a colorless syrup (0.2 g, 87%). Recrystalization from *n*-C_6H_{14}–EtOAc gave **5b** (95 mg, 41%). Mp 110–111 °C; $[\alpha]_D^{25}$ +10.8° (*c* 0.5, $CHCl_3$); IR (KBr): 1745 (*ν* OAc), 1695 cm^{-1} (*ν* C=O); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.31–7.21 (m, 2 H, H-2′, H-6′, Ph-H), 7.08–7.00 (m, 3 H, H-3′, H-4′, H-5′, Ph–H), 5.07 (s, 1 H, H-1), 4.63 (d, 1 H, $J_{3,2}$ 9.8 Hz, H-2), 4.05 (dd, 1 H, $J_{5,6}$ 3.8, $J_{5,6'}$ 2.4 Hz, H-5), 4.22 (m, 1 H, OCH), 3.99 (dd, 1 H, $J_{6,6'}$ 10.9, $J_{6,5}$ 3.8 Hz, H-6), 3.85 (dd, 1 H, $J_{6',6}$ 10.9, $J_{6',5}$ 2.4 Hz, H-6′), 3.76 (b, $J_{CH_2N,3}$ 7.9 Hz, 2 H, CH_2N), 3.18 (t, J_{3,CH_2N} 8.7 Hz, 1 H, H-3), 2.19 (s, 3 H, CH_3), 1.79–1.58 (m, 8 H, 4 CH_2); ^{13}C NMR (75 MHz, $CDCl_3$): δ 205.0 (C-4), 169.7 (CO_2), 152.0 (C-1′), 129.4 (C-3′, C-5′), 128.7 (C-4′), 116.0 (C-2′, C-6′), 96.7 (C-1), 81.3 (C-5), 78.5 (C-2), 77.0 (OCH), 59.3 (C-6), 51.1 (CH_2N), 41.0 (C-3), 33.5 and 238 (CH_2, aglycone), 21.1 (CH_3). Anal. Calcd for $C_{20}H_{25}NO_6$ (375.22): C, 63.98; H, 6.71; N, 3.73. Found: C, 64.18; H, 6.92; N, 3.87.

3.6.5. Cyclopentyl 6-*O*-*tert*-butyldimethylsilyl-α-D-*lyxo*-hexopyranosid-(2,3:5′,4′)-2′-phenylisoxazolidin-4-ulose (6b). Compound **4b** (0.2 g, 6 mmol) was dissolved in DMF (2 mL) and the solution cooled to 0 °C. Imidazole (0.13 g, 1.97 mmol) and TBDMSiCl (0.15 g, 0.46 mmol) was added. The mixture was stirred at rt for 22 h. TLC in 9:1 CH_2Cl_2–EtOAc showed a new product with R_f 0.68. The mixture was extracted with petroleum ether (3 × 20 mL), the organic solution was washed with water (2 × 20 mL), then with a saturated aq soln of NaCl (2 × 20 mL), and dried over Na_2SO_4. Fitration and solvent removal under reduced pressure gave a viscous material which was chromatographed over silica gel using initially petroleum ether (40–60 °C), followed by petroleum ether–EtOAc (9:1) as the eluent to give **6b** (0.21 g, 78%) as a semisolid; $[\alpha]_D^{25}$ −125° (*c* 1, $CHCl_3$); IR (KBr): 1745 (*ν* C=O), 1060 cm^{-1} (*ν* C–O); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.31–7.26 (m, 2 H, H-2′, H-6′, Ph-H), 7.08–7.00 (m, 3 H, H-3′, H-4′, H-5′, Ph–H), 5.16 (s, 1 H, H-1), 4.37 (d, 1 H, $J_{2,3}$ 8.9 Hz, H-2), 4.30 (m, 1 H, OCH), 4.14 (dd, 1 H, $J_{5,6}$ 3.6, $J_{5,6'}$ 2.3 Hz, H-5), 4.07 (dd, 1 H, $J_{H,H}$ 10.9, $J_{6,5}$ 3.6 Hz, H-6), 3.93 (dd, 1 H, $J_{H,H}$ 10.9, $J_{6,5}$ 2.3 Hz, H-6′), 3.90-3.8 (bd, $J_{CH_2N,3}$ 10.9 Hz, 2 H, CH_2N), 3.28 (dt, 1 H, $J_{3,2}$ 8.9, $J_{3,7}$ 10.9 Hz, H-3), 1.75–1.58 (m, 8 H, 4 CH_2), 0.90 (s, 9 H, CMe_3), 0.09 (s, 6 H, $SiCH_3$); ^{13}C NMR (75 MHz, $CDCl_3$): δ 206.5 (C=O), 150.4 (C-1′), 129.3 (C-3′, C-5′), 123.1 (C-4‘), 115.6 (C-2′, C-6′), 95.6 (C-1), 81.3 (C-5), 79.2 (C-2), 76.9 (O-C), 63.4 (C-6), 55.9 (CH_2N), 53.2 (C-3), 33.6 (2 CH_2), 23.9 (2 CH_2), 26.2 $(CH_3)_3CSi$), 23.6 $(CH_3)_3$, −4.92 and −5.08 (CH_3Si). Anal. Calcd for $C_{24}H_{37}NO_5Si$ (447.65): C, 64.39; H, 8.33; N, 3.12. Found: C, 64.13; H, 8.14; N, 2.93.

