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'Click' Preparation of Carbohydrate 1-Benzotriazoles, 1,4-Disubstituted, and 1,4,5-Trisubstituted Triazoles and their Utility as Glycosyl Donors*

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Glycosyl triazoles can be prepared from readily available anomeric azides through various 'click' methodologies: thermal Huisgen cycloaddition with alkynes, strain-promoted Huisgen cycloaddition of benzynes, and Cu^{I}-catalyzed azide-alkyne cycloaddition of terminal alkynes (CuAAC reaction). Here we investigate the formation of glycosyl 1-benzotriazoles from anomeric and non-anomeric carbohydrate azides using benzynes derived from substituted anthranilic acids. The reactivity of the resulting anomeric 1-benzotriazoles as glycosyl donors was investigated and compared with 1,4-disubstituted glycosyl triazoles (from the CuAAC reaction) and 1,4,5-trisubstituted glycosyl triazoles (prepared by Huisgen cycloaddition of glycosyl azides and dimethyl acetylene dicarboxylate). The 1,4,5-trisubstituted glycosyl triazoles were activated by Lewis acids and could be converted to *O*-glycosides, *S*-glycosides, glycosyl chlorides, and glycosyl azides. By contrast, under all conditions investigated, the 1,4-disubstituted glycosyl triazoles were unreactive as glycosyl donors. Glycosyl 1-benzotriazoles were generally inert as glycosyl donors; however, a tetrafluorobenzotriazole derivative, which bears electron-withdrawing substituents on the benzotriazole group, was a moderate glycosyl donor and could be converted to an *S*-glycoside by treatment with thiocresol and tin(IV) chloride.

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Introduction

Since the recent introduction of the Cu^{I}-catalyzed azide-terminal alkyne cycloaddition (CuAAC)[1] and the independent realization of improved rates and regioselectivities as reported by the Meldal[2] and Sharpless[3] groups, there has been a boom in applications of this reaction in the carbohydrate field. These include the preparation of triazoles used to both inhibit[4] and define the substrate specificity[5] of glycosyltransferases, its application in the detection of azide-bearing cell-surface carbohydrates,[6] and the synthesis of complex neoglycoconjugates including triazole-linked oligosaccharides, glycopeptides and carbohydrate macrocycles.[7]

The CuAAC reaction yields 1,4-disubstituted 1,2,3-triazoles in high yields with essentially perfect regioselectivity[8] and the ready accessibility of glycosyl azides makes them ideal substrates for the reaction. Several other types of N-linked glycosyl 1,2,3-triazoles have been reported in the literature, most notably 1,4,5-trisubstituted 1,2,3-triazoles, and 1- and 2-substituted benzotriazoles (Fig. 1). 1,4,5-Trisubstituted 1,2,3-triazoles have been prepared through the classical Huisgen [3 + 2] cycloaddition of glycosyl azides and activated symmetrical alkynes such as dimethyl acetylene dicarboxylate.[9] Glycosyl benzotriazoles have been prepared by the glycosidation of benzotriazole salts or trimethylsilylbenzotriazole, resulting in mixtures of the 1- and 2-substituted regioisomers.[10,11] Each of these reactions has been described as a 'click' process that conforms to the ideals of modularity, high yield, stereospecificity and ease of isolation and purification.[12,13]

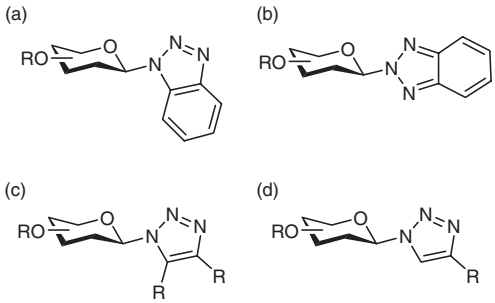

Fig. 1. Generic examples of glycosyl triazoles: (a) 1-benzotriazole, (b) 2-benzotriazole, (c) 1,4,5-trisubstituted triazole, and (d) 1,4-disubstituted triazole.

Although the attractions of the glycosyl triazole group have mostly been as an inert linker, several reports have investigated the chemical reactivity of various glycosyl triazoles. The N-linkage of 1,4-disubstituted glycosyl triazoles is stable to strong acid or base for prolonged periods,[14] is inert

* The present paper is dedicated to Professor Bob Stick to mark the occasion of his retirement and 65th birthday.

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to enzymatic cleavage by glycosidases,[15] and is stable to a range of common reaction conditions, such as those used for the acetylation and benzylation of alcohols, as well as for the removal of these protecting groups.[16] Moreover, the linkage is stable to the conditions used for Lewis acid-catalyzed ($BF_3 \cdot Et_2O$) and Koenigs–Knorr (AgOTf) glycosidations.[16] By contrast, Miethchen and coworkers have shown that trisubstituted triazoles with an electron-withdrawing trifluoromethyl substituent are acid-sensitive[17] and Bröder and Kunz have demonstrated that 1,4,5-trisubstituted glycosyl triazoles can act as glycosyl donors in the presence of Lewis acids including TMSOTf, $ZnCl_2$, and $BF_3 \cdot Et_2O$,[9] and can be converted to glycosyl fluorides by treatment with HF–pyridine.[18,19] Interestingly, 1,4,5-trisubstituted glycosyl triazoles derived from the thermal cycloaddition of di-*t*-butyl acetylene dicarboxylate were found to be better glycosyl donors than those obtained from dimethyl acetylene dicarboxylate, a result Bröder and Kunz attributed to loss of the *t*-butyloxycarbonyl group under the reaction conditions, and the formation of a glycosyl triazole, which was proposed to be the actual glycosyl donor.[18] Finally, to the best of our knowledge, the utility of glycosyl benzotriazoles as glycosyl donors has not been assessed, possibly owing to the lack of reliable methods for their synthesis and the difficulty of preparing pure regioisomers.

Given the current interest in glycosyl triazoles, we sought to develop a route enabling the synthesis of glycosyl 1-benzotriazoles as single regioisomers, and to investigate their reactivity as glycosyl donors relative to 1,4-disubstituted and 1,4,5-trisubstituted glycosyl triazoles.

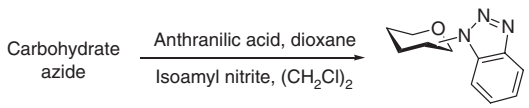
Results and Discussion

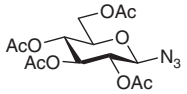
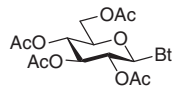
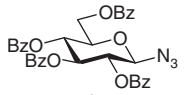
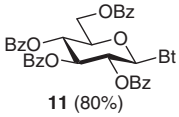
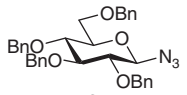
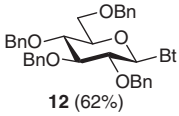
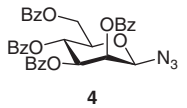
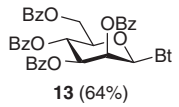
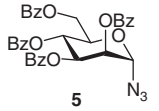
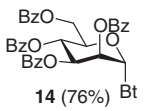
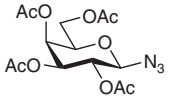
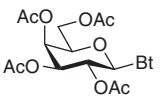
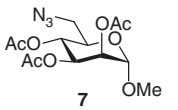
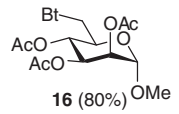
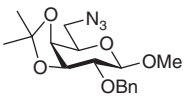
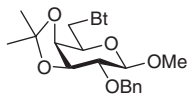
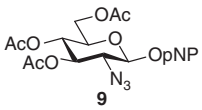
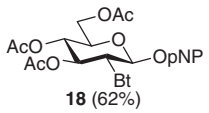
Synthesis of Glycosyl Triazoles

Although there are several extremely mild methods for the generation of benzyne, most of the precursors require lengthy and complicated syntheses,[13,20] and modification of the benzotriazole nucleus is not trivial. Wittig and Hoffman,[21] and shortly thereafter Reynolds,[22] reported that the cycloaddition of benzyne (obtained by thermal decomposition of diazonium benzenecarboxylate) to azides affords only 1-substituted benzotriazoles. This procedure seemed particularly appealing as it allows the synthesis of glycosyl 1-benzotriazoles from readily available glycosyl azides, avoiding the formation of the 2-substituted regioisomers. However, preparation of benzyne by thermal decomposition of diazonium benzenecarboxylate can suffer from a risk of explosion.[23] This has led to the avoidance of this useful reaction, with a focus instead on the development of alternative reagents.[13] However, the ready availability of substituted anthranilic acids and their potential as benzyne precursors must not be overlooked. The explosive potential of the intermediate benzenediazonium-2-carboxylates can be readily minimized by the simple expedient of avoiding the isolation of the shock-sensitive solid through forming it in situ under conditions where it can thermally decompose to benzyne. A convenient procedure involves the syringe-pump addition of a solution of anthranilic acid to a solution of the carbohydrate azide and an excess of isoamyl nitrite in 1,2-dichloroethane at reflux.[24] By this under-appreciated approach, such anthranilic acids remain experimentally competitive reagents for the formation of benzotriazoles by virtue of their ready availability, and the potential safety concerns are overcome. As can be seen in Table 1, good to excellent results were seen for the glycosyl azides **1**,[25] **2**,[26] **3**,[25] **4**,[27] **5**,[27] and **6**,[28] protected with acetyl, benzoyl, or benzyl groups. In order to extend the scope of the reaction, the non-anomeric azides **7**,[5] **8**, and **9** (K. Loft and S. J. Williams, unpubl. data) were converted to the non-anomeric 1-benzotriazoles **16**, **17**, and **18**. Of particular note is the tolerance of the reaction conditions for a range of common protecting groups including esters, benzyl ethers, an isopropylidene acetal, and an aromatic nitro group.

