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Note

Triazole-fused sugars from nitroalkene-containing C-glycosides by a tandem 1,3-dipolar cycloaddition and intramolecular Michael addition

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ABSTRACT

A synthetic method to triazole-fused sugars by treatment of nitroalkene-containing C-glycosides with sodium azide is described. Initial experiments conducted at room temperature gave only the 1,3-dipolar cycloaddition products. However, at elevated reaction temperature the tandem β-elimination/cycloaddition/Michael addition yielded 1,5-disubstituted triazole-fused sugars.

1,2,3-Triazoles are often synthesized from organic azides and alkynes by 1,3-dipolar cycloaddition.[1] The reaction can be induced thermally and by Cu(I) catalysts.[2] In addition to being structural entities of antibacterial and anti-tumour agents,[3] the formation of triazoles is widely used in molecular ligation of bioactive carbohydrates with various carrier molecules.[4] Our interest in triazole-fused sugars as potential glycosidase inhibitors[5] has prompted the current synthetic study.

Triazole-fused sugars have been synthesized by intramolecular 1,3-dipolar cycloadditions of an azido group to a carbon–carbon multiple bond of substrates such as an unsaturated ester[6] and an alkyne group.[7] More recently, an $In(OTf)_3$-catalyzed one-pot reaction between trimethylsilylazide ($TMSN_3$) and 1,1-dimethoxyhex-5-yne derivatives also afforded triazole-fused sugars.[8] There are also reports in which aromatic nitroalkenes were used as a replacement of the alkyne to react with sodium azide[9] and $TMSN_3$[10] leading to 1,2,3-triazoles (Scheme 1). The products obtained by Zefirov et al.[9] were assigned as *2H*-1,2,3-triazoles, while those reported by Vaccaro et al.[10] were assigned as *1H*-1,2,3-triazoles. The 1,3-dipolar cycloaddition between nitroalkene and azido compounds is affected by electronic polarization of the substrates. An electron-donating substituent at C2 of 1-nitroalkene, for example, a substituted aryl group, is often required to facilitate the reaction. In this report, we describe a tandem 1,3-dipolar cycloaddition and intramolecular Michael addition from nitroalkene C-glycosides and sodium azide, leading to the formation of fused triazole-sugars.

Previously, we have used nitroalkyl 2′-(oxoalkyl)-C-glycosides for the synthesis of hydroxylated indoles and oxindoles by an intramolecular Michael addition.[11] The intermediates in that study, D-ribosyl derivative **1** and L-arabinosyl derivative **5**, can be easily converted into nitroalkene C-glycosides (**4** and **7**) by oxidation of the allyl group to a ketone (**3** and **6**) prior to the dehydration to nitroalkenes (Scheme 2). 2′-Oxidation of **1** and **5** was achieved effectively using $Hg(OAc)_2$ and Jones reagent as previously described,[12] which was followed by the treatment of **3** and **6** with MsCl/TEA[13] to afford nitroalkenes **4** and **7**, respectively.

When nitroalkenes **2** and **4** were treated overnight with sodium azide at room temperature, triazoles **8** and **9** were obtained in moderate yields (see Scheme 3). Improved yields (60–70%) were obtained when the substrate (e.g., **7**) was treated with $TMSN_3$ and *t*-butylammonium fluoride (TBAF)[10] (see Scheme 3). 1*H*-1,2,3-Triazole and 2*H*-1,2,3-triazole are tautomeric structures presented in **8–10** as evidenced by missing the C5 and C6 resonances in their C-13 spectra. However, the cycloaddition likely produced the latter because when 1-nitrocyclohexene (**11**) was treated with sodium azide, the major product obtained was 2-N-substituted triazole **12**. Apparently, the intermediate 2*H*-1,2,3-triazole **13** was initially formed and then trapped immediately by nitroalkene **11** via an intermolecular Michael-type addition (Scheme 4). Six distinctive ^{13}C NMR signals for the nitrohexyl moiety and an additional three on triazolo-[4,5]-cyclohexane were observed. ^1H NMR also showed only two sets of chemical shifts for protons of

