Synthesis and Reactivity of Halogenated 1,2,4-Triazole Nucleoside Analogues with High Potential for Chemical Modifications

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In tribute to Prof. Dr. Hans Beyer (University of Greifswald) on the occasion of his 100th birthday

Abstract: 1,2,4-Triazole nucleoside analogues bonded at N-1 of the base were synthesized by addition of N-halo-3,5-dibromo-1,2,4-triazoles to 1,2-unsaturated carbohydrate derivatives (glycals). Examples are given for 1,5-anhydro-3,4,6-tri-O-acetyl-2-deoxy-D-arabinohex-1-enitol (tri-O-acetyl-D-glucal), and 1,5-anhydro-3,4,6-tri-O-benzyl-2-deoxy-D-arabinohex-1-enitol (tri-O-benzyl-D-glucal), respectively. The graduated reactivity of the three halogens [C-5 (triazole) > C-2 (sugar) > C-3 (triazole)] in the addition products allows subsequent regioselective replacement and deprotection reactions like hydrodehalogenations, nucleophilic substitutions (by methoxide, hydrazine, benzylamine, thiophenolate), deacetylations, and debenzylations, respectively. Thus, the paper opens a new synthetic approach to triazole nucleoside analogues of 2-deoxy-sugars. X-ray analyses support the structures of nine products.

Key words: nucleoside analogues, 1,2,4-triazoles, additions to D-glucals, nucleophilic substitutions, hydrodehalogenations

1,3,5-Tribromo-1,2,4-triazole (I), synthesized by a very simple procedure in 1967,1 attracted interest as a brominating reagent shortly after publication.2 Addition products of I to suitable unsaturated compounds offer valuable synthetic potential due to the graduated reactivities of the halogens in nucleophilic addition–elimination reactions. Thus, investigations on 3,5-dibromo-1-methyl-1,2,4-triazole have shown that the halogen atom located on C-5 is significantly more reactive than that on C-3.3,4 This observation was convincingly confirmed by recent studies on various 1-alkyl-3,5-dibromo-1,2,4-triazoles5 and on 1-(2,3,5-tri-O-acetyl-β-D-ribofuransyl)-3(5)-bromo-5(3)-carbamido-1,2,4-triazole6 as well as reactions with 1-phenyl-5-bromo-1,2,4-triazole.7,8 It is assumed that the mesomorphic discrimination of intermediate A relative to B is the reason for the difference in reactivity of the halogens (Scheme 1).

Various methods for regiospecific and stereoselective electrophilic addition reactions of azole and azine derivatives to pyranoid and furanoid glycals were reported in the literature as key steps in nucleoside syntheses.9–12 Herdeewijn et al.13,14 and Eschenmoser et al.15 synthesized pyranose nucleosides and investigated their incorporation into oligonucleotides, respectively. The biological activity of 1,2,4-triazole nucleoside analogues has been widely demonstrated,16–19 thus our efforts were focused on providing a new synthetic strategy towards 2-deoxy-sugar derivatives. The strategy presented in this paper allows the design of triazole nucleoside analogues with a variable pattern of groups on the C-5 of the triazole ring. This was achieved by regioselective additions of 1,3,5-trihalogeno-1,2,4-triazoles to 1,2-unsaturated sugars (glycals) combined with subsequent regioselective replacement of the halogens by nucleophiles or by hydrogen. Indeed, the enol ether unit of a glycal ensures, above all, the addition step is highly regioselective but rarely diastereoselective.20–22 However, the loss of stereochemistry becomes less important because the halogen atom, introduced into C-2 of the sugar moiety, is finally removed by hydrodehalogenation.

Additions of 1,3,5-tribromo-1,2,4-triazole (1) and 3,5-dibromo-1-iodo-1,2,4-triazole (2) to 3,4,6-tri-O-acetyl-1,5-anhydro-2-deoxy-D-arabinohex-1-enitol (3) and 1,5-anhydro-3,4,6-tri-O-benzyl-2-deoxy-D-arabinohex-1-enitol (4), respectively, at room temperature in 1,4-dioxane had been reported previously (Scheme 2).23 Three diastereomeric nucleoside analogues are formed, the α-configured major products with ‘D-manno’ and ‘D-gluc’ configuration and the corresponding ‘β-D-gluco’ N-glycoside (minor product). The dominance of the α anomers in the product mixture is caused by the anomeric effect. Components 5–7 (overall yield 83%) can be separated by column chromatography. Figure 1 shows the result of X-ray structural analyses for these compounds.

The overall yield of the three diastereomers hardly changed if the acetyl protecting groups of the starting material 3 were replaced by benzyl protecting groups (starting material 4). However, the ratio of the three diastereomers within the mixture changed after this re-

Scheme 1

Additions of 1,3,5-tribromo-1,2,4-triazole (1) and 3,5-dibromo-1-iodo-1,2,4-triazole (2) to 3,4,6-tri-O-acetyl-1,5-anhydro-2-deoxy-D-arabinohex-1-enitol (3) and 1,5-anhydro-3,4,6-tri-O-benzyl-2-deoxy-D-arabinohex-1-enitol (4), respectively, at room temperature in 1,4-dioxane had been reported previously (Scheme 2).23 Three diastereomeric nucleoside analogues are formed, the α-configured major products with ‘D-manno’ and ‘D-gluc’ configuration and the corresponding ‘β-D-gluco’ N-glycoside (minor product). The dominance of the α anomers in the product mixture is caused by the anomeric effect. Components 5–7 (overall yield 83%) can be separated by column chromatography. Figure 1 shows the result of X-ray structural analyses for these compounds.

The overall yield of the three diastereomers hardly changed if the acetyl protecting groups of the starting material 3 were replaced by benzyl protecting groups (starting material 4). However, the ratio of the three diastereomers within the mixture changed after this re-
placement. The benzylated starting material 4 produced a noticeably higher percentage of the \textit{a-D-glucos}-configured diastereomer 9 at the expense of the \textit{a-D-manno} diastereomer 8, than the acetylated starting material 3 yielding 6 and 5, respectively. The sum of the two \textit{a}-diastereomers remained nearly unchanged at 66–68% (Table 1).

The \textit{N}-glycosylated halotriazoles proved to be suitable candidates for regioselective variation of the substituent pattern. Separation of the two \textit{a}-diastereomers is not required if the sugar linked halogen is hydrodehalogenated in a final synthetic step. In this case, the ‘\textit{a-D-manno}’ and ‘\textit{a-D-glucos}’ precursors will give the same product. Thus, it is sufficient to separate the \textit{\beta}-anomer from the diastereomeric mixture of addition products.