Table 1. Cycloaddition of benzyne with carbohydrate azides

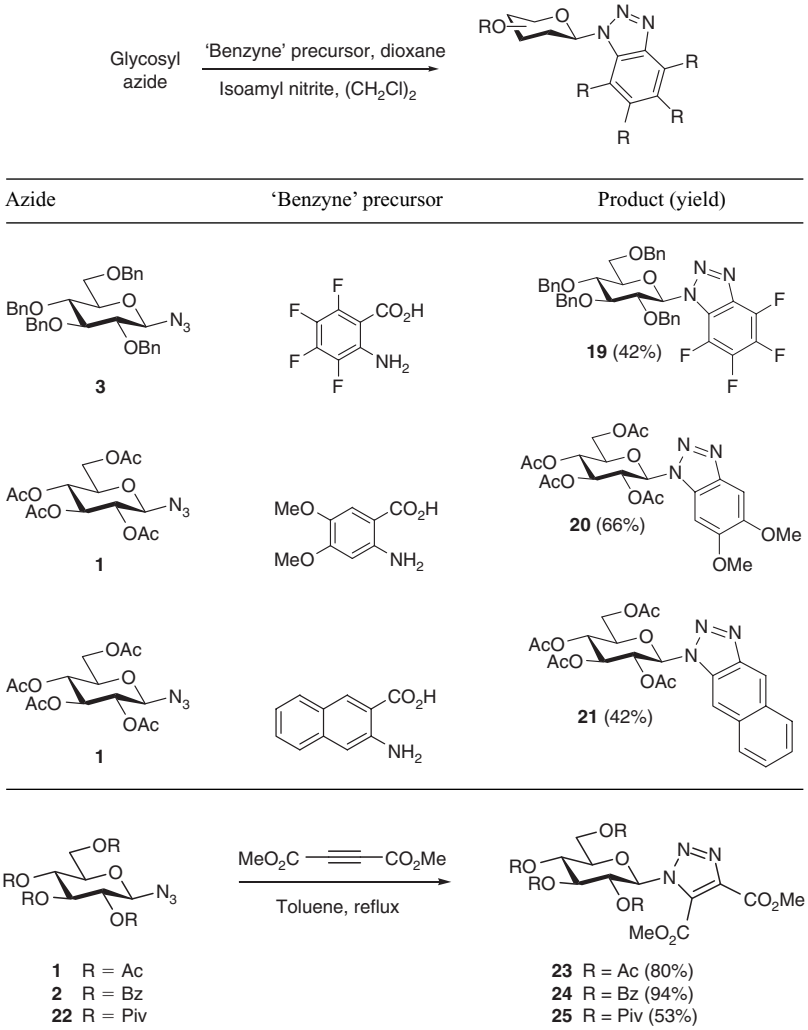
Reagents and conditions: azide (1 equiv.), anthranilic acid (3 equiv.), isoamyl nitrite (5 equiv.); Bt = 1*H*-benzo[*d*][1,2,3]triazol-1-yl



Azide	Product (yield)
 **1**	 **10** (77%)
 **2**	 **11** (80%)
 **3**	 **12** (62%)
 **4**	 **13** (64%)
 **5**	 **14** (76%)
 **6**	 **15** (73%)
 **7**	 **16** (80%)
 **8**	 **17** (71%)
 **9**	 **18** (62%)

Cycloaddition of benzyne and a carbohydrate azide should result in only the 1-benzotriazole isomer; however, there is precedent for the thermal rearrangement of 1-substituted

Table 2. Cycloaddition of substituted 'benzyne' precursors with glycosyl triazoles
Reagents and conditions: 1 equiv. of azide, 3 equiv. of anthranilic acid, 5 equiv. isoamyl nitrite



Scheme 1. Preparation of 1,4,5-trisubstituted 1,2,3-triazoles from glycosyl azides.

triazoles to their 2-substituted isomers.[29] In previous work, the structures of 1- and 2-benzotriazole isomers were deduced by careful comparison of UV/visible spectra with literature compounds;[30] here, direct evidence for only the 1-benzotriazole was obtained by two-dimensional $^{1}H–^{15}N$ heteronuclear multiple quantum coherence (HMQC) analysis of the acetylated adduct **10**, which revealed three nitrogen signals, with coupling between the anomeric proton H1 and both N1 and N2, and coupling between H2 and N1.

The potential of this method for the preparation of glycosyl 1-benzotriazoles bearing electron-donating and electron-withdrawing substituents on the benzotriazole nucleus was explored next (Table 2). Symmetrically substituted anthranilic acid precursors were chosen to avoid the problem of the formation of regioisomers. Use of 4,5-dimethoxyanthranilic acid, 3-amino-2-naphthoic acid and tetrafluoroanthranilic acid as benzyne precursors afforded the corresponding benzo- and naphtho-triazoles in good yields. This facile entry into substituted glycosyl 1-benzotriazoles may be of potential value for medicinal chemistry investigations and, as will be seen, can be used to tune the reactivity of the benzotriazole group.

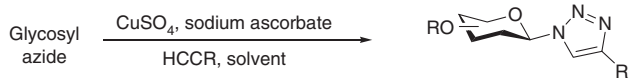
In order to allow comparison of the reactivity of the glycosyl 1-benzotriazoles with other glycosyl triazoles, a series of 1,4,5-trisubsituted glycosyl triazoles and 1,4-disubstituted glycosyl triazoles were prepared. 1,4,5-Trisubstituted glycosyl triazoles were synthesized from glycosyl azides **1**, **2**, and **22**[18] by thermal Huisgen [3 + 2] cycloaddition with dimethyl acetylene dicarboxylate in refluxing toluene (Scheme 1).[9]

1,4-Disubstituted glycosyl triazoles were prepared by the CuAAC reaction from the glycosyl azides **2** or **4** and phenylacetylene, *t*-butyl propiolate, or methyl propiolate (Table 3). The last two alkynes were chosen as they afforded 1,4-disubstituted triazoles with substituents that matched the 1,4,5-trisubsituted triazoles prepared here and by Bröder and Kunz.[9] Cu^{I} was produced in situ by reduction of $CuSO_4$ with sodium ascorbate in DMSO/water or *t*-butanol/water[3] and reactions were conducted in the presence of the Cu^{I}-stabilizing ligand tris-(benzyltriazolylmethyl)amine (TBTA).[31]

Investigation of the Ability of Glycosyl Triazoles to Act as Glycosyl Donors

With a series of glycosyl triazoles in hand, their ability to act as glycosyl donors was investigated (Table 4). Initially, we sought to reinvestigate the work of Bröder and Kunz, who had shown that various Lewis acids can activate 1,4,5-trisubstituted glycosyl triazoles towards *O*-glycosidation. Glycosyl triazole **24** and

Table 3. Cu^{I}-catalyzed cycloaddition of glycosyl azides and terminal alkynes



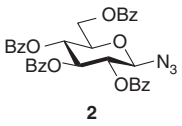
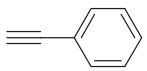
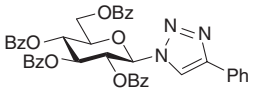
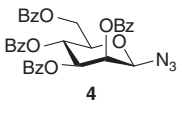
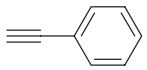
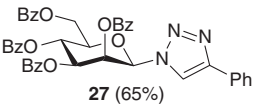
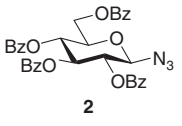
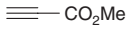
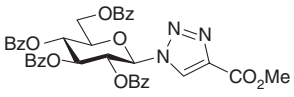
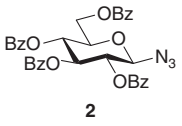
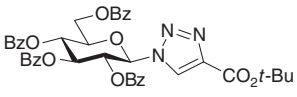
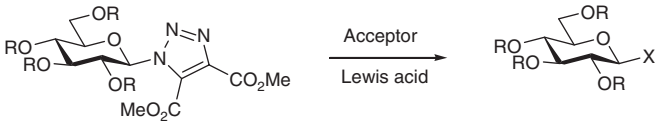
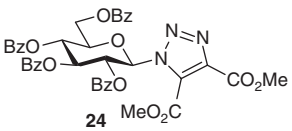
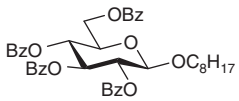
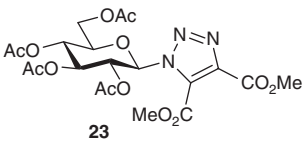
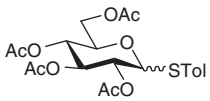
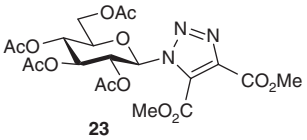
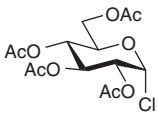
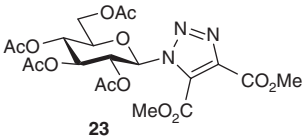
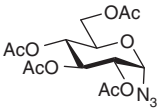
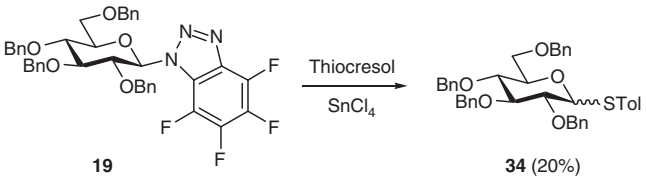
Azide	Alkyne	Product (yield)
 **2**		 **26** (95%)
 **4**		 **27** (65%)
 **2**		 **28** (87%)
 **2**		 **29** (60%)

Table 4. 1,4,5-Trisubstituted glycosyl triazoles as glycosyl donors



Glycosyl donor	Reagents	Product (yield)
 **24**	1-Octanol, TMSOTf	 **30** (50%)
 **23**	Thiocresol, $SnCl_4$	 **31** (77%) α:β 1:5
 **23**	TMSCl, $SnCl_4$	 **32** (51%)
 **23**	$TMSN_3$, $SnCl_4$	 **33** (38%)



Scheme 2. Use of a tetrafluorobenzotriazole as a glycosyl donor.

octanol, in the presence of TMSOTf, afforded the β-glycoside **30** in 50% yield. In order to broaden the potential applicability of these triazoles as synthetic intermediates, their conversion into a range of other known glycosyl donors was investigated. Thus, treatment of **23** with thiocresol and $SnCl_4$ afforded the corresponding *S*-glycoside **31** (77%) as a mixture of anomers. Similarly, the triazole **23** could be converted to the glycosyl chloride **32** (51%) by treatment with chlorotrimethylsilane and $SnCl_4$. Finally, in an example of an *N*-glycosidation, the triazole **23** was converted to the glycosyl azide **33** (38%), with inversion of configuration, by treatment with $TMSN_3$ and $SnCl_4$.

