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Unexpected formation of complex bridged tetrazoles via intramolecular 1,3-dipolar cycloaddition of 1,2-*O*-cyanoalkylidene derivatives of 3-azido-3-deoxy-D-allose

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Abstract—An unexpected and interesting intramolecular side reaction occurred during the attempted synthesis of glycosyl cyanides upon treatment of 1-*O*-acetyl-3-azido-3-deoxyallose derivatives with TMSCN and different Lewis acids. Exo-1,2-*O*-cyanoalkylidene derivatives formed by neighboring group participation and attack of cyanide underwent, after Lewis-acid mediated isomerization to the endo-isomer, intramolecular azide–cyanide cycloaddition leading to the formation of tetrazoles embedded in bridged tetracyclic ring systems. The efficiency of cycloaddition is dependent on the ring structure of the sugar (pyranose or furanose). Of the studied molecules, 3-azido-1,2-*O*-cyanoethylidene-3-deoxy-allopyranose provides the most suitable scaffold for intramolecular [2+3] cycloaddition under exceptionally mild conditions. Our results highlight the capability of carbohydrates to act as scaffolds for the precise positioning of functional groups productive for a specific chemical reaction.

Keywords: *C*-Glycosyl compounds; Cyanides; Cyanoethylidene; Cycloaddition; Neighboring group participation

1. Introduction

Tetrazoles are becoming an increasingly popular functionality. They can serve as bioisosteres of carboxylic acids,[1,2] as precursors of nitrogen-containing heterocycles, and as lipophilic spacers in pharmaceuticals. Recently reported was their use as β-secretase inhibitors,[3,4] Kv1.5 blockers,[5] and as carboxylate bioisosteres of gabapentin and pregabalin.[6,7] A potentially useful method for the preparation of 1,5-disubstituted tetrazoles is the [2+3] cycloaddition of organic azides to nitriles. To date, however, only a few electron deficient nitriles are known that undergo this reaction in an intermolecular way under very forcing conditions.[8–10] High yields have been reported for the reaction of sulfonyl and acyl cyanides with unhindered aliphatic azides by neat, thermal fusion.[11,12] Intramolecular [2+3] cycloaddition reactions of organic azides to nitriles occur more readily.[13–17] Still, they require high reaction temperatures to proceed and yields are with few exceptions[18] not satisfactory. In the course of our investigations toward the Lewis-acid promoted synthesis of glycosyl cyanides, we now observed an unexpected side reaction leading for the first time to complex bridged tetracyclic ring systems via 1,3-dipolar cycloaddition of intermediate cyanoethylidene derivatives of 3-azidoallose even at room temperature.

The formation of cyanoethylidene compounds is a common side reaction in C-glycosylation reactions. They are formed when ester protecting groups are used at O-2 and the C-nucleophile is cyanide.[19–21] Kochetkov and coworkers utilized cyanoethylidene compounds in O-glycosylation reactions and showed that the C–C bond between the dioxolane carbon and the carbon of the cyano group is relatively weak and can be cleaved with catalytic amounts of Lewis acids such as trityl perchlorate.[22–24] Myers et al. showed that cyanoethylidene

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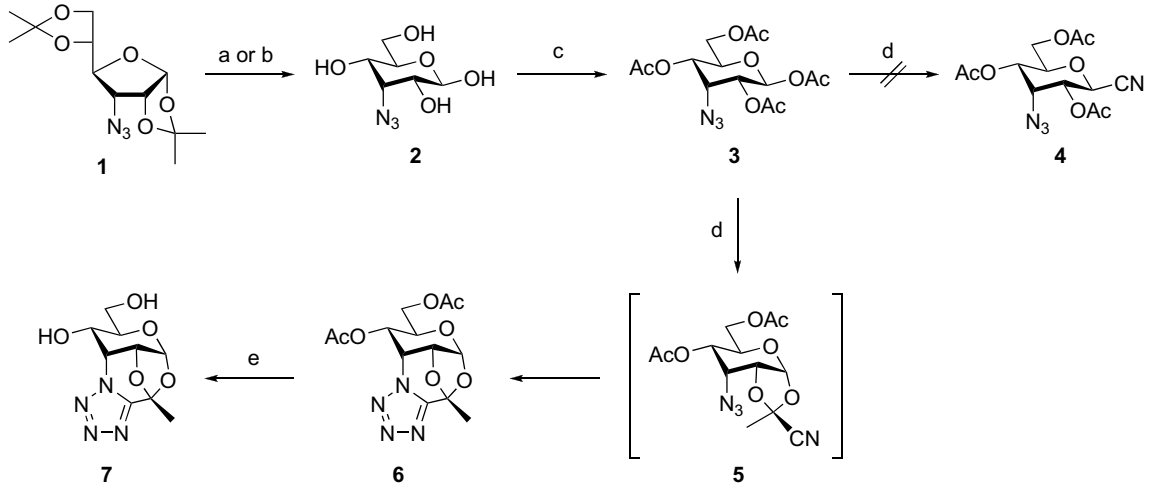
compounds of mannose, glucose, and galactose can be converted to anomeric cyanides under acid promotion without an exogenous cyanide source.[19] Intra- or intermolecular cycloaddition reactions of cyanoethylidene compounds have not been reported before.

2. Results and discussion

In the course of our program directed at the synthesis of sugar diamino acids (SDAs) as building blocks of oligosaccharide mimetics,[25] we were interested in glycosyl cyanide **4** of 3-azido-3-deoxy-D-allopyranose (Scheme 1). Starting from 3-azido-3-deoxy-1,2:5,6-di-*O*-isopropylidene-α-D-allofuranose **1**[26] we obtained the peracetylated allopyranose derivative **3** using two different pathways. When using 60% formic acid for the cleavage of the isopropylidene protecting groups of **1**, we observed the formation of two different formylated side products, which could subsequently be converted with NaOMe/MeOH to the completely deprotected 3-azido-3-deoxy-D-allose **2** existing predominantly as β-pyranose. Treatment with acetic anhydride in pyridine afforded peracetylated β-pyranose **3** in 91% yield over 3 steps besides small amounts of the corresponding α- and β-furanose and α-pyranose forms. Alternatively, stirring of **1** with 2 M HCl directly resulted in the formation of **2**, which was again peracetylated under the same conditions. In this case, however, the yield of β-pyranose **3** was somewhat lower (70% over 2 steps). For both reaction pathways the amounts of α-pyranose and the α- and β-furanose forms were negligible and completely separable by HPLC purification.

To synthesize glycosyl cyanide **4**, peracetate **3** was treated with excess of trimethylsilyl cyanide (TMSCN) and equimolar amounts of tin tetrachloride as Lewis acid promoter. However, we were not able to find even traces of the desired *C*-glycosyl compounds under these conditions. Instead, we observed a new compound that, after extensive analysis by NMR and IR spectroscopy and mass spectrometry, turned out to be tetrazole **6**. As an intermediate, *exo*-cyanoethylidene derivative **5** was identified (see below). Figure 1 depicts characteristic NMR data of **5** and **6**. Tetrazole **6** shows a ^{13}C NMR



Scheme 1. Reagents and conditions: (a) (i) 60% HCOOH, 16 h; (ii) NaOMe, MeOH, 2 h; (b) 2 M HCl, 6 h; (c) Ac_2O, pyr, overnight, 91% [(a) + (c)], 70% [(b) + (c)]; (d) 5 equiv TMSCN, 1.2 equiv $SnCl_4$, CH_2Cl_2, 60 °C, 65%; (e) NaOMe, MeOH, 14 h, 84%.

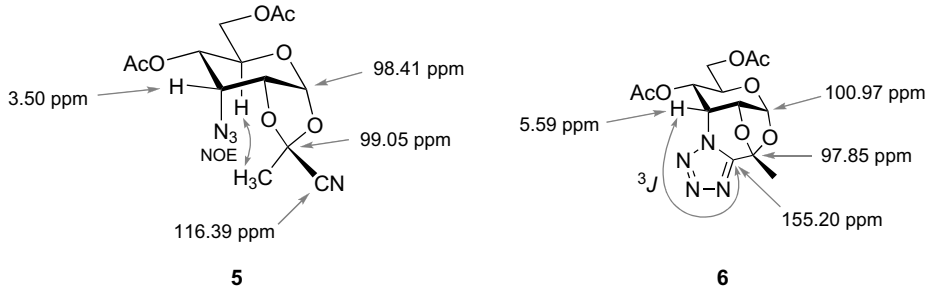


Figure 1. Comparison of significant ^1H and ^{13}C NMR chemical shifts of compounds **5** and **6**. Also indicated are an NOE between H-5 and the cyanoethylidene methyl group of **5** indicative for the exo-configuration and a $^3J_{C,H}$ long-range coupling observed in a $^1H,^{13}C$ HMBC NMR spectrum characteristic for tetrazole **6**.

resonance at 155.20 ppm, which is typical for a tetrazole carbon[27,28] and a strong signal in a $^{1}H,^{13}C$ HMBC NMR spectrum due to a $^{3}J_{C,H}$ long-range coupling between the tetrazole carbon and H-3. In addition, the cyanide resonance in a ^{13}C NMR spectrum and the nitrile and azide resonances in an IR spectrum (between 2100 and 2130 cm^{-1}, medium intensity) were missing for **6**. Tetrazole **6** could be deacetylated with NaOMe in methanol leading to the formation of diol **7** in 84% yield. Further investigations of the tetrazole formation using different solvents and Lewis acids at different temperatures revealed that **6** emerged as the major product in every case and no anomeric cyanide **4** was formed. Table 1 gives an overview over some of the experiments we carried out.