In order to explore the regioselectivity of subsequent reactions, first of all all hydrodebrominations were investigated. It was found that hydrogen activated by Pd/C allows the complete hydrodebromination of halogenated precursors in one step. Thus, 1-(3,4,6-tri-O-acetyl-2-bromo-2-deoxy-\textit{a-D-mannopyranosyl})-3,5-dibromo-1\textit{H}-1,2,4-triazole (5) gave at room temperature the bromine-free product 12 in 90% yield (Scheme 3). The hydrodebromination of the mixture of 5, 6, and 7 formed from 1 and 3 (Scheme 2) yielded \textit{a}-nucleoside 12 (61%) and its \textit{\beta}-isomer 18 (12%) as shown in Scheme 3 (Table 1). Additionally, small amounts of two by-products were identified, the glucal 3 and 3,4,6-tri-O-acetyl-1,5-anhydro-2-deoxy-\textit{D-arabin}o-hexitol. The use of the \textit{H}_2/Pd/C/\textit{Et}_3\textit{N} reagent system allows simultaneous hydrodebromination and de-benzylation of the compounds in the case of benzylated precursors of mixtures such as 8 and 9 or 19 and 26 (Scheme 5).

It should be mentioned that the Bu_4Sn/AIBN system was less suitable as a selective reagent and led to mixtures of products. A reagent combination of ethylmagnesium chloride/[Fe(acac)]_3 in THF/NMP neither facilitated selective hydrodebromination nor a cross-coupling reaction.\textsuperscript{24} The detection of 1-(3,4,6-tri-O-acetyl-2-deoxy-\textit{a-D-mannopyranosyl})-3-bromo-1\textit{H}-1,2,4-triazole along with dibromo compound 13 indicated that the bromine atom linked to the heteroaromatic C-3 of starting material 5 is the most stable.\textsuperscript{25}

Selective hydrodebrominations of the most reactive bromine atom on C-5 of the heteroaromatic ring was achieved by heating the corresponding trihalogen derivative with dimethyl phosphite dissolved in trimethyl phosphate. This is demonstrated with the precursors 5, 6, 7, 9, and 11 (Scheme 3). Regioselective hydrodebromination of iodo derivative 11 to 1-(3,4,6-tri-O-acetyl-2-deoxy-2-iodo-\textit{a-D-mannopyranosyl})-3-bromo-1\textit{H}-1,2,4-triazole (17) demonstrated also that dimethyl phosphite did not attack the iodo substituent linked to the sugar moiety (Scheme 3). There was no evidence of an Arbuzov phosphorylation by trimethyl phosphate, even when trihalogen derivative 5 was heated in pure trimethyl phosphate.

The high reactivity of the bromine linked to C-5 of the triazole ring allowed various regioselective nucleophilic substitutions in this position. Thus, methoxylation of the benzylated precursors 9 and 10 by methanolic sodium methoxide at room temperature yielded the corresponding 5-methoxy derivatives 19 and 20, in 92% and 88% yields, respectively. In a further experiment, the crude mixture of 8, 9, and 10 obtained from the reaction of tribromotriazole 1 and glucal 4 was methoxylated under analogous conditions to give 19, 20, and 26. After the \textit{\beta}-anomeric 5-methoxy-isomer 20 had been separated from the mixture by column chromatography, the mixed fraction of the two \textit{a}-products 19 and 26 was deprotected as shown in Scheme 5.

Moreover, 5-phenylthio derivative 23 was generated from \textit{a-D-manno} derivative 8 by treatment with thiophenolate at room temperature. The thiophenolate was generated in situ from thiophenol and potassium carbonate. Furthermore, the starting materials 8 and 9 were reacted with hydrazine hydrate at room temperature to give the corresponding 5-hydrazino derivatives. Compound 24 obtained from 8 was isolated as a syrupy substance, whereas the crude 5-hydrazino derivative generated from 9 was treated with acetone before isolation. The hydrazone 21 obtained in this manner at room temperature, is a crystalline compound (Scheme 4; Table 1).

At increased reaction temperatures, nucleophilic substitutions can be accompanied by \textit{\beta}-elimination of HBr. It is a precondition for the elimination that the bromine atom on C-2 of the sugar moiety and the vicinal protons are in a \textit{trans} relationship. Such a situation exists with the C-3 proton of \textit{a-D-manno}-configured halotriazole nucleosides.

\begin{scheme}[H]
\centering
\includegraphics[width=\textwidth]{Scheme2.png}
\caption{Addition of 1,3,5-tribromo-1,2,4-triazole (1) and 3,5-dibromo-1-iodo-1,2,4-triazole (2), respectively, to the glycals 3 and 4: i) 1 (or 2), 1,4-dioxane, r.t., 5–6 h.}
\end{scheme}
and the C-1 proton of α-D-gluco-configured halotriazole nucleosides.

The introduction of a benzylamino function onto C-5 of 1-(3,4,6-tri-O-benzyl-2-bromo-2-deoxy-α-D-mannopyranosyl)-3,5-dibromo-1H-1,2,4-triazole (8) required a reaction temperature of about 100 °C. The reaction proceeded to furnish the 2,3-unsaturated nucleoside analogue 25.

On refluxing α-D-glucose diastereomer 16 in methanolic sodium methoxide, only HBr elimination was observed with no methoxylation of the heteroaromatic C-3. β-Elimina-
tion of HBr is facile as H-1 and bromine are in a trans relationship. The corresponding glycal derivative 22 was isolated in 93% yield.