The ability of 1,4-disubstituted glycosyl triazoles to act as glycosyl donors was investigated next. Not unexpectedly, in light of previous work,[14,16] no reaction was observed on treatment of the phenyltriazole **26** and 1-octanol with a range of Lewis acids such as $Cu(OTf)_2$, AgOTf, TfOH, or TMSOTf. The poor reactivity observed here is somewhat at odds with the reactivity seen for 1,4,5-trisubstituted glycosyl triazoles, especially in light of the mechanism proposed by Bröder and Kunz wherein unsubstituted glycosyl triazoles were proposed to be intermediates in Lewis acid-catalyzed glycosidations.[18] Thus, the ability of the methoxycarbonyl- and *t*-butyloxycarbonyl-substituted 1,4-triazoles **28** and **29** to act as glycosyl donors was investigated. Notably, TfOH was unable to activate either of these triazoles towards glycosidation. This result suggests that the ability of the trisubstituted triazoles to act as glycosyl donors is simply due to the presence of the strongly electron-withdrawing ester groups, and not due to loss of the *t*-butyloxycarbonyl group.

Finally, we examined the ability of the glycosyl 1-benzotriazoles to act as glycosyl donors. Katritzky has published extensively on the ability of benzotriazoles to act as synthetic auxiliaries in organic synthesis, including as 'tamed' halogen equivalents in nucleophilic substitutions.[32] However, to the best of our knowledge, the reactions of glycosyl 1-benzotriazoles have not been systematically investigated. Surprisingly, the unsubstituted glycosyl 1-benzotriazoles **10** and **11** proved refractory as glycosyl donors in the presence of a range of Lewis acids including TMSOTf, TfOH, $SnCl_4$, $BF_3{\cdot}Et_2O$, or AgOTf. Katritzky has shown that tetrahydropyranyl 1-benzotriazole reacts with Grignard reagents to afford 2-aryl-tetrahydropyrans.[32] However, **12** was inert to either PhMgBr or diethylzinc. Having established the requirement for electron-withdrawing groups to effect glycosidation with trisubstituted glycosyl triazoles, we investigated the ability of the 'armed'[33] benzylated tetrafluorobenzotriazole **19** to act as a glycosyl donor (Scheme 2). Gratifyingly, this could be converted to the *S*-glycoside **34** using thiocresol and $SnCl_4$, albeit in low yield (20%).

Conclusions

Carbohydrate 1-benzotriazoles can be readily accessed by cycloaddition of benzynes (derived by diazotization of anthranilic acids), without formation of the 2-substituted regioisomer. In contrast to the introduction of the benzotriazole group by nucleophilic substitution, this cycloaddition approach allows the direct preparation of non-anomeric benzotriazoles. The method was used for the synthesis of substituted benzotriazoles from the corresponding substituted anthranilic acid precursors. The anomeric 1-benzotriazole derivatives are nucleoside analogues, and have previously been investigated as anticancer agents;[34] the non-anomeric 1-benzotriazoles are isonucleosides, and may also prove to have interesting biological activities.[35]

Investigation of the ability of glycosyl triazoles to act as glycosyl donors revealed that 1,4,5-trisubstituted glycosyl triazoles bearing two electron-withdrawing groups were effective glycosyl donors and could be converted to *O*-glycosides, *S*-glycosides, glycosyl chlorides, and glycosyl azides. By contrast, 1,4-disubstituted glycosyl triazoles were unreactive as glycosyl donors under all of the conditions investigated. Finally, glycosyl 1-benzotriazoles were typically inert as glycosyl donors; however, a glycosyl tetrafluorobenzotriazole could be converted to an *S*-glycoside. Thus, the number and nature of electron-withdrawing substituents on the triazole group appears to dictate their ability to act as leaving groups.

Experimental

General Methods

Petroleum spirits refers to a mixed fraction boiling at 40–60°C. TLC was performed with Merck silica gel 60 F_{254}, using mixtures of petroleum spirits/ethyl acetate unless otherwise stated. Detection was effected by either charring in a mixture of 5% sulfuric acid/MeOH or by visualization in UV light. Melting points were obtained on a Reichert–Jung hot-stage apparatus and are corrected. NMR spectra were obtained on Varian Inova 400 or 500 instruments. Flash chromatography was performed according to the method of Still et al. with Merck silica gel 60, using adjusted mixtures of ethyl acetate/petroleum spirits unless otherwise stated.[36] Dichloromethane and pyridine were dried over CaH_2. Solvents were evaporated under reduced pressure using a rotary evaporator. High resolution mass spectrometry (HRMS) was performed on a Finnigan hybrid LTQ-FT mass spectrometer. Elemental analysis was performed by Chemical and Microanalytical Services, Belmont, Victoria. $[\alpha]_D$ values are given in 10^{-1} degrees $cm^2\ g^{-1}$. *J* values are given in Hz. The two-dimensional HMQC spectrum was obtained on an Inova 400 with pulse sequence delays optimized for $^nJ(H,N) = 8$ Hz; pulse width (N) 44 ms, (H) 7.4 ms; relaxation delay (N) 2.5 s. Nitromethane (0 ppm) was used as an external reference for the ^{15}N spectrum.

Representative Procedure for the Preparation of 1-Benzotriazoles

A solution of anthranilic acid (3 equiv.) in dioxane (10 mL per mmol of azide) was added over 30 min to a refluxing solution of the azide (1 equiv.) and isoamyl nitrite (5 equiv.) in 1,2-dichloroethane (20 mL per mmol of azide) under N_2. The reaction mixture was heated for a further 1 h, then diluted with CH_2Cl_2 and washed with water (2×50 mL) and brine (1×50 mL). The solvent was removed under reduced pressure to give a dark residue, which was purified by flash chromatography to give the benzotriazole.

*1-(2,3,4,5-Tetra-*O*-acetyl-β-D-glucosyl)-1*H*-benzo[*d*][1,2,3]triazole* ***10***

According to the representative procedure, the azide **1**[25] (165 mg, 0.5 mmol) gave, after flash chromatography (30–40% EtOAc/pet. spirits), the benzotriazole **10** as a yellow oil (152 mg, 77%). A portion was recrystallized to give pale brown needles, mp 133–135.5°C (from EtOH; lit.[11,37] 118–119°C). $[\alpha]_D^{24}$ −61 (*c* ∼0.8 in $CHCl_3$; lit.[37] $[\alpha]_D$ −61.7, lit.[11] $[\alpha]_D$ −61). δ_H (500 MHz; $CDCl_3$) 1.77, 2.04, 2.09, 2.11 (4 × 3H, 4s, Me), 4.10 (1H, ddd, $J_{4,5}$ 10.0, $J_{5,6}$ 2.0, $J_{5,6}$ 5.0, H5), 4.22 (1H, dd, $J_{5,6}$ 2.5, $J_{6,6}$ 13.0, H6), 4.33 (1H, dd, $J_{5,6}$ 5.0, $J_{6,6}$ 13.0, H6), 5.38 (1H, dd, $J_{3,4}$ 9.5, $J_{4,5}$ 10.0, H4), 5.52 (1H, dd, $J_{2,3}$ 9.5, $J_{3,4}$ 9.5, H3), 5.78 (1H, dd, $J_{1,2}$ 9.5, $J_{2,3}$ 9.5, H2), 6.21 (1H, d, $J_{1,2}$ 9.5, H1), 7.43 (1H, dd, *J* 8.0, 7.5, Ar), 7.57 (1H, dd, *J* 7.5, 8.0, Ar), 7.73 (1H, d, *J* 8.0, Ar), 8.08 (1H, d, *J* 8.5, Ar). δ_C (125.6 MHz; $CDCl_3$) 20.08, 20.57, 20.60, 20.70 (4C, Me), 61.64, 67.78, 69.22, 72.68, 75.01 (5C, C2,3,4,5,6), 86.03 (1C, C1), 10.65, 120.32, 124.79, 128.38, 131.70, 146.53 (6C, Ar), 168.62, 169.45, 170.05, 170.51 (4C, C=O).