Acknowledgements

One of us (J.R.d.F.F.) is thankful to the Brazilian National Research Council (CNPq) for a fellowship. We are grateful to CAPES-COFECUB and CNPq for financial assistance. We also thank Professor T. Brocksom, Chemistry Department, Federal University of São Carlos for allowing his technician, Antônio Pinto Loureiro Filho, to measure the specific rotations of compounds **4b**–**c**, **7a**–**c** and **8a**–**b**, and to Wagner de Mendonça Faustino for his help in performing the molecular orbital calculations.

References

1. Sibi, M. P.; Lu, J.; Edwards, J. *J. Org. Chem.* **1997**, *62*, 5864–5872 and references cited therein.
2. Pelyvás, I. V.; Monneret, C.; Herczegh, P. *Synthetic Aspects of Aminodeoxy Sugars of Antibiotics*; Springer: Berlin, 1988; pp 123–162.
3. Lindberg, B. *Carbohydr. Chem. Biochem.* **1990**, *48*, 279–318.
4. El Khadem, H. S. *Anthracycline Antibiotics*; Academic Press: New York, 1982; pp 1–285.
5. Fraser-Reid, B.; McLean, A.; Usherwood, E. W.; Yunker, M. *Can. J. Chem.* **1970**, *48*, 2877–2884 and references cited therein.
6. Holder, N. L.; Fraser-Reid, B. *Can. J. Chem.* **1973**, *51*, 3357–3365 and references cited therein.
7. Brimacombe, J. S. *Angew. Chem., Int. Ed. Engl.* **1971**, *10*, 236–248.
8. Brimacombe, J. S. *Angew. Chem., Int. Ed. Engl.* **1969**, *8*, 401–409.
9. Grisebach, H.; Schmid, R. *Angew. Chem., Int. Ed. Engl.* **1972**, *11*, 159–173.
10. Holder, N. L. *Chem. Rev.* **1982**, *82*, 287–332.
11. Kliegel, W. *Pharmazie* **1977**, *32*, 643–664.
12. Tufariello, J. J. *Acc. Chem. Res.* **1979**, *12*, 396–403.
13. DeShong, P.; Leginus, J. M. *J. Am. Chem. Soc.* **1983**, *105*, 1686–1688.
14. Panfil, I.; Chmielewski, M. *Tetrahedron* **1985**, *41*, 4713–4716.
15. Toshima, K.; Ishizuka, T.; Matsuo, G.; Nakata, M. *Synlett* **1995**, *4*, 306.
16. Filho, J. R. F.; Srivastava, R. M.; Soro, Y.; Cottier, L.; Descotes, G. *J. Carbohydr. Chem.* **2001**, *20*, 561–568.
17. Panfil, I.; Belzecki, C.; Urbanczyk-Lipkowska, Z.; Chmielewski, M. *Tetrahedron* **1991**, *47*, 10087–10094.