Finally, selected deprotection reactions were investigated. The glycosidic bond of triazole nucleoside analogues is quite stable towards acids as long as the triazole ring contains bromine. Cleavage of the glycosidic bond is effected by acids, when the triazole ring does not contain electron withdrawing substituents like halogens due to the increased basicity of the triazole moiety. Thus, compounds 5 and 13 underwent selective deacetylation at room temperature by 1% methanolic HCl yielding 27 and 30, respectively, whereas the bromine-free nucleoside 12 was attacked by the same reagent under the same reaction conditions. A diastereomeric mixture of methyl 2-deoxy-\(\alpha/\beta\)-D-glucopyranosides (67%; \(\alpha/\beta\) 10:1) resulted, along with only 12% of the desired 1-(2-deoxy-\(\alpha\)-D-glucopyranosyl)-1H-1,2,4-triazole (28). The latter was therefore synthesized by simultaneous debenzylation and hydrodebromination of benzyl-protected precursors. Thus, a mixture of \(\alpha\)-anomeric tribromo derivatives 8 and 9 was treated with \(\text{H}_2/\text{Pd/C/Et}_3\text{N in EtOAc–MeOH at room temperature. 1-(2-Deoxy-\(\alpha\)-D-glucopyranosyl)-1H-1,2,4-triazole (28) was the only reaction product in this case, as C-2 of the sugar moiety is no longer a chiral center as a result of the hydrodebromination (Scheme 5). In a second experiment, which required only a few consecutive synthetic steps relating to the preliminary addition reaction, the diastereomeric mixture of the two methoxylated \(\alpha\)-diastereomers 19 and 26, obtained from 8, 9, and 10 (Scheme 4), was hydrogenated by \(\text{H}_2/\text{Pd/C/Et}_3\text{N. The expected product, 1-(2-deoxy-\(\alpha\)-D-glucopyranosyl)-5-methoxy-1H-1,2,4-triazole (29), was isolated in 59% yield (Scheme 5, Table 1) along with two by-products, incompletely deprotected derivatives of the starting material. It is important to mention that the hydrogenation of the starting materials 19 and 26 was accompanied by cleavage of the methoxy group unless triethylamine was added to the reaction mixture.}

The structures of the new products are supported by microanalyses, GC-MS analyses, and NMR data (correlation spectra and NOE measurements included). Crystals of compounds 5–8, 11, 13, 14, 17, and 30 were suitable for X-ray structural analyses. Thereby, it was confirmed that the compounds with acetyl protecting groups adopt a more or less distorted \(\text{C}_1\) chair conformation, whereas the pyranose ring of the benzylated product 8 adopts a skew conformation in the crystalline state. The puckering parameters of the compounds are given in Table 2. Moreover, the regioselective hydrodehalogenations on C-5 could be confirmed for nucleosides 13, 14, and 17. Figures 1–3 show the X-ray structures of compounds 5, 6, 7, 8, 11, 17, 13, 14, and 30.27 The deprotected nucleoside 30 crystallizes together with one mole of methanol per mole of nucleoside.
The 1H NMR spectra of the mono-hydrodebrominated heteroaromatic rings (compounds 13–17) show proton signals between 8.00 and 8.29 ppm. The completely hydrodebrominated triazole rings of 12, 18, and 28 are characterized by two singlets (7.98–8.01 and 8.29–8.64 ppm, respectively). The methoxy groups of 19, 20, 26, and 29 appear at 4.12–4.16 ppm and 59.3 ppm in the 1H and 13C NMR spectra, respectively. The singlet corresponding to the NH proton of compound 21 was monitored at 7.69 ppm. The chemical shift of the heteroaromatic carbon atom bonded to the bromine changes significantly when the bromine atom was replaced by another atom or group; therefore it was possible to determine the reaction center by monitoring both the 1H and 13C NMR spectra.

Interestingly, the synthesized α-D-manno-configured products (5, 11, 13, 17, 23, 24, 27, and 30) exhibit different conformations in solution. This is indicated by the large variation in the proton couplings $J_{1,2}$ and $J_{4,5}$ for these compounds. The values of the $J_{1,2}$ coupling constants range from 1.9 Hz in compound 24 up to 7.6 Hz in compound 17. The corresponding values for $J_{4,5}$ are 8.7 Hz for compound 24 and 4.7 Hz for 17. The coupling values for 17 do not match the expected C1-conformation, found in the crystal structure (Figure 2).

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### Table 2

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<td>287 (3)</td>
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<td>6</td>
<td>0.530 (3)</td>
<td>3.6 (3)</td>
<td>17.15 (5)</td>
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<td>7</td>
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<td>6.2 (4)</td>
<td>305 (3)</td>
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<tr>
<td>8</td>
<td>0.780 (2)</td>
<td>91.7 (1)</td>
<td>318.17 (17)</td>
</tr>
<tr>
<td>11</td>
<td>0.523 (4)</td>
<td>3.4 (4)</td>
<td>318.7 (7)</td>
</tr>
<tr>
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<td>0.513 (2)</td>
<td>7.7 (2)</td>
<td>208.2 (18)</td>
</tr>
<tr>
<td>14</td>
<td>0.510 (3)</td>
<td>12.2 (2)</td>
<td>352.5 (14)</td>
</tr>
<tr>
<td>17</td>
<td>0.522 (1)</td>
<td>5.9 (1)</td>
<td>309.8 (15)</td>
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<td>30</td>
<td>0.495 (2)</td>
<td>1.1 (2)</td>
<td>142 (13)</td>
</tr>
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</table>

Scheme 4 Deprotection and regioselective replacement reactions: i) NaOMe/MeOH, r.t., 12 h; ii) H2NNH2·H2O, 1,4-dioxane, r.t., 12 h; iii) acetone, r.t., 15 min; iv) NaOMe/MeOH, reflux, 6 h; v) thiophenol, K2CO3, DMF, r.t., 6 h; vi) excess BnNH2, 100 °C, 6–8 h.
In summary, trihalogenated triazole nucleoside analogues were accessible from simple precursors, i.e., 1,3,5-tribromo-1H-1,2,4-triazole and 1,2-unsaturated carbohydrates. The three bromine atoms linked to C-2 (pyranose) and C-3, C-5 (triazole) of the target molecules showed graduated reactivities C-5 > C-2 > C-3. This sequence allowed regioselective variations of the substituent pattern, culminating in nucleoside analogues of halogen free 2-deoxy-sugars. The most reactive bromine on C-5 could be regioselectively replaced by nucleophiles or by hydrogen.

**Figure 1** Molecular structures of 1-(3,4,6-tri-O-acetyl-2-bromo-2-deoxy-a-D-mannopyranosyl)-3,5-dibromo-1H-1,2,4-triazole (5), 1-(3,4,6-tri-O-acetyl-2-bromo-2-deoxy-a-D-glucopyranosyl)-3,5-dibromo-1H-1,2,4-triazole (6) and 1-(3,4,6-tri-O-acetyl-2-iodo-2-deoxy-a-D-glucopyranosyl)-3,5-dibromo-1H-1,2,4-triazole (7) with 30% probability of the thermal ellipsoids.

The favored attack of the heteroaromatic position 5 by nucleophiles can be explained by the formation of a more stabilized intermediate in an addition–elimination SN mechanism (see Scheme 1).