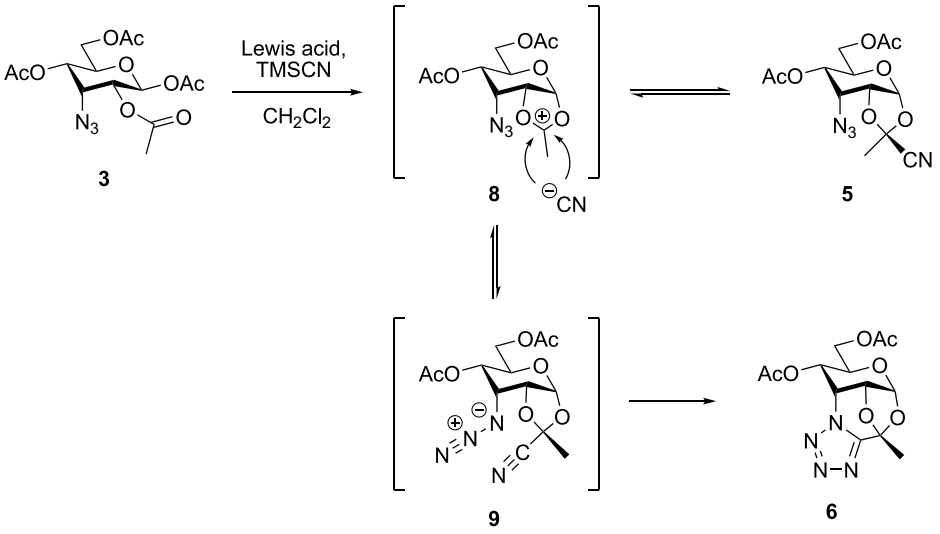
To isolate and characterize cyanoethylidene intermediate **5**, we reacted **3** with TMSCN (5 equiv) and catalytic amounts of Lewis acid (0.2 equiv $SnCl_4$) at room temperature. After column chromatography, **5** was isolated in 22% yield beside tetrazole **6** (33%) and starting material **3** (12%). NOE experiments carried out with cyanoethylidene derivative **5** using a mixing time of 300 ms revealed an NOE between the dioxolane methyl group and H-5 indicating that **5** is the *exo*-cyanoethylidene isomer. Pure **5** was treated with TMSCN and $SnCl_4$ or with $SnCl_4$ alone. In both cases we observed that tetrazole **6** was formed as the only product beside some decomposition. Addition of TMSCN to a solution of $SnCl_4$ and **5** in CH_2Cl_2 increased the speed of reaction but had no effect on the yield, which was approximately 70%. We always had to use at least equimolar amounts of Lewis acid to effect complete consumption of starting material **5**.

Scheme 2 shows the proposed mechanism by which tetrazole **6** is formed. Starting from **3**, neighboring group participation leads to acetoxonium ion **8** that can be attacked by cyanide either from the exo or the endo side. Formation of *exo*-cyanoethylidene **5** is expected to be kinetically favored due to an attack from the sterically less hindered convex side of bicyclic **8**. Formation of *exo*-cyanoethylidenes has been described earlier by others to be favored over the formation of *endo*-cyanoethylidenes[22–24,29] and also corresponds to the preferred formation of exo-isomeric forms of ortho esters.[30] Under the reaction conditions, however, cyanide attack is reversible giving also access to *endo*-cyanoethylidene **9**. Proper spatial orientation of azido and cyano groups within *endo*-cyanoethylidene **9** obviously leads to a fast irreversible intramolecular cycloaddition forming tetrazole **6**. In agreement with a fast cycloaddition step is the observation that we were never able to detect any of the *endo*-cyanoethylidene isomer **9**.

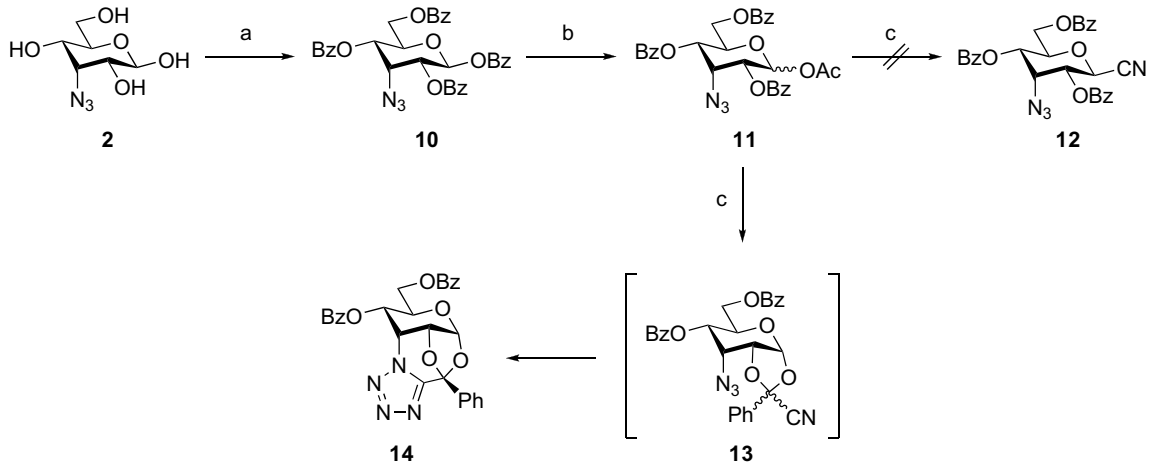
To investigate whether tetrazole formation also occurs with protecting groups that are known to reduce the amount of cyanoethylidene formation,[31,32] we

Table 1. Results of reactions of 3-azido-3-deoxy-allopyranose **3** with 5 equiv of TMSCN under varying conditions

Solvent	Lewis acid	*T* (°C)	Time	Yield **5** (%)	Yield **6** (%)	Recovered **3** (%)
CH_2Cl_2	0.4 equiv $SnCl_4$	60	5 h	14	8	52
CH_2Cl_2	1.2 equiv $SnCl_4$	60	2 h	—	65	—
CH_2Cl_2	0.2 equiv $SnCl_4$	20	18 h	22	9	65
H_3CNO_2	0.9 equiv $BF_3{\cdot}OEt_2$	20	1 h 20 min	8	60	—
H_3CNO_2	1.2 equiv $BF_3{\cdot}OEt_2$	60	20 min	—	35	—



Scheme 2. Proposed mechanism for intramolecular tetrazole formation.

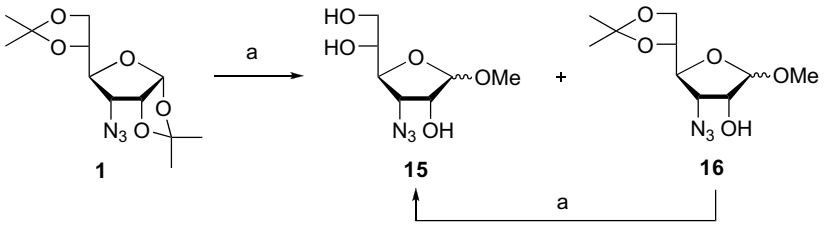


Scheme 3. Reagents and conditions: (a) BzCl, pyr, 24 h, 77%; (b) (i) $H_2N–NH_2$·HOAc, DMF, 50 °C, 3 h; (ii) Ac_2O, pyr, 12 h, 41% (2 steps); (c) 10 equiv TMSCN, 1.6 equiv BF_3·OEt_2, H_3CNO_2, 50%.

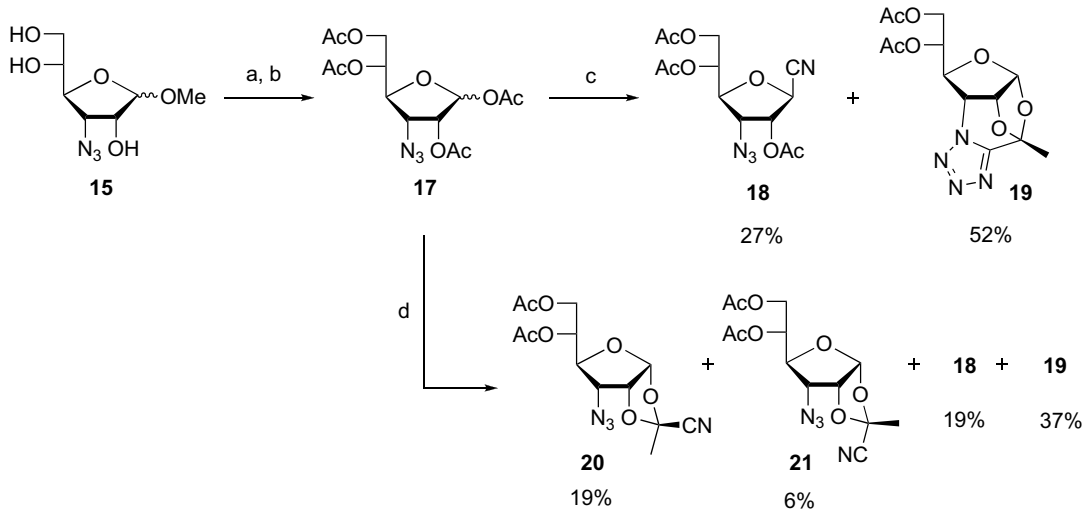
decided to introduce a benzoyl group as protection for O-2. Azidoallose **2** was perbenzoylated with benzoyl chloride in pyridine to give **10** in a yield of 77% (Scheme 3). Experiments to react **10** directly with TMSCN and $SnCl_4$ failed. Obviously, the anomeric benzoyl group cannot act as a leaving group under these conditions and starting material was recovered completely. Anomeric deprotection of **10** by treatment with hydrazinium acetate for 3 h at 50 °C and subsequent acetylation with pyridine/Ac_2O led to the formation of **11** as a mixture of anomers (α:β = 1:2.9) in 41% yield over 2 steps. Compound **11** was treated with TMSCN and BF_3·OEt_2 in nitromethane and, again, the formation of a tetrazole (**14**) was observed (50% yield). Glycosyl cyanide **12** was not found. In this case, the yield of **14** dropped to 12% when dichloromethane was used instead of nitromethane.