*1-(2,3,4,5-Tetra-*O*-benzoyl-β-D-glucosyl)-1*H*-benzo[*d*][1,2,3]triazole* ***11***

According to the representative procedure, the azide **2**[26] (311 mg, 0.5 mmol) gave, after flash chromatography (30–40% EtOAc/pet. spirits), the benzotriazole **11** as a yellow gum (280 mg, 80%). This was recrystallized to give an orange powder, mp 98–100°C (from EtOH). $[\alpha]_D^{24}$ −74 (*c* ∼1.2 in $CHCl_3$). (Found: C 68.91, H 4.52, N 6.07. $C_{40}H_{31}N_3O_9$ requires C 68.86, H 4.48, N 6.02%). δ_H (400 MHz; $CDCl_3$) 4.51–4.55 (2H, m, H6,6), 4.77 (1H, m, H5), 5.99 (1H, dd, $J_{1,2}$ 9.2, $J_{2,3}$ 9.2, H2), 6.19 (1H, dd, $J_{3,4}$ 9.6, $J_{4,5}$ 9.2, H4), 6.26 (1H, dd, $J_{2,3}$ 9.2, $J_{3,4}$ 9.6, H3), 6.59 (1H, d, $J_{1,2}$ 8.8, H1), 7.24–8.06 (24H, m, Ar). δ_C (100.5 MHz; $CDCl_3$) 62.40, 68.87, 69.93, 73.17, 75.51 (5C, C2,3,4,5,6), 86.61 (1C, C1), 110.06–133.76 (30C, Ar), 164.46, 165.21, 165.68, 165.99 (4C, C=O).

*1-(2,3,4,5-Tetra-*O*-benzyl-β-D-glucosyl)-1*H*-benzo[*d*][1,2,3]triazole* ***12***

According to the representative procedure, the azide **3**[25] (196 mg, 0.347 mmol) gave, after flash chromatography (15% EtOAc/pet. spirits), the benzotriazole **12** (137 mg, 62%) as a brown gum. $[\alpha]_D^{25}$ −15.1 (*c* ∼0.59, $CHCl_3$; lit.[38] $[\alpha]_D^{20}$ −22.8). δ_H (400 MHz; $CDCl_3$) 3.74–3.87, 3.93–3.96 (6H, 2m), 4.29–4.35 (2H, m), 4.48 (1H, d, *J* 12.0, CH_2Ph), 4.55 (1H, d, *J* 12.0, CH_2Ph), 4.67 (1H, d, *J* 10.6), 4.91 (1H, d, *J* 10.6), 4.91–4.98 (2H, m), 5.96 (1H, d, $J_{1,2}$ 9.2, H1), 6.73–8.09 (20H, Ar). δ_C (100.5 MHz; $CDCl_3$) 68.55, 73.65, 74.67, 75.51, 76.08 (5C, C2,3,4,5,6), 78.23, 79.64, 85.81, 87.45 (5C, PhCH_2,C1), 110.91–146.57 (Ar).

*1-(2,3,4,5-Tetra-*O*-benzoyl-β-D-mannosyl)-1*H*-benzo[*d*][1,2,3]triazole* ***13***

According to the representative procedure, the azide **4**[27] (311 mg, 0.5 mmol) gave, after flash chromatography (30–50% EtOAc/pet. spirits) the benzotriazole **13** as a yellow gum (224 mg, 64%). A portion was recrystallized to give an off-white powder, mp 207–211°C (from EtOH). $[\alpha]_D^{24}$ −104 (*c* ∼0.8 in $CHCl_3$). (Found: C 68.8, H 4.35, N 5.9. $C_{40}H_{31}N_3O_9$ requires C 68.9, H 4.5, N 6.0%). δ_H (500 MHz; $CDCl_3$) 4.56 (1H, ddd, $J_{4,5}$ 10.0, $J_{5,6}$ 2.5, $J_{5,6}$ 3.5, H5), 4.62 (1H, dd, $J_{5,6}$ 4.0, $J_{6,6}$ 12.5, H6), 4.99 (1H, dd, $J_{5,6}$ 2.5, $J_{6,6}$ 12.5, H6), 6.00 (1H, dd, $J_{2,3}$ 3.0, $J_{3,4}$ 10.0, H3), 6.38 (1H, dd, $J_{3,4}$ 10.0, $J_{5,6}$ 10.0, H4), 6.41 (1H, dd, $J_{1,2}$ 1.5, $J_{2,3}$ 3.0, H2), 6.83 (1H, d, $J_{1,2}$ 1.5, H1), 6.96–8.23 (24H, m, Ar). δ_C (125.6 MHz; $CDCl_3$) 62.06, 65.78, 70.62, 71.60, 75.76 (5C, C2,3,4,5,6), 86.62 (1C, C1), 112.46–146.09 (30C, Ar), 164.54, 165.35, 165.93 (4C, C=O).

*1-(2,3,4,5-Tetra-*O*-benzoyl-α-D-mannosyl)-1*H*-benzo[*d*][1,2,3]triazole* ***14***

According to the representative procedure, the azide **5**[27] (311 mg, 0.5 mmol) gave, after flash chromatography (30–50% EtOAc/pet. spirits), the benzotriazole **14** as a dark yellow gum (264 mg, 76%). A portion was recrystallized to give yellow needles, mp 159–162°C (from EtOH). $[\alpha]_D^{24}$ +7 (*c* ∼0.8 in $CHCl_3$). δ_H (400 MHz; $CDCl_3$) 4.12 (1H, ddd, $J_{4,5}$ 10.0, $J_{5,6}$ 2.4, $J_{5,6}$ 4.8, H5), 4.51 (1H, dd, $J_{5,6}$ 5.2, $J_{6,6}$ 12.4, H6), 4.57 (1H, dd, $J_{5,6}$ 2.8, $J_{6,6}$ 12.4, H6), 6.31 (1H, dd, $J_{3,4}$ 10.0, $J_{4,5}$ 10.0, H4), 6.61 (1H, s, H1), 6.72–6.76 (2H, m, H2,3), 7.25–8.18 (24H, m, Ar). δ_C (100.5 MHz; $CDCl_3$) 62.44, 66.92, 69.76, 70.27, 71.69 (5C, C2,3,4,5,6), 83.27 (1C, C1), 110.33–146.17 (30C, Ar), 165.19, 165.43, 165.58, 165.98 (4C, C=O).

*1-(2,3,4,5-Tetra-*O*-acetyl-β-D-galactosyl)-1*H*-benzo[*d*][1,2,3]triazole* ***15***

According to the representative procedure, the azide **6**[28] (0.19 g, 0.50 mmol) gave, after flash chromatography (30–50% EtOAc/pet. spirits), the benzotriazole **15** (0.16 g, 73%) as a brown gum. $[\alpha]_D^{22}$ −56.3 (*c* ∼1.00 in $CHCl_3$; lit.[11] $[\alpha]_D$ −53.2). δ_H (400 MHz; $CDCl_3$) 1.75, 1.98, 2.00, 2.27 (4 × 3H, s, Ac), 4.15–4.17, 4.21–4.26 (2H, 2m, $J_{5,6}$ 6.4, H6,6), 4.31 (1H, t, $J_{5,6}$ 6.4, H5), 5.33 (1H, dd, $J_{1,2}$ 3.2, $J_{2,3}$ 10.0, H2), 5.60 (1H, d, $J_{1,2}$ 3.2, H1), 5.85 (1H, t, $J_{3,4}$ 9.6, H3), 6.17 (1H, d, $J_{3,4}$ 9.6, H4), 7.38, 7.53 (2H, 2t, *J* 7.6, Ar), 7.66, 8.03 (2H, 2d, *J* 8.4, Ar). δ_C (125.6 MHz; $CDCl_3$) 20.37, 20.80, 20.91, 21.03 (4C, CH_3), 61.63, 66.97, 67.33, 71.23, 73.95 (5C, C2,3,4,5,6), 86.90 (1C, C1), 111.12, 120.56, 124.97, 128.50, 132.02, 146.77 (6C, Ar), 169.01, 170.19, 170.21, 170.66 (4C, C=O).

*1-(Methyl 2,3,4,-Tri-*O*-acetyl-6-deoxy-α-D-mannosid-6-yl)-1*H*-benzo[*d*][1,2,3]triazole* ***16***

According to the representative procedure, the azide **7**[5] (173 mg, 0.500 mmol) gave, after flash chromatography (25–55% EtOAc/pet. spirits), the benzotriazole **16** (169 mg, 80%) as a brown oil. $[\alpha]_D^{23}$ +41.2 (*c* ∼1.91 in $CHCl_3$). (Found: C 54.2, H 5.65, N 10.0. $C_{19}H_{23}N_3O_8$ requires C 54.15, H 5.5, N 10.0%). δ_H (400 MHz; $CDCl_3$) 2.00, 2.12, 2.13 (3 × 3H, 3s, Ac), 2.85 (3H, s, OCH_3), 4.30–4.36 (1H, m, H5), 4.57 (1H, d, $J_{1,2}$ 1.6, H1), 4.75–4.85 (2H, m, H6,6), 5.20 (1H, dd, $J_{2,3}$ 3.6, $J_{1,2}$ 1.6, H2), 5.26 (1H, dd, $J_{3,4}$ 9.6, $J_{4,5}$ 9.6, H4), 5.35 (1H, dd, $J_{3,4}$ 9.6, $J_{2,3}$ 3.2, H3), 7.38 (1H, dd, *J* 7.6, 7.6, Ar), 7.50 (1H, dd, *J* 7.6, 7.6, Ar), 7.67 (1H, d, *J* 8.4, Ar), 8.05 (1H, d, *J* 8.4, Ar). δ_C (100.5 MHz; $CDCl_3$) 20.56, 20.73 (×2), (3C, CH_3), 49.21 (1C, C6), 54.86 (1C, OCH_3), 67.66, 68.70, 69.35, 69.64 (4C, C2,3,4,5), 98.13 (1C, C1), 110.12, 119.76, 123.86, 127.33, 133.65, 145.77 (6C, Ar), 169.68, 169.81, 170.11 (3C, C=O).