Dimethylphosphite was found to be a highly selective hydrodehalogenation reagent for the most reactive bromine at the heteroaromatic C-5. The complete removal of residual halogens was achieved by treatment with H2, Pd/C, Et3N. This procedure can be carried out at any point in the synthesis. Simultaneous debenzylation was achieved by H2, Pd/C, Et3N, so that completely deprotected and dehydrobrominated 1,2,4-triazole nucleosides were accessible by this procedure from benzyl-protected precursors. Prod-
Zumbrunn recently showed that the less reactive bromine stereoselectivity of the initial addition step. This possibility reduces the dis-advantages considerably, which results from the poor interaction of the sugar moiety. This potential exists for consecutive reactions with the com-
pounds reported in this paper.

Mps were obtained using a Leitz polarizing microscope (Laborlux 12 Pol) equipped with a hot stage (Mettler FP 90) and are uncorrected. Microanalyses were carried out with a CHNS-analyser Thermoquest Flash EA 1112. ¹H and ¹³C NMR spectra were recorded on Bruker instruments: AC 250 and ARX 300, with TMS as the internal standard for ¹H and ¹³C NMR spectra. Optical rotations were measured on a polar LpM (BIZ Melleotechnik) instrument. Column chromatography was carried out with Merck Silica Gel 60 (63–200 µm) and TLC on Merck Silica Gel 60 F₂₅₄ sheets.

All crystal structure investigations were done on a Bruker X8 Apex diffractometer with CCD area detector, Mo-Kα radiation and graphite monochromator at 100–243 K. The structures were solved by direct methods and refined by the full matrix least squares method with the Bruker SHELXTL software package. Due to the higher values of the absorption coefficient semiemipirical absorption correction calculations were done on the basis of the intensities of equivalent reflections; for selected crystal data of compounds 5–8, 11, 13, 14, 17, and 30, see Table 3.

Addition of 1,3,5-Trihalogeno-1,2,4-triazoles to Glycals; Typical Procedure
To a stirred solution of glucal 3 (1.5 g, 5.5 mmol) in anhyd 1,4-dioxane (25 mL), tribromotriazole 1 (2.0 g, 6.6 mmol) was added at r.t. under an argon atmosphere. The suspension was stirred until the glucal could no longer be detected by TLC (ca. 1 h). After filtration, the solution was concentrated under reduced pressure, and the residue was separated by column chromatography (heptane–EtOAc, 10:1→7:1) to give 1.2 g (38%) of α-manno derivative 5, 954 mg (30%) of α-glucos derivative 6, and 477 mg (15%) of β-glucos derivative 7.

1-(3,4,6-Tri-O-acetyl-2-bromo-2-deoxy-α-D-mannopyranosyl)-3,5-dibromo-1H-1,2,4-triazole (5)
¹H NMR (250 MHz, CDCl₃); δ = 6.14 (d, 1 H, J₁₂₁ = 5.3 Hz, H-1), 5.68 (dd, 1 H, J₂₃₂ = 3.8, J₃₄₃ = 6.2 Hz, H-3), 5.24 (dd, 1 H, J₃₄₃ = 6.2, J₃₈₃ = 7.0 Hz, H-4), 5.00 (dd, 1 H, J₁₂₁ = 5.3, J₁₃₁ = 3.8 Hz, H-2), 4.43 (q, 1 H, J₅₆₅ = 6.1 Hz, J₆₇₆ = 12.2, H-6a), 4.21 (ddd, 1 H, J₅₆₅ = 7.0, J₅₆₆ = 6.1, J₆₇₆ = 3.0 Hz, H-5), 4.11 (dd, 1 H, J₅₆₅ = 3.0, J₆₇₆ = 12.2 Hz, H-6b), 2.19, 2.14, 2.09 (3 s, 9 H, 3 × CH₃).
¹³C NMR (63 MHz, CDCl₃); δ = 170.6, 169.4, 169.4 (3 × C=O), 141.7, 131.4 (C-3 triazole, C-5 triazole), 83.9 (C-1), 73.3 (C-5), 69.9 (C-3), 66.9 (C-4), 61.2 (C-6), 45.7 (C-2), 20.9, 20.9, 20.8 (3 × CH₃).

Anal. Calc. for C₁₄H₁₄Br₃N₃O₇ (578.01): C, 29.09; H, 2.79; N, 7.27. Found: C, 29.18; H, 2.77; N, 7.32.

1-(3,4,6-Tri-O-acetyl-2-bromo-2-deoxy-α-D-glucopyranosyl)-3,5-dibromo-1H-1,2,4-triazole (6)
¹H NMR (250 MHz, CDCl₃); δ = 6.19 (dd, 1 H, J₁₂₁ = 10.8, J₁₃₁ = 9.3 Hz, H-3), 6.18 (d, 1 H, J₁₂₁ = 5.8 Hz, H-1), 5.20 (dd, 1 H, J₃₄₃ = 9.3, J₁₃₁ = 10.3 Hz, H-4), 4.54 (dddd, 1 H, J₅₆₅ = 3.8, J₆₇₆ = 3.8, J₆₇₆ = 12.6 Hz, H-6b), 4.00 (dd, 1 H, J₅₆₅ = 2.1, J₆₇₆ = 12.6 Hz, H-6a), 2.09, 2.08 (3 s, 9 H, 3 × CH₃).
¹³C NMR (63 MHz, CDCl₃); δ = 170.6, 169.8, 169.6 (3 × C=O), 141.7, 132.5 (C-3 triazole, C-5 triazole), 82.9 (C-1), 71.8 (C-5), 71.3 (C-3), 68.8 (C-4), 61.3 (C-6), 44.9 (C-2), 20.8, 20.7, 20.6 (3 × CH₃).
Scheme 5  Deprotection of halotriazole nucleoside analogues: i) 1% methanolic HCl, r.t., 10–12 h; ii) H3, Pd/C, Et3N, EtOAc–MeOH, r.t., 12–15 h.


1-(3,4,6-Tri-O-acetyl-2-bromo-2-deoxy-β-D-glucopyranosyl)-5,6-dibromo-1H,1,2,4-triazole (7)

1H NMR (250 MHz, CDCl3): δ = 5.66 (d, 1 H, JH2 = 9.6 Hz, H-1), 5.47 (dd, 1 H, JH2 = 10.6, JH2 = 9.3 Hz, H-3); 5.11 (dd, 1 H, JH5 = 9.3, JH6 = 10.1 Hz, H-4), 4.61 (dd, 1 H, JH5 = 9.8, JH6 = 10.6 Hz, H-2), 4.27 (dd, 1 H, JH5a = 4.9, JH6b = 12.6 Hz, H-6a), 4.12 (dd, 1 H, JH5b = 2.2, JH6a = 12.6 Hz, H-6b), 4.05–3.97 (m, 1 H, JH4 = 10.1, JH5a = 4.9, JH6b = 2.2 Hz, H-5), 2.09, 2.05, 2.02 (3 s, 9 H, 3 × CH3).