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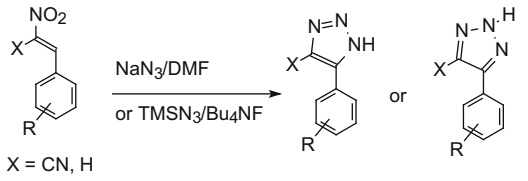
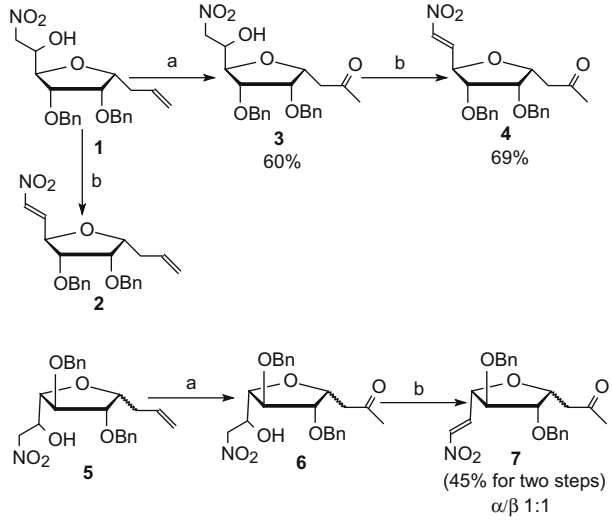
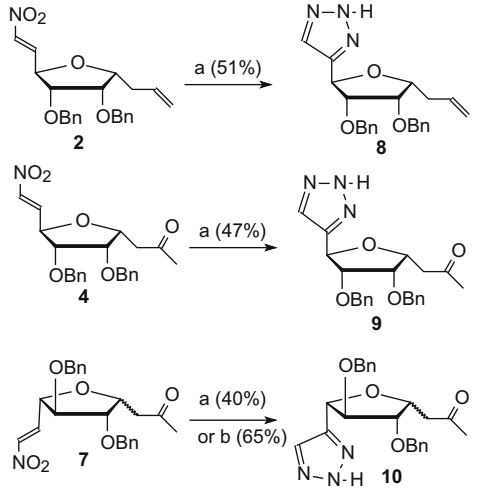


Scheme 1.



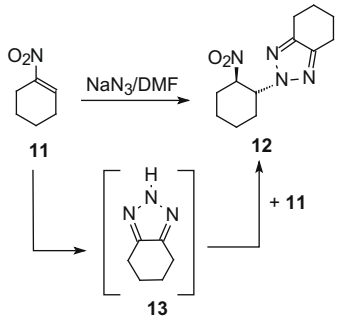
Scheme 2. Reagents and conditions: (a) $Hg(OAc)_2$/Jones reagent; (b) MsCl/TEA in DCM.



Scheme 3. Reagents and conditions: (a) NaN_3 in DMF at rt overnight; (b) $TMSN_3$/TBAF.

triazolo-[4,5]-cyclohexane, δ_H 1.81 (broad singlet, 4H, 2 × N=C–CH_2CH_2) and 2.66 (broad singlet, 4H, 2 × N=C–CH_2CH_2), confirming the structure of **12** and that the 2*H*-triazole was indeed formed from 1,3-dipolar addition.

The formation of adduct **12** prompted us to attempt an intramolecular Michael addition using triazoles **9** and **10** as substrates after β-elimination under basic conditions yielded an α,β-conjugated ketone. However, both **9** and **10** were relatively stable under basic conditions (1% NaOMe and K_2CO_3 in methanol), indicating that

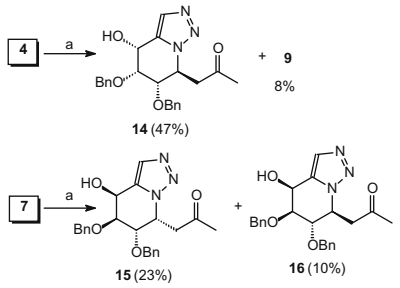


Scheme 4.

the presence of a triazole moiety may actually hinder β-elimination. Treatment of **4** and **7** with sodium azide at elevated temperature, however, afforded fused triazole-sugars (Scheme 5). It appears that β-elimination at high temperature was followed by 1,3-dipolar cycloaddition of the azide to the nitroalkene group. The open-chain intermediate, a conjugated ketone containing a triazole moiety, then underwent an intramolecular Michael addition to give a triazole-fused sugar. The stereochemistry of the reaction was controlled similarly by thermodynamic stability of the transition state as previously reported,[14] which led to the formation of a fused triazole (**14**) from nitroalkene **4** and an anomeric mixture of **15** and **16** from nitroalkene **7**. The low chemical yield was likely the result of a series of side-reactions, including intermolecular couplings similar to that reported in Scheme 4 as indicated by a significant amount of very polar byproducts observed on TLC.