Since we observed tetrazole formation even with a benzoyl group at O-2, we wanted to know if azidoallose acts as a template for the intramolecular cycloaddition reaction only in its pyranose constitution or if this cyclization can also be achieved with the corresponding acetylated furanose (**17**). To synthesize **17**, furanose **1** was treated with a solution of HCl in methanol (Scheme 4). After stirring for 48 h, the formation of a mixture of methyl glycosides **15** and **16** was observed. Quenching of the reaction mixture with triethylamine and subsequent chromatographic purification afforded the desired triol **15** in a yield of 56% and 5,6-*O*-isopropylidene derivative **16** in 34% yield. Neutralization of the reaction mixture was necessary, as direct solvent removal gave small amounts of the corresponding methyl α- and β-D-3-azido-3-deoxy-allopyranosides, which were not separable from **15** by column chromatography. Conversion of **16** into **15** was possible using the same conditions as before, thus raising the overall yield of **15** to 78%. Subsequently **15** was converted into the peracetylated furanose **17** in 2 steps in a yield of 83% (Scheme 5).

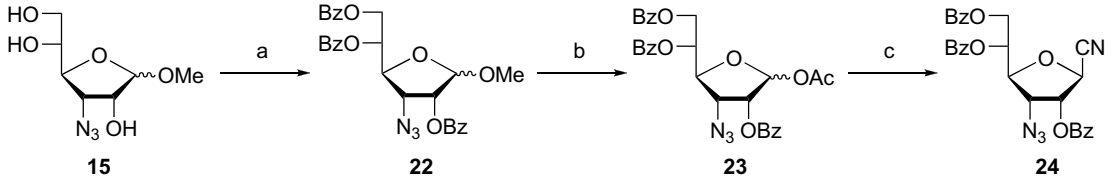
Treatment of **17** with 5 equiv of TMSCN and 1.1 equiv of $SnCl_4$ in CH_2Cl_2 at 60 °C led to complete consumption of the starting material and a product mixture of glycosyl cyanide **18** (27%) and tetrazole **19** (52%) was isolated. NMR studies of this reaction in CD_2Cl_2 revealed that two major intermediates were formed. To isolate these intermediates, **17** was treated with 5 equiv of TMSCN and only 0.5 equiv of $SnCl_4$ at room temperature. Under these conditions we were able to isolate the two intermediates **20** (19%) and **21** (6%) by HPLC beside **18** (19%) and **19** (37%). Analysis by NMR spectroscopy revealed that the intermediates were the two isomeric cyanoethylidenes (Scheme 1), which were formed in an exo/endo ratio of approximately 3:1. Since the *endo*-cyanoethylidene derivative **21** could be isolated in the allofuranose case, we conclude that



Scheme 4. Reagents and conditions: (a) (i) MeOH, HCl, 48 h; (ii) Et_3N, pH 7, 78%.



Scheme 5. Reagents and conditions: (a) Ac_2O, pyr, 12 h; (b) 75 equiv HOAc, 12 equiv Ac_2O, 6 equiv concd H_2SO_4, 30 min, 83% (2 steps); (c) 5 equiv TMSCN, 1.1 equiv $SnCl_4$, CH_2Cl_2, 60 °C; (d) 5 equiv TMSCN, 0.5 equiv $SnCl_4$, CH_2Cl_2, rt.



Scheme 6. Reagents and conditions: (a) BzCl, pyr, 24 h, 89%; (b) 70 equiv HOAc, 10 equiv Ac_2O, 5 equiv concd H_2SO_4, 36 min, 90%; (c) 5 equiv TMSCN, 1.1 equiv $SnCl_4$, CH_2Cl_2, 4 h, 60 °C, 65%.

in this case the spatial orientation of the cyano and azido groups is not as favorable for a subsequent cycloaddition as in the allopyranose case, leading to a slower rate of the tetrazole formation.

The observation, that glycosyl cyanide **18** was formed beside tetrazole **19** in the allofuranose case, led us to the speculation that the introduction of a benzoyl group at O-2 this time could lead to the formation of the anomeric cyanide as the major product. To prove this, **15** was perbenzoylated with benzoyl chloride in pyridine to yield **22** in 89% yield (Scheme 6). Subsequently, the anomeric acetyl group was introduced by acetolysis of **22** with concd H_2SO_4, HOAc and Ac_2O to give **23** in 90% yield. Treatment of **23** with 5 equiv of TMSCN and 1.1 equiv of $SnCl_4$ in CH_2Cl_2 led to the formation of the glycosyl cyanide **24** as the major product (65%), as expected. This time, we did not observe any tetrazole formation.

3. Conclusion

In summary, we investigated an unexpected and interesting side reaction during the attempted synthesis of glycosyl cyanides by treatment of 1-*O*-acetyl-3-azido-3-deoxyallose derivatives with TMSCN and different Lewis acids. *exo*-1,2-*O*-Cyanoalkylidene derivatives formed by neighboring group participation and attack of cyanide underwent, after Lewis-acid mediated isomerization to the endo-isomer, intramolecular azide–cyanide cycloaddition leading to the formation of tetrazoles embedded in bridged tetracyclic ring systems. The efficiency of cycloaddition is dependent on the ring structure of the sugar. Of the studied molecules, 3-azido-1,2-*O*-cyanoethylidene-3-deoxy-allopyranose provides the most suitable scaffold for intramolecular [2+3] cycloaddition under exceptionally mild conditions. Tetrazole formation is even observed with a 2-*O*-benzoyl protecting group that is known to give diminished amounts of cyanoalkylidene derivatives. In the case of 3-azido-3-deoxy-allofuranose, production of a glycosyl cyanide was observed beside tetrazole formation when O-2 was acetylated indicating a less precise positioning of azide and cyanide. Tetrazole formation can be completely prevented in the furanose case by introducing a benzoyl group at O-2. In this case, the glycosyl cyanide is the major product.

It has been shown that carbohydrates can function as scaffolds for the spatially defined presentation of pharmacophores.[33] Our results highlight the capability of carbohydrates to act as scaffolds for the precise positioning of functional groups productive for a specific

chemical reaction. It is conceivable that pyranose forms of other sugars, having a similar stereochemical structure at C-2 and C-3, like gulose or ribose, could also act as scaffolds for the same reaction.

4. Experimental

4.1. General methods

All solvents were dried and freshly distilled using standard procedures.[34] Organic solutions were concentrated under diminished pressure with bath temperatures <40 °C. Cation exchange resin Amberlite IR-120 (H^+) was pre-washed with dry MeOH before use. Thin-layer chromatography (TLC) was performed on aluminum-backed, pre-coated silica gel plates (Silica Gel 60 F_{254}, E. Merck). Silica Gel 60 (200–400 mesh) was used for column chromatography. MALDI-TOF mass spectra were recorded on a Bruker Biflex III spectrometer in positive, linear mode. High resolution ESI mass spectra were recorded on an Apex II spectrometer using an Apollo ESI source. FT-IR spectra were recorded on a Perkin Elmer System 2000 FT-IR spectrometer. NMR spectra were recorded either with a Bruker DRX 600 (600 MHz for ^1H and 150 MHz for ^{13}C) or a Bruker AC 250 (250 MHz for ^1H and 62.5 MHz for ^{13}C) spectrometer. Resonance assignments were made by the aid of COSY, HSQC, HMQC, HMBC, and NOESY experiments, when necessary. Chemical shifts are reported relative to $CHCl_3$ (δ_H 7.26, δ_C 77.0 ppm), DMSO (δ_H 2.50, δ_C 39.43 ppm), or MeOH (δ_C 49.50 ppm) as internal standard for D_2O. In the case of α/β and endo/exo mixtures, elemental analysis was carried out using a mixture of both isomers, even when the isomers were separated for the recording of NMR spectra.

4.2. 3-Azido-3-deoxy-β-D-allopyranose (2)

A 0.4 M soln of NaOMe in MeOH (2.6 mL, 0.1 equiv) was added to a stirred soln of **3** (3.9 g, 10.45 mmol) in dry MeOH (20 mL). After 6 h, ion exchange resin Amberlite IR-120 (H^+ form) was added until the pH was 7. Evaporation to dryness afforded **2** as a white wax-like solid (1.93 g, 9.4 mmol, 90%). Beside the β-pyranose form, minor signals from the α-pyranose and the α- and β-furanose forms were detected in the NMR spectrum of compound **2** in a ratio of β_{Pyr}: α_{Pyr}: β_{Fur}:α_{Fur} = 100:4:3: < 1. These minor products were not completely characterized.