13C NMR (63 MHz, CDCl3): δ = 170.6, 169.7, 169.3 (3 × C-O), 142.1, 131.7 (C-3 triazole, C-5 triazole), 85.8 (C-1), 75.3 (C-5), 74.4 (C-3), 68.6 (C-4), 61.6 (C-6), 46.7 (C-2), 20.8, 20.6, 20.6 (3 × CH3).

Addition of Tribromotriazole 1 to Glucal 4

Glucal 4 (3.0 g, 7.21 mmol) and tribromotriazole 1 (2.6 g, 8.58 mmol) were reacted as described for glucal 3. Column chromatography (heptane–EtOAc, 20:1→15:1) gave 1.46 g (28%) of 8. 1.98 g (38%) of 9, and 0.99 g (19%) of 10.

Table 3  Crystal Data of 5–8, 11, 13, 14, 17, 30

<table>
<thead>
<tr>
<th>Product</th>
<th>Formula</th>
<th>Space group</th>
<th>Unit cell dimensions</th>
<th>Parameters/ Independent reflections</th>
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<td>5</td>
<td>C14H15Br2N3O4</td>
<td>P212121</td>
<td>a = 8.9674(7) Å, b = 10.7922(8) Å, c = 21.1264(16) Å, α = β = γ = 90°, V = 2044.6(3) Å³</td>
<td>247/2666</td>
<td>0.0215/0.0233</td>
</tr>
<tr>
<td>6</td>
<td>C14H15Br2N3O4</td>
<td>P21</td>
<td>a = 10.738(5) Å, b = 8.9274(4) Å, c = 11.7147(6) Å, α = γ = 90°, β = 115.462(2)°, V = 1013.96(8) Å³</td>
<td>247/5767</td>
<td>0.0274/0.0318</td>
</tr>
<tr>
<td>7</td>
<td>C14H15Br2N3O4</td>
<td>P21</td>
<td>a = 8.181(6) Å, b = 8.4251(17) Å, c = 15.1963(3) Å, α = γ = 90°, β = 98.40(3)°, V = 1063.1(4) Å³</td>
<td>247/3519</td>
<td>0.0296/0.0304</td>
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<tr>
<td>8</td>
<td>C2H3Br2N3O4</td>
<td>P21</td>
<td>a = 4.9548(1) Å, b = 14.8212(4) Å, c = 19.5384(5) Å, α = γ = 90°, β = 96.678(2)°, V = 1425.09(6) Å³</td>
<td>352/9316</td>
<td>0.0322/0.0496</td>
</tr>
<tr>
<td>11</td>
<td>C14H15Br2N3O4</td>
<td>P21</td>
<td>a = 10.2246(7) Å, b = 11.2241(9) Å, c = 18.2309(15) Å, α = β = γ = 90°, V = 2092.2(3) Å³</td>
<td>248/6241</td>
<td>0.0387/0.0432</td>
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<tr>
<td>13</td>
<td>C14H15Br2N3O4</td>
<td>P21</td>
<td>a = 10.1049(2) Å, b = 8.2230(2) Å, c = 11.5463(3) Å, α = γ = 90°, β = 91.230(1)°, V = 959.19(4) Å³</td>
<td>238/4397</td>
<td>0.0236/0.0244</td>
</tr>
<tr>
<td>14</td>
<td>C14H15Br2N3O4</td>
<td>P21</td>
<td>a = 9.4075(7) Å, b = 13.1334(11) Å, c = 15.1824(13) Å, α = γ = 90°, β = 1875.8(3) Å³</td>
<td>235/9588</td>
<td>0.0522/0.0846</td>
</tr>
<tr>
<td>17</td>
<td>C14H15Br2N3O4</td>
<td>P21</td>
<td>a = 10.582(4) Å, b = 11.2945(4) Å, c = 16.8889(6) Å, α = β = γ = 90°, V = 2020.44(13) Å³</td>
<td>238/12388</td>
<td>0.0306/0.0570</td>
</tr>
<tr>
<td>30</td>
<td>C9H15Br2N3O3</td>
<td>P21</td>
<td>a = 7.7126(3) Å, b = 8.7008(4) Å, c = 21.0408(9) Å, α = β = γ = 90°, V = 1411.96(10) Å³</td>
<td>174/9291</td>
<td>0.0345/0.0636</td>
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concentrated under reduced pressure, and the residue was purified by column chromatography (heptane–EtOAc, 1:2) and filtration, the residue was washed with EtOAc, and the combined filtrate was added after a further 60 min. Stirring of the mixture was continued at r.t. for about 15 h (TLC). After filtration, the residue was washed with EtOAc, and the combined solution was concentrated under reduced pressure. The crude product was purified by column chromatography (heptane–EtOAc, 1:2) to give 28% (97%) of desired 12 (R,0.09) along with 5% (2%) of 3,4,6-tri-acetyl-1,5-anhydro-2-deoxy-d-arabino-hexitol (R,0.44).

1-(3,4,6-Tri-O-acetyl-2-deoxy-d-glycopyranosyl)-1H-1,1,4-triazole (12)

1H NMR (250 MHz, CDCl3): δ = 8.29, 8.00 (2 s, 2 H, H-3 triazole, H-5 triazole), 6.05 (dd, 1 H, J2a,2b = 1.8, J2a,2b = 5.7 Hz, H-1), 5.77 (dd, 1 H, J2a,2b = 5.5, J2a,2b = 10.7, J2a,2b = 8.9 Hz, H-3), 5.10 (dd, 1 H, J2a,2b = 8.9, J2a,2b = 9.5 Hz, H-4), 4.30 (dd, 1 H, J2a,2b = 4.9, J2a,2b = 12.5 Hz, H-6a), 3.96 (dd, 1 H, J2a,2b = 2.4, J2a,2b = 12.5 Hz, H-6b). 3.82 (dd, 1 H, J2a,2b = 9.5, J2a,2b = 4.9, J2a,2b = 2.4 Hz, H-5), 2.82 (dd, 1 H, J2a,2b = 1.8, J2a,2b = 13.8, J2a,2b = 5.5 Hz, H-2a), 2.26 (m, 1 H, J2a,2b = 5.7, J2a,2b = 13.8, J2a,2b = 10.7 Hz, H-2b), 2.05, 2.04, 2.03 (3 s, 9 H, 3 × CH3).

