Pergamon

Tetrahedron 55 (1999) 10511–10526

TETRAHEDRON

N-Azole Substituted Carbohydrates. Synthesis and Transformations of 1-(3'-Deoxy-1',2':5',6'-di-*O*-isopropylidene-α-D-glucofuranos-3'-yl)-Azole Derivatives

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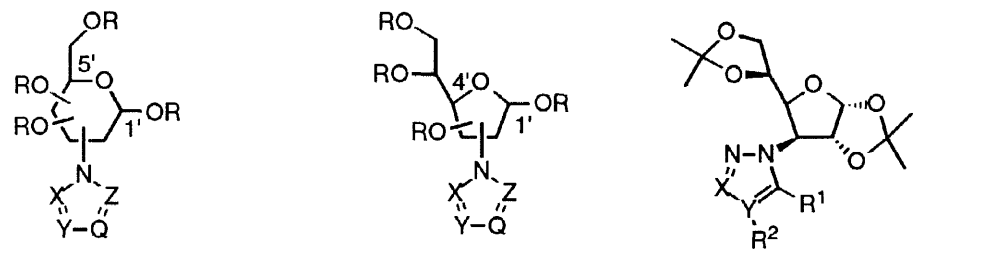
Received 26 April 1999; revised 7 June 1999; accepted 25 June 1999

Abstract: The synthesis and chemical manipulation of some 1-(3'-deoxy-1',2':5',6'-di-*O*-isopropylidene-α-D-glucofuranos-3'-yl)-azole derivatives is described. © 1999 Elsevier Science Ltd. All rights reserved.

INTRODUCTION

In the course of a project aimed at the synthesis and biological evaluation of a series of new aminosugars and nucleosides, we were particularly attracted by simple *N*-azole derivatives where the azole nucleus is located at carbon 2, 3 or 4 in the carbohydrate core of a pyranosyl ring (**A**), or at carbon 2 or 3 of a furanosyl structure (**B**) (Fig. 1).



A R= H, alkyl, acyl
X, Y, Z, Q= C, O, N, S

B

C
X= N, Y= C; R^1, R^2= H, COOR
X= CH, Y= N; R^1= H
X, Y= N; R^1= H

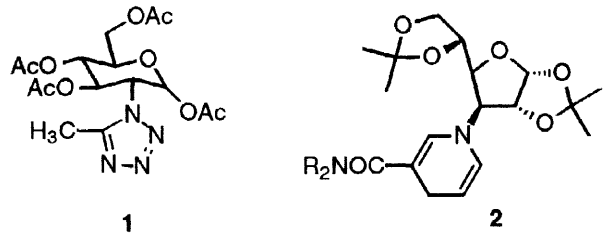
Figure 1. Structures A-C

Careful revision of the literature reveals that the synthesis of such a family of compounds has been almost neglected and only scarce examples have been documented (see for instance, molecules **1**[1] and **2**,[2] Fig. 2). This is really surprising in view of the potential ready availability of these glycomimetics[3] by using simple synthetic schemes and the large number of possible molecules resulting for biological screening and chemical manipulation.

Very recently, in our laboratory we have addressed this problem and in this work we report our preliminary results on this subject. We have selected as azole the 1,2,3-triazole, 1,2,4-triazole and the tetrazole nucleus. These heterocyclic rings have been systematically used in medicinal chemistry due to the pronounced biological activities of the substances containing this heterocycle.[4] We describe here the synthesis and chemical

PII: S0040-4020(99)00575-X

manipulation of some 1-(3'deoxy-1',2':5',6'-di-*O*-isopropylidene-α-D-glucofuranos-3'-yl)-azole derivatives of type **C** (Fig. 1).[5]



1 **2**

Figure 2. *N*-Azoles 1 and 2

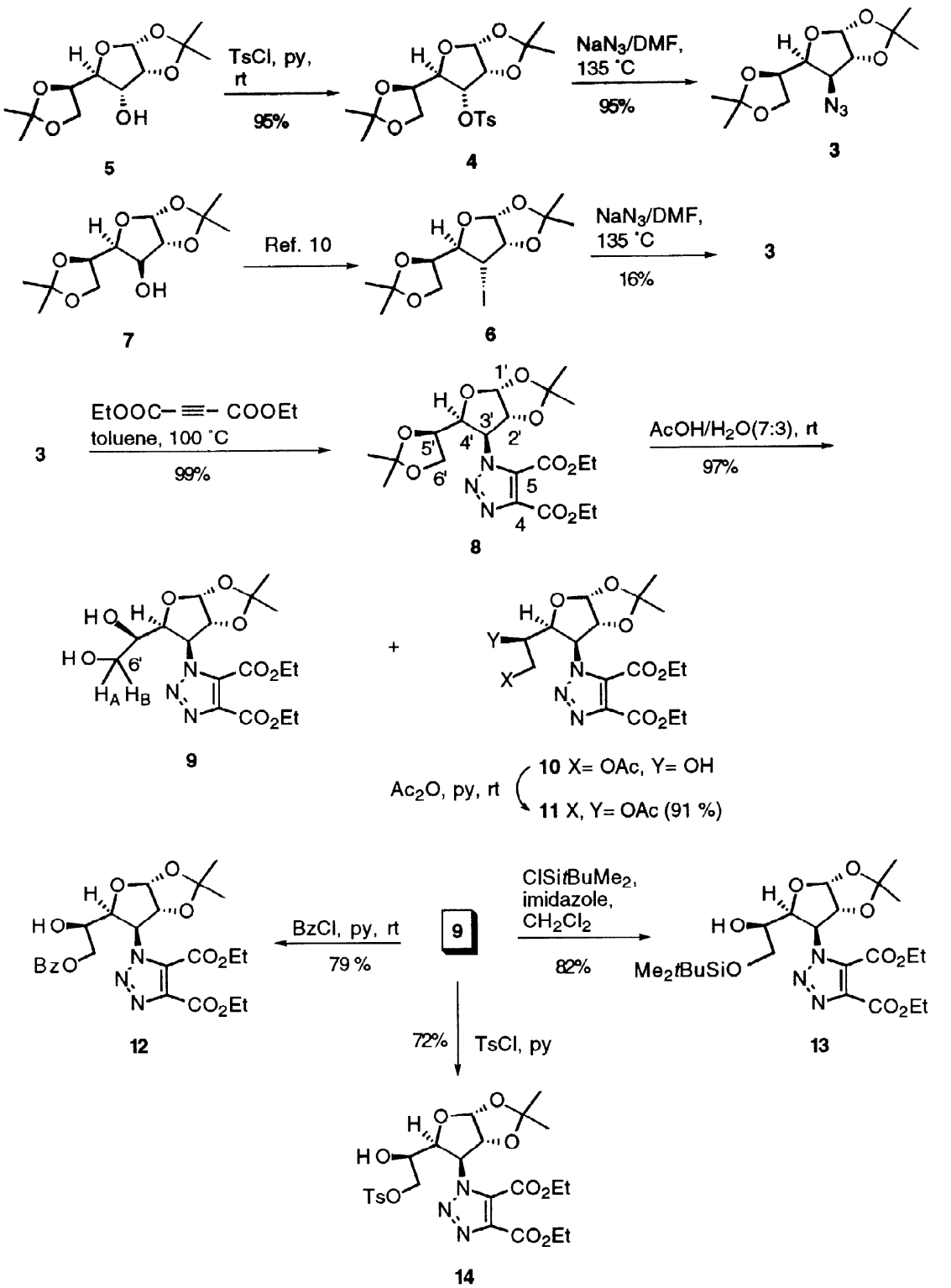
RESULTS AND DISCUSSION

We began this project with the synthesis of 1-(3'-deoxy-1',2':5',6'-di-*O*-isopropylidene-α-D-glucofuranos-3'-yl)-1,2,3-triazole derivatives. The choice of the 1,2,3-triazole heterocyclic ring was also in part due to the easily available azido sugar **3** (Scheme 1). In fact, the most common method described in the literature for the preparation of the 1,2,3-triazole ring is the 1,3-dipolar cycloaddition (1,3-DC) reaction between substituted acetylenes and an azide.[6] This reaction has been performed with azido sugars[7] and nucleosides, such as AZT, in order to improve its biological profile.[8]

3-Azido-3-deoxy-1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (**3**) was prepared, according to the method previously described (DMF, 135 °C), from 1,2:5,6-di-*O*-isopropylidene-3-*O*-*p*-toluenesulfonyl-α-D-allofuranose[9] (**4**) (Scheme 1), easily synthesized by tosylation of commercially available 1,2:5,6-di-*O*-isopropylidene-α-D-allofuranose (**5**), in 90% overall yield. Alternatively, reaction of 3-deoxy-3-iodo-1,2:5,6-di-*O*-isopropylidene-α-D-allofuranose (**6**),[10] obtained from 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (**7**), with sodium azide in DMF, gave a lower overall yield of compound **3** (16%) and was discarded. Finally, Mitsunobu inversion[11] protocols on 1,2:5,6-di-*O*-isopropylidene-α-D-allofuranose (**5**) [with diphenylphosphoryl azide[12] (19% yield) or with zinc azide/bis-pyridine complex[13] (no reaction)] as a method for the "one-pot-reaction" synthesis of compound **3** from sugar **5**, were disappointing in terms of yields and purification, and were not further used.