Based on the reaction illustrated in Scheme 4 2,4-disubstituted triazoles would be the likely products (see Chart 1). However, structural analysis of **14–16** by NMR, including the measurement of coupling constants and NOE's and comparison of our NMR data ($J_{1,2}$ = 8.4 Hz, $J_{3,4}$ = 4 Hz observed in **14**, all small couplings in **15**, $J_{1,2}$ = 3.2 Hz, $J_{2,3}$ = 5.6 Hz and $J_{3,4}$ = 4.0 Hz in **16** and $^{***}\delta$c 132–133 ppm for C-6 and 135–136 ppm for C-5) with those reported in the literature[6–8] suggest that the products could be 1,5-disubstituted triazoles.

To determine unambiguously the bicyclic structure, we decided to introduce ^{15}N-atom into triazole **14** by treatment of 1-^{15}N-sodium azide with nitroalkene **4**. The triazole product obtained (**14**-^{15}N) was analyzed by ^{1}H and ^{13}C NMR. Because of the ^{15}N label at N-1 and N-3 of the triazole, based on ^{15}N–^{13}C and/or ^{15}N–^{1}H couplings one would be able to definitively assign the structure of **14**. Although ^{15}N–^{1}H-6 coupling was observed in **14**-^{15}N at δ_H 7.69 ppm, ^{15}N–^{1}H-1 coupling was not conclusive due to the overlap of H-1 and benzyl CH_2 proton resonances. However, the observation of ^{15}N–^{13}C-5, ^{15}N–^{13}C-6 and ^{15}N–^{13}C-1 coupling in **14**-^{15}N at



Scheme 5. Reagents and conditions: (a) NaN_3 in DMF at 80 °C overnight.

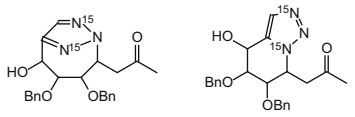


Chart 1.

136.0 ppm (C-5), 132.5 ppm (C-6) and 54.0 ppm (C-1) indicates that the products are indeed 1,5-disubstituted triazoles.

In summary, we described a synthetic method to triazole-fused sugars from nitroalkene-containing C-glycosides. Initial experiments conducted at room temperature gave only the 1,3-dipolar cycloaddition products. However, at elevated reaction temperature the tandem β-elimination/cycloaddition/Michael addition yielded 1,5-disubstituted triazole-fused sugars.

1. Experimental

1.1. General methods

^{1}H and ^{13}C NMR spectra were recorded at 400 MHz and 100 MHz, respectively, with a Varian instrument at 293 K. Chemical shifts were given in ppm downfield to the signal of internal TMS, and were assigned on the basis of 2D ^{1}H-COSY and ^{1}H–^{13}C chemical-shift correlated experiments. To maintain consistency in NMR assignments, carbon and proton numberings of the sugar were used despite the compounds being named otherwise. For high resolution mass spectroscopic analysis, samples in CH_2Cl_2–MeOH, 1:1 were mixed with Agilent ES tuning mix for internal mass calibration and infused into an AB/MDS-Sciex (Concord, ON) QSTAR mass spectrometer at a flow-rate of 4 μL/min. All chemicals were purchased from Aldrich Co. and used without further purification.

1.2. General procedure

1.2.1. Method A

The nitroalkene (100 mg) and sodium azide (20 mg) in DMF (2 mL) were stirred overnight at room temperature. The mixture was diluted by the addition of water, and extracted with EtOAc. The organic phase was dried and concentrated. Purification by column chromatography gave the triazole sugars.