Hydrodehalogenations with Hydrogen in the Presence of Pd/C; Typical Procedure

To a stirred solution of 5 (500 mg, 0.87 mmol) in EtOAc (10 mL) and Et3N (1.0 mL), 10% Pd/C (100 mg, 0.09 mmol) was added under an argon atmosphere. Argon was then replaced by hydrogen (1 atm) and stirring was continued at r.t. for about 15 h (TLC). After filtration, the residue was washed with EtOAc, and the combined solution was concentrated under reduced pressure. The crude product was purified by column chromatography (heptane–EtOAc, 1:2) to give 28% (97%) of desired 12 (R,0.09) along with 5% (2%) of 3,4,6-tri-O-acetyl-1,5-anhydro-2-deoxy-d-arabino-hexitol (R,0.44).

1-(3,4,6-Tri-O-acetyl-2-deoxy-d-glycopyranosyl)-1H-1,1,4-triazole (18)

1H NMR (250 MHz, CDCl3): δ = 8.31, 7.98 (2 s, 2 H, H-3 triazole, H-5 triazole), 5.65 (dd, 1 H, J2a,2b = 2.3, J2a,2b = 11.2 Hz, H-1), 5.23–5.09 (2 m, 2 H, J2a,2b = 4.6, J2a,2b = 5.8, J2a,2b = 9.8, J2a,2b = 5.8 Hz, H-4), 4.30 (dd, 1 H, J2a,2b = 4.9, J2a,2b = 12.5 Hz, H-6a), 4.14 (dd, 1 H, J2a,2b = 2.3, J2a,2b = 12.3 Hz, H-6b). 3.87 (dd, 1 H, J2a,2b = 9.8, J2a,2b = 4.9, J2a,2b = 2.4 Hz, H-5), 2.69 (dd, 1 H, J2a,2b = 2.3, J2a,2b = 12.7, J2a,2b = 4.6 Hz, H-2a), (m, 1 H, J2a,2b = 11.2, J2a,2b = 12.7, J2a,2b = 5.8 Hz, H-2b), 2.07, 2.05 (3 s, 9 H, 3 × CH3).

Hydrodehalogenations with Dimethylphosphite; Typical Procedure

To a stirred solution of 5 (300 mg, 0.52 mmol) in P(OCH3)3 (5 mL), O=P(OH)(OCH3)2 (60 mg, 0.54 mmol) and Et3N (0.2 mL) were added under an argon atmosphere. Stirring was continued for 3 h at r.t. (TLC). The mixture was concentrated under reduced pressure and the residue was co-distilled with EtOAc several times until the residue...
ide was free of the pungent smell. Column chromatography (heptane–EtOAc, 3:1) gave 246 mg (95%) of the crystalline compound 13.

1-(3,4,6-Tri-O-acetyl-2-bromo-2-deoxy-α-D-mannopyranosyl)-3-bromo-1H-1,2,4-triazole (13)

1H NMR (250 MHz, CDCl3): δ = 8.20 (s, 1 H, H-5 triazole), 6.14 (dd, 1 H, J3,6a = 6.9 Hz, H-1), 5.57 (dd, 1 H, J2,3 = 3.5, J4,5 = 5.4 Hz, H-3), 5.09 (dd, 1 H, J1,4 = 5.4, J1,5 = 5.2 Hz, H-4), 5.03 (dd, 1 H, J2,6b = 6.9, J3,6a = 3.5 Hz, H-2), 4.80 (dd, 1 H, J5,6a = 8.1, J6a,6b = 12.5 Hz, H-6a), 4.24 (dd, 1 H, J1,4 = 5.2, J1,5 = 8.1, J6a,6b = 2.9 Hz, H-5), 3.95 (dd, 1 H, J1,6b = 2.9, J2,6b = 12.5 Hz, H-6b), 2.19, 2.15, 2.07 (3 s, 9 H, 3 x CH3).

13C NMR (75 MHz, CDCl3): δ = 170.1, 169.5, 169.0 (3 x C=O), 146.1 (C-5 triazole), 141.5 (C-3 triazole), 82.8 (C-1), 75.1 (C-5), 69.7 (C-3), 67.0 (C-4), 60.3 (C-6), 45.4 (C-2), 20.9, 20.8, 20.8 (3 x CH3).


Found: C, 33.69; H, 3.47; N, 8.27.

1,2,4-Triazole Nucleoside Analogues
1-(3,4,6-Tri-O-benzyl-2-bromo-2-deoxy-β-D-glucopyranosyl)-3-bromo-5-methoxy-1H,1,2,4-triazole (20)

Compound 10 (500 mg, 0.69 mmol) was methoxylated as described for compound 19. The crude product was purified by column chromatography (heptane–EtOAc, 5:1) to give 408 mg (88%) of 20.

1H NMR (250 MHz, CDCl3): δ = 7.44–7.11 (m, 15 H, Ph), 5.07, 4.42 (2 d, 2 H, JHa,Hb = 12.6 Hz, CH2Ph), 4.89, 4.65 (2 d, 2 H, JHa,Hb = 10.8 Hz, CH2Ph), 4.91 (dd, 1 H, Jα,β = 8.8, J1,2 = 10.4 Hz, H-3), 4.89, 4.65 (2 d, 2 H, JHa,Hb = 11.1 Hz, CH2Ph), 4.58, 4.50 (2 d, 2 H, JHa,Hb = 12.1 Hz, CH2Ph), 4.40 (dd, 1 h, J1,2 = 2.0 Hz, J2,3 = 3.6 Hz, J5,6a = 10.1 Hz, H-5), 4.36, 1 H, J1,2 = 5.9 Hz, J3,4 = 10.4 Hz, H-2), 3.82 (dd, 1 H, J1,2 = 8.8 Hz, J3,4 = 10.0 Hz, H-4), 3.77 (dd, 1 H, J1,2 = 3.6 Hz, J6,5a = 11.1 Hz, H-6a), 3.66 (dd, 1 H, J1,2 = 2.0 Hz, J6,5b = 11.1 Hz, H-6b), 2.08, 1.89 [2 s, 6 H, Ne(C6H5)].