Following the projected synthetic sequence, 1,3-DC[14] of azidosugar **3** with diethyl acetylenedicarboxylate[15] (toluene, reflux, 6 h) gave adduct **8** (Scheme 1) in almost quantitative yield. The new triazole-sugar derivative showed analytical and spectroscopic data in good agreement with this structure ($C_{20}H_{29}N_3O_9$). In the IR spectrum the typical band for the azido group was absent, showing a new and strong band at 1735 cm^{-1} due to the carbonyl of the ester group. In the ^1H and ^{13}C NMR spectra, after standard experiments (2D COSY, HMQC, DEPT), we could assign all the signals for the protons and carbons (see **Experimental Part**). Very interestingly, the proton on the carbon where the azole has been incorporated, H-3', appears at 5.80 ppm, as a doublet with a vicinal coupling constant $J_{3',4'}$= 3.9 Hz ($J_{2',3'}$= 0 Hz), showing that the cycloaddition has occurred with retention of configuration; in addition, an unexpected highly shielded signal at 2.98 ppm was assigned to H-5' [compare with the shift of H-5 (m, 4.30-4.00 ppm) in compound **3**]. In the ^{13}C NMR spectrum, the carbons of the triazole, C-4 and C-5, appear at 140.5 ppm and 132.1 ppm, respectively.[16]

The high yield and the short synthetic sequence leading to adduct **8** prompted us to transform and manipulate this material in order to obtain new *N*-1,2,3-triazole sugar derivatives. Following simple or standard protocols compounds **9-17** (Schemes 1, 2 and 3) were synthesized.



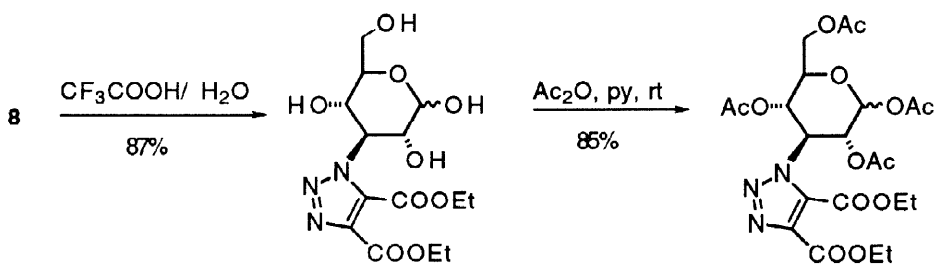
Scheme 1. Synthesis and transformations of 4,5-dicarbethoxy-1-(3'-deoxy-1',2':5',6'-di-*O*-isopropylidene-α-D-glucofuranos-3'-yl)-1,2,3-triazole (**8**).

Acid hydrolysis under mild acid conditions (acetic acid/water, 7/3) gave the 1,2-*O*-isopropylidene derivative **9** in excellent yield (97%) and traces of the monoacetate **10** (Scheme 1). Compound **9** was also obtained, but in lower yield (59%), using ethanol/*p*-toluenesulfonic acid as reagent. In the ^{1}H NMR spectrum of compound **9** the signals at δ 2.89 (d, *J*= 5.1 Hz, 1H, OH) and 2.40 (br s, 1H, OH) disappeared after D_2O

addition; and the resonances for 2 H6': 3.81-3.67 ppm (m, 1H, HA6') and 3.65-3.52 ppm (m, 1H, HB6') were significantly simplified, appearing now as doublets of doublets: δ 3.81-3.67 (dd, $J_{6'A,6'B}$= 13.2 Hz, $J_{5',6'A}$= 2.2 Hz, 1H, HA6') and 3.65-3.52 (dd, $J_{5',6'B}$= 4.0 Hz,1H, HB6'). Comparing with product **9**, as expected, compound **10** showed an additional acetyl group (accordingly, in the ^{1}H NMR, a new singlet appears at 2.04 ppm, and in the ^{13}C NMR spectrum, two new signals at 171.9 ppm and 20.8 ppm). The observed shifts at C-6 on going from product **9** to **10** (H6'A: Δδ= + 0.53 ppm and H6'B: Δδ= + 0.46 ppm; C6': Δδ= +3.2 ppm) in the NMR spectra, while H-5' and C-5' remained almost unchanged (H5': Δδ= + 0.17 ppm; C5': Δδ= - 0.8 ppm), suggest that the acetyl group was located at C-6'. Full acetylation of compound **10** gave compound **11** in 91% yield (Scheme 1), whose spectroscopic and analytical data were in good agreement with this structure.

Selective and standard benzoylation, silylation or tosylation of **9** at the primary hydroxyl group was achieved in very good yield affording products **12**, **13** and **14** (Scheme 1), respectively. Compounds **12-14** showed analytical and spectroscopic data in full agreement with these structures (see **Experimental Part**). These compounds are conveniently functionalized intermediates for further synthetic developments.[17]

We have also analyzed the acid hydrolysis of the 1',2'-isopropylidene ring in compound **8**. Treating this molecule with trifluoroacetic acid/water provided the fully deprotected material **15**, that was acetylated to give derivative **16** (Scheme 2). Both reactions occurred in very good yield (~85%). The ^{1}H NMR spectrum of compound **15** was very complex due to the presumed mixture of the pyrano and furano forms with the corresponding anomers, a typical situation in free sugars.[18] After D_2O addition, in this spectrum we could identify signals for H-1α and H-1β at 5.25 ppm (d, $J_{1eq,\ 2ax}$= 3.6 Hz) and at 4.68 ppm (d, $J_{1ax,\ 2ax}$= 7.2 Hz), in a 2.5 to 1 ratio, respectively. These data are in good agreement with the expected values for H-1 in the pyrano form for the α and β anomers in D-glucose derivatives.[18] The ^{13}C NMR spectrum was more simple and easy to analyze. In fact, signals for only two compounds were apparent. Particularly significant were the chemical shifts for C-1α at 91.1 ppm and for C-1β at 96.7 ppm. This is also in accordance with the recorded typical values for C-1 in free sugars and the observed ratios for the anomers.[18] Similar chemical shifts in product **16** confirmed again unambiguously this assignment (see **Experimental Part**).



15 **16**

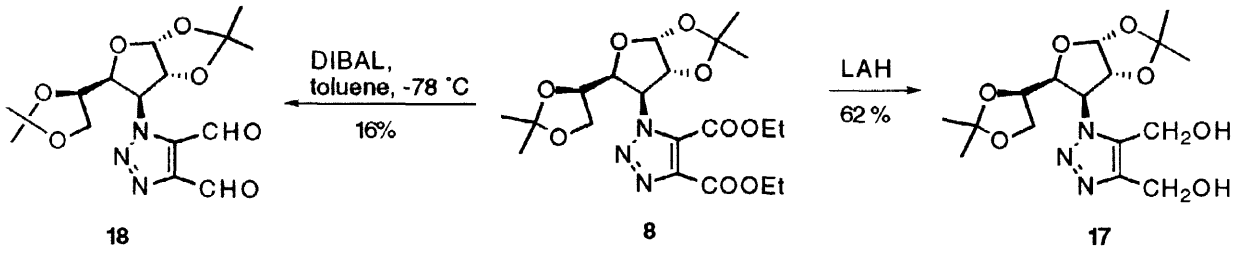
Scheme 2. Acid hydrolysis of 4,5-dicarbethoxy-1-(3'-deoxy-1',2':5',6'-di-*O*-isopropylidene-α-D-glucofuranos-3'-yl)-1,2,3-triazole (**8**).

We have also tested some reactions involving the triazole nucleus (Scheme 3).

The lithium alumnium hydride reaction of product **8** gave the expected diol **17**, while diisobutylaluminium hydride, in toluene, at -78 °C, afforded a complex reaction mixture; we could only isolate the aldehyde **18** in a poor yield that we did not try to optimize. All these compounds showed analytical and spectroscopic data as expected for these structures.

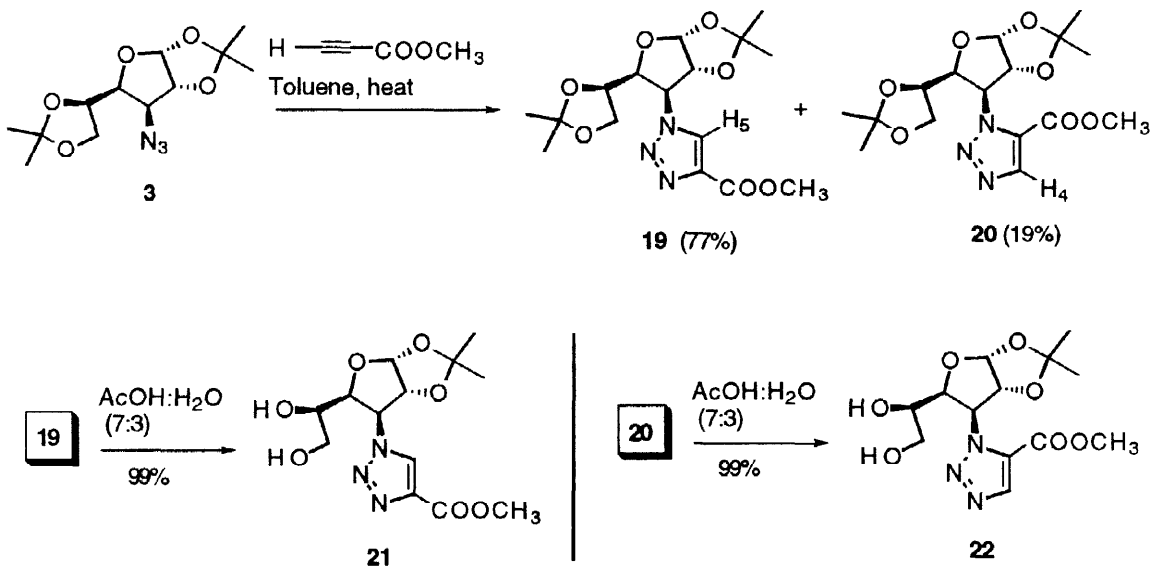
Continuing with our project, we investigated the 1,3-DC of methyl propiolate with the azido sugar **3**. As expected,[19] two isomers were isolated in almost quantitative overall yield (Scheme 4). In the ^{1}H NMR spectrum

major isomer (**19**, 77% yield) showed H-5 at 8.22 ppm as a singlet, while in the minor isomer **20** (19% yield) H-4 appeared more shielded, at 8.04 ppm as a singlet. These data are in agreement with the known reactivity of azides with unsymmetrical alkynes, and with the observed chemical shifts for H-4 or H-5 in substituted alkoxycarbonyl 1,2,3-triazoles.[19] Additional NMR experiments (HMQC, ^{13}C, DEPT) allowed us to assign all the signals to the protons and carbons. It is interesting to note that in the ^{1}H NMR spectra of these molecules, H-3' resonates at 5.03 ppm in the ester **19**, while this proton appears more deshielded (at 6.12 ppm, $\Delta\delta$= +1.09 ppm) in ester **20**. This significant shift is probably due to the proximity of the carbonyl of the carbethoxy group at C-5 respect to H-3' in a coplanar arrangement of these functional groups, that would effectively deshield the proton H-3' in the furanose nucleus.



