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D-RIBOFURANOSYL AZIDES. A DIRECT CONVERSION OF 1-*O*-ACYL-2,3-*O*-ISOPROPYLIDENE-D-RIBOFURANOSE INTO D-RIBOFURANOSYL AZIDES

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ABSTRACT

Reactions of azidotrimethylsilane with 1-*O*-acetyl-2,3,5-tri-*O*-benzoyl-β-D-ribofuranose (**2**), and the 1,5-di-*O*-*p*-nitrobenzoyl and 1,5-di-*O*-acetyl derivatives, **4** and **5** respectively, of 2,3-*O*-isopropylidene-β-D-ribofuranose, in the presence of the Lewis acids aluminum chloride, titanium tetrachloride, or boron trifluoride etherate were studied. All three Lewis acids readily catalyze the quantitative conversion of **2** into its β-D-ribofuranosyl azide, whereas only aluminum chloride is a suitable catalyst for conversion of **4** and **5** into their azides; boron trifluoride etherate is ineffective, and titanium tetrachloride causes partial decomposition. Contrary to the behavior of **2**, which gives only the β azide, **4** and **5** give, in excellent yield, anomeric mixtures of azides in which the β azide preponderates. Although dichloromethane and acetonitrile are appropriate solvents for the reaction of **2**, only acetonitrile is suitable for **4** and **5**, as use of the former results in the co-production of related D-ribofuranosyl chlorides.

INTRODUCTION

Glycosyl azides are valuable in that they are intermediates in the synthesis of 1,2,3-triazole nucleosides[1–3], and can serve as a source (*via* reduction) of glycosylamines which can serve as precursors for the synthesis of pyrimidine nucleosides[4]. In the past, glycosyl azides had been obtained by the action of sodium or silver azide upon glycosyl halides[5–8]. More recently, they have been prepared, from sugars having the anomeric hydroxyl group free, by the action of hydrazoic acid in the presence of triphenylphosphine and diethyl azodicarboxylate[9], or by the action of mesityloxytris(dimethylamino)phosphonium azide on their derived glycosyloxytris(dimethylamino)phosphonium chlorides[10]. At present, the best

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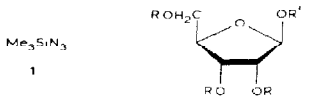
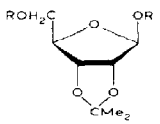
method for the preparation of glycosyl azides appears to be the reaction of 1-*O*-acylated sugars with azidotrimethylsilane (**1**) in the presence of the Lewis acids stannic chloride[11,12] and trimethylsilyl trifluoromethanesulfonate[9]. Although the last method appears to provide the best route to glycosyl azides, it has been applied only to per-*O*-acylated sugars, and, with the exception of 1-*O*-acetyl-2,3,5-tri-*O*-benzoyl-β-D-ribofuranose[9] (**2**) and 1,2,3,5-tetra-*O*-acetyl-β-D-ribofuranose[12] (**3**), these have all been per-*O*-acetylpyranoses[13].



2 R = Bz, R' = Ac
3 R = R' = Ac
Bz = PhCO

Because 2,3-isopropylidene acetals of sugars, especially of ribofuranoses, are used extensively in nucleoside synthesis, a study of their suitability as substrates for reaction with **1** seemed appropriate. We now report on a study of the effect of additional Lewis acid catalysts on the reaction of **2** with **1**, and on the reaction of 2,3-*O*-isopropylidene-1,5-di-*O*-*p*-nitrobenzoyl-β-D-ribofuranose (**4**) and 1,5-di-*O*-acetyl-2,3-*O*-isopropylidene-β-D-ribofuranose (**5**) with **1**. The Lewis acids examined were boron trifluoride etherate, aluminum chloride, titanium tetrachloride, and bromotrimethylsilane.



4 R = $COC_6H_4NO_2$-*p*
5 R = Ac

RESULTS AND DISCUSSION

In contrast to the reaction conditions (3.5 to 24 h at room temperature) previously used for the conversion of **2** and **3** into the corresponding azides by reactions with **1** catalyzed by stannic chloride or trimethylsilyl trifluoromethanesulfonate, we have found that **2** is converted, essentially quantitatively, into 2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl azide (**6**) on treatment with **1** and the catalysts boron trifluoride etherate, aluminum chloride, or titanium tetrachloride in dichloromethane for 10