1.2.2. Method B

A solution of the nitroalkene (100 mg) in DMF (1 mL) was mixed at 80 °C with sodium azide (20 mg) in DMF (1 mL). The mixture was stirred overnight at that temperature. Upon cooling, the mixture was diluted by the addition of water, and extracted with EtOAc. The organic phase was dried and concentrated. Purification by column chromatography gave fused triazoles.

1.2.2.1. 1-C-(2,3-Di-*O*-benzyl-6-C-nitro-6-deoxy-α-D-ribo-hex-5-eno-furanosyl)acetone (4). To a solution of compound **1** (3.5 g, 8.46 mmol) and $Hg(OAc)_2$ (1.6 g, 5.0 mmol) in acetone–water (37.5 mL:5 mL) was added dropwise a solution of Jones reagent (0.84 M, 21 mL) over 30 min. The dark greenish-brown mixture was stirred for 1 h and then poured into water and extracted with EtOAc. The combined organic solution was washed with water, aq $NaHCO_3$, and brine, dried and concentrated. Purification by chromatography (hexane–EtOAc 2:1) yielded compound **3** (2.2 g, 60%) as a solid. To a solution of the compound **3** (2 g, 4.7 mmol) and TEA (1.4 mL, 9.8 mmol) at 0 °C in DCM (30 mL) was added $MeSO_2Cl$ (435 μL, 5.6 mmol) dropwise. After 30 min, the mixture was poured into cold 5% HCl and extracted with EtOAc. The organic phase was washed with brine, dried and evaporated. Purification by chromatography (hexane–EtOAc 8:1) yielded 1.33 g of product (69%). ^{1}H NMR ($CDCl_3$) δ: 2.08 (s, 3H, CH_3), 2.79 (dd, 1H, H-1′a, J = 6.4, 17.6 Hz), 2.91 (dd, 1H, H-1′b, J = 8.0, 17.6 Hz), 3.86 (dd, 1H, H-2, J = 4.0, 8.4 Hz), 4.19 (dd, 1H, H-3, J = 4.0, 4.0 Hz), 4.45 and 4.83 (d and d, 1H each, CH_2Ph, J = 11.2 Hz), 4.51 (m, 1H, H-1), 4.54 and 4.71 (d and d, 1H each, CH_2Ph, J = 12.0 Hz), 4.64 (m, 1H, H-4), 7.06–7.15 (m, 2H, H-5, 6), 7.23–7.39 (m, 10H, 2 × Ph); ^{13}C NMR ($CDCl_3$) δ: 30.8 (C-3′), 43.9 (C-1′), 73.6 (CH_2Ph), 74.3 (CH_2Ph), 75.9 (C-4), 76.9 (C-1 and C-3), 84.2 (C-2), 128.2, 128.4, 128.7, 137.0 (C-5), 138.1 (C-6), 139.8, 140.2, 206.9 (C-2′). HRMS: calcd for $C_{23}H_{26}NO_6$ (M + H) 412.1760, found 412.1748.

1.2.2.2. 1-*C*-(2,3-Di-*O*-benzyl-6-C-nitro-6-deoxy-α/β-D-arabino-hex-5-eno-furanosyl)acetone (7). The compound (syrup) was synthesized as an anomeric mixture (45%) from **5** following the same procedure described for compound **4**. Date for **7-α**: ^{1}H NMR ($CDCl_3$) δ: 2.15 (s, 3H, CH_3), 2.70–2.93 (m, 2H, H-1′a,b), 3.91 (s, 1H, H-2), 3.96 (s, 1H, H-3), 4.37 (d, J = 11.6 Hz, 1H, CH_2Ph), 4.44–4.68 (m, 5H, H-1, 4, 1.5 × CH_2Ph), 7.06–7.20 (m, 2H, H-5, H-6), 7.26–7.40 (m, 10H, 2 × Ph); ^{13}C NMR ($CDCl_3$) δ: 30.6 (C-3′), 46.5 (C-1′), 71.9 (CH_2Ph), 72.6 (CH_2Ph), 79.7 (C-1), 79.7 (C-4), 85.8 (C-2), 87.1 (C-3), 127.7-128.8 (Ph), 136.8 (Ph), 137.4 (Ph), 139.8 (C-6), 139.1(C-6), 139.9 (C-5), 206.1 (C-2′). Data for **7-β**: ^{1}H NMR ($CDCl_3$) δ: 2.16 (s, 3H, CH_3), 2.70–2.93 (m, 2H, H-1′a, 1′b), 3.87 (m, 1H, H-3), 4.08 (d, J = 3.6 Hz, 1H, H-2), 4.37 (d, J = 11.6 Hz, 1H, CH_2Ph), 4.44–4.68 (m, 5H, H-1, H-4, CH_2Ph), 7.06–7.20 (m, 2H, H-5, H-6), 7.26–7.40 (m, 10H, 2 × Ph); ^{13}C NMR ($CDCl_3$) δ: 30.5 (C-3′), 42.7 (C-1′), 72.3 (CH_2Ph), 72.2 (CH_2Ph), 78.1 (C-1), 79.9 (C-4), 82.5 (C-2), 86.1(C-3), 127.7-128.8 (Ph), 136.8 (Ph), 137.4 (Ph), 139.4 (C-6), 139.7 (C-5), 206.3 (C-2′). HRMS: calcd for $C_{23}H_{26}NO_6$ (M+H) 412.1760, found 412.1768.