Scheme 3. Hydride reduction of compound **8**. Synthesis of 1-(3'-deoxy-1',2':5',6'-di-*O*-isopropylidene-α-D-glucofuranos-3'-yl)-1,2,3-triazole derivatives **17** and **18**.

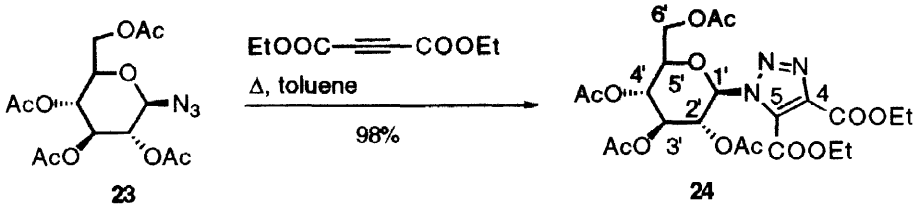
Compounds **19** and **20** were submitted to mild acid hydrolysis to give the partially deprotected sugars **21** and **22** in good yield (Scheme 4).



Scheme 4. Synthesis of 4-carbomethoxy-1-(3'-deoxy-1',2':5',6'-di-*O*-isopropylidene-α-D-glucofuranos-3'-yl)-1,2,3-triazole (**19**), 5-carbomethoxy-1-(3'-deoxy-1',2':5',6'-di-*O*-isopropylidene-α-D-glucofuranos-3'-yl)-1,2,3-triazole (**20**) and derivatives (**21**, **22**).

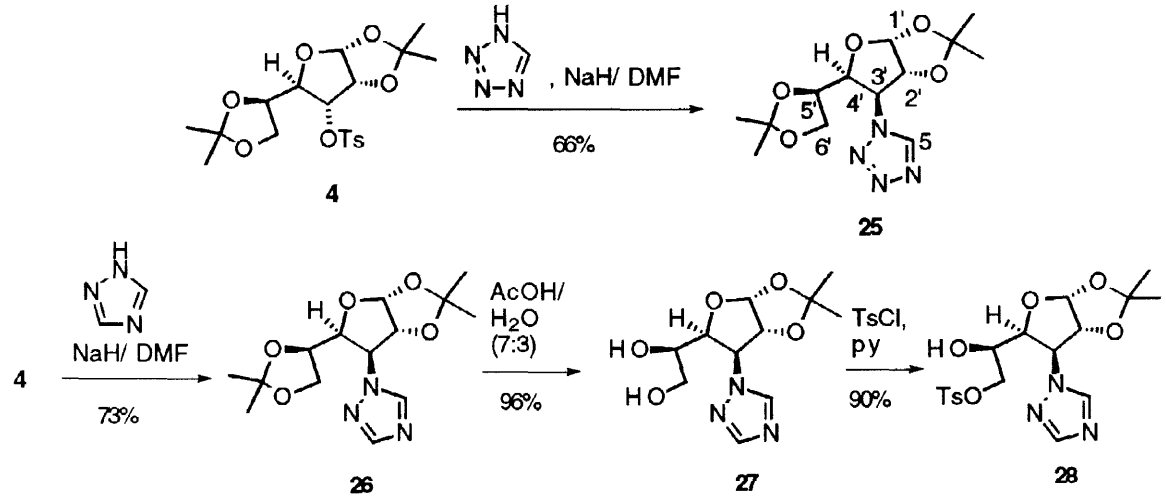
In this context, we considered also the reaction of azido sugar **3** with methyl acrylate. It is known that this protocol yields the corresponding Δ^2-1,2,3-triazolines[20] and some example in sugar chemistry with 1-azido sugars has been reported with moderate success.[21] Unfortunately, in our hands and with substrate **3**, this reaction, at reflux or at room temperature, gave a complex reaction mixture that was not further investigated.

Prompted by the successful results obtained in the reaction of azide **3** with different acetylene derivatives, we extended this chemistry to other azides, such as the commercially available **23**.



Scheme 5. Synthesis of 4,5-dicarbethoxy-1-(2',3',4',6'-tretra-*O*-acetyl-β-D-glucopyranosyl)-1,2,3-triazole (**24**).

In fact, a careful revision of the literature reveals that the 1,3-DC of methyl propiolate and this glycosyl azide has been described,[19a] but similar 1,3-DC reactions of symmetrical dialkyl acetylenedicarboxylates with glycosyl azides have not been reported.



Scheme 6. Synthesis and transformations of 1-(3'-deoxy-1',2':5',6'-di-*O*-isopropylidene-α-D-glucofuranos-3'-yl)-1,2,3,4-tetrazole (**25**) and 1-(3'-deoxy-1',2':5',6'-di-*O*-isopropylidene-α-D-glucofuranos-3'-yl)-1,2,4-triazole (**26**).

Equimolecular quantities of 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl azide (**23**) and diethyl acetylenedicarboxylate were heated in toluene at reflux for 10 h. After work-up and chromatography compound **24** (Scheme 5) was isolated in almost quantitative yield. The structure of this compound was established on the basis of its elemental analysis, spectroscopic data and chemical reactivity. Since the IR spectrum of **24** did not show absorption in the diazo region, it was assumed that this compound was the expected cycloaddition adduct. In the ^{1}H NMR spectrum of **24** the anomeric proton (H-1') appeared at 6.12 ppm as a doublet ($J_{1',2'}$= 9.4 Hz). This value for the vicinal coupling constant confirms the axial-axial arrangement between these protons, securing that during the cycloaddition the absolute stereochemistry at carbon (C-1') has not been affected. Additional experiments (selective decoupling irradiations, ^{13}C NMR, DEPT, 2D COSY, HMQC) allowed us to assign the resonances for the rest of the carbons and protons of the molecule.

Another interesting synthetic alternative for the incorporation of the azole nucleus in these sugar templates is the Mitsunobu inversion reaction[22] or the intermolecular S_N2 reaction of the azole salts with good leaving

groups on suitable carbohydrate derivatives. These transfromations have been considered in the literature before and there are some precedents.[23]

With these ideas in mind we treated tosylate **4** with imidazole and sodium hydride in dry DMF. The reaction was very slow and, after 12 days, a complex mixture resulted that was not further investigated. A more satisfying result was obtained using tetrazole as the heterocyclic ring. Under the same conditions, we isolated and characterized compound **25** in 66% yield (Scheme 6). Following the same protocol, triazole gave compound **26** in good yield (73%) (Scheme 6). In both successful cases, inversion of the configuration at C-3' has taken place in view of the vicinal coupling constants of H-2' and H-3' (0 Hz), a typical value for these structures with this configurational disposition.

Standard acid hydrolysis and tosylation gave compounds **27** and **28** in good yield, respectively. These compounds showed spectroscopic data coherent with these structures.

In summary, a series of *N*-azole carbohydrate derivatives have been prepared by 1,3-DC of diethylacetylenedicarboxylate, methyl propiolate and 3-azido-3-deoxy-1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (**3**) and 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl azide (**23**) or by S_N2 reaction of tosylate **4** with the appropriate azole nucleus. These reactions proceed in high yields, in multigram quantities, providing access to a large number of new, chiral molecules for additional chemical manipulation and biological screening,[5] such as fused azole-piperidinoses.[5,24]

EXPERIMENTAL SECTION

General Methods. Reactions were monitored by TLC using precoated silica gel aluminium plates containing a fluorescent indicator (Merck, 5539). Detection was done by UV (254 nm) followed by charring with sulfuric-acetic acid spray, 1% aqueous potassium permanganate solution or 0.5% phosphomolybdic acid in 95% EtOH. Anhydrous $MgSO_4$ was used to dry organic solutions during workups and the removal of solvents was carried out under vacuum with a rotary evaporator. Flash column chromatography was performed using Kieselgel 60 (230-400 mesh, Merck) and hexane-ethyl acetate mixtures as eluent unless otherwise stated. Optical rotations were determined with a Perkin-Elmer 257 instrument. ^1H and ^{13}C NMR spectra were recorded with a Varian VXR-300S spectrometer, using tetramethylsilane as internal standard. Compound **5** was used as received (Pfanstiehl). Tosylate **4** was prepared according to the described method (ref. 9).