13C NMR (63 MHz, CDCl3): δ = 154.0 (C-1), 151.7 (s, Ne(C6H5)3), 138.3, 130.8, 137.8, 137.3 (C-3-triazole, 3 × Ne(C6H5)Ph), 128.0, 128.3, 128.1, 128.0, 127.9 (15 C, Ph), 82.6 (C-1), 81.6 (C-3), 79.5 (C-4), 76.0, 75.4, 73.7 (3 s, 3 × CH2Ph), 74.3 (C-5), 68.2 (C-6), 49.6 (C-2), 25.3, 16.0 [2 s, Ne(C6H5)].

Anal. Calcd for C33H27BrN2O5S: C, 55.74; H, 4.43; N, 5.59. Found: C, 55.73; H, 4.49; N, 5.37.

1-(3,4,6-Tri-O-benzyl-2-bromo-2-deoxy-a-D-mannopyranosyl)-3-bromo-5-phénylthiolo-1H,1,2,4-triazole (23)

A solution of 8 (200 mg, 0.3 mmol), thiophenol (0.3 mL, 3.0 mmol), and K2CO3 (0.08 g, 0.6 mmol) in anhyd DMF (15 mL) was stirred for 6 h at r.t. After addition of H2O (50 mL), the aqueous phase was extracted with EtOAc (3 × 20 mL), the combined organic layers were washed with H2O (2 × 50 mL), dried (Na2SO4), and concentrated under reduced pressure. Column chromatography of the residue (heptane–EtOAc, 5:1; Rf 0.2) gave 0.17 g (82%) of the syrupy compound 23.

1H NMR (300 MHz, CDCl3): δ = 7.56–7.12 (m, 20 H, Ph), 6.29 (d, 1 H, J1,2 = 4.5 Hz, H-5), 4.92 (dd, 1 H, Jα,β = 4.4 Hz, J1,2 = 3.5 Hz, H-2), 4.76, 4.68 (2 d, 2 H, JHa,Hb = 11.6 Hz, OCH2), 4.69, 4.46 (d, 2 H, JHa,Hb = 11.1 Hz, OCH2), 4.62, 4.46, 4.26 (2 H, JHa,Hb = 12.1 Hz, OCH2), 3.45 (dd, 1 H, J1,2 = 3.5 Hz, J3,4 = 0.3 Hz, H-3), 3.99 (dd, 1 H, J3,4 = 6.4 Hz, J4,5 = 8.0 Hz, H-4), 3.94–3.85 (m, 1 H, J1,2 = 2.9 Hz, J6,5a = 4.4 Hz, H-5), 3.77 (dd, 1 H, J1,2 = 4.5 Hz, J6,5a = 11.1 Hz, H-6a), 3.56 (dd, 1 H, J1,2 = 2.9 Hz, J6,5a = 11.1 Hz, H-6b).

13C NMR (63 MHz, CDCl3): δ = 154.0 (C-1), 140.2 (C-2 triazole), 138.0, 137.7, 137.3 (3 × Ne(C6H5)Ph), 139.2, 129.7, 129.3, 128.6, 128.5, 128.2, 128.0, 127.8 (20 C, Ph), 84.3 (C-1), 77.2, 75.2, 74.2 (C-3, C-4, C-5), 74.1, 73.5, 72.7 (3 s, 3 × OCH2), 68.2 (C-6), 49.0 (C-2).

Anal. Calcd for C32H24BrN2O5S: C, 55.43; H, 4.43; N, 5.59. Found: C, 55.73; H, 4.49; N, 5.37.

1,3,4,6-Tri-O-benzyl-2-bromo-2-deoxy-a-D-mannopyranosyl-3-bromo-5-hydrazido-1H,1,2,4-triazole (24)

To a stirred solution of 8 (300 mg, 4.6 mmol) in 1,4-dioxane (15 mL), H2NNH2·H2O (0.6 g, 12 mmol) was added at t.r. and stirring was continued for 4–5 h (TLC). Then the mixture was concentrated under reduced pressure and the residue was purified by column chromatography (heptane–EtOAc, 2:1; Rf 0.13) to give 0.25 g (91%) of 24.

1H NMR (250 MHz, CDCl3): δ = 7.46–7.09 (m, 15 H, Ph), 5.77 (dd, 1 H, J1,2 = 1.9 Hz, H-1), 5.23 (dd, 1 H, J1,2 = 1.9 Hz, J3,4 = 3.6 Hz, H-2), 4.84 (d, 1 H, J1,2 = 10.9 Hz, OCH2), 4.78, 4.61 (2 d, 2 H, JHa,Hb = 11.6 Hz, OCH2), 4.56–4.41 (m, 3 H, OCH2), 4.02 (dd, 1 H, J1,2 = 3.7 Hz, J4,5 = 8.5 Hz, H-3), 3.83–3.53 (m, 4 H, J4,5 = 8.5 Hz, H-4), 4.5–3.6 (H-5, H-6a, H-6b).

13C NMR (63 MHz, CDCl3): δ = 159.4 (C-5 triazole), 137.5 (C-3 triazole), 137.6, 137.6, 137.1 (3 × Ne(C6H5)Ph), 128.8, 128.7, 128.6, 128.2, 128.1 (15 C, Ph), 86.0 (C-1), 76.5 (C-3), 74.3 (C-5), 74.0 (C-4), 75.2, 73.7, 71.6 (3 × OCH2), 68.8 (C-6), 48.6 (C-2).

Anal. Calcd for C31H21BrN2O5S: C, 51.73; H, 4.64; N, 10.40. Found: C, 52.21; H, 4.82; N, 10.15.

1,3,4,6-Tri-O-benzyl-2-bromo-2-deoxy-a-erythro-hex-2-enopyranosyl-5-benzylamino-3-bromo-1H,1,2,4-triazole (25)

A solution of 8 (100 mg, 0.14 mmol) in benzylamine (8 mL) was stirred for 8 h at 100 °C, then stirring was continued for 4–5 h at r.t. (TLC). The solution was concentrated under reduced pressure and...
the residue was purified by column chromatography (heptane–
EtOAc–MeOH 1:1:20, V/V/V) and recrystallized from hexane–
EtOAc as a colorless syrup. Prepared from AcCl (0.4 mL) and
anhyd MeOH (16 mL) was stirred on the phosphite reagent.

1-(2-Bromo-2-deoxy-D-mannopyranosyl)-3,5-dibromo-1H-
1,2,4-triazole (27)

A mixture of diastereomers 8 and 9 (400 mg, 0.55 mmol)
in EtOAc–MeOH (1:1, 20 mL), Pd/C (100 mg, 0.09 mmol) was
added under an argon atmosphere. Argon was replaced by 
hydrogen (1 atm) and stirring was continued at r.t. for about
15 h (TLC). The solution was filtered, the residue was washed
and extracted with EtOAc–MeOH (1:1) and the combined solutions 
were concentrated under reduced pressure. The crude product was purified by column chromatography (toluene–
EtOAc–EtOH, 15:1:1) to give 71 mg (60%) of 25.