*1-(Methyl 2-*O*-Benzyl-6-deoxy-3,4-*O*-isopropylidene-β-D-galactosid-6-yl)-1*H*-benzo[*d*][1,2,3]triazole* ***17***

*(i) Methyl 6-Azido-2-*O*-benzyl-6-deoxy-3,4-*O*-isopropylidene-β-D-galactopyranoside* ***8***

A mixture of methyl 2-*O*-benzyl-6-deoxy-6-iodo-3,4-*O*-isopropylidene-β-D-galactopyranoside[39] (0.76 g, 1.74 mmol) and sodium azide (0.17 g, 2.57 mmol) in DMF (50 mL) was stirred at 100°C for 24 h. The reaction mixture was then

poured over ice (100 mL) and extracted with dichloromethane (3 × 50 mL). The organic extract was washed with brine (3 × 75 mL) and water (3 × 75 mL), then dried ($MgSO_4$), filtered and concentrated under reduced pressure to give a crude brown gum. The gum was purified by flash chromatography (10–40% EtOAc/pet. spirits) to give the azide **8** as a pale yellow gum (309 mg, 51%) that crystallized on standing. Recrystallization afforded a fluffy white solid, mp 81–83°C (from EtOH/H_2O). $[\alpha]_D^{23}$ +17.9 (*c* ~0.89 in $CHCl_3$). (Found: C 58.5, H 6.7, N 12.0. $C_{17}H_{23}N_3O_5$ requires C 58.4, H 6.6, N 12.0%). δ_H (500 MHz; $CDCl_3$) 1.33, 1.36 (2 × 3H, 2s, CMe_2), 3.29–3.32 (1H, dd, $J_{5,6}$ 4.0, $J_{6,6}$ 13.0, H6), 3.40 (1H, t, $J_{2,3}$ 7.5, H2), 3.59 (3H, s, OMe), 3.72 (1H, dd, $J_{5,6}$ 4.0, $J_{6,6}$ 13.0, H6), 3.88–3.91 (1H, m, H5), 4.08 (1H, dd, $J_{2,3}$ 2.5, $J_{3,4}$ 6.0, H3), 4.20 (1H, t, $J_{3,4}$ 6.0, H4), 4.27 (1H, d, $J_{1,2}$ 8.0, H1), 4.78–4.85 (2H, app. q, CH_2Ph), 7.28–7.41 (5H, m, Ph). δ_C (125.6 MHz; $CDCl_3$) 26.59, 27.91 (2C, CMe_2), 51.40 (1C, CH_2Ph), 57.22 (1C, OMe), 72.92, 73.78, 74.08, 79.12, 79.52 (5C, C2,3,4,5,6), 104.10 (1C, C1), 110.53 (1C, CMe_2), 127.87, 128.44, 128.51, 138.36 (Ph). ν_{max}(thin film)/cm^{-1} 2097 (N_3).

(ii) 1-(Methyl 2-O-Benzyl-6-deoxy-3,4-O-isopropylidene-β-D-galactosid-6-yl)-1H-benzo[d][1,2,3]triazole ***17***

According to the representative procedure, the azide **8** (140 mg, 0.41 mmol) gave, after flash chromatography (20–50% EtOAc/pet. spirits), the benzotriazole **17** as a brown plates (120 mg, 71%), mp 155–156°C. $[\alpha]_D^{22}$ +16.1 (*c* ~0.91 in $CHCl_3$). (Found: C 65.0, H 6.5, N 9.9. $C_{19}H_{23}N_3O_8$ requires C 64.9, H 6.4, N 9.9%). δ_H (500 MHz; $CDCl_3$) 1.30, 1.44 (2 × 3H, 2s, CMe_2), 3.19 (3H, s, OMe), 3.42 (1H, t, $J_{1,2}$ 7.5, H2), 4.06–4.11 (2H, m, H1,3), 4.18 (1H, t, $J_{3,4}$ 6.0, H4), 4.24–4.27 (1H, m, H5), 4.77 (2H, app. q, CH_2Ph), 4.92 (1H, dd, $J_{5,6}$ 8.0, $J_{6,6}$ 14.5, H6), 5.10 (1H, dd, $J_{5,6}$ 4.5, $J_{6,6}$ 14.5, H6,6), 7.24–7.38 (6H, m, Ar), 7.49 (1H, t, *J* 7.0, Ar), 7.73, 8.04 (2H, 2d, *J* 8.5, 8.5, Ar). δ_C (125.6 MHz; $CDCl_3$) 26.60, 28.02 (2C, CMe_2), 48.89 (1C, CH_2Ph), 56.95 (1C, OMe), 72.74, 73.74, 73.77, 79.10, 79.44 (5C, C2,3,4,5,6), 103.94 (1C, C1), 110.64, 110.85 (2C, CMe_2,Bt), 119.90, 124.24, 127.53, 127.87, 128.36, 128.50, 134.14, 138.29, 145.97 (Ar).

1-(p-Nitrophenyl 3,4,6-Tri-O-acetyl-2-deoxy-β-D-glucosid-2-yl)-1H-benzo[d][1,2,3]triazole ***18***

According to the representative procedure, the azide **9** (63.9 mg, 0.141 mmol) gave, after flash chromatography (20% EtOAc/toluene), the benzotriazole **18** (46.3 mg, 62%). This was recrystallized to give off-white needles, mp 240–241.5°C (from EtOH). $[\alpha]_D^{25}$ +55.6 (*c* ~0.57 in $CHCl_3$). (Found C 54.65, H 4.6, N 10.5. $C_{24}H_{24}N_4O_{10}$ requires C 54.55, H 4.6, N 10.6%). δ_H (400 MHz; $CDCl_3$) 1.66, 2.07, 2.14 (3 × 3H, 3s, Ac), 4.23 (1H, ddd, $J_{5,6}$ 1.9, $J_{5,6}$ 5.2, H5), 4.28 (1H, dd, $J_{5,6}$ 1.9, $J_{6,6}$ 12.4, H6), 4.46 (1H, dd, $J_{5,6}$ 5.2, $J_{6,6}$ 12.4, H6), 5.06 (1H, dd, *J* 8.2, 10.6, one of H3,4), 5.38 (1H, t, *J* 9.4, one of H3,4), 6.01–6.06 (2H, m, H1,2), 6.85–8.11 (8H, Ar). δ_C (100.5 MHz; $CDCl_3$) 20.36, 20.81, 20.95 (3C, 3 × CH_3), 61.48, 61.94, 68.63, 72.89, 98.89 (5C, C2,3,4,5,6), 109.12 (1C, C1), 117.18, 120.68, 124.79, 125.89, 128.46, 134.44, 143.73, 145.72, 160.79 (Ar), 169.03, 169.94, 170.63 (3C, C=O). ν_{max}(thin film)/cm^{-1} 1049, 1072, 1205 (C–O), 1226 (C–O), 1347 (NO_2), 1520 (NO_2), 1750 (C=O).

1-(2,3,4,5-Tetra-O-benzyl-β-D-glucosyl)-3,4,5,6-tetrafluoro-1H-benzo[d][1,2,3]triazole ***19***

According to the representative procedure, the azide **3**[25] (283 mg, 0.50 mmol) and 2-amino-3,4,5,6-tetrafluorobenzoic acid (314 mg, 1.5 mmol) gave, after flash chromatography (5–20% EtOAc/pet. spirits), a yellow residue, which was recrystallized to give the tetrafluorobenzotriazole **19** as a white solid (150 mg, 42%), mp 113.5–116.5°C (from EtOH). $[\alpha]_D^{27}$ −59 (*c* ~1.18 in $CHCl_3$). (Found: C 67.4, H 5.0, N 5.9. $C_{40}H_{35}F_4N_3O_9$ requires C 67.3, H 4.9, N 5.9%). δ_H (400 MHz; $CDCl_3$) 3.68–5.02 (14H, m, H1,2,3,4,5,6,6,OCH_2Ph), 5.94 (1H, d, $J_{1,2}$ 8.8, H1), 6.77–7.38 (20H, m, Ar). δ_C (100.5 MHz; $CDCl_3$) 68.35, 73.36, 74.55, 75.29, 76.00 (5C, C2,3,4,5,6), 78.12, 78.26, 86.09, 87.61 (5C, C1,OCH_2Ph), 127.55–128.58, 136.60, 137.73, 137.81, 137.97 (Ar). HRMS (electrospray ionization (ESI^+), *m*/*z*) calc. for $C_{40}H_{35}F_4N_3O_9Na$ $[M + Na]^+$ 736.2407, found 736.2411.