R_f 0.33 (EtOAc/MeOH). ^1H NMR (D_2O, 250 MHz): δ 4.76 (dd, 1H, $J_{1,2}$ 8.2 Hz, H-1), 4.19 (t, 1H, $J_{2,3} \approx J_{3,4}$ 3.5 Hz, H-3), 3.75–3.82 (m, 2H, H-6, H-4), 3.58–3.69 (m, 2H, H-5, H-6′), 3.51 (dd, 1H, $J_{2,3}$ 3.5 Hz, H-2); ^{13}C NMR (D_2O + 2 drops MeOH-d_4, 150 MHz): δ 94.97 (C-1), 75.56 (C-5), 72.11 (C-2), 68.00 (C-3), 67.93 (C-4), 62.33 (C-6). MALDIMS (positive mode, DHB, MeCN/H_2O 1:1) m/z calcd for $C_6H_{11}N_3O_5$: 228.1 $[M+Na]^+$. Found: 228.0. Anal. Calcd for $C_6H_{11}N_3O_5 \cdot 0.75H_2O$: C, 32.95; H, 5.76; N, 19.22. Found: C, 33.04; H, 5.71; N, 19.25.

4.3. 1,2,4,6-Tetra-*O*-acetyl-3-azido-3-deoxy-β-D-allopyranose (3)

Compound **3** was synthesized in two different ways.

(a) Compound **1** (5.3 g, 18.57 mmol) was suspended in 60% formic acid (180 mL) and stirred at room temperature for 16 h. The solvent was removed under diminished pressure and the completely deprotected product was separated from formylated side product by column chromatography (EtOAc). The side product was then dissolved in MeOH (70 mL) and a 0.4 M soln of NaOMe in MeOH (2.15 mL) was added. After 2 h ion exchange resin Amberlite IR-120 (H^+ form) was added until the soln showed a pH of 7. The solvent was removed under diminished pressure and the white crystalline residue was combined with the completely deprotected product. Combined products were dissolved in pyridine (260 mL) followed by the addition of Ac_2O (130 mL) and stirred overnight. Solvent removal under diminished pressure followed by chromatographic purification (4:1 petroleum ether–EtOAc) afforded **3** as a colorless oil (6.31 g, 16.91 mmol, 91%).

(b) Compound **1** (2.18 g, 7.64 mmol) was dissolved under ultrasonic agitation in 2 M HCl (76.4 mL) and stirred for 6 h at room temperature. The solvent was removed under diminished pressure. The remaining dark brown oil was redissolved in pyridine (110 mL) under ultrasonic agitation. Subsequently, Ac_2O (55 mL) was added and the soln was stirred overnight. Solvent removal under diminished pressure followed by chromatographic purification (4:1 petroleum ether–EtOAc) afforded **3** as a colorless oil (2.0 g, 5.35 mmol, 70%).

In both cases (a) and (b) minor signals from the α-pyranose and the α- and β-furanose forms were detected in the NMR spectrum of compound **3**.

R_f 0.26 (3:1 petroleum ether–EtOAc). IR (film): ν 2109 (N_3), 1751 cm^{-1} (CO). ^1H NMR ($CDCl_3$, 250 MHz): δ 5.96 (d, 1H, $J_{1,2}$ 8.5 Hz, H-1), 4.92–4.99 (m, 2 H, H-2, H-4), 4.47 (t, 1H, $J_{2,3} \approx J_{3,4}$ 3.4 Hz, H-3), 4.29 (dd, 1H, $J_{5,6}$ 4.2 Hz, $J_{6,6'}$ 12.3 Hz, H-6), 4.10–4.21 (m, 2H, $J_{5,6'}$ 1.9 Hz, H-5, H-6′), 2.13 (s, 3H, CH_3CO), 2.12 (s, 3H, CH_3CO), 2.11 (s, 3H, CH_3CO), 2.08 (s, 3H, CH_3CO); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 170.57 (CO), 169.32 (CO), 169.21 (CO), 168.90 (CO), 89.81 (C-1), 70.88 (C-5$_\beta$), 69.30 (C-2), 66.87 (C-4), 61.82 (C-6), 60.79 (C-3), 20.82 (CH_3CO), 20.67 (CH_3CO), 20.48 (CH_3CO), 20.45 (CH_3CO). MALDIMS (positive mode, DHB, dioxane) m/z calcd for $C_{14}H_{19}N_3O_9$: 396.2 $[M+Na]^+$. Found: 396.2. Anal. Calcd: C, 45.04; H, 5.13; N, 11.26. Found: C, 45.24; H, 5.23; N, 11.17.

4.4. 4,6-Di-*O*-acetyl-3-azido-3-deoxy-1,2-*O*-(1-*exo*-cyanoethylidene)-α-D-allopyranose (5)

Trimethylsilyl cyanide (316.7 μL, 2.53 mmol, 5 equiv) and a 1 M soln of $SnCl_4$ in CH_2Cl_2 (101 μL, 101 μmol, 0.2 equiv) were added to a stirred soln of **3** (189 mg, 506 μmol) in dry CH_2Cl_2 (7.5 mL) under argon. After 18 h the reaction soln was poured on a satd aq $NaHCO_3$ soln (23 mL). The aq layer was extracted with CH_2Cl_2 (3 × 30 mL). The combined extracts were concentrated and the dark brown residue was subjected to column chromatography to yield **5** (37.8 mg, 110.8 μmol, 22%) as colorless crystals, **6** (57 mg, 168 μmol, 33%) as pale yellow needles and starting material **3** (23 mg, 61.7 μmol, 12%).

R_f 0.34 (3:1 petroleum ether–EtOAc). ^{1}H NMR ($CDCl_3$, 250 MHz): δ 5.81 (d, 1H, $J_{1,2}$ 5.6 Hz, H-1), 5.35 (m, 1H, $J_{3,4} \approx J_{4,5}$ 6.4 Hz, H-4), 4.69 (ddd, 1H, $J_{2,3}$ 2.72 Hz, $J_{2,4}$ 1.0 Hz, H-2), 4.26 (dd, 1H, $J_{5,6}$ 3.4 Hz, $J_{6,6'}$ 12.1 Hz, H-6), 4.18 (dd, 1H, $J_{5,6'}$ 5.2 Hz, H-6′), 3.97 (ddd, 1H, H-5), 3.50 (dd, 1H, H-3), 2.16 (s, 3H, CH_3CO), 2.09 (s, 3H, CH_3CO), 1.96 (s, 3H, dioxolane CH_3); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 170.35 (CO), 169.93 (CO), 116.39 (CN), 99.08 (dioxolane *C*), 98.48 (C-1), 74.13 (C-2), 70.25 (C-5), 65.50 (C-4), 63.48 (C-6), 55.03 (C-3), 24.01 (dioxolane *C*H_3), 20.61 (*C*H_3CO), 20.60 (*C*H_3CO). MALDIMS (positive mode, CHCA, MeCN) *m*/*z* calcd for $C_{13}H_{16}N_4O_7$: 363.1 $[M+Na]^+$. Found: 363.1. Anal. Calcd: C, 45.88; H, 4.74; N, 16.46. Found: C, 45.62; H, 4.55; N, 16.31.

4.5. Tetrazole 6

Trimethylsilyl cyanide (263 μL, 2.10 mmol, 5 equiv) and a 1 M soln of $SnCl_4$ in CH_2Cl_2 (505 μL, 505 μmol, 1.2 equiv) were added to a stirred soln of **3** (157 mg, 420.5 μmol) in dry CH_2Cl_2 (4 mL) under argon at 60 °C. After 2 h the reaction soln was poured on a satd aq $NaHCO_3$ soln. The aq layer was extracted with CH_2Cl_2. The combined extracts were dried ($MgSO_4$) concentrated and the dark brown residue was subjected to column chromatography (2:1 petroleum ether–EtOAc) to yield **6** (93.0 mg, 273 μmol, 65%) as a yellow oil.

R_f 0.32 (2:1 petroleum ether–EtOAc). ^{1}H NMR ($CDCl_3$, 250 MHz): δ 5.73 (d, 1H, $J_{1,2}$ 3.9 Hz, H-1), 5.59 (dd, 1H, $J_{2,3}$ 5.8, $J_{3,4}$ 3.1 Hz, H-3), 5.08 (dd, 1H, $J_{4,5}$ 10.5 Hz, H-4), 4.89 (dd, 1H, H-2), 4.28 (dd, 1H, $J_{5,6}$ 3.9 Hz, $J_{6,6'}$ 12.4 Hz, H-6), 4.16 (dd, 1H, $J_{5,6'}$ 2.1 Hz, H-6′), 3.45 (m, 1H, H-5), 2.16 (s, 3H, CH_3CO), 1.98 (s, 3H, CH_3CO), 1.95 (s, 3H, dioxolane CH_3); ^{1}H NMR (DMSO-d_6 600 MHz): $\delta = 5.76$ (d, 1H, $J_{1,2}$ 3.9 Hz, H-1), 5.74 (dd, 1H, $J_{2,3}$ 5.6 Hz, $J_{3,4}$ 3.1 Hz, H-3), 5.43 (dd, 1H, H-2), 5.20 (dd, 1H, H-4), 4.15 (dd, 1H, $J_{5,6}$ 4.3 Hz, $J_{6,6'}$ 12.5 Hz, H-6), 4.03 (dd, 1H, $J_{5,6'}$ 1.5 Hz, H-6′), 3.34 (m, 1H, H-5), 2.16 (s, 3H, CH_3CO), 1.98 (s, 3H, CH_3CO), 1.95 (s, 3H, dioxolane CH_3); ^{13}C NMR (DMSO-d_6, 150 MHz): δ 169.97 (CO), 169.13 (CO), 155.20 (C-tetrazole), 100.97 (dioxolane *C*), 97.85 (C-1), 68.32 (C-2), 65.22 (C-4), 63.68 (C-5), 61.38 (C-6), 55.52 (C-3), 20.67 (*C*H_3CO), 20.51 (*C*H_3CO), 19.73 (dioxolane *C*H_3). MALDIMS (positive mode, CHCA, dioxane) *m*/*z* calcd for $C_{13}H_{16}N_4O_7$: 363.1 $[M+Na]^+$. Found: 363.1. Anal. Calcd: C, 45.88; H, 4.74; N, 16.46. Found: C, 45.83; H, 4.79; N, 16.52.