4,5-Dicarbethoxy-1-(3'-deoxy-1',2':5',6'-di-*O*-isopropylidene-α-D-glucofuranos-3'-yl)-1,2,3-triazole (8)

Azide **3** (880 mg, 3.09 mmol) was dissolved in toluene (12 mL) and diethyl acetylenedicarboxylate (526 mg, 3.09 mmol, 1 equiv) was added. The mixture was refluxed for 6 h, the solvent was evaporated and the residue submitted to flash chromatography (hexane, ethyl acetate 20%) to give compound **8** (1.30 g, 99%): oil; $[\alpha]_D^{25}$ +126 (*c* 0.45, $CHCl_3$); IR (film) υ 2990, 2940, 1735, 1550, 1375, 1280, 1160, 1070 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 6.25 (d, $J_{1',2'}$= 3.5 Hz, 1 H, H1'), 5.80 (d, $J_{3',4'}$= 3.9 Hz, 1 H, H3'), 4.97 (d, 1 H, H2'), 4.53-4.29 (m, 5 H, 2 x $COOCH_2CH_3$, H4'), 3.91 (d, $J_{5',6'}$= 5.3 Hz, 2 H6'), 2.98 (dt, $J_{4',5'}$= 9.3 Hz, 1 H, H5'), 1.58 (s), 1.44-1.35, 1.12 (s) [18 H, 2 x $OC(CH_3)_2O$, 2 x $COOCH_2CH_3$]; ^{13}C NMR (75 MHz, $CDCl_3$) δ 160.5 and 158.7 (2 x$COOCH_2CH_3$), 140.5 (C4), 132.1 (C5), 113.1 and 110.2 [2 x $OC(CH_3)_2O$], 107.3 (C1'), 84.8 (C2'), 81.3 (C4'), 73.0 (C5'), 68.0 (C6'), 65.3 (C3'), 63.1 and 62.4 (2 x $COOCH_2CH_3$), 27.4, 26.7 and 25.2 [2 x $OC(CH_3)_2O$], 14.6 and 14.3 (2 x $COOCH_2CH_3$); MS (70 eV) *m/z* 456 ($M+1^+$, 1), 440 (M^+-15, 100),

410 (15), 397 (2), 382 (30), 314 (6), 254 (8), 214 (75), 142 (8), 113 (44), 101 (39), 43 (38). Anal. Calcd for $C_{20}H_{29}N_3O_9$: C, 52.74; H, 6.42; N, 9.23. Found: C, 52.56; H, 6.53; N 9.03.

4,5-Dicarbethoxy-1-(3'-deoxy-1',2'-*O*-isopropylidene-α-D-glucofuranos-3'-yl)-1,2,3-triazole (9) and 4,5-dicarbethoxy-1-(6'-*O*-acetyl-3'-deoxy-1',2'-*O*-isopropylidene-α-D-glucofuranos-3'-yl)-1,2,3-triazole (10)

Triazole **8** (1.17 g, 2,59 mmol) was treated with acetic acid/water (10 mL, 7/3) at room temperature for 18 h. The solvent was evaporated, co-distilling with toluene, and the residue was submitted to flash chromatography (hexane, ethyl acetate 30%) to give compound **9** (0.99 g, 92%) and **10** (52 mg, 4%). **9**: oil; $[\alpha]_D^{25}$ +139 (*c* 0.49, $CHCl_3$); IR (film) υ 3600-3400, 3000, 2940, 1740, 1550, 1380, 1285, 1165, 1070 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 6.19 (d, $J_{1',2'}$= 3.6 Hz, 1 H, H1'), 5.64 (d, $J_{3',4'}$= 4.2 Hz, 1 H, H3'), 5.01 (d, 1 H, H2'), 4.42-4.30 (m, 5 H, 2 x $COOCH_2CH_3$, H4'), 3.81-3.67 (m, 1 H, HA6'), 3.65-3.52 (m, 1 H, HB6'), 2.89 (d, *J*= 5.1 Hz, 1 H, OH), 2.71-2.55 (m, 1 H, H5'), 2.40 (br s, 1 H, OH), 1.51 (s), 1.34-1.31 [12 H, $OC(CH_3)_2O$, 2 x $COOCH_2CH_3$]; ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.9 and 158.7 (2 x$COOCH_2CH_3$), 139.4 (C4), 131.9 (C5), 112.5 [$OC(CH_3)_2O$], 106.3 (C1'), 84.1 (C2'), 79.0 (C4'), 68.9 (C5'), 65.1 (C3'), 63.5 (C6'), 63.1 and 61.9 (2 x $COOCH_2CH_3$), 26.6 and 26.1 [$OC(CH_3)_2O$], 14.0 and 13.7 (2 x $COOCH_2CH_3$); MS (70 eV) *m/z* 400 (M^+-15, 22), 384 (15), 354 (22), 324 (15), 254 (14), 214 (68), 167 (28), 127 (40), 122 (72), 113 (78), 85 (54), 43 (100). Anal. Calcd for $C_{17}H_{25}N_3O_9$: C, 49.15; H, 6.07; N, 10.12. Found: C, 49.28; H, 6.16; N 10.13. **10**: oil; $[\alpha]_D^{25}$ +128 (*c* 0.63, $CHCl_3$); IR (film) υ 3600-3200, 3000, 1735, 1550, 1380, 1300-1210, 1165, 1070 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 6.25 (d, $J_{1',2'}$= 3.6 Hz, 1 H, H1'), 5.72 (d, $J_{3',4'}$= 4.2 Hz, 1 H, H3'), 5.04 (d, 1 H, H2'), 4.46-4.35 (m, 5 H, 2 x $COOCH_2CH_3$, H4'), 4.28 (dd, $J_{6'A,6'B}$= 13.2 Hz, $J_{5',6'A}$= 2.2 Hz, 1 H, HA6'), 4.06 (dd, $J_{5',6'B}$= 4.0 Hz, 1 H, HB6'), 2.90-2.75 (m, 2 H, H5', OH), 2.04 (s, 3 H, $OCOCH_3$), 1.56 (s), 1.42-1.33 [12 H, $OC(CH_3)_2O$, 2 x $COOCH_2CH_3$]; ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.9 ($OCOCH_3$), 160.0 and 158.8 (2 x$COOCH_2CH_3$), 139.6 (C4), 132.0 (C5), 112.7 [$OC(CH_3)_2O$], 106.6 (C1'), 84.2 (C2'), 78.9 (C4'), 68.1 (C5'), 66.7 (C6'), 64.8 (C3'), 63.1 and 62.0 (2 x $COOCH_2CH_3$), 26.8 and 26.3 [$OC(CH_3)_2O$], 20.8 ($OCOCH_3$), 14.1 and 13.9 (2 x $COOCH_2CH_3$); MS (70 eV) *m/z* 458 (M^++1, 1), 442 (M^+-15, 22), 384 (10), 354 (21), 324 (26), 254 (12), 214 (52), 194 (44), 167 (22), 150 (10), 140 (13), 122 (35), 43 (100). Anal. Calcd for $C_{19}H_{27}N_3O_{10}$: C, 49.89; H, 5.95; N, 9.19. Found: C, 49.78; H, 6.11; N 9.13.

4,5-Dicarbethoxy-1-(5',6'-di-*O*-acetyl-3'-deoxy-1',2'-*O*-isopropylidene-α-D-glucofuranos-3'-yl)-1,2,3-triazole (11)

Monoacetate **10** (60 mg, 0.13 mmol) was treated with acetic anhydride/pyridine (1 mL/1 mL) at room temperature for 3 h. The solvents were removed and the residue was submitted to flash chromatography (hexane, ethyl acetate 40%) to give compound **11** (59 mg, 91%). **11**: oil; $[\alpha]_D^{25}$ +65 (*c* 0.67, $CHCl_3$); IR (film) υ 2960, 1735, 1535, 1380, 1260-1200, 1165, 1070 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 6.24 (d, $J_{1',2'}$= 3.6 Hz, 1 H, H1'), 5.72 (d, $J_{3',4'}$= 4.0 Hz, 1 H, H3'), 4.85 (d, 1 H, H2'), 4.76 (dd, $J_{4',5'}$= 8.6 Hz, 1 H, H4'), 4.55-4.37 (m, 6 H, 2 x $COOCH_2CH_3$, H5', HA6'), 4.09 (dd, $J_{6A',6'B}$= 12.4 Hz, $J_{5',6'B}$= 4.8 Hz, 1 H, HB6'), 2.04 (s, 3 H, $OCOCH_3$), 1.94 (s, 3 H, $OCOCH_3$), 1.60 and 1.40 [s, s, 6 H, $OC(CH_3)_2O$)], 1.41 [t, *J*= 7.0 Hz, 6 H, 2 x $COOCH_2CH_3$]; ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.3 and 169.1 (2 x $OCOCH_3$), 159.9 and 158.4 (2 x$COOCH_2CH_3$), 140.5 (C4), 132.3 (C5), 112.9 [$OC(CH_3)_2O$], 105.9 (C1'), 84.8 (C2'), 77.1 (C4'), 67.9 (C5'), 64.6 (C3'), 63.1 (C6'), 62.5 and 61.9 (2 x $COOCH_2CH_3$), 26.8 and 26.4 [$OC(CH_3)_2O$], 20.6 (2 x

$OCOCH_3$), 14.1 and 13.8 (2 x $COOCH_2CH_3$); MS (70 eV) *m/z* 484 (M^+-15, 100), 454 (6), 426 (6), 384 (6), 354 (8), 267 (10), 254 (16), 194 (55), 167 (38), 122 (27), 85 (10), 43 (100). Anal. Calcd for $C_{21}H_{29}N_3O_{11}$: C, 50.50; H, 5.85; N, 8.41. Found: C, 50.27; H, 5.75; N 8.66.