1.2.2.3. 4-(1-*C*-Allyl-2,3-di-*O*-benzyl-α-D-erythrofuranoside-4s)-2*H*-1,2,3-triazole (8). A syrup with $[\alpha]_D$ +39 (c 0.5, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ: 2.56 (dd, 2H, 1′-CH_2, J = 6.8, 6.8 Hz), 4.09 (dd, 1H, H-2, J = 4.0, 4.4 Hz), 4.25 (dt, 1H, H-1, J = 4.4, 6.8 Hz), 4.32 (dd, 1H, H-3, J = 4.0, 7.2 Hz), 4.55 and 4.61 (d and d, 1H each, CH_2Ph, J = 12.4 Hz), 4.62 and 4.89 (d and d, 1H each, CH_2Ph, J = 11.6 Hz), 5.06 (br d, 1H, CH_2=, J = 10.4 Hz), 5.12 (br d, 1H, CH_2=, J = 17.2 Hz), 5.26 (d, 1H, H-4, J = 6.8 Hz), 5.80 (m, 1H, –CH=), 7.29–7.38 (m, 10H, 2 × Ph), 7.59 (s, 1H, H-6); ^{13}C NMR ($CDCl_3$) δ: 34.5 (C-1′), 73.0 (CH_2Ph), 73.8 (CH_2Ph), 74.3 (C-4), 77.9 (C-2), 80.6 (C-1), 84.7 (C-3), 117.4 (CH_2=), 127.9, 128.0, 128.1, 128.5, 128.6, 134.8 (–CH=), 137.7, 138.5. HRMS: calcd for $C_{23}H_{26}N_3O_3$ (M+H) 392.1976, found 392.1991.

1.2.2.4. 4-(1-*C*-Acetylmethyl-2,3-di-*O*-benzyl-α-D-erythrofuranoside-4s)-2*H*-1,2,3-triazole (9). Obtained in 47% as a syrup. $[\alpha]_D$ +26 (c 0.9, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ: 2.07 (s, 3H, CH_3), 2.85 (dd, 1H, H-1′a, J = 6.4, 17.2 Hz), 2.97 (dd, 1H, H-1′b, J = 7.2, 17.2 Hz), 4.23 (dd, 1H, H-2, J = 4.4, 3.2 Hz), 4.28 (dd, 1H, H-3, J = 4.4, 6.0 Hz), 4.43 and 4.81 (d and d, 1H each, CH_2Ph, J = 11.2 Hz), 4.53 and 4.60 (d and d, 1H each, CH_2Ph, J = 12.0 Hz), 4.65 (m, 1H, H-1), 5.18 (d, 1H, H-4, J = 6.8 Hz), 7.29–7.38 (m, 10H, 2 × Ph), 7.59 (s, 1H, H-6); ^{13}C NMR ($CDCl_3$) δ: 30.9 (C-3′), 44.2 (C-1′), 73.1 (CH_2Ph), 74.0 (CH_2Ph), 74.5 (C-4), 76.4 (C-1), 78.1 (C-2), 84.2 (C-3), 128.0, 128.1, 128.2, 128.3, 128.6, 128.7, 137.7, 138.3, 207.8 (C-2′). HRMS: calcd for $C_{23}H_{26}N_3O_4$ (M+H) 408.1923, found 408.1890.