4.6. Tetrazole 7

A 0.05 M soln of NaOMe in MeOH (0.41 mL, 0.05 equiv) was added to a stirred soln of compound **6** (140.2 g, 0.412 mmol) in dry MeOH (4.1 mL). After 14 h ion exchange resin Amberlite IR-120 (H^+ form) was added until the soln showed a pH of 7. Evaporation to dryness and subsequent chromatographic purification (1:9 petroleum ether–EtOAc) afforded compound **6** as a white wax-like solid (88.3 mg, 0.345 mmol, 84%).

R_f 0.19 (1:9 petroleum ether–EtOAc). ^{1}H NMR (D_2O, 600 MHz): δ 5.85 (d, 1H, $J_{1,2}$ 4.0 Hz, H-1), 5.57 (dd, 1H, $J_{2,3}$ 5.5 Hz, $J_{3,4}$ 3.0 Hz, H-3), 5.23 (dd, 1H, H-2), 4.30 (dd, 1H, $J_{4,5}$ 10.2 Hz, H-4), 3.74–3.80 (m, 2H, H-6, H-6′), 3.07 (m, 1H, H-5), 2.07 (dioxolane *C*H_3); ^{13}C NMR (D_2O + 2 drops MeOH-d_4, 150 MHz): δ 156.41 (C-tetrazole), 102.15 (dioxolane *C*), 99.16 (C-1), 70.35 (C-2), 68.88 (C-5), 65.27 (C-4), 60.63 (C-6), 59.83 (C-3), 19.87 (dioxolane *C*H_3). Anal. Calcd for $C_9H_{12}N_4O_5 \cdot H_2O$: C, 41.46; H, 4.83; N, 21.49. Found: C, 41.62; H, 5.12; N, 21.54.

4.7. 3-Azido-1,2,4,6-tetra-*O*-benzoyl-3-deoxy-β-D-allopyranose (10)

Compound **2** (1.01 g, 4.92 mmol) was dissolved in pyridine (8 mL) at room temperature. The colorless soln was cooled in an ice bath and benzoyl chloride (11.44 mL, 98.5 mmol, 5 equiv per OH group) was added. After stirring for 24 h at room temperature, the soln was concentrated under diminished pressure. The residue was suspended in EtOAc and washed with water (80 mL) and satd aq $NaHCO_3$ soln (100 mL). The organic phase was dried ($MgSO_4$) and concentrated. Chromatographic purification (8:1→5:1→3:1 petroleum ether–EtOAc) afforded **10** (2.34 g, 3.78 mmol, 77%) as a colorless foam. Minor amounts of the corresponding α- and β-furanose were formed as side products. They were completely separable by column chromatography.

R_f 0.42 (4:1 petroleum ether–EtOAc). ^{1}H NMR ($CDCl_3$, 250 MHz): δ 7.99–8.09 (m, 8H, Ph), 7,36–7,65 (m, 12H, Ph) 6.49 (d, 1H, $J_{1,2}$ 8.5 Hz, H-1), 5.59 (dd, 1H, $J_{2,3}$ 3.4 Hz, H-2), 5.52 (dd, 1H, $J_{3,4}$ 3.3 Hz, $J_{4,5}$ 9.7 Hz, H-4), 4.82 (t, 1H, H-3), 4.62–4.69 (m, 2H, H-5, H-6), 4.47 (dd, 1H, $J_{5,6'}$ 5.0 Hz, $J_{6,6'}$ 12.9 Hz, H-6′, Hz); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 166.10 (CO), 165.02 (CO), 164.98 (CO), 164.67 (CO), 133.85, 133.74,

133.70, 133.09, 130.14, 130.03, 129.81, 129.65, 128.75, 128.64, 128.60, 128.58, 128.51, 128.47, 128.40, 128.36 (24 C, C-arom.), 90.81 (C-1), 71.24 (C-5), 69.81 (C-2), 68.05 (C-4), 62.97 (C-6), 61.56 (C-3). MALDIMS (positive mode, DHB, dioxane) *m*/*z* calcd for $C_{34}H_{27}N_3O_9$: 644.2 $[M+Na]^+$. Found: 644.5. ESIHRMS *m*/*z* calcd for $C_{34}H_{27}N_3O_9$: 644.1645 $[M+Na]^+$. Found: 644.1663.

4.8. 1-*O*-Acetyl-3-azido-2,4,6-tri-*O*-benzoyl-3-deoxy-α,β-D-allopyranose 11

Compound **10** (1.54 g, 2.48 mmol) was dissolved in DMF (10 mL) at 50 °C and stirred for 10 min. Hydrazinium acetate (274.4 mg, 2.97 mmol, 1.2 equiv) suspended in DMF (2 mL) was added and the resulting soln was stirred for 3 h at 50 °C. The reaction mixture was diluted with 70 mL EtOAc and washed with 50 mL portions of a satd aq NaCl soln until the precipitation of salt had stopped. The organic phase was dried ($MgSO_4$) and concentrated. After passing the residue through a short bed of silica (3:1 petroleum ether–EtOAc), the solvent mixture was removed under diminished pressure and dried for 3 days under vacuum over P_2O_5. The remaining pale yellow solid was dissolved in pyridine (2.5 mL) and then stirred with Ac_2O (3 mL) for 12 h. The soln was concentrated and coevaporated three times with toluene. The crude product was purified by column chromatography to yield **11** (470 mg, 0.84 mmol, 41%, α:β = 1:2.9) as a colorless foam.

R_f 0.37 (3:1 petroleum ether–EtOAc). ^{1}H NMR ($CDCl_3$, 250 MHz): δ 7.41–8.09 (3m, $3Ph_\alpha$, $3Ph_\beta$), 6.48 (d, $J_{1,2}$ 3.9 Hz, H-1_α), 6.28 (d, $J_{1,2}$ 8.4 Hz, H-1_β), 5.54 (t, $J_{2,3} \approx 3.8$ Hz, H-2_α), 5.46 (dd, $J_{3,4}$ 3.2 Hz, $J_{4,5}$ 10.0 Hz, H-4_β), 5.40 (dd, $J_{3,4}$ 3.3 Hz, $J_{4,5}$ 10.1 Hz, H-4_α), 5.33 (dd, H-2_β, $J_{2,3}$ 3.4 Hz), 4.80 (t, H-3_α), 4.77 (t, 3-H_β), 4.69 (m, H-5_α), 4.66 (dd, $J_{5,6}$ 2.5 Hz, $J_{6,6'}$ 12.4 Hz, H-6_α), 4.62 (dd, $J_{5,6}$ 2.2 Hz, $J_{6,6'}$ 12.3 Hz, H-6_β), 4.56 (m, H-5_β), 4.48 (dd, $J_{5,6'}$ 4.1 Hz, H-$6'_\alpha$), 4.43 (dd, $J_{5,6'}$ 4.6 Hz, H-$6'_\beta$), 2.24 (s, 3H, CH_3CO_α), 2.07 (s, 3H, CH_3CO_β); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 169.12 (CO_α), 169.07 (CO_β), 166.11 (CO_β), 166.09 (CO_α), 164.89 (CO_α), 164.87 (2 × CO_β), 164.85 (CO_α), 128.39–133.89 (36C, 3 × Ph_α, 3 × Ph_β), 89.99 (C-1_β), 88.46 (C-1_α), 71.05 (C-5_β), 69.75 (C-2_β), 68.40 (C-2_α), 67.75 (C-4_β), 67.21 (C-4_α), 66.14 (C-5_α), 62.84 (C-6_β), 62.54 (C-6_α), 61.25 (C-3_β), 58.88 (C-3_α), 20.98 (CH_3CO_α), 20.87 (CH_3CO_β). MALDIMS (positive mode, DHB, dioxane) *m*/*z* calcd for $C_{29}H_{25}N_3O_9$: 582.2 $[M+Na]^+$. Found: 582.3. Anal. Calcd for $C_{29}H_{25}N_3O_9$: C, 62.25; H, 4.50; N, 7.51. Found: C, 62.22; H, 4.41; N, 7.65.

4.9. Tetrazole 14

Trimethylsilyl cyanide (110.5 μL, 883 μmol, 10 equiv) was added to a stirred soln of **11** (49.4 mg, 88.3 μmol) in nitromethane (2 mL) at room temperature under argon. $BF_3{\cdot}OEt_2$ was added in portions of 2 μL every 30 min, until TLC indicated complete consumption of starting material. The soln was poured on a satd aq $NaHCO_3$ soln (20 mL) and the aq layer was extracted with CH_2Cl_2 (3 × 30 mL). The combined extracts were concentrated and the dark brown residue was subjected to column chromatography (4:1 petroleum ether–EtOAc) to yield **14** (23.4 mg, 44.2 μmol, 50%) as a pale yellow syrup.