1-(2,3,4,5-Tetra-O-acetyl-β-D-glucosyl)-5,6-dimethoxy-1H-benzo[d][1,2,3]triazole ***20***

According to the representative procedure, the azide **1**[25] (165 mg, 0.500 mmol) and 4,5-dimethylanthranilic acid gave, after flash chromatography (25–45% EtOAc/pet. spirits), the benzotriazole **20** (169 mg, 66%) as a brown solid. A portion was recrystallized to afford a pink powder, mp 139–141°C (from EtOH). $[\alpha]_D^{23}$ −82.1 (*c* ~1.25 in $CHCl_3$). (Found: C 51.8, H 5.3, N 8.3. $C_{22}H_{27}N_3O_{11}$ requires C 51.9, H 5.3, N 8.25%). δ_H (500 MHz; $CDCl_3$) 1.80, 2.05, 2.08, 2.11 (4 × 3H, 4s, Ac), 3.97, 4.05 (2 × 3H, 2s, OCH_3), 4.07–4.12 (1H, m, H5), 4.19 (1H, dd, $J_{6,6}$ 12.5, $J_{5,6}$ 2.0, H6), 4.39 (1H, dd, $J_{6,6}$ 12.5, $J_{5,6}$ 5.0, H6), 5.37 (1H, dd, *J* 10.0, 10.0, one of H2,3,4), 5.50 (1H, dd, *J* 9.5, 9.5, one of H2,3,4), 5.69 (1H, dd, *J* 9.5, 9.5, one of H2,3,4), 6.13 (1H, d, $J_{1,2}$ 9.0, H1), 7.00, 7.36 (2 × 1H, 2s, Ar). δ_C (100.5 MHz; $CDCl_3$) 20.09, 20.55, 20.58, 20.64 (4C, COCH_3), 56.20, 56.40 (2C, OCH_3), 61.65, 67.81, 69.09, 72.89, 75.10 (5C, C2,3,4,5,6), 86.12, 90.91, 99.13, 126.97, 140.98, 149.02, 152.00 (7C, C1,Ar), 168.68, 169.51, 169.96, 170.35 (4C, C=O).

1-(2,3,4,5-Tetra-O-acetyl-β-D-glucosyl)-1H-naphtho[2,3-d][1,2,3]triazole ***21***

According to the representative procedure, the azide **1**[25] (165 mg, 0.500 mmol) and 3-amino-2-naphthoic acid gave, after flash chromatography (25–55% EtOAc/pet. spirits), the naphthotriazole **21** (106 mg, 42%) as a brown oil. $[\alpha]_D^{25}$ −92 (*c* ~0.27 in $CHCl_3$). (Found: C 57.6, H 5.1, N 8.5. $C_{24}H_{25}N_3O_9$ requires C 57.7, H 5.05, N 8.4%). δ_H (400 MHz; $CDCl_3$) 1.76, 2.05, 2.11, 2.13 (4 × 3H, 4s, Ac), 4.13–4.18 (1H, m, H5), 4.25 (1H, dd, $J_{6,6}$ 12.8, $J_{5,6}$ 2.4, H6), 4.37 (1H, dd, $J_{6,6}$ 12.4, $J_{5,6}$ 4.8, H6), 5.46 (1H, dd, *J* 10.0, 10.0, one of H2,3,4), 5.57 (1H, dd, *J* 10.4, 10.4, one of H2,3,4), 5.92 (1H, dd, *J* 9.6, 9.6, one of H2,3,4), 6.33 (1H, d, $J_{1,2}$ 9.6, H1), 7.48 (1H, dd, *J* 7.2, 7.2, Ar), 7.56 (1H, dd, *J* 7.2, 7.2, Ar), 8.02 (1H, d, *J* 8.4, Ar), 8.06 (1H, d, *J* 8.4, Ar), 8.14 (1H, s, Ar), 8.65 (1H, s, Ar). δ_C (100.5 MHz; $CDCl_3$) 20.02, 20.52, 20.56, 20.66 (4C, CH_3), 61.66, 67.84, 69.00, 73.01, 74.90 (5C, C2,3,4,5,6), 85.99 (1C, C1), 106.57, 118.59, 125.08, 127.13, 128.01, 129.35, 129.87, 130.89, 133.31, 145.55 (10C, Ar), 168.57, 169.45, 170.01, 170.44 (4C, C=O).

3,4-Bis-(methoxycarbonyl)-1-(2,3,4,6-tetra-O-acetyl-β-D-glucosyl)-1H-1,2,3-triazole ***23***

A solution of the azide **1**[25] (1.02 g, 2.73 mmol) and dimethyl acetylene dicarboxylate (0.60 mL, 4.91 mmol) in toluene

(30 mL) was heated at reflux overnight. The solvent was evaporated under reduced pressure and the residue was dissolved in EtOAc (30 mL), washed with water (3 × 30 mL), and dried ($MgSO_4$). The solvent was evaporated under reduced pressure and the crude residue was recrystallized to give the triazole **23** as light yellow cubic crystals (1.12 g, 80%), mp 148–151.5°C (from EtOH; lit.[40] 153°C). $[\alpha]_D^{25}$ −24.9 (*c* ~0.8 in $CHCl_3$). δ_H (400 MHz; $CDCl_3$) 1.90, 2.05, 2.07, 2.08 (4 × 3H, s, Ac), 3.97, 4.04 (2 × 3H, 2s, OMe), 4.79 (1H, ddd, $J_{4,5}$ 10.0, $J_{5,6}$ 2.0, $J_{5,6}$ 4.8, H5), 4.14 (1H, dd, $J_{5,6}$ 2.0, $J_{6,6}$ 12.8, H6), 4.29 (1H, dd, $J_{5,6}$ 4.8, $J_{6,6}$ 12.8, H6), 5.25 (1H, dd, $J_{3,4}$ 9.6, $J_{4,5}$ 10.0, H4), 5.42 (1H, dd, *J* 9.2, 9.6), 5.94 (1H, dd, *J* 9.2, 9.6, H2,3) 6.13 (1H, d, $J_{1,2}$ 9.2, H1). δ_C (100.5 MHz; $CDCl_3$) 20.26, 20.53, 20.55, 20.65 (4C, $COCH_3$), 52.84, 53.68 (2C, OMe), 61.37, 67.36, 69.75, 72.87, 75.23 (5C, C2,3,4,5,6), 85.60 (C1), 130.85, 140.10 (2C, Ar), 158.51, 159.97 (2C, CO_2Me), 168.53, 169.21, 170.14, 170.40 (4C, C=O).

3,4-Bis-(methoxycarbonyl)-1-(2,3,4,6-tetra-O-benzoyl-β-D-glucosyl)-1H-1,2,3-triazole ***24***

A solution of the azide **2**[26] (2.01 g, 3.24 mmol) and dimethyl acetylene dicarboxylate (0.71 mL, 5.83 mmol) in toluene (50 mL) was heated at reflux overnight. The solvent was evaporated under reduced pressure and the residue dissolved in EtOAc (60 mL) and washed with water (3 × 50 mL) and dried ($MgSO_4$). The solvent was evaporated under reduced pressure and the residue was purified by flash chromatography (30–40% EtOAc/pet. spirits) to give the triazole **24** as a yellow foam (2.32 g, 94%). A portion was crystallized from EtOH to give a white solid, mp 97–101°C. $[\alpha]_D^{25}$ +5.5 (*c* ~0.8 in $CHCl_3$). (Found: C 63.0, H 4.4, N 5.6. $C_{40}H_{33}N_3O_{13}$ requires C 62.9, H 4.4, N 5.5%). δ_H (500 MHz; $CDCl_3$) 3.88, 3.92 (2 × 3H, 2s, Me), 4.47–4.53 (2H, m, H5,6), 4.64–4.68 (1H, m, H6), 5.89, 6.14, 6.51–6.56 (4H, 3m, H1,2,3,4), 7.26–8.07 (20H, m, Ph). δ_C (125.6 MHz; $CDCl_3$) 52.72, 53.57 (2C, Me), 62.44, 68.53, 70.35, 73.10, 75.63 (5C, C2,3,4,5,6), 86.08 (C1), 128.23–140.15 (Ar), 158.62, 159.93 (2C, CO_2Me), 164.30, 164.98, 165.69, 165.97 (4C, C=O). HRMS (ESI^+, *m/z*) calc. for $C_{40}H_{33}N_3O_{13}Na$ $[M+Na]^+$ 786.1906, found 786.1907.

2,3,4,6-Tetra-O-pivalyl-β-D-glucosyl Azide ***22***[18]

The azide **1**[25] (485 mg, 1.3 mmol) was stirred with a small piece of sodium metal in MeOH until TLC indicated conversion to a less polar product. Cation exchange resin (Amberlyst IR-120, H^+ form) was used to neutralize the solution and the solvent was evaporated under reduced pressure. Pivalyl chloride (1.57 mL, 10.4 mmol) and 4-dimethylaminopyridine (DMAP) (0.195 mg, 1.3 mmol) were added to a solution of the crude tetraol (267 mg, 1.3 mmol) in pyridine (10 mL) and the mixture was stirred at room temperature for 20 h. A further 4 equiv. of pivalyl chloride were added (0.78 mL, 5.2 mmol) and the temperature was raised to 50°C and the reaction stirred for a further 24 h. The solvent was co-evaporated with toluene and the remaining residue was crystallized to give the azide **22** (707 mg, 83%), mp 103–109°C (from EtOH/water). $[\alpha]_D^{24}$ −9.9 (*c* ~0.6 in $CHCl_3$). δ_H (500 MHz; $CDCl_3$) 1.10–130 (36H, m, *t*-Bu), 3.82 (1H, ddd, $J_{4,5}$ 10.0, $J_{5,6}$ 2.0, $J_{5,6}$ 5.0, H5), 4.10 (1H, dd, $J_{5,6}$ 5.0, $J_{6,6}$ 12.0, H6), 4.24 (1H, dd, $J_{5,6}$ 2.0, $J_{6,6}$ 12.0, H6), 4.63 (1H, d, $J_{1,2}$ 8.6, H1), 4.99 (1H, dd, $J_{1,2}$ 9.0, $J_{2,3}$ 9.5, H2), 5.16 (1H, dd, $J_{3,4}$ 10.0, $J_{4,5}$ 10.0, H4), 5.33 (1H, dd, $J_{2,3}$ 9.5, $J_{3,4}$ 9.5, H3). δ_C (125.6 MHz; $CDCl_3$) 27.22, 27.28, 27.33 (12C, CH_3), 38.94, 38.97, 39.00, 39.11 (4C, $C(CH_3)_3$), 61.69, 67.61, 70.72, 72.15, 74.67 (5C, C2,3,4,5,6), 88.48 (C1), 176.50, 176.73, 177.31, 178.23 (4C, C=O).