4,5-Dicarbethoxy-1-(6'-*O*-benzoyl-3'-deoxy-1',2'-*O*-isopropylidene-α-D-glucofuranos-3'-yl)-1,2,3-triazole (12)

Diol **9** (113 mg, 0.27 mmol) and DMAP (3 mg) were dissolved in dry pyridine (2 mL). Distilled benzoyl chloride (96 mg, 0.68 mmol, 2.5 equiv) was slowly added to this cooled mixture in an ice bath, under argon and stirring. After 3 h water was added and the mixture extracted with ethyl acetate. The combined organic layer was dried, filtered, evaporated and the residue was submitted to flash chromatography (hexane, ethyl acetate 30%) to give compound **12** (110 mg, 79%) **12**: mp 99-100 °C; $[\alpha]_D^{25}$ +83 (*c* 0.59, $CHCl_3$); IR (KBr) υ 3600-3200, 2950, 1700, 1440, 1355, 1255, 1165 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.05-7.98 (m, 2 H, aromatic), 7.60-7.26 (m, 3 H, aromatic), 6.30 (d, $J_{1',2'}$= 3.6 Hz, 1 H, H1'), 5.77 (d, $J_{3',4'}$= 4.0 Hz, 1 H, H3'), 5.07 (d, 1 H, H2'), 4.62-4.12 (m, 7 H, 2 x $COOCH_2CH_3$, H4', 2 H6'), 3.40-3.15 (br s, 1 H, OH), 2.96 (ddd, $J_{4',5'}$= 7.8 Hz, $J_{5',6A'}$= 2.0 Hz, $J_{5',6B'}$= 3.6 Hz, 1 H, H5'), 1.56 (s), 1.43-1.24 [12 H, $OC(CH_3)_2O$, 2 x $COOCH_2CH_3$]; ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.6 ($OCOC_6H_5$), 159.9 and 158.7 (2 x$COOCH_2CH_3$), 139.6 (C4), 132.0 (C5), 133.4, 129.7, 129.4, 128.4 ($OCOC_6H_5$), 112.7 [$OC(CH_3)_2O$], 106.5 (C1'), 84.2 (C2'), 78.9 (C4'), 68.5 (C5'), 67.2 (C6'), 64.7 (C3'), 63.0 and 61.8 (2 x $COOCH_2CH_3$), 26.8 and 26.3 [$OC(CH_3)_2O$], 14.1 and 13.8 (2 x $COOCH_2CH_3$); MS (70 eV) *m/z* 504 (17), 474 (5), 458 (15), 382 (15), 354 (13), 324 (32), 214 (54), 194 (26), 122 (13), 113 (22), 105 (100), 77 (20). Anal. Calcd for $C_{24}H_{29}N_{310}$: C, 55.49; H, 5.63; N, 8.09. Found: C, 55.31; H, 5.40; N 7.89.

4,5-Dicarbethoxy-1-(6'-*O*-*t*-butyldimethylsilyl-3'-deoxy-1',2'-*O*-isopropylidene-α-D-glucofuranos-3'-yl)-1,2,3-triazole (13)

Diol **9** (200 mg, 0.48 mmol) was dissolved in dry pyridine (4 mL). Then, DMAP (10 mg) and *t*-butyldimethylsilyl chloride (212 mg, 1.40 mmol, 3.0 equiv) were added to the cooled mixture in an ice bath, under argon and stirring. After 7 h at room temperature toluene was added, the suspension filtered, the solvents evaporated and the residue was submitted to flash chromatography (hexane, ethyl acetate 20%) to give compound **13** (208 mg, 82%). **13**: oil; $[\alpha]_D^{25}$ +47 (*c* 0.32, $CHCl_3$); IR (film) υ 3600-3200, 2950, 1730, 1450, 1355, 1260, 1165, 1090 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 6.24 (d, $J_{1',2'}$= 3.6 Hz, 1 H, H1'), 5.78 (d, $J_{3',4'}$= 4.0 Hz, 1 H, H3'), 5.07 (d, 1 H, H2'), 4.47-4.37 (m, 5 H, 2 x $COOCH_2CH_3$, H4') 3.63 (br s, 2 H, 2 H6'), 2.55-2.51 (m, 1 H, H5'), 2.41 (d, *J*= 6.6 Hz, 1 H, OH), 1.54 (s), 1.48-1.24 [12 H, $OC(CH_3)_2O$, 2 x $COOCH_2CH_3$], 0.86 [9 H, OSi*t*-$C(CH_3)_3(CH_3)_2$], 0.04 [6 H, OSi*t*-$C(CH_3)_3(CH_3)_2$]; ^{13}C NMR (75 MHz, $CDCl_3$) δ 160.0 and 158.5 (2 x$COOCH_2CH_3$), 139.6 (C4), 132.0 (C5), 112.4 [$OC(CH_3)_2O$], 106.4 (C1'), 84.2 (C2'), 78.6 (C4'), 68.6 (C5'), 64.8 (C3'), 63.7 (C6'), 62.7 and 61.8 (2 x $COOCH_2CH_3$), 26.6 and 26.2 [$OC(CH_3)_2O$], 25.7 [OSi*t*-$C(CH_3)_3(CH_3)_2$], 18.2 [OSi*t*-$C(CH_3)_3(CH_3)_2$], 14.0 and 13.7 (2 x $COOCH_2CH_3$), -5.5 [OSi*t*-$C(CH_3)_3(CH_3)_2$]; MS (70 eV) *m/z* 514 (M^+-15, 8), 473 (20), 414 (32), 382 (14), 214 (67), 201 (41), 194 (15), 155 (12), 143 (11), 117 (100), 75 (53). Anal. Calcd for $C_{23}H_{39}N_3O_{10}Si$: C, 50.63; H, 7.20; N, 7.70. Found: C, 50.68; H, 7.31; N 7.53.

4,5-Dicarbethoxy-1-(6'-*O*-*p*-toluenesulfonyl-3'-deoxy-1',2'-*O*-isopropylidene-α-D-glucofuranos-3'-yl)-1,2,3-triazole (14)

Diol **9** (101 mg, 0.24 mmol) was dissolved in dry pyridine (2.6 mL). DMAP (26 mg, 0.24 mmol) and *p*-toluenesulfonyl chloride (92 mg, 0.48 mmol, 2.0 equiv) were added to the cooled mixture in an ice bath, under argon and stirring. After 24 h at room temperature toluene was added, the solvent evaporated and the residue was submitted to flash chromatography (hexane, ethyl acetate 40%) to give compound **14** (99 mg, 72%). **14**: mp 124-126 °C; $[\alpha]_D^{25}$ +130 (*c* 0.6, $CHCl_3$); IR (KBr) υ 3480, 2990, 1730, 1710, 1550, 1375, 1365, 1225, 1180, 1065 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.73 (d, *J*= 8.2 Hz, 2 H, aromatic), 7.33 (d, 2 H, aromatic), 6.20 (d, $J_{1',2'}$= 3.4 Hz, 1 H, H1'), 5.73 (d, $J_{3',4'}$= 4.2 Hz, 1 H, H3'), 5.04 (d, 1 H, H2'), 4.49-4.37 (m, 5 H, 2 x $COOCH_2CH_3$, H4'), 4.12 (dd, $J_{6A',6'B}$= 10.5 Hz, $J_{5',6'A}$= 2.2 Hz, 1 H, HA6'), 4.01 (dd, $J_{5',6'B}$= 6.0 Hz, 1 H, HB6'), 2.83-2.78 (m, 2 H, OH, H5'), 2.44 (s, 3 H, $CH_3SO_2C_6H_5$), 1.54 (s), 1.48-1.24 [12 H, $OC(CH_3)_2O$, 2 x $COOCH_2CH_3$]; ^{13}C NMR (75 MHz, $CDCl_3$) δ 160.3 and 159.1 (2 x$COOCH_2CH_3$), 140.0 (C4), 132.6 (C5), 145.7, 132.3, 130.4, 128.4 ($CH_3SO_2C_6H_5$), 113.2 [$OC(CH_3)_2O$], 107.0 (C1'), 84.5 (C2'), 78.9 (C4'), 72.1 (C5'), 67.8 (C3'), 65.1 (C6'), 63.6 and 62.4 (2 x $COOCH_2CH_3$), 27.2 and 26.7 [$OC(CH_3)_2O$], 22.1 ($CH_3SO_2C_6H_5$), 14.6 and 14.3 (2 x $COOCH_2CH_3$); MS (70 eV) *m/z* 569 (M^+, 20), 554 (M^+-15, 14), 511 (5), 382 (13), 354 (23), 324 (26), 268 (10), 254 (18), 214 (59), 139 (17), 113 (46), 91 (100). Anal. Calcd for $C_{24}H_{31}N_3O_{11}S$: C, 50.61; H, 5.49; N, 7.38; S, 5.63. Found: C, 50.80; H, 5.64; N 7.30; S, 5.45.

4,5-Dicarbethoxy-1-(α,β-D-glucofuranos-3'-yl)-1,2,3-triazole (15)

Compound **8** (200 mg, 0.44 mmol) was treated with 60% aqueous trifluoroacetic acid (5 mL). After 7 h at room temperature, the solvents were removed using toluene, and the residue was submitted to flash chromatography (ethyl acetate) to give compound **15** (143 mg, 87%) as a solid. **15**: mp 118-120 °C; IR (KBr) υ 3600-3000, 2950, 2900, 1710, 1610, 1540, 1355, 1260, 1200, 1030 cm^{-1}; ^1H NMR (300 MHz, DMSO) (mixture of α and β anomers at C-1') δ 6.01 (d, $J_{1',OH}$= 3.6 Hz, 1 H, OH-α), 5.28 (t, $J_{1',2'}$= 3.6 Hz, 1 H, H1'-α), 5.15 (t, $J_{3',2'}$= $J_{3',4'}$= 10.0 Hz, 1 H, H3'-α), 4.86-4.74 (m, 3 H, H1'-β, H3'-β, OH-β), 4.50-3.50 (m, 9 H, 2 x $COOCH_2CH_3$, H2', H4', H5', 2 H6'), 1.33 and 1.32 [t, *J*= 7.2 Hz, 6 H, 2 x $COOCH_2CH_3$]; ^{13}C NMR (75 MHz, DMSO) (mixture of α and β anomers at C-1') δ 159.4 and 158.0 (2 x$COOCH_2CH_3$), 138.0 (C4), 132.5 (C5), 96.7 (C1'-β), 91.1 (C1'-α), 76.8 (C2'-β, C5'-β), 71.9 (C4'-β), 71.3 (C5'-α), 69.6 (C2'-α), 67.5 (C4'-α), 64.8 (C3'), 61.7 (C6'), 60.4 and 60.3 (2 x $COOCH_2CH_3$), 12.6 and 12.4 (2 x $COOCH_2CH_3$); MS (70 eV) *m/z* 344 (1), 256 (5), 226 (4), 214 (100), 186 (19), 168 (38), 140 (58), 85 (26), 69 (34). Anal. Calcd for $C_{14}H_{21}N_3O_9$: C, 44.80; H, 5.64; N, 11.20 Found: C, 44.64; H, 5.65; N 11.09.