R_f 0.28 (4:1 petroleum ether–EtOAc). ^{1}H NMR ($CDCl_3$, 250 MHz): δ 7.41–8.17 (4m, 15H, arom.), 5.94 (d, 1H, $J_{1,2}$ 3.9 Hz, H-1), 5.79 (dd, 1H, $J_{2,3}$ 5.8 Hz, $J_{3,4}$ 3.0 Hz, H-3), 5.68 (dd, 1H, $J_{4,5}$ 10.4 Hz, H-4), 5.17 (dd, 1H, H-2), 4.68 (dd, 1H, $J_{5,6}$ 4.1 Hz, $J_{6,6'}$ 12.5 Hz, H-6), 4.44 (dd, 1H, H-6′), 3.86 (m, 1H, H-5); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 165.9 (CO), 165.3 (CO), 134.14, 133.33, 131.83, 130.85, 130.30, 129.74, 129.32, 128.74, 128.62, 128.45, 128.36, 126.38 (18 C, C-arom.), 102.9 (dioxolane *C*), 98.6 (C-1), 69.4 (C-2), 66.4 (C-4), 64.7 (C-5), 62.0 (C-6), 56.1 (C-3). MALDIMS (positive mode, DHB, dioxane) *m*/*z* calcd for $C_{28}H_{22}N_4O_7$: 549.2 $[M+Na]^+$. Found: 549.2. ESIHRMS *m*/*z* calcd for $C_{28}H_{22}N_4O_7$: 565.1112 $[M+K]^+$. Found: 565.1111.

4.10. Methyl 3-azido-3-deoxy-α,β-D-allofuranoside (15) and methyl 3-azido-3-deoxy-5,6-*O*-isopropylidene-α,β-D-allofuranoside (16)

Acetyl chloride (86 μL, 1.2 mmol) was added to a stirred soln of compound **1** (857 mg, 3 mmol) in 11.8 mL of MeOH under nitrogen at 0 °C. The ice bath was removed and the reaction mixture was stirred for 48 h at room temperature. The soln was neutralized with Et_3N and concentrated under diminished pressure. The pale yellow residue was subjected to column chromatography to yield **15** (367 mg, 1.69 mmol, 56%) and **16** (250 mg, 0.97 mmol, 34%) as colorless crystals.

Compound **15**: R_f 0.23 (1:4 petroleum ether–EtOAc). ^{1}H NMR (MeOH-d_4, 600 MHz): δ 4.82 (d, $J_{1,2}$ 4.4 Hz, H-1_α), 4.74 (s, $J_{1,2} < 1$ Hz, H-1_β), 4.22 (dd, $J_{2,3}$ 7.6 Hz, H-2_α), 4.10 (d, $J_{2,3}$ 4.2 Hz, H-2_β), 3.92–3.97 (m, H-3_α, H-3_β, H-4_β), 3.90 (t, $J_{3,4} \approx J_{4,5}$ 4.2 Hz, H-4_α), 3.75 (dd, $J_{5,6}$ 3.3 Hz, $J_{6,6'}$ 11.4 Hz, H-6_β), 3.56–3.63 (m, H-5_α, H-$6'_\beta$, H-6_α, H-$6'_\alpha$), 3.51 (m, H-5_α), 3.39 (s, OMe_α), 3.32 (OMe_β); ^{13}C NMR (MeOH-d_4, 150 MHz): δ 109.76 (C-1_β), 103.64 (C-1_α), 83.72 (C-4_α), 81.65 (C-4_β), 77.16 (C-2_β), 75.39 (C-5_β), 74.20 (C-2_α), 73.28 (C-5_α), 65.39 (C-3_β), 64.82 (2 C, C-6_α, C-6_β), 61.60 (C-3_α), 55.37 (OMe_β), 55.31 (OMe_α). Anal. Calcd: C, 38.36; H, 5.98; N, 19.17. Found: C, 38.50; H, 6.05; N, 19.01.

Compound **16**: R_f 0.27 (1:2 petroleum ether–EtOAc). ^{1}H NMR ($CDCl_3$, 600 MHz): δ 4.80 (d, $J_{1\alpha,2\alpha}$ 4.5 Hz, H-1_α), 4.75 (s, $J_{1\beta,2\beta} < 1$ Hz, H-1_β), 4.20 (m, H-2_α), 4.02–4.12 (m, H-6_β, H-2_β, H-3_β, H-5_α, H-6_α), 3.89–3.97

(m, H-6′$_\beta$, H-5$_\beta$, H-4$_\beta$, H-3$_\alpha$, H-6$_\alpha$), 3.84 (dd, $J_{3\alpha,4\alpha}$ 3.4 Hz, $J_{4\alpha,5\alpha}$ 5.9 Hz, H-4$_\alpha$), 3.80 (m, H-6$_\alpha$), 3.40 (s, OMe$_\alpha$), 3.26 (OMe$_\beta$), 1.41 (s, 1CH$_{3\beta}$, 1CH$_{3\alpha}$), 1.31 (s, CH$_{3\beta}$), 1.30 (s, CH$_{3\alpha}$); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 109.86 (C-isopropylidene$_\alpha$), 109.77 (C-isopropylidene$_\beta$), 107.83 (C-1$_\beta$), 101.92 (C-1$_\alpha$), 82.58 (C-4$_\alpha$), 81.99 (C-4$_\beta$), 77.56 (C-5$_\beta$), 75.50 (C-5$_\alpha$), 75.48 (C-2$_\beta$), 72.38 (C-2$_\alpha$), 67.67 (C-6$_\beta$), 66.34 (C-6$_\alpha$), 65.31 (C-3$_\beta$), 60.95 (C-3$_\alpha$), 55.33 (OMe$_\alpha$), 54.82 (OMe$_\beta$), 26.33 (CH$_{3\beta}$), 26.27 (CH$_{3\alpha}$), 25.03 (CH$_{3\beta}$), 24.61 (CH$_{3\alpha}$). Anal. Calcd: C, 46.33; H, 6.61; N, 16.21. Found: C, 46.41; H, 6.74; N, 16.00.

4.11. 1,2,5,6-Tetra-*O*-acetyl-3-azido-3-deoxy-α,β-D-allofuranose (17)

Ac_2O (5 mL) was added to a stirred soln of compound **15** (271 mg, 1.24 mmol) in pyridine (10 mL). After 12 h the reaction mixture was concentrated under diminished pressure and the yellow residue was filtered through a short silica column (2:1 petroleum ether–EE). The combined product fractions were dried and subsequently dissolved in a mixture of Ac_2O (1.29 mL), HOAc (4.92 mL) and concd H_2SO_4 (360 μL). After 90 min, the reaction mixture was poured on a satd aq $NaHCO_3$ soln. The aq layer was extracted with CH_2Cl_2 (3 × 30 mL). The combined extracts were concentrated and the dark brown residue was subjected to column chromatography to yield **17** (386 mg, 1.03 mmol, 83%) as a colorless oil.

R_f 0.26 (2:1 petroleum ether–EtOAc). ^{1}H NMR ($CDCl_3$, 600 MHz): δ 6.31 (d, $J_{1,2}$ 4.4 Hz, H-1$_\alpha$), 6.12 (s, $J_{1,2} < 1$ Hz, H-1$_\beta$), 5.31 (d, $J_{2,3}$ 4.9 Hz, H-2$_\beta$), 5.09–5.18 (m, H-2$_\alpha$, H-5$_\beta$, H-5$_\alpha$), 4.45 (dd, $J_{5,6}$ 3.2 Hz, $J_{6,6'}$ 12.2 Hz, H-6$_\beta$), 4.38 (dd, $J_{5,6}$ 3.9 Hz, $J_{6,6'}$ 12.3 Hz, H-6$_\alpha$), 4.26 (t, $J_{3,4} \approx J_{4,5}$ 4.3 Hz, H-4$_\alpha$), 4.17–4.22 (m, H-4$_\beta$, H-3$_\alpha$), 4.11–4.16 (m, H-3$_\beta$, H-6′$_\alpha$), 4.08 (dd, $J_{5,6'}$ 5.6 Hz, H-6′β), 2.16 (s, 1CH$_{3\beta}$, 1CH$_{3\alpha}$), 2.12 (s, 1CH$_{3\beta}$, 1CH$_{3\alpha}$), 2.09 (s, CH$_{3\alpha}$), 2.08 (s, 1CH$_{3\beta}$, 1CH$_{3\alpha}$), 2.06 (s, CH$_{3\beta}$). ^{13}C NMR ($CDCl_3$, 150 MHz): δ 170.42 (CO$_\beta$), 170.27 (CO$_\alpha$), 169.96 (2C, 1CO$_\alpha$, 1CO$_\beta$), 169.63 (CO$_\alpha$), 169.62 (CO$_\alpha$), 169.39 (CO$_\beta$), 168.57 (CO$_\beta$), 98.03 (C-1$_\beta$), 93.29 (C-1$_\alpha$), 82.13 (C-4$_\alpha$), 79.80 (C-4$_\beta$), 75.74 (C-2$_\beta$), 71.75 (2 C, C-5$_\beta$, C-2$_\alpha$), 70.34 (C-5$_\alpha$), 62.24 (C-6$_\beta$), 61.97 (C-6$_\alpha$), 61.53 (C-3$_\beta$), 58.24 (C-3$_\alpha$), 20.94, 20.77, 20.56, 20.15 (4C, *C*H$_3$CO$_\alpha$), 20.89, 20.78, 20.62, 20.43 (4 C, *C*H$_3$CO$_\beta$). MALDI-HRMS (positive mode, DHB, dioxane) *m*/*z* calcd for $C_{14}H_{19}N_3O_9$: 396.1091 $[M+Na]^+$. Found: 396.0990.