3,4-Bis-(methoxycarbonyl)-1-(2,3,4,6-tetra-O-pivalyl-β-D-glucosyl)-1H-1,2,3-triazole ***25***[18]

A solution of the azide **22** (506 mg, 0.93 mmol) and dimethyl acetylene dicarboxylate (207 μL, 1.68 mmol) in refluxing toluene (10 mL) was heated under reflux overnight. The solvent was evaporated under reduced pressure and the residue was dissolved in EtOAc (40 mL) and washed with water (3 × 30 mL). The organic phase was dried ($MgSO_4$) and the solvent evaporated under reduced pressure. The crude crystalline residue was purified by flash chromatography (30% EtOAc/pet. spirits) to give the triazole **25** as white needles (338 mg, 53%), mp 131–133°C. $[\alpha]_D^{25}$ −22.1 (*c* ~0.7 in $CHCl_3$). δ_H (400 MHz; $CDCl_3$) 0.95, 1.13, 1.18 (48H, 3s, *t*-Bu), 3.97, 4.02 (2 × 3H, 2s, CO_2CH_3), 4.01 (1H, ddd, $J_{4,5}$ 10.0, $J_{5,6}$ 2.0, $J_{5,6}$ 5.2, H5), 4.12 (1H, dd, $J_{5,6}$ 5.2, $J_{6,6}$ 12.8, H6), 4.18 (1H, dd, $J_{5,6}$ 2.0, $J_{6,6}$ 12.8, H6), 5.30 (1H, dd, $J_{3,4}$ 10.0, $J_{4,5}$ 9.8, H4), 5.52 (1H, dd, $J_{2,3}$ 9.6, $J_{3,4}$ 9.6, H2), 6.03 (1H, dd, $J_{2,3}$ 9.2, $J_{3,4}$ 9.2, H3), 6.18 (1H, d, $J_{1,2}$ 9.6, H1). δ_C (125.6 MHz; $CDCl_3$) 26.71, 26.98, 27.10 (12C, $C(CH_3)_3$), 38.56, 38.76, 38.80 (4C, $C(CH_3)_3$), 52.78, 53.62 (CO_2CH_3), 61.29, 66.97, 69.45, 72.42, 75.75 (5C, C2,3,4,5,6), 85.56 (C1), 130.60, 140.11 (2C, Ar), 158.37, 159.95 (CO_2Me), 175.59, 176.19, 177.15, 177.86 (4C, C=O).

1-(2,3,4,6-Tetra-O-benzoyl-β-D-glucosyl)-4-phenyl-1H-1,2,3-triazole ***26***

Sodium ascorbate (60.0 mg, 0.302 mmol) was added to a mixture of the azide **2**[26] (2.18 g, 3.52 mmol), phenylacetylene (0.598 mL, 5.44 mmol), $CuSO_4$ (9.6 mg, 0.06 mmol) and TBTA (32.0 mg, 0.06 mmol) in *t*-BuOH/water (2:1, 22.5 mL). After 4 days, TLC showed consumption of starting material. The reaction was extracted with $CHCl_3$ and the organic phase washed with H_2O (3 × 100 mL). The solvent was evaporated under reduced pressure and the resulting residue was purified by passage through a plug of silica (95% $CHCl_3$/MeOH) to give the triazole **26** as a yellow flaky solid (2.41 g, 95%). $[\alpha]_D^{21}$ −21.8 (*c* ~0.8 in $CHCl_3$). δ_H (400 MHz; $CDCl_3$) 4.51–4.72 (3H, m, H5,6,6), 5.93 (1H, dd, $J_{3,4}$ 9.6, $J_{4,5}$ 10.0, H4), 6.08 (1H, dd, $J_{1,2}$ 9.2, $J_{2,3}$ 9.6, H2), 6.17 (1H, dd, $J_{2,3}$ 9.6, $J_{3,4}$ 9.6, H3), 6.35 (1H, d, $J_{1,2}$ 9.2, H1), 7.24–8.03 (30H, m, Ph), 8.17 (1H, s, triazole). δ_C (100.5 MHz; $CDCl_3$) 62.89, 69.11, 71.12, 73.25, 75.23 (5C, C2,3,4,5,6), 86.34 (C1), 118.09–133.85, 148.64 (Ph), 165.01, 165.34, 165.76, 166.22 (4C, C=O).

1-(2,3,4,6-Tetra-O-benzoyl-β-D-mannosyl)-4-phenyl-1H-1,2,3-triazole ***27***

Sodium ascorbate (62.0 mg, 0.313 mmol) was added to a mixture of the azide **4**[25] (194 mg, 0.31 mmol), phenylacetylene (62 μL, 0.56 mmol), $CuSO_4$ (1.0 mg, 0.006 mmol) and TBTA (3.3 mg, 0.006 mmol) in DMSO (9:1, 5 mL). After 24 h, water was added to the reaction mixture and the precipitate was collected to give the triazole **27** as a pale blue solid (148 mg, 65%). A portion was recrystallized from EtOH to give white crystals, mp 219–221°C (from EtOH and water). $[\alpha]_D^{21}$ −103.2 (*c* ~0.750 in $CHCl_3$). δ_H (500 MHz; $CDCl_3$) 4.54 (1H, ddd, $J_{4,5}$ 10.5, $J_{5,6}$ 2.5, $J_{5,6}$ 4.5, H5), 4.61 (1H, dd, $J_{5,6}$ 4.5, $J_{6,6}$ 12.5, H6), 4.91 (1H, dd, $J_{5,6}$ 2.5, $J_{6,6}$ 12.5, H6), 5.92 (1H, dd, $J_{2,3}$ 3.0, $J_{3,4}$ 10.0, H3), 6.25 (1H, dd, $J_{3,4}$ 10.0, $J_{4,5}$ 10.5, H4), 6.30 (1H, dd, $J_{1,2}$ 1.0, $J_{2,3}$ 3.0, H2), 6.66 (1H, d, $J_{1,2}$ 1.0, H1), 7.26–8.18 (31H, m,

Ar). δ_C (125.6 MHz; $CDCl_3$) 62.68, 66.03, 70.13, 71.93, 76.06 (5C, C2,3,4,5,6), 85.82 (C1), 118.00–148.17 (32C, Ar), 164.51, 165.51, 165.58, 166.29 (4C, C=O). HRMS (ESI^+, *m/z*) calc. for $C_{42}H_{33}N_3O_9Na$ $[M + Na]^+$ 746.2109, found 746.2118.

1-(2,3,4,6-Tetra-O-benzoyl-β-D-glucosyl)-4-methoxycarbonyl-1H-1,2,3-triazole ***28***

Sodium ascorbate (9.7 mg, 0.049 mmol) was added to a stirred suspension of the azide **2**[26] (305 mg, 0.49 mmol), methyl propiolate (61.5 μL, 0.74 mmol), $CuSO_4$ (0.0098 mmol), and TBTA (5.2 mg, 9.8 μmol) in a mixture of *t*-BuOH/water (4:1, 10 mL). Additional sodium ascorbate (0.2 equiv.) was added after 24 and 48 h and stirring was continued for a total of 72 h. Water was added, resulting in the formation of a precipitate. The solid was collected and recrystallized, to give the triazole **28** as a yellow solid (300 mg, 87%), mp 201–203.5°C (from EtOAc/pet. spirits). $[\alpha]_D^{21}$ −33.3 (*c* ~0.95 in $CHCl_3$). (Found: C 64.35, H 4.6, N 6.1. $C_{38}H_{31}N_3O_{11}$ requires C 64.7, H 4.4, N 5.95%). δ_H (400 MHz; $CDCl_3$) 3.91 (3H, s, Me), 4.45–4.68 (3H, m, H5,6,6), 5.85 (1H, dd, $J_{3,4}$ 9.6, $J_{4,5}$ 9.6, H4), 5.91 (1H, dd, $J_{2,3}$ 10.0, $J_{3,4}$ 9.4, H3), 6.11 (1H, dd, $J_{1,2}$ 9.6, $J_{2,3}$ 10.0, H2), 6.29 (1H, d, $J_{1,2}$ 9.6, H1), 7.24–8.00 (20H, m, Ar), 8.47 (s, 1H, triazole CH). δ_C (100.5 MHz; $CDCl_3$) 52.52 (1C, CH_3), 62.69, 68.85, 71.33, 72.87, 76.03 (5C, C2,3,4,5,6), 86.54 (C1), 127.86, 129.42 (2C, Ar), 128.61–134.04 (24C, Ar), 160.77 (MeO*C*=O), 164.94, 165.27, 165.72, 166.20 (4C, Ph*C*=O). HRMS (ESI^+, *m/z*) calc. for $C_{38}H_{31}N_3O_{11}Na$ $[M + Na]^+$ 728.1849, found 728.1884.