4,5-Dicarbethoxy-1-(1',2',4',6'-tetra-*O*-acetyl-α,β-D-glucofuranos-3'-yl)-1,2,3-triazole (16)

Compound **15** (120 mg, 0.32 mmol) was acetylated under standard conditions (acetic anhydride/pyridine, 1/1, 2 mL) to give compound **16** (147 mg, 85%). **16**: oil; IR (film) υ 2950, 1760-1725, 1540, 1440, 1355, 1250-1180, 1100-1010 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) (mixture of α and β anomers at C-1') δ 6.48 (d, $J_{1',2'}$= 3.4 Hz, 1 H, H1'-α), 5.83-5.16 (m, H1'-β, 3 H: H2', H3' and H4'), 4.57-3.94 (m, 7 H, 2 x $COOCH_2CH_3$, H5', 2 H6'), 2.21, 2.12, 2.09, 2.03, 1.88, 1.87 and 1.85 (s, s, s, s, s, s, s, 12 H, 4 x $OCOCH_3$), 1.40 [t, *J*= 7.2 Hz, 6 H, 2 x $COOCH_2CH_3$)]; ^{13}C NMR (75 MHz, $CDCl_3$) (mixture of α and β anomers at C-1') δ 171.0, 169.4, 169.2, 168.8, 168.7, 167.1 and 166.4 (4 x $OCOCH_3$), 160.2 and 158.9 (2 x$COOCH_2CH_3$), 138.0 (C4), 132.5 (C5), 92.8 (C1'-β), 89.1 (C1'-α), 74.4 (C5'-α), 70.9 (C2'-α, C4'), 70.6 (C2'-β), 69.2 (C5'-β), 69.2 and 68.0 (C3'), 63.8 and 63.7 (C6'), 62.4 and 61.9 (2 x $COOCH_2CH_3$), 20.6 and

20.5 (4 x $OCOCH_3$), 14.6 and 14.3 (2 x $COOCH_2CH_3$); MS (70 eV) *m/z* 353 (23), 293 (20), 280 (15), 256 (22), 214 (62), 169 (22), 43 (100). Anal. Calcd for $C_{22}H_{29}N_3O_{13}$: C, 48.62; H, 5.38; N, 7.73 Found: C, 48.53; H, 5.52; N 7.55.

4,5-Dihydroxymethyl-1-(3'-deoxy-1',2':5',6'-di-*O*-isopropylidene-α-D-glucofuranos-3'-yl)-1,2,3-triazole (17)

Compound **8** (100 mg, 0.22 mmol) was dissolved in dry THF (3 mL), the solution was cooled in an ice-bath and lithium aluminium hydride (13 mg, 0.33 mmol, 1.8 equiv) was added. The mixture was stirred at room temperature for 10 h. The excess of lithium aluminium hydride was destroyed by addition of an aqueous solution of potassium bisulfite, the mixture was extracted with ethyl acetate, and the combined organic layer was washed with brine, dried, evaporated and the residue was submitted to flash chromatography (hexane, ethyl acetate 80%) to give compound **17** (57 mg, 62%). **17**: mp 116-118 °C; $[\alpha]_D^{25}$ +25 (*c* 0.85, $CHCl_3$); IR (KBr) υ 3600-3100, 2940, 1600, 1440, 1560, 1550, 1190, 1140, 1050 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 6.20 (d, $J_{1',2'}$= 3.5 Hz, 1 H, H1'), 5.02 (d, $J_{3',4'}$= 4.0 Hz, 1 H, H3'), 4.92 (d, 1 H, H2'), 4.80-4.62 (m, 4 H, 2 x $COOCH_2CH_3$), 4.32 (dd, $J_{4',5'}$= 9.5 Hz, 1 H, H4'), 3.98 (dd, $J_{5',6A'}$= 4.3 Hz, $J_{6A',6B'}$= 9.1 Hz, 1 H, H6A'), 3.91 (dd, $J_{5',6B'}$= 6.0 Hz, 1 H, H6B'), 3.40 (br s, 1 H, OH), 3.04 (ddd, 1 H, H5'), 1.97 (d, *J*= 10.4 Hz, 1 H, OH), 1.58, 1.35, 1.30 and 1.14 [s, s, s, s, 12 H, 2 x $OC(CH_3)_2O$]; ^{13}C NMR (75 MHz, $CDCl_3$) δ 144.6 (C4), 135.6 (C5), 112.5 and 110.0 [2 x $OC(CH_3)_2O$], 106.4 (C1'), 84.5 (C2'), 80.4 (C4'), 72.1 (C5'), 67.4 (C6'), 63.2 (C3'), 55.0 and 51.6 (2 x CH_2OH), 26.8, 26.7, 26.1 and 24.9 [2 x $OC(CH_3)_2O$]; MS (70 eV) *m/z* 371 (1), 356 (34), 254 (18), 196 (11), 170 (12), 130 (63), 113 (40), 101 (55), 43 (100). Anal. Calcd for $C_{16}H_{25}N_3O_7$: C, 51.75; H, 6.78; N, 11.31. Found: C, 51.90; H, 6.57; N 11.20.

4,5-Dicarbaldehyde-1-(3'-deoxy-1',2':5',6'-di-*O*-isopropylidene-α-D-glucofuranos-3'-yl)-1,2,3-triazole (18)

Compound **8** (160 mg, 0.35 mmol) was dissolved in dry toluene (10 mL), the solution was cooled in a bath at -78 °C and diisobutylaluminium hydride (1.05 mL, 1.05 mmol, 3.0 equiv, 1 M in toluene) was slowly added. The mixture was stirred at this temperature for 5 h. The excess of reagent was destroyed by careful addition of methanol, the salts were filtered, the filtrate was evaporated and the residue submitted to flash chromatography (hexane, ethyl acetate 50%) to give compound **18** (20 mg, 16%). **18**: mp 113-116 °C; $[\alpha]_D^{25}$ +77 (*c* 0.62, $CHCl_3$); IR (KBr) υ 2950, 1680, 1440, 1360, 1370, 1200, 1050, 1000 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 10.31 (s, 1 H, CHO), 10.28 (s, 1 H, CHO), 6.25 (d, $J_{1',2'}$= 3.4 Hz, 1 H, H1'), 6.05 (d, $J_{3',4'}$= 4.4 Hz, 1 H, H3'), 5.05 (d, 1 H, H2'), 4.42 (dd, $J_{4',5'}$= 9.1 Hz, 1 H, H4'), 3.98-3.81 (m, 2 H, 2 H6'), 2.90 (ddd, $J_{5',6A'}$= 4.4 Hz, $J_{5',6B'}$= 9.0 Hz, 1 H, H5'), 1.57, 1.34, 1.32 and 1.07 [s, s, s, s, 12 H, 2 x $OC(CH_3)_2O$]; ^{13}C NMR (75 MHz, $CDCl_3$) δ 185.7 and 180.0 (2 x CHO), 147.1 (C4), 134.3 (C5), 112.8 and 109.9 [2 x $OC(CH_3)_2O$], 106.7 (C1'), 84.2 (C2'), 81.1 (C4'), 72.8 (C5'), 67.5 (C6'), 65.4 (C3'), 26.8, 26.2 and 25.0 [2 x $OC(CH_3)_2O$]; MS (70 eV) *m/z* 352 (5), 312 (16), 150 (16), 127 (32), 85 (45), 43 (100). Anal. Calcd for $C_{16}H_{21}N_3O_7$: C, 52.31; H, 5.76; N, 11.44. Found: C, 52.28; H, 5.62; N 11.39.

4-Carbomethoxy-1-(3'-deoxy-1',2':5',6'-di-*O*-isopropylidene-α-D-glucofuranos-3'-yl)-1,2,3-triazole (19) and 5-carbomethoxy-1-(3'-deoxy-1',2':5',6'-di-*O*-isopropylidene-α-D-glucofuranos-3'-yl)-1,2,3-triazole (20)