1H NMR (500 MHz, CDCl3): δ = 7.60–7.13 (20 H, Ph), 6.10 (d, 1
H, J2,2b = 3.1 Hz, H-1), 5.97 (t, 1 H, J2,3 = 5.8 Hz, NH), 5.02 (d, 1
H, J3,4 = 3.2 Hz, H-2), 4.92, 4.83 (2 d, 2 H, J2,9ab = 11.4 Hz,
OCH3), 4.67, 4.49 (2 d, 2 H, J2,9ab = 11.5 Hz, OCH3), 4.46 (d, 1 H,
J9ab,9ac = 12.1 Hz, OCH3), 4.43–4.38 (3 m, 3 H, J9ac,9bc = 5.8 Hz, 
OCH3, NCH), 4.25–4.19 (m, 1 H, J3,4 = 4.4, J4,5 = 5.7 Hz, H-5),
4.07 (d, 1 H, J3,4 = 5.7 Hz, H-4), 3.66 (dd, 1 H, J2,9ab = 5.8, 
J9ab,9ac = 10.3 Hz, H-6a), 3.54 (dd, 1 H, J3,4 = 4.5, J9ab,9bc = 10.3 Hz,
H-6b).

13C NMR (63 MHz, CDCl3): δ = 156.7, 156.5 (C-5 triazole, C-3),
138.9, 137.8, 137.0, 136.1 (4 s, 4 CquatPh), 131.9 (C-3 triazole),
131.1, 129.0, 128.8, 128.7, 128.6, 128.3, 128.2, 127.9, 127.7
(20 C, Ph), 93.8 (C-2), 81.7 (C-1), 74.0 (C-5), 73.8, 73.7, 70.2 (3 s, 
3 C, OCH3), 71.4 (C-4), 68.6 (C-6), 47.6 (NHCH2).


1-(2-Deoxy-a-d-glucopyranosyl)-5-methoxy-1H-
1,2,4-triazole (29)

A mixture of diastereomers 19 and 26 (870 mg, 1.29 mmol) in
EtOAc–MeOH (1:1, 30 mL) was treated with Pd/C in a hydrogen
atmosphere as described for compound 28. Column chromatogra-
phy (toluene–EtOAc–EtOH, 3:1:1; Rf 0.19) gave 198 mg (59%) of 
29 along with two completely deprotected by-products [Rf 0.25
(20 mg) and Rf 0.32 (70 mg)].

1H NMR (250 MHz, CD3OD): δ = 7.56 (s, 1 H, triazole-H), 5.91 (d, 1
H, J2,2b = 6.1 Hz, H-1), 4.56 (dd, 1 H, J2,9ab = 5.5, J9ab,9ac = 8.5,
J9ac,9bc = 11.1 Hz, H-3), 4.09 (s, 3 H, OCH3), 3.74 (dd, 1 H, 
J3,4 = 2.5, J9ab,9bc = 11.9 Hz, H-6a), 3.64 (dd, 1 H, J1,2a = 4.8,
J2a,3 = 1.6 Hz, H-5), 3.41–3.33 (m, 1 H, H-4), 3.40 (dd, 1 H, 
J3,4 = 1.0, J9ac,9bc = 5.6, J9ab,9ac = 13.7 Hz, H-2a), 2.02 (dd, 1 H, 
J2,9ab = 6.2, J9ab,9bc = 11.1, J2a,3 = 13.7 Hz, H-2b).

13C NMR (63 MHz, CD3OD): δ = 161.1 (C-5 triazole), 148.1 (C-3 triazole),
80.0 (C-1), 76.6, 72.9, 70.0 (C-3, C-4, C-5), 62.6 (C-6),
59.1 (OCH3), 36.4 (C-2).

Acknowledgment

We are grateful to Doz. Dr. Arno Balszuweit for helpful discussions
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References

(2) Becker, H. G. O.; Eisenschmidt, V.; Bubig, M.; Jähnisch, K.; 
Klein, N.; Kowalski, W.; Misselwitz, R.; Müller, R.; 
Reimann, P.; Roth, C.; Sauter, W.-D.; Schößler, W.; 
Thorein, B. Z. Chem. 1969, 9, 325.
(3) Unlike 3,5-dibromo-1,2,4-triazole itself, which is 
deprotonated and so deactivated by sodium hydroxide, the corresponding N-alkyl derivative reacts with this reagent via
3-bromo-5-hydroxy-1-methyl-1,2,4-triazole to the 
tautomeric 3-bromo-1-methyl-1,2,4-triazolone-(5). The 
reaction stops at this stage, because the 3-bromo-1-methyl-
1,2,4-triazolone-(5) is now likewise deactivated by 
de protonation: Miethchen, R.; Kröger, C.-F. unpublished 
results.
(4) The data reported for nucleophilic substitutions on 3,5-
dibromo-1,2,4-triazole with alkali hydroxides and alkoxides 
in following patent are not correct: Becker, H. G. O.; 
Eisenschmidt, V.; Wehner, K. Ger. Pat. DD 19670415, 

(23) The use of solvents like CHCl₃ and NMP gave only low yields of the desired compounds. THF proved to be unsuitable, because it was attacked by 1,3,5-tribromo-1,2,4-triazole (1) resulting in ring-opening and insertion of the 1-oxy-tetramethylene chain between the glycosidic position and N-1 of the triazole ring. The diastereomeric O-glycosides (54%) were formed along with about 26% of the desired products: Christiansen, A.; Miethchen, R. unpublished results.
(24) Tribromo derivative 5, EtMgCl/[Fe(acac)]₃ in THF/NMP gave 1-(3,4,6-tri-O-acetyl-2-deoxy-a-D-mannopyranosyl)-3-bromo-1H-1,2,4-triazole along with dibromo compound 13.
(27) Crystallographic data for the structures in this paper have been deposited at the Cambridge Crystallographic Data Centre as supplementary publication nos. CCDC 265777 (11), 265778 (17), 276274 (5), 276275 (6), 276276 (7), 276277 (8), 276278 (13), 276279 (14), and 276280 (30). Copies of these data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44(1223)336033 or e-mail: deposit@ccdc.cam.ac.uk or via www.ccdc.cam.ac.uk/conts/retrieving.html.