TABLE I

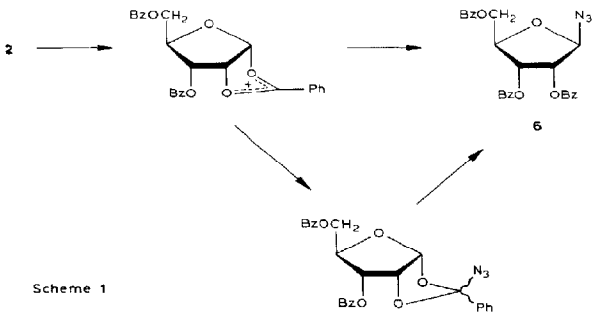
REACTIONS[a] OF **2** WITH **1**

Catalyst	*Solvent*	*Temp. (degrees)*	*Time (min)*	*Yield[b] (%)*
$BF_3 \cdot Et_2O$	CH_2Cl_2	0	10	97
$AlCl_3$	CH_2Cl_2	0	10	98
$TiCl_4$	CH_2Cl_2	0	10	96
$BF_3 \cdot Et_2O$	MeCN	25	30	96
$AlCl_3$	MeCN	25	10	98
$TiCl_4$	MeCN	25	30	95

[a]With 1:1:5 molar ratios of **2**:catalyst:**1**. [b]Isolated yields.

min at 0° (see Table I). Use of the more polar solvent acetonitrile required longer reaction times at higher temperatures to obtain comparable, percent conversions. That **6** does, indeed, possess the β configuration assigned is supported by its n.m.r. spectrum. The observed $J_{1,2}$ value of 1.5 Hz for the H-1 doublet at δ 5.67 is indicative of the β configuration[13]. Because $J_{1,2}$ should be $\leq$1.0 Hz for an unequivocal assignment of the β configuration[13], we converted **6** into its 5-*O*-benzoyl-2,3-*O*-isopropylidene derivative, which should exhibit a smaller $J_{1,2}$ value[14]. The signal of H-1 as a singlet at δ 5.58 in the n.m.r. spectrum of the isopropylidene derivative thus unequivocally established the β configuration of **6**.

Both the exclusive formation of the β anomer **6** and the solvent effect observed can be rationalized by the intermediacy of a benzoxonium ion (see Scheme 1). If **6** is formed by the attack of **1** on the anomeric carbon atom of the benzoxonium ion, which is formed by the action of Lewis acids on **2**, the β azide must be formed, as only the β face of the benzoxonium ion is open to attack by **1**. Alternatively, the benzoxonium ion could react with **1** at the benzylic carbon atom, to form an azido orthoester derivative, which could then undergo an acid-catalyzed

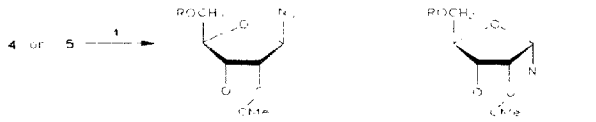


Scheme 1

rearrangement to **6**. Similar, mechanistic alternatives have been suggested for the stereoselective β-glycosylation of alcohols by **2** in the presence of stannic chloride[15], and azido orthoester derivatives of 1,2-glycols are known to undergo stereoselective, thermal isomerizations to the corresponding 1,2-azido esters[16]. The solvent effect observed in going from dichloromethane to acetonitrile is, most probably, a manifestation of (*1*) a weakening of the acid strengths of the catalysts due to their greater extent of solvation by the more-polar acetonitrile, (*2*) an increased stability of the benzoxonium ion in acetonitrile, or (*3*) a combination of both of these effects.

The use of boron trifluoride etherate, aluminum chloride, or titanium tetrachloride requires, as with stannic chloride, one equivalent of the catalyst, and its removal by aqueous processing at the end of the reaction. Because of the necessity of an aqueous work-up with these Lewis acids, we tried bromotrimethylsilane as a Lewis acid catalyst for the reaction, as its low boiling point would allow its removal, along with the other volatile reagents, during evaporation of solvent. Furthermore, as with trimethylsilyl trifluoromethanesulfonate, only catalytic amounts of it should be necessary, as it would be regenerated during the reaction. However, when an equimolar mixture of **2** and bromotrimethylsilane in dichloromethane was heated at reflux for 21 h in the presence of **1**, compound **2** was recovered unchanged.