4.12. 2,5,6-Tri-*O*-acetyl-3-azido-3-deoxy-β-D-allofuranosyl cyanide (18) and tetrazole 19

Trimethylsilyl cyanide (136 μL, 1.09 mmol, 5 equiv) and a 1 M soln of $SnCl_4$ in CH_2Cl_2 (239 μL, 239 μmol, 1.1 equiv) were added to a stirred soln of compound **17** (81 mg, 217 μmol) in dry CH_2Cl_2 (4 mL) under argon. The mixture was heated in an oil bath (60 °C). After 90 min the reaction soln was poured on a satd aq $NaHCO_3$ soln (30 mL). The aq layer was extracted with CH_2Cl_2 (3 × 50 mL). The combined extracts were concentrated and the dark brown residue was subjected to column chromatography to yield **18** (20 mg, 58.8 μmol, 27%) as a colorless oil and **19** (38 mg, 112 μmol, 52%) as a pale yellow oil.

Compound **18**: R_f 0.44 (3:2 petroleum ether–EtOAc). ^{1}H NMR ($CDCl_3$, 250 MHz): δ 5.55 (dd, 1H, $J_{1,2}$ 3.2 Hz, $J_{2,3}$ 5.2 Hz, H-2), 5.34 (dd, 1H, H-5), 4.67 (d, 1H, H-1), 4.35–4.43 (m, 2H, H-3, H-6), 4.12–4.21 (m, 2H, H-4, H-6′), 2.21 (s, 3H, CH_3CO), 2.17 (s, 3H, CH_3CO), 2.10 (s, 3H, CH_3CO); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 170.329 (CO), 169.76 (CO), 169.38 (CO), 115.41 (CN), 80.95 (C-4), 75.82 (C-2), 69.71 (C-5), 69.32 (C-1), 61.59 (C-6), 60.75 (C-3), 20.91 (*C*H$_3$CO), 20.61 (*C*H$_3$CO), 20.35 (*C*H$_3$CO). MALDIMS (positive mode, CHCA, MeCN) *m*/*z* calcd for $C_{13}H_{16}N_4O_7$: 363.1 $[M+Na]^+$. Found: 363.1. Anal. Calcd: C, 45.88; H, 4.74; N, 16.46. Found: C, 45.78; H, 4.80; N, 16.51.

Compound **19**: R_f 0.28 (1:1 petroleum ether–EtOAc). ^{1}H NMR ($CDCl_3$, 600 MHz): δ 5.84 (d, 1H, $J_{1,2}$ 3.9 Hz, H-1), 5.62 (dd, 1H, $J_{2,3}$ 5.5 Hz, H-2), 5.41 (d, 1H, $J_{3,4} < 1$ Hz, H-3), 5.02 (m, 1H, H-5), 4.55 (d, 1H, $J_{4,5}$ 6.5 Hz, H-4), 4.44 (dd, 1H, $J_{5,6}$ 3.3 Hz, $J_{6,6'}$ 12.5 Hz, H-6), 4.20 (dd, 1H, $J_{5,6'}$ 4.6 Hz, H-6′), 2.19 (s, 3H, CH_3CO), 2.12 (s, 3H, CH_3CO), 2.05 (s, 3H, dioxolane CH_3); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 170.24 (CO), 169.79 (CO), 154.60 (C-tetrazole), 103.43 (C-1), 102.79 (dioxolane *C*), 84.78 (C-4), 77.73 (C-2), 70.27 (C-5), 61.90 (C-6), 57.414 (C-3), 20.93 (dioxolane *C*H$_3$), 20.63 (*C*H$_3$CO), 19.04 (*C*H$_3$CO). MALDIMS (positive mode, CHCA, MeCN) *m*/*z* calcd for $C_{13}H_{16}N_4O_7$: 363.1 $[M+Na]^+$. Found: 363.1. Anal. Calcd: C, 45.88; H, 4.74; N, 16.46. Found: C, 45.80; H, 4.76; N, 16.48.

4.13. 5,6-Di-*O*-acetyl-3-azido-3-deoxy-1,2-*O*-(1-*exo*-cyanoethylidene)-α-D-allofuranose (20) and 5,6-Di-*O*-acetyl-3-azido-3-deoxy-1,2-*O*-(1-*endo*-cyanoethylidene)-α-D-allofuranose (21)

Trimethylsilyl cyanide (150 μL, 0.1.20 mmol, 6 equiv) and a 1 M soln of $SnCl_4$ in CH_2Cl_2 (100 μL, 100 μmol, 0.5 equiv) were added to a stirred soln of compound **17** (75 mg, 201 μmol) in dry CH_2Cl_2 (4 mL) under argon. After 15 h the reaction soln was poured on satd aq $NaHCO_3$ soln (25 mL). The aq layer was extracted with CH_2Cl_2 (3 × 20 mL). The combined extracts were concentrated and the dark brown residue was taken up in acetonitrile and filtered. Purification of the remaining soln by HPLC afforded **21** (13 mg, 38 μmol, 19%) as a white powder and **21** (4 mg, 12 μmol, 6%) as a colorless oil. In addition, cyanide **18** (13 mg, 38 μmol, 19%) and tetrazole **19** (25 mg, 73.5 μmol, 37%) were isolated.

Compound **20**: R_f 0.34 (3:1 petroleum ether–EtOAc). ^{1}H NMR ($CDCl_3$, 250 MHz): δ 5.99 (d, 1H, $J_{1,2}$ 4.0 Hz, H-1), 5.32 (m, 1H, H-5), 4.94 (dd, 1H, $J_{2,3}$ 4.93 Hz, H-2), 4.40 (dd, 1H, $J_{5,6}$ 3.8 Hz, $J_{6,6'}$ 12.1 Hz, H-6), 4.17 (dd, 1H, $J_{5,6'}$ 6.5 Hz, H-6′), 4.11 (dd, 1H, $J_{3,4}$ 9.6 Hz, $J_{4,5}$ 5.7 Hz, H-4), 3.62 (dd, 1H, H-3), 2.14 (s, 3H, CH_3CO), 2.08 (s, 3H, CH_3CO), 1.91 (s, 3H, dioxolane CH_3); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 170.36 (CO), 169.83 (CO), 116.38 (CN), 104.74 (C-1), 100.84 (dioxolane *C*), 81.11 (C-2), 76.11 (C-4), 69.97 (C-5), 62.17 (C-6), 61.47 (C-3), 24.31 (dioxolane *C*H_3), 20.71 (*C*H_3CO), 20.59 (*C*H_3CO). MALDIMS (positive mode, CHCA, MeCN) *m*/*z* calcd for $C_{13}H_{16}N_4O_7$: 363.1 $[M+Na]^+$. Found: 363.1. Anal. Calcd: C, 45.88; H, 4.74; N, 16.46. Found: C, 45.62; H, 4.55; N, 16.31.

Compound **21**: R_f 0.34 (3:1 petroleum ether–EtOAc). ^{1}H NMR ($CDCl_3$, 600 MHz): δ 6.14 (d, 1H, $J_{1,2}$ 3.8 Hz, H-1), 5.29 (m, 1H, H-5), 5.18 (t, 1H, H-2), 4.41 (dd, 1H, $J_{5,6}$ 3.5 Hz, $J_{6,6'}$ 12.2 Hz, H-6), 4.19 (dd, 1H, $J_{5,6'}$ 6.1 Hz, H-6′), 4.13 (dd, 1H, $J_{3,4}$ 9.5 Hz, $J_{4,5}$ 6.1 Hz, H-4), 3.47 (dd, 1H, $J_{2,3}$ 5.1 Hz, H-3), 2.14 (s, 3H, CH_3CO), 2.09 (s, 3H, CH_3CO), 1.87 (s, 3H, dioxolane CH_3); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 170.44 (CO), 169.93 (CO), 115.59 (CN), 106.11 (C-1), 104.67 (dioxolane *C*), 83.60 (C-2), 76.40 (C-4), 70.18 (C-5), 62.18 (C-6), 61.86 (C-3), 20.77 (CH_3), 20.66 (CH_3), 20.63 (CH_3). MALDIMS (positive mode, CHCA, MeCN) *m*/*z* calcd for $C_{13}H_{16}N_4O_7$: 363.1 $[M+Na]^+$. Found: 363.1.

4.14. Methyl 3-azido-2,5,6-tri-*O*-benzoyl-3-deoxy-α,β-D-allofuranoside (22)

Compound **15** (948 mg, 4.32 mmol) was dissolved in pyridine (10 mL) at room temperature. The colorless soln was cooled in an ice bath and benzoyl chloride (2.26 mL, 19.44 mmol, 4.5 equiv per OH group) was added. After stirring for 48 h at room temperature the soln was concentrated under diminished pressure. The residue was suspended in EtOAc (100 mL) and washed with water (100 mL) and sat. NaCl soln (100 mL). The organic phase was dried ($MgSO_4$) and concentrated. Chromatographic purification (8:1→5:1 petroleum ether–EtOAc) afforded **22** (2.05 g, 3.86 mmol, 89%) as a colorless foam.