1.2.2.5. 4-(1-*C*-Acetylmethyl-2,3-di-*O*-benzyl-α/β-L-threofuranoside-4r)-2*H*-1,2,3-triazole (10). Obtained as an anomeric mixture (α:β 1:1) following method A (40%) and method B (65%) as a syrup. ^{1}H NMR ($CDCl_3$) δ: 2.16 and 2.17 (2s, α- and β-CH_3), 2.75–

2.97 (m, 2H, 1′-CH_2), 3.96 and 4.14 (2m, 1H, H-2), 4.18 and 4.31 (2m, 1H, H-3), 4.33–4.62 (m, 5H, H-1, 2 × CH_2Ph), 5.11 and 5.27 (2d, 1H, H-4), 7.29–7.38 (m, 10H, 2 × Ph), 7.60 and 7.65 (2*s*, 1H, H-6); ^{13}C NMR ($CDCl_3$) δ: 30.8 and 30.9 (C-3′), 43.1 and 46.7 (C-1′), 72.1, 72.18, 72.2, 72.5, 78.0, 78.1, 79.3, 83.2, 86.9, 87.2, 88.4, 128.0, 128.1, 128.2, 128.3, 128.7, 137.4, 137.5, 137.6, 206.7 and 206.8 (C-2′).

1.2.2.6. 2-(1,2-*trans*-2-Nitrocyclohexyl)-1,2,3-triazolo-[4,5]-cyclohexane (12). Obtained as a syrup. ^1H NMR ($CDCl_3$) δ: 1.45–1.53 (m, 2H, H-4ax, 5ax), 1.81 (br s, 4H, 2 × N=C–CH_2CH_2), 1.80–2.03 (m, 4H, H-3ax, 6ax, 4eq, 5eq), 2.26 (dm, 1H, H-6eq), 2.50 (dm, 1H, H-3eq), 2.66 (br s, 4H, 2 × N=C–CH_2), 4.99 (ddd, 1H, H-2, *J* = 4.0, 11.2, 11.2 Hz), 5.15 (ddd, 1H, H-1, *J* = 4.0, 11.2, 11.2 Hz); ^{13}C NMR ($CDCl_3$) δ: 21.9 (2 × N=C–CH_2CH_2), 23.2 (2 × N=C–CH_2CH_2), 24.0 (C-4), 24.2 (C-5), 31.8 (C-6), 32.0 (C-3), 64.4 (C-1), 87.8 (C-2), 144.4 (2 × N=C–CH_2CH_2); MS: *m*/*z* 251.4 (M+H), 268.3 (M+NH_4).

1.2.2.7. (3*r*,4*s*,5*s*,6*s*)-6-Acetylmethyl-4,5-di-*O*-benzyl-3-hydroxy-pyrido[1,5-*c*]-1,2,3-triazole (14). Obtained from **4** in 47% as a syrup. $[\alpha]_D$ −21 (*c* 1.5, $CHCl_3$); ^1H NMR ($CDCl_3$) δ: 2.12 (s, 3H, CH_3), 3.07 (d, 1H, 4-OH, *J* = 12.0 Hz), 3.12 (dd, 1H, H-1′a, *J* = 4.0, 17.6 Hz), 3.28 (dd, 1H, H-1′b, *J* = 6.0, 17.6 Hz), 4.12 (d, 1H, H-2, *J* = 8.4 Hz); 4.15 (d, 1H, H-3, *J* = 4.0 Hz), 4.62 and 4.77 (d and d, 1H each, CH_2Ph, *J* = 11.6 Hz), 4.70 and 4.94 (d and d, 1H each, CH_2Ph, *J* = 11.6 Hz), 4.87 (dd, 1H, H-4, *J* = 4.0, 12.0 Hz), 4.92 (m, 1H, H-1), 7.29–7.38 (m, 10H, 2 × Ph), 7.69 (s, 1H, H-6); ^{13}C NMR ($CDCl_3$) δ: 30.9 (C-3′), 42.6 (C-1′), 54.0 (C-1), 63.3 (C-4), 72.8 (CH_2Ph), 73.9 (C-3), 74.1 (CH_2Ph), 77.2 (C-2), 128.3, 128.4, 128.5, 128.7, 128.9, 129.0, 132.6 (C-6), 136.0 (C-5), 136.8, 137.4, 205.2 (C-2′). HRMS: calcd for $C_{23}H_{26}N_3O_4$ (M+H) 408.1923, found 408.1919.