Azide **3** (500 mg, 1.75 mmol) was dissolved in toluene (6 mL) and methyl propiolate (526 mg, 3.09 mmol, 1 equiv) was added. The mixture was refluxed for 4 h, the solvent was evaporated and the residue submitted to flash chromatography (hexane, ethyl acetate 25%) to give compounds **19** (500 mg, 77%) and **20** (120 mg, 19%). **19**: mp 180-181 °C; $[\alpha]_D^{25}$ +3 (*c* 0.48, $CHCl_3$); IR (KBr) υ 3140, 2990, 2940, 1730, 1545, 1380, 1375, 1260-1215, 1160, 1070 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.22 (s, 1 H, H5), 6.23 (d, $J_{1',2'}$= 3.6 Hz, 1 H, H1'), 5.17 (d, 1 H, H2'), 5.04 (d, $J_{3',4'}$= 3.8 Hz, 1 H, H3'), 4.33 (dd, $J_{4',5'}$= 9.4 Hz, 1 H, H4'), 3.95-3.90 (m, 5 H, $COOCH_3$, 2 H6'), 3.07 (dt, $J_{5',6A'}$=$J_{5',6B'}$= 5.4 Hz, 1 H, H5'), 1.57, 1.43, 1.36, 1.19 [s, s, s, s12 H, 2 x $OC(CH_3)_2O$]; ^{13}C NMR (75 MHz, $CDCl_3$) δ 160.9 ($COOCH_3$), 139.5 (C4), 129.4 (C5), 112.6 and 109.8 [2 x $OC(CH_3)_2O$], 106.2 (C1'), 83.2 (C2'), 80.3 (C4'), 72.1 (C5'), 67.4 (C6'), 66.1 (C3'), 52.2 ($COOCH_3$), 26.8, 26.6, 26.1 and 24.8 [2 x $OC(CH_3)_2O$]; MS (70 eV) *m/z* 354 (44), 168 (20), 142 (28), 128 (40), 113 (63), 101 (64), 95 (36), 43 (100). Anal. Calcd for $C_{16}H_{23}N_3O_7$: C, 52.03; H, 6.28; N, 11.38. Found: C, 52.30; H, 6.30; N, 11.25. **20**: mp 145-147 °C; $[\alpha]_D^{25}$ +97 (*c* 0.56, $CHCl_3$); IR (KBr) υ 3100, 2990, 2940, 1720, 1545, 1380, 1375, 1260-1215, 1160, 1070 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.11 (s, 1 H, H4), 6.27 (d, $J_{1',2'}$= 3.5 Hz, 1 H, H1'), 6.12 (d, $J_{3',4'}$= 4.3 Hz, 1 H, H3'), 5.12 (d, 1 H, H2'), 4.43 (dd, $J_{4',5'}$= 9.0 Hz, 1 H, H4'), 3.92 (s, 3 H, $COOCH_3$), 3.86 (d, $J_{5',6'}$= 5.5 Hz, 2 H, 2 H6'), 2.85 (dt, 1 H, H5'), 1.59, 1.37, 1.35 and 1.09 [s, s, s, s, 12 H, 2 x $OC(CH_3)_2O$]; ^{13}C NMR (75 MHz, $CDCl_3$) δ 158.7 ($COOCH_3$), 136.9 (C4), 129.9 (C5), 112.5 and 109.4 [2 x $OC(CH_3)_2O$], 106.7 (C1'), 84.3 (C2'), 81.3 (C4'), 72.7 (C5'), 67.6 (C6'), 64.3 (C3'), 52.3 ($COOCH_3$), 26.9, 26.7, 26.2 and 24.8 [2 x $OC(CH_3)_2O$]; MS (70 eV) *m/z* 354 (50), 296 (21), 228 (13), 168 (12), 142 (14), 128 (52), 95 (22), 43 (100). Anal. Calcd for $C_{16}H_{23}N_3O_7$: C, 52.03; H, 6.28; N, 11.38. Found: C, 52.26; H, 6.01; N, 11.44.

4-Carbomethoxy-1-(3'-deoxy-1',2'-*O*-isopropylidene-α-D-glucofuranos-3'-yl)-1,2,3-triazole (21)

Compound **19** (265 mg, 0.71 mmol) was treated with acetic acid/water (5 mL, 7/3) at room temperature for 18 h. The solvent was evaporated co-distilling with toluene, and the residue was submitted to flash chromatography (hexane, ethyl acetate 50%) to give compound **21** (230 mg, 99%). **21**: mp 118-121 °C; $[\alpha]_D^{25}$ +55 (*c* 1.7, $CHCl_3$); IR (KBr) υ 3640, 3500-3150, 3115, 2990, 2940, 2850, 1700, 1545, 1380, 1375, 1260-1215, 1160, 1070 cm^{-1}; ^1H NMR (300 MHz, CD_3OD) δ 8.72 (s, 1 H, H5), 6.39 (d, $J_{1',2'}$= 3.7 Hz, 1 H, H1'), 5.51 (d, 1 H, H2'), 5.29 (d, $J_{3',4'}$= 3.8 Hz, 1 H, H3'), 4.68 (dd, $J_{4',5'}$= 9.4 Hz, 1 H, H4'), 4.11 (s, 3 H, $COOCH_3$), 3.81 (dd, $J_{5',6A'}$= 2.8 Hz, $J_{6A',6B'}$= 11.7 Hz, 1 H, H6A'), 3.71 (dd, $J_{5',6B'}$= 5.1 Hz, 1 H, H6B'), 2.81 (ddd, 1 H, H5'), 1.75 and 1.19 [s, s, 6 H, $OC(CH_3)_2O$]; ^{13}C NMR (75 MHz, CD_3OD) δ 162.4 ($COOCH_3$), 139.9 (C4), 131.5 (C5), 113.7 [$OC(CH_3)_2O$], 107.5 (C1'), 84.9 (C2'), 79.8 (C4'), 70.6 (C5'), 67.8 (C3'), 64.8 (C6'), 52.5 ($COOCH_3$), 26.9 and 26.4 [$OC(CH_3)_2O$]; MS (70 eV) *m/z* 314 (M^+-15, 16), 298 (15), 181 (21), 168 (29), 128 (33), 85 (52), 43 (100). Anal. Calcd for $C_{13}H_{19}N_3O_7$: C, 47.42; H, 5.82; N, 12.76. Found: C, 47.41; H, 5.71; N, 12.69.

5-Carbomethoxy-1-(3'-deoxy-1',2'-*O*-isopropylidene-α-D-glucofuranos-3'-yl)-1,2,3-triazole (22)

Compound **20** (260 mg, 0.71 mmol) was treated with acetic acid/water (5 mL, 7/3) at room temperature for 18 h. The solvent was evaporated co-distilling with toluene, and the residue was submitted to flash chromatography (hexane, ethyl acetate 50%) to give compound **22** (229 mg, 99%). **22**: oil; $[\alpha]_D^{25}$ +80 (*c* 0.88,

$CHCl_3$); IR (film) υ 3640, 3500-3100, 2990, 2940, 1720, 1525, 1370, 1300, 1245, 1200, 1145, 1050 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.04 (s, 1 H, H4), 6.18 (d, $J_{1',2'}$= 3.6 Hz, 1 H, H1'), 6.06 (d, $J_{3',4'}$= 4.0 Hz, 1 H, H3'), 4.98 (d, 1 H, H2'), 4.43 (dd, $J_{4',5'}$= 9.2 Hz, 1 H, H4'), 3.88 (s, 3 H, $COOCH_3$), 3.57-3.37 (m, 3 H, 2 H6', OH), 2.46-2.37 (m, 1 H, H5'), 1.51 and 1.31 [s, s, 6 H, $OC(CH_3)_2O$]; ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.0 ($COOCH_3$), 136.8 (C4), 129.7 (C5), 112.3 [$OC(CH_3)_2O$], 106.2 (C1'), 84.2 (C2'), 79.3 (C4'), 68.9 (C5'), 64.4 (C3'), 63.4 (C6'), 52.7 ($COOCH_3$), 26.5 and 25.9 [$OC(CH_3)_2O$]; MS (70 eV) *m/z* 330 (M^++1, 1), 314 (M^+-15, 39), 282 (17), 268 (40), 240 (15), 122 (71), 85 (95), 43 (100). Anal. Calcd for $C_{13}H_{19}N_3O_7$: C, 47.42; H, 5.82; N, 12.76. Found: C, 47.36; H, 5.97; N, 12.86.

4,5-Dicarbethoxy-1-(2',3',4',6'-tetra-*O*-acetyl-β-D-glucopyranosyl)-1,2,3-triazole (24)

Diethyl acetylenedicarboxylate (273 mg, 1.6 mmol) and 2,3,4,6-tretra-*O*-acetyl-β-D-glucopyranosyl azide (**23**) (299 mg, 0.8 mmol) were dissolved in toluene (4 mL). The mixture was refluxed for 15 h, the solvent was evaporated and the residue submitted to flash chromatography (hexane, ethyl acetate 20%) to give compound **24** (427 mg, 98%). **24**: mp 131-133 °C; IR (KBr) υ 2995, 1745, 1710, 1550, 1445, 1350, 1240-1180, 1020 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 6.12 (d, $J_{1',2'}$= 9.4 Hz, 1 H, H1'), 5.96 (t, $J_{2',3'}$= 9.4 Hz, 1 H, H2'), 5.39 (t, $J_{3',4'}$= 9.4 Hz, 1 H, H3'), 5.23 (t, $J_{4',5'}$= 9.4 Hz, 1 H, H4'), 4.44 (q, *J*= 7.2 Hz, 2 H, $CO_2CH_2CH_3$), 4.42 (q, *J*= 7.2 Hz, 2 H, $CO_2CH_2CH_3$), 4.26 (dd, $J_{6A',5'}$= 4.9 Hz, $J_{6A',6B'}$= 12.7 Hz, 1 H, H6A'), 4.12 (dd, $J_{6B',5'}$= 2.0 Hz, 1 H, H6B'), 3.98 (ddd, 1 H, H-5'), 2.06, 2.05, 2.02 and 1.88 (s, s, s, s, 12 H, 4 x CH_3CO), 1.42 (t, 3 H, $CO_2CH_2CH_3$), 1.39 (t, 3 H, $CO_2CH_2CH_3$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.2, 169.9, 169.0 and 168.3 (4 x CH_3CO), 159.4 and 157.9 (2 x $CO_2CH_2CH_3$), 140.2 (C4), 130.6 (C5), 85.2 (C1'), 75.0 (C5'), 72.8 (C3'), 69.5 (C2'), 67.2 (C4'), 6.3.0 and 61.8 (2 x $CO_2CH_2CH_3$), 61.2 (C6'), 20.4 , 20.3 and 20.1 (4 xCH_3CO), 13.9 and 13.7 (2 x $CO_2CH_2CH_3$); MS (70 eV) *m/z* 331 (31), 278 (17), 259 (38), 221 (16), 186 (25), 169 (83), 139 (100), 109 (67), 81 (15). Calcd for $C_{22}H_{29}N_3O_{13}$: C, 48.62; H, 5.38; N, 7.73. Found: C, 48.52; H, 5.49; N, 7.60.