Compound β-**22**: R_f 0.38 (4:1 petroleum ether–EtOAc). IR (thin film): ν 2113 (N_3), 1725 cm^{-1} (CO). ^{1}H NMR ($CDCl_3$, 250 MHz): δ 7.99–8.09 (m, Ph_β), 7.36–7.65 (m, Ph_β), 5.75 (m, H-5$_\beta$), 5.54 (d, $J_{1,2} < 1$ Hz, $J_{2,3}$ 4.7 Hz, H-2$_\beta$), 5.07 (s, H-1$_\beta$), 4.88 (dd, $J_{5,6}$ 3.1 Hz, $J_{6,6'}$ 12.1 Hz, H-6$_\beta$), 4.68 (dd, $J_{5,6'}$ 6.3 Hz, H-6′$_\beta$), 4.57 (t, $J_{3,4} \approx J_{4,5} \approx 7.6$ Hz, H-4$_\beta$), 4.51 (dd, $J_{2,3}$ 4.7 Hz, H-3$_\beta$), 4.47 (s, OMe_β). ^{13}C NMR ($CDCl_3$, 150 MHz): δ 165.74 (CO_β), 165.37 (CO_β), 164.98 (CO_β), 128.36–134.26 (12 C, C-arom.), 106.11 (C-1$_\beta$), 78.76 (C-4$_\beta$), 76.61 (C-2$_\beta$), 72.33 (C-5$_\beta$), 62.93 (C-6$_\beta$), 61.75 (C-3$_\beta$), 55.19 (OMe_β). MALDIMS (positive mode, CHCA, dioxane) *m*/*z* calcd for $C_{28}H_{25}N_3O_8$: 554.2 $[M+Na]^+$. Found: 554.4. Anal. Calcd: C, 63.27; H, 4.74; N, 7.91. Found: C, 63.13; H, 4.86; N, 7.76.

Compound α-**22**: R_f 0.38 (4:1 petroleum ether–EtOAc). ^{1}H NMR ($CDCl_3$, 250 MHz): δ 7.99–8.09 (m, Ph_α), 7.38–7.56 (m, Ph_α), 5.75 (m, H-5$_\alpha$), 5.29 (d, $J_{1,2}$ 4.2 Hz, H-1$_\alpha$), 5.25 (dd, $J_{2,3}$ 4.2, H-2$_\alpha$), 4.82 (dd, $J_{5,6}$ 3.4 Hz, $J_{6,6'}$ 12.2, H-6$_\alpha$), 4.69 (dd, $J_{5,6'}$ 6.2 Hz, H-6′$_\alpha$), 4.55 (dd, $J_{3,4}$ 7.2 Hz, H-3$_\alpha$), 4.46 (t, H-4$_\alpha$), 3.44 (s, OMe_α). ^{13}C NMR ($CDCl_3$, 150 MHz): δ 128.36—133.37 (12 C, C-arom.), 100.93 (C-1$_\alpha$), 79.71 (C-4$_\alpha$), 73.02 (C-2$_\alpha$), 71.22 (C-5$_\alpha$), 62.70 (C-6$_\alpha$), 58.87 (C-3$_\alpha$), 55.19 (OMe_α). MALDIMS (positive mode, CHCA, dioxane) *m*/*z* calcd for $C_{28}H_{25}N_3O_8$: 554.2 $[M+Na]^+$. Found: 554.4.

4.15. 1-*O*-Acetyl-3-azido-2,5,6-tri-*O*-benzoyl-3-deoxy-α,β-D-allofuranose (23)

Compound **22** (2.01 g, 3.78 mmol) was dissolved in Ac_2O (3.55 mL), HOAc (15.12 mL), and concd H_2SO_4 (990 μL). After 35 min the reaction mixture was poured on a satd aq $NaHCO_3$ soln. The aq layer was extracted with CH_2Cl_2 (3 × 50 mL). The combined extracts were dried ($MgSO_4$), concentrated, and the dark brown residue was subjected to column chromatography to yield **23** (1.90 g, 3.40 mmol, 90%) as a colorless oil.

Compound β-**23**: R_f 0.38 (4:1 petroleum ether–EtOAc). ^{1}H NMR ($CDCl_3$, 250 MHz): δ 8.07–8.11 (m, 4H, arom.), 8.00–8.03 (m, 2H, arom.), 7.54–7.63 (m, 3H, arom.), 7.41–7.50 (m, 6H, arom.), 6.34 (s, 1H, $J_{1,2} < 1$ Hz, H-1), 5.76 (m, 1H, H-5), 5.62 (d, 1H, $J_{2,3}$ 4.3 Hz, H-2), 4.79 (dd, 1H, $J_{5,6}$ 3.6 Hz, $J_{6,6'}$ 12.1 Hz, H-6), 4.60 (dd, 1H, $J_{5,6'}$ 6.4 Hz, H-6′), 4.50–4.56 (m, 2H, H-4, H-3), 1.92 (s, 3H, CH_3CO). ^{13}C NMR ($CDCl_3$, 150 MHz): δ 168.70 (CO), 168.03 (CO), 165.51 (CO), 165.18 (CO), 133.87, 133.64, 133.27, 130.03, 129.89, 129.69, 129.45, 129.15, 128.61, 128.58, 128.50, 128.47 (18 C, C-arom.), 98.21 (C-1), 80.36 (C-4), 76.39 (C-2), 71.81 (C-5), 62.92 (C-6), 61.36 (C-3), 20.67 (CH_3). MALDIMS (positive mode, CHCA, dioxane) *m*/*z* calcd for $C_{29}H_{25}N_3O_9$: 582.2 $[M+Na]^+$. Found: 582.4. Anal. Calcd: C, 62.25; H, 4.50; N, 7.51. Found: C, 62.13; H, 4.70; N, 7.56.

Compound α-**23**: R_f 0.38 (4:1 petroleum ether–EtOAc). ^{1}H NMR ($CDCl_3$, 250 MHz): δ 8.01–8.09 (m, 6H, arom.), 7.55–7.64 (m, 3H, arom.), 7.43–7.50 (m, 6H, arom.), 6.57 (s, 1H $J_{1,2}$ 4.4 Hz, H-1), 5.68 (m, 1H, H-5), 5.45 (dd, 1H, $J_{2,3}$ 7.6 Hz, H-2), 4.76 (dd, 1H, $J_{5,6}$ 3.9 Hz, $J_{6,6'}$ 12.3 Hz, H-6), 4.63 (dd, 1H, $J_{5,6'}$ 5.5 Hz, H-6′), 4.58 (t, 1H, $J_{4,5} \approx 4.4$ Hz, H-4), 4.54 (dd, 1H, $J_{3,4}$ 4.0 Hz, H-3), 2.14 (s, 3H, CH_3CO). ^{13}C NMR ($CDCl_3$, 150 MHz): δ 169.39 (CO), 165.98 (CO), 165.35 (CO), 165.32 (CO), 133.88, 133.70, 133.36, 129.95, 129.83, 129.71, 129.34, 129.02, 128.68, 128.55, 128.43

(18 C, C-arom.), 93.63 (C-1), 82.50 (C-4), 72.49 (C-2), 71.19 (C-5), 62.78 (C-6), 58.68 (C-3), 21.04 (CH_3). MALDIMS (positive mode, CHCA, dioxane) *m/z* calcd for $C_{29}H_{25}N_3O_9$: 582.2 $[M+Na]^+$. Found: 582.4.

4.16. 3-Azido-2,5,6-tri-*O*-benzoyl-3-deoxy-β-D-allofuranosyl cyanide (24)

Trimethylsilyl cyanide (369 μL, 2.95 mmol, 5 equiv) and a 1 M soln of $SnCl_4$ in CH_2Cl_2 (650 μL, 650 μmol, 1.1 equiv) were added to a stirred soln of **23** (331 mg, 591 μmol) in dry CH_2Cl_2 (12 mL) under argon. The mixture was heated in an oil bath (60 °C). After 4 h the reaction soln was poured on a satd aq $NaHCO_3$ solution (60 mL). The aq layer was extracted with CH_2Cl_2 (3×50 mL). The combined extracts were dried ($MgSO_4$), concentrated, and the dark brown residue was subjected to column chromatography to yield **24** (202 mg, 384 μmol, 65%) as a colorless oil.

R_f 0.33 (5:1 petroleum ether–EtOAc). IR (thin film): *v* 2116 (N_3), 1728 cm^{-1} (CO). ^1H NMR ($CDCl_3$, 250 MHz): δ 8.02–8.11 (m, 6H, arom.), 7.43–7.51 (m, 9H, arom.), 5.83 (dd, $J_{1,2}$ 3.8 Hz, $J_{2,3}$ 5.2 Hz, H-2), 5.76 (m, H-5), 4.86 (d, H-1), 4.78 (dd, $J_{5,6}$ 3.8 Hz, $J_{6,6'}$ 12.3 Hz, H-6), 4.65–4.69 (m, H-6′, H-3), 4.45 (t, $J_{3,4} \approx J_{4,5}$ 6.4 Hz, H-4). ^{13}C NMR ($CDCl_3$, 150 MHz): δ 165.96 (CO), 165.49 (CO), 165.15 (CO), 134.27, 133.75, 133.38, 130.08, 129.90, 129.69, 129.28, 128.85, 128.75, 128.60, 128.52, 127.79 (18 C, C-arom.), 115.28 (CN), 80.91 (C-4), 76.10 (C-2), 71.00 (C-5), 69.35 (C-1), 62.59 (C-6), 61.96 (C-3). MALDIMS (positive mode, DHB, dioxane) *m/z* calcd for $C_{28}H_{22}N_4O_7$: 549.1 $[M+Na]^+$. Found: 549.2. ESIHRMS *m/z* calcd 549.1386 $[M+Na]^+$. Found: 549.1367. Anal. Calcd: C, 63.87; H, 4.21; N, 10.64. Found: C, 63.20; H, 4.49; N, 10.04.

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