1.2.2.8. (3*s*,4*r*,5*s*,6*r*)-6-Acetylmethyl-4,5-di-*O*-benzyl-3-hydroxy-pyrido[1,5-*c*]-1,2,3-triazole (15). Major product (23%) obtained from **7** as a syrup. $[\alpha]_D$ +63 (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$) δ: 2.15 (s, 3H, CH_3), 2.81 (d, 1H, 3-OH, *J* = 11.2 Hz), 3.04 (dd, 1H, H-1′a, *J* = 9.6, 18.4 Hz), 3.82 (dd, 1H, H-1′b, *J* = 4.0, 18.4 Hz), 4.02 (dd, 1H, H-3, *J* = 4.4, 4.4 Hz), 4.30 (dd, 1H, H-2, *J* = 3.6, 4.4 Hz), 4.38 and 4.51 (d and d, 1H each, CH_2Ph, *J* = 11.6 Hz), 4.61 and 4.70 (d and d, 1H each, CH_2Ph, *J* = 11.6 Hz), 4.97 (m, 1H, H-1), 5.01 (dd, 1H, H-4, *J* = 4.0, 11.2 Hz), 7.29-7.38 (m, 10H, 2 × Ph), 7.72 (s, 1H, H-6); ^{13}C NMR ($CDCl_3$) δ: 30.5 (C-3′), 41.9 (C-1′), 52.8 (C-1), 63.0 (C-4), 73.6 (C-2, 3), 73.7 (CH_2Ph), 73.8 (CH_2Ph), 128.5, 128.6, 128.8, 128.9, 129.0, 132.6 (C-6), 136.0 (C-5), 136.7, 136.8, 205.9 (C-2′). HRMS: calcd for $C_{23}H_{26}N_3O_4$ (M + H) 408.1923, found 408.1944.

1.2.2.9. (3*s*,4*r*,5*s*,6*s*)-6-Acetylmethyl-4,5-di-*O*-benzyl-3-hydroxy-pyrido[1,5-*c*]-1,2,3-triazole (16). Minor product (10%) obtained from **7** as a syrup. ^1H NMR ($CDCl_3$) δ: 2.10 (s, 3H, CH_3), 2.79 (d, 1H, 4-OH, *J* = 10.0 Hz), 3.17 (dd, 1H, H-1″a, *J* = 8.8, 17.6 Hz), 3.28 (dd, 1H, H-1′b, *J* = 4.0, 17.6 Hz), 3.98 (dd, 1H, H-3, *J* = 4.0, 5.6 Hz), 4.19 (dd, 1H, H-2, *J* = 2.8, 5.6 Hz), 4.58 and 4.64 (d and d, 1H each, CH_2Ph, *J* = 11.6 Hz), 4.75 and 4.80 (d and d, 1H each, CH_2Ph, *J* = 12.0 Hz), 5.04 (m, 1H, H-1), 5.09 (dd, 1H, H-4, *J* = 4.0, 10.0 Hz), 7.29–7.38 (m, 10H, 2 × Ph), 7.73 (s, 1H, H-6); ^{13}C NMR ($CDCl_3$) δ: 30.3 (C-3′), 46.3 (C-1′), 55.4 (C-1), 62.2 (C-4), 72.8 (CH_2Ph), 73.8 (CH_2Ph), 74.3 (C-3), 77.9 (C-2), 128.3, 128.4, 128.8, 128.9, 129.1, 132.3 (C-6), 134.9 (C-5), 136.7, 137.5, 205.8 (C-2′). HRMS: calcd for $C_{23}H_{26}N_3O_4$ (M+H) 408.1923, found 408.1912.

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.carres.2009.03.007.

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