1-(2,3,4,6-Tetra-O-benzoyl-β-D-glucosyl)-4-t-butyloxycarbonyl-1H-1,2,3-triazole ***29***

Sodium ascorbate (16.2 mg, 0.082 mmol) was added to a stirred mixture of the azide **2**[26] (506 mg, 0.815 mmol), *t*-butyl propiolate (179 μL, 1.47 mmol), $CuSO_4$ (2.6 mg, 0.016 mmol), and TBTA (8.6 mg, 0.016 mmol) in *t*-BuOH/water (2:1, 12 mL) and DMSO (1 mL). After 2 days, TLC showed consumption of the starting material. Water (10 mL) was added, resulting in the formation of a precipitate. The solid was collected and recrystallized from EtOH to give the triazole **29** as white crystals (368 mg, 60%). $[\alpha]_D^{19}$ −26.6 (*c* ~0.7 in $CHCl_3$). δ_H (400 MHz; $CDCl_3$) 1.57 (9H, s, *t*-butyl), 4.46–4.52 (2H, m, H5,6), 4.66 (1H, m, H6), 5.86 (1H, dd, $J_{3,4}$ 9.6, $J_{4,5}$ 9.6, H4), 5.94 (1H, dd, $J_{1,2}$ 9.2, $J_{2,3}$ 9.6, H2), 6.11 (1H, dd, $J_{2,3}$ 9.6, $J_{3,4}$ 9.6, H3), 6.29 (1H, d, $J_{1,2}$ 9.2, H1), 7.26–8.00 (20H, m, Ar), 8.38 (1H, s, triazole CH). δ_C (125.5 MHz; $CDCl_3$) 28.42 (3C, C(*Me*)$_3$), 62.79, 68.92, 71.32, 73.09, 76.01 (5C, C2,3,4,5,6), 82.90 (C1), 86.49 (*C*(Me)$_3$), 125.90–134.04 (24C, Ar), 128.01, 129.48 (2C, Ar), 164.92, 165.27, 165.72, 166.22 (4C, C=O). HRMS (ESI^+, *m/z*) calc. for $C_{41}H_{37}N_3O_{11}Na$ $[M + Na]^+$ 770.2317, found 770.2320.

Octyl 2,3,4,6-Tetra-O-benzoyl-β-D-glucoside ***30***

TMSOTf (97.5 μL, 0.54 mmol) was added to a stirred suspension of the trisubstituted triazole **24** (206 mg, 0.269 mmol), 1-octanol (51 μL, 0.32 mmol), and 4-Å molecular sieves in dry 1,2-dichloroethane (10 mL) at room temperature. After 24 h, additional TMSOTf (97.5 μL, 0.539 mmol) was added and the reaction stirred for a further 24 h. The mixture was filtered through Celite and the filtrate was washed with water (3 × 30 mL) and dried ($MgSO_4$). The solvent was evaporated under reduced pressure and the residue was purified by flash chromatography (20–30% EtOAc/pet. spirits) to give the glycoside **30** as a yellow oil (95.7 mg, 50%). $[\alpha]_D^{20}$ 15.7 (*c* ~0.4 in $CHCl_3$). δ_H (400 MHz; $CDCl_3$) 0.80–1.56 (15H, m, heptyl), 3.54, 3.92 (2H, 2 × ddd, OCH_2), 4.17 (1H, ddd, $J_{4,5}$ 9.6, $J_{5,6}$ 3.2, $J_{5,6}$ 4.8, H5), 4.52 (1H, dd, $J_{5,6}$ 5.2, $J_{6,6}$ 12.0, H6), 4.64 (1H, dd, $J_{5,6}$ 3.2, $J_{6,6}$ 12.0, H6), 4.85 (1H, d, $J_{1,2}$ 7.6, H1), 5.54 (1H, dd, $J_{1,2}$ 8.0, $J_{2,3}$ 9.6, H2), 5.69 (1H, dd, $J_{2,3}$ 9.6, $J_{3,4}$ 10.0, H3), 5.92 (1H, dd, $J_{3,4}$ 10.0, $J_{4,5}$ 9.6, H4), 7.24–8.03 (20H, m, Ar). δ_C (100.5 MHz; $CDCl_3$) 14.24, 22.77, 25.94, 29.28, 29.36, 29.56, 21.88 (7C, $OCH_2(CH_3)_6CH_3$), 63.42 ($OCH_2(CH_3)_6CH_3$), 70.05, 70.55, 72.09, 72.61, 73.12 (5C, C2,3,4,5,6), 101.48 (C1), 128.45–133.58 (24C, Ar), 165.26, 165.38, 166.02, 166.34 (4C, C=O).

4-Methylphenyl 2,3,4,6-Tetra-O-acetyl-1-thio-β-D-glucoside ***31***

$SnCl_4$ (117 μL, 2.0 mmol) was added to a stirred solution of the trisubstituted triazole **23** (258 mg, 0.50 mmol) and thiocresol (93 mg, 0.75 mmol) in dry CH_2Cl_2 (5 mL) at room temperature. After 75 min, the reaction mixture was extracted with CH_2Cl_2 and the organic phase was washed with 1 M HCl (3 × 30 mL) and H_2O (2 × 30 mL). The organic layer was dried ($MgSO_4$) and the solvent was evaporated under reduced pressure. The crude yellow residue was purified by flash chromatography (30–40% EtOAc/pet. spirits) to give the thioglycoside **31** as a yellow oil (165 mg, 77%; 1:5 α:β). δ_H (500 MHz; $CDCl_3$) 4.64 (1H, d, $J_{1,2}$ 10.0, H1β), 6.29 (1H, d, $J_{1,2}$ 4.5, H1α). δ_C (125.7 MHz; $CDCl_3$) 85.78 (C1β), 90.05 (C1α).

2,3,4,6-Tetra-O-acetyl-α-D-glucosyl Chloride ***32***

$SnCl_4$ (240 μL, 2.0 mmol) was added to a stirred suspension of the trisubstituted triazole **23** (258 mg, 0.50 mmol), TMSCl (255 μL, 2.0 mmol), and 4-Å molecular sieves in CH_2Cl_2 (5 mL) with under nitrogen at room temperature. The mixture was stirred for 2 h and was diluted with CH_2Cl_2 and filtered through Celite. The filtrate was washed with 1 M HCl (3 × 40 mL) and water (2 × 40 mL), dried ($MgSO_4$) and the solvent evaporated under reduced pressure. The residue was purified by flash chromatography (35–40% EtOAc/pet. spirits) to give **32** as a pale yellow crystalline residue (92.9 mg, 51%). A portion was recrystallizsed from diethyl ether/pet. spirits to give white needles, mp 72–75°C (lit.[41] 72–73.5). $[\alpha]_D^{27}$ 166 (*c* ~0.8 in $CHCl_3$; lit.[42] $[\alpha]_D^{27}$ 166). δ_H (400 MHz; $CDCl_3$) 1.99–2.06 (4 × 3H, m, Ac), 4.08–4.11 (1H, m, H6), 4.25–4.30 (2H, m, H5,6), 4.97 (1H, dd, $J_{1,2}$ 4.0, $J_{2,3}$ 10.0, H2), 5.09 (1H, dd, $J_{3,4}$ 9.6, $J_{4,5}$ 9.6, H4), 5.52 (1H, dd, $J_{2,3}$ 10.0, $J_{3,4}$ 9.6, H3), 6.25 (1H, d, $J_{1,2}$ 4.0, H1). δ_C (100.5 MHz; $CDCl_3$) 20.56, 20.59, 20.63, 20.68 (4C, Me), 61.13, 67.44, 69.44, 70.40, 70.75 (5C, C2,3,4,5,6), 169.35, 169.88, 170.53 (4C, C=O).

2,3,4,6-Tetra-O-acetyl-α-D-glucosyl Azide ***33***

$TMSN_3$ (66.4 μL, 0.50 mmol) and $SnCl_4$ (73 μL, 0.50 mmol) were added to a suspension of the trisubstituted triazole **23** (129 mg, 0.25 mmol) and 4-Å molecular sieves in dry 1,2-dichloroethane (8 mL) and the mixture was stirred at 50°C. After 2 h, additional $SnCl_4$ (1 equiv.) and $TMSN_3$ (1 equiv.) were added and the reaction stirred for another 2 h. At this point, TLC showed consumption of the starting material and the reaction was filtered. The filtrate was washed with 1 M HCl (3 × 40 mL) and H_2O (2 × 40 mL), dried ($MgSO_4$) and the solvent evaporated under reduced pressure. The crystalline residue was purified by flash chromatography (30–45% EtOAc/pet. spirits) to give the azide **33** as an off-white solid (35.3 mg, 38%), mp 52.5–55°C. $[\alpha]_D^{25}$ +2.9 (*c* ~0.6 in $CHCl_3$). ^1H NMR and ^{13}C NMR data were consistent with the literature.[43]

4-Methylphenyl 2,3,4,6-Tetra-O-benzyl-1-thio-D-glucoside ***34***

A solution of the tetrabenzylated tetrafluorobenzotriazole **19** (64.6 mg, 0.09 mmol), $SnCl_4$ (21.7 μL, 0.18 mmol), and thiocresol (16.8 mg, 0.14 mmol) in dry CH_2Cl_2 (5 mL) was stirred under nitrogen at room temperature. After 4 h, further $SnCl_4$ (21.7 μL, 0.18 mmol) was added. At 6 h, the reaction mixture was diluted with CH_2Cl_2 and washed with 1 M HCl (3 × 20 mL) and H_2O (2 × 20 mL). The organic layer was dried ($MgSO_4$) and the solvent was evaporated under reduced pressure. The crude residue was purified by flash chromatography (10–20% EtOAc/pet. spirits) to give the thioglycoside **34** as yellow residue (12.0 mg, 20%). δ_H (400 MHz; $CDCl_3$) 4.88 (1H, d, $J_{1,2}$ 10.8, H1β), 5.58 (1H, d, $J_{1,2}$ 4.4, H1α). The ^{1}H NMR data for the β-anomer are consistent with the literature.[44]

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