1-(3'-Deoxy-1',2':5',6'-di-*O*-isopropylidene-α-D-glucofuranos-3'-yl)-1,2,3,4-tetrazole (25)

Tetrazole (34 mg, 0.48 mmol) was dissolved in dry DMF (1.5 mL). Crown-6-ether (26 mg, 0.097 mmol) and sodium hydride (12 mg, 0.48 mmol, 2 equiv) were added. The mixture was heated at 80 °C for 1 h.Then tosylate **4** (100 mg, 0.24 mmol) was added, and the mixture warmed at 130-140 °C for 12 days. The solvent was evaporated, the residue dissolved in ethyl acetate and washed with aqueous bicarbonate solution and brine. The organic layer was dried, filtered, evaporated and the residue submitted to flash chromatography (hexane, ethyl acetate 20%) to give compound **25** (30 mg, 66%). **25**: mp 103-104 °C; $[\alpha]_D^{25}$ -1 (*c* 0.49, $CHCl_3$); IR (KBr) υ 3110, 2960, 2870, 1375, 1355, 1195, 1055 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 6.25 (d, $J_{1',2'}$= 3.5 Hz, 1 H, H1'), 5.59 (d, $J_{3',4'}$= 3.8 Hz, 1 H, H3'), 4.98 (d, 1 H, H2'), 4.48 (dd, $J_{4',5'}$= 8.9 Hz, 1 H, H4'), 3.92 (dd, $J_{6A',5'}$= 4.7 Hz, $J_{6A',6B'}$= 8.8 Hz, 1 H, H6A'), 3.84 (dd, $J_{6B',5'}$= 5.8 Hz, 1 H, H6B'), 3.16 (ddd, 1 H, H5'), 1.60, 1.44, 1.38 and 1.20 [s, s, s, s, 12 H, 2 x $OC(CH_3)_2O$]; ^{13}C NMR (75 MHz, $CDCl_3$) δ 152.9 (C5), 112.9 and 109.9 [2 x $OC(CH_3)_2O$], 105.9 (C1'), 83.4 (C2'), 80.1 (C4'), 72.1 (C5'), 68.1 (C3'), 66.9 (C6'), 26.8, 26.6, 26.1 and 24.9 [2 x $OC(CH_3)_2O$]; MS (70 eV) *m/z* 297 (M^+-15, 54), 239 (17), 142 (20), 113 (28), 101 (80), 43 (100). Anal. Calcd for $C_{13}H_{20}N_4O_5$: C, 49.99; H, 6.45; N, 17.94. Found: C, 50.11; H, 6.51; N, 17.83.

1-(3'-Deoxy-1',2':5',6'-di-*O*-isopropylidene-α-D-glucofuranos-3'-yl)-1,2,4-triazole (26)

Following the same protocol (see above) 1,2,4-triazole (33 mg, 0.48 mmol) and tosylate **4** (100 mg, 0.24 mmol), after work-up and flash chromatography (hexane, ethyl acetate 40%) gave compound **26** (38 mg, 73%). **26**: mp 101-103 °C; $[\alpha]_D^{25}$ -17 (*c* 0.43, $CHCl_3$); IR (KBr) υ 3090, 2960, 2870, 1485, 1375, 1255, 1245, 1195, 1050 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.17 (s, 1 H, H3), 7.90 (s, 1 H, H5), 6.18 (d, $J_{1',2'}$= 3.6 Hz, 1 H, H1'), 4,96 (d, 1 H, H2'), 4.92 (d, $J_{3',4'}$= 3.8 Hz, 1 H, H3'), 4.27 (dd, $J_{4',5'}$= 9.3 Hz, 1 H, H4'), 3.94-3.91 (m, 2 H, 2 H6'), 3.08 (dt, $J_{5',6A'}$=$J_{5',6B'}$= 5.7 Hz, 1 H, H5'), 1.56, 1.41, 1.34 and 1.17 [s, s, s, s, 12 H, 2 x $OC(CH_3)_2O$]; ^{13}C NMR (75 MHz, $CDCl_3$) δ 152.1 (C5), 144.7 (C3), 112.4 and 109.6 [2 x $OC(CH_3)_2O$], 106.5 (C1'), 83.4 (C2'), 80.7 (C4'), 72.3 (C5'), 67.5 (C6'), 64.3 (C3'), 26.9, 26.7, 26.1 and 24.9 [2 x $OC(CH_3)_2O$]; MS (70 eV) *m/z* 311 (M^+, 1), 296 (M^+-15, 58), 211 (19), 101 (100), 43 (84). Anal. Calcd for $C_{14}H_{21}N_3O_5$: C, 54.01; H, 6.80; N, 13.50. Found: C, 54.11; H, 6.71; N, 13.63.

1-(3'-Deoxy-1',2'-*O*-isopropylidene-α-D-glucofuranos-3'-yl)-1,2,4-triazole (27)

Triazole **26** (160 mg, 0.51 mmol) was treated with acetic acid/water (4 mL, 7/3) at room temperature for 18 h. The solvent was evaporated co-destilling with toluene, and the residue was submitted to flash chromatography (ethyl acetate) to give compound **27** (134 mg, 96%). **27**: mp 184-186 °C; $[\alpha]_D^{25}$ + 36 (*c* 0.68, CH_3OH); IR (KBr) υ 3500-3100, 3300, 3180, 2910, 1495, 1370, 1205, 1070 cm^{-1}; ^1H NMR (300 MHz, CD_3OD) δ 8.70 (s, 1 H, H3), 8.18 (s, 1 H, H5), 6.36 (d, $J_{1',2'}$= 3.6 Hz, 1 H, H1'), 5.37 (d, $J_{3',4'}$= 3.8 Hz, 1 H, H3'), 5.14 (d, 1 H, H2'), 4.62 (dd, $J_{4',5'}$= 9.7 Hz, 1 H, H4'), 3.81 (dd, $J_{6A',6B'}$= 9.5 Hz,$J_{5',6A'}$= 2.8 Hz, 1 H, HA6'), 3.70 (dd,$J_{5',6B'}$= 5.2 Hz, 1 H, HB6'), 2.84 (ddd, 1 H, H5'), 1.76 and 1.54 [s, s, 6 H, $OC(CH_3)_2O$]; ^{13}C NMR (75 MHz, CD_3OD) δ 152.6 (C5), 146.9 (C3), 113.7 [$OC(CH_3)_2O$], 107.9 (C1'), 85.1 (C2'), 80.3 (C4'), 70.9 (C5'), 66.3 (C3'), 65.2 (C6'), 27.3 and 26.7 [$OC(CH_3)_2O$]; MS (70 eV) *m/z* 271 (M^+-15, 24), 210 (19), 142 (30), 127 (46), 85 (100). Anal. Calcd for $C_{11}H_{17}N_3O_5$: C, 48.70; H, 6.32; N, 15.49. Found: C, 48.55; H, 6.51; N, 15.62.

1-(6'-*O*-*p*-Toluenesulfonyl-3'-deoxy-1',2'-*O*-isopropylidene-α-D-glucofuranos-3'-yl)-1,2,4-triazole (28)

Diol **27** (109 mg, 0.4 mmol) was dissolved in dry pyridine (1.5 mL) and *p*-toluenesulfonyl chloride (99 mg, 0.52 mmol, 1.3 equiv) was added to the cooled mixture in an ice bath, under argon and stirring. After 24 h at room temperature, toluene was added, the solvent evaporated and the residue was submitted to flash chromatography (hexane, ethyl acetate 80%) to give compound **28** (64 mg, 90%). **28**: mp 124-127 °C; IR (KBr) υ 3600-3300, 3200-3100, 2950, 1580, 1495, 1350, 1160, 1060, 1000 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.27 (s, 1 H, H-3), 8.00 (s, 1 H, H-5), 7.74 (d, *J*= 8.2 Hz, 2 H, aromatic), 7.31 (d, 2 H, aromatic), 6.38 (br s, 1 H, OH), 6.15 (d, $J_{1',2'}$= 3.4 Hz, 1 H, H1'), 5.07 (d, $J_{3',4'}$= 3.7 Hz, 1 H, H3'), 4.94 (d, 1 H, H2'), 4.32 (dd, $J_{4',5'}$= 9.0 Hz, 1 H, H4'), 4.12 (br d, $J_{6A',6B'}$= 9.0 Hz, 1 H, HA6'), 3.97 (t, $J_{5',6B'}$= $J_{6A',6B'}$= 9.0 Hz, 1 H, HB6'), 2.76 (br m, 1 H, H5'), 2.43 (s, 3 H, $CH_3SO_2C_6H_5$), 1.53 and 1.34 [s, s, 6 H, $OC(CH_3)_2O$]; ^{13}C NMR (75 MHz, $CDCl_3$) δ 151.8 (C5), 144.9 (C3), 144.4, 132.3, 129.8, 128.0 ($CH_3SO_2C_6H_5$), 112.4 [$OC(CH_3)_2O$], 106.4 (C1'), 82.9 (C2'), 78.6 (C4'), 73.1 (C6'), 66.3 (C5'), 64.5 (C3'), 26.6 and 26.0 [$OC(CH_3)_2O$], 21.5 ($CH_3SO_2C_6H_5$); MS (70 eV) *m/z* 425 (M^+, 13), 410 (M^+-15, 22), 281 (11), 238 (28), 210

(42), 155 (84), 173 (27), 167 (38), 124 (70), 113 (64), 91 (100). Anal. Calcd for $C_{18}H_{23}N_3SO_7$: C, 50.82; H, 5.45; N, 9.88; S, 7.54. Found: C, 50.91; H, 5.51; N, 9.64; S, 7.42.

ACKNOWLEDGMENTS

JMC warmly thanks Miss Mercedes Rodríguez Fernández for the great effort in summarizing the unavailable C. A. Jiménez's report regarding the experimental material. JMC thanks Janssen-Cilag (Toledo, Spain) for support, the biological evaluation of most of the products reported here and for the permission to publish these results.

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