Having determined that boron trifluoride etherate, aluminum chloride, and titanium tetrachloride are equally effective catalysts for the reaction of **2** with **1**, we examined the feasibility of using the isopropylidenated sugars **4** and **5** as substrates for the reaction. Indeed, **4** and **5** produce azides in excellent yield. However, of the three catalysts effective with **2**, only aluminum chloride is suitable for use with **4** and **5**. Use of titanium tetrachloride results in partial decomposition, to give, in ad-



dition to azides **7**–**10**, unidentified products devoid of isopropylidene groups. On the other hand, **4** and **5** are unreactive towards **1** in the presence of boron trifluoride etherate, both **4** and **5** being recovered in 92% yield. Evidently, boron trifluoride etherate is too weak an acid, under the present conditions, to form an oxonium ion from **4** or **5**, which lack the neighboring-group participation by a 2-*O*-acyl group that is possible for **2**. Furthermore, although dichloromethane and acetonitrile are both suitable solvents for the reaction of **2** with **1**, dichloromethane is unsuitable for the aluminum chloride-catalyzed reactions of **4** and **5**. When the

TABLE II

REACTIONS[a] OF **4** AND **5** WITH **1** AND $AlCl_3$

Substrate	*Temp. (degrees)*	*Time (h)*	*Yield*[b]	
			α anomer	*β anomer*
4	60	3	41.2	51.1
5	55	3	29.8	69.8

[a]With 1:1:5 molar ratios of substrate: $AlCl_3$:**1**. [b]Isolated yields.

latter are conducted in dichloromethane, additional compounds are produced besides azides **7**–**10**. These additional compounds, which can be isolated in up to 43% yield by column chromatography, have been tentatively identified as the corresponding β-D-ribofuranosyl chlorides, on the basis of precipitation of copious amounts of silver chloride on treatment of them with alcoholic silver nitrate, and the presence of singlets in their n.m.r. spectra at chemical shifts intermediate between those for the H-1 signals for the azides and those for **4** or **5**. The D-ribofuranosyl chlorides may also be produced when acetonitrile is the solvent; however, with an upper limit of 8%, they would most probably not survive column chromatography and would therefore escape detection.

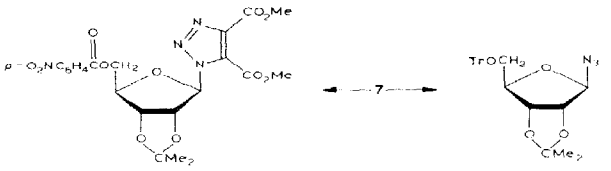
Unlike **2** which produces only the β azide, compounds **4** and **5** react with **1** in the presence of aluminum chloride in acetonitrile to give anomeric mixtures of azides, **7** + **9** and **8** + **10**, respectively (see Table II). The anomeric mixtures can be cleanly separated by column chromatography on silica gel. Structure assignments for the components of the anomeric mixtures were made on the basis of their n.m.r. spectra and specific optical rotations. For the mixture of **7** and **9**, the faster-moving component has a one-proton singlet (H-1) at δ 5.62 in its spectrum, and $[\alpha]_D$ −152.4°, whereas that of the slower-moving component has a one-proton doublet (H-1) at δ 5.13 ($J_{1,2}$ 3 Hz), and the compound has $[\alpha]_D$ −17.0°. Thus, the faster component can be assigned the structure of β anomer **7**, and the slower component, that of α anomer **9**. Similarly, with the mixture of **8** and **10**, the faster-moving component {one-proton singlet (H-1) at δ 5.56, and $[\alpha]_D$ −228.8°} can be assigned the structure of β anomer **8**, and the slower-moving component {one-proton doublet (H-1) at δ 5.06 ($J_{1,2}$ 3 Hz), and $[\alpha]_D$ −16.0°} that of α anomer **10**. Further confirmation of the structural assignments for **7**–**10** was accomplished by the interconversions of **7** and **9** into **8** and **10**, and the conversions of **7** and **9** into their respective triazole derivatives **11** and **13**[†].

Removal of the *p*-nitrobenzoyl groups from **7** and **9** with methanolic ammonia, and acetylation of the resultant deblocked azides with acetic anhydride in

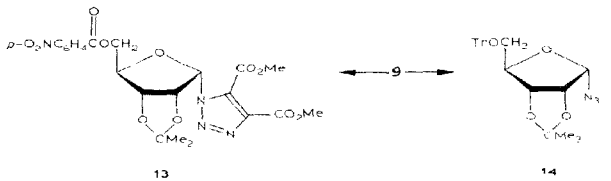
[†]Combustion analyses were then obtained on **11** and **13**, instead of **7**–**10**, because of the labile nature of organic azides.

pyridine gave **8** and **10**, respectively, identical in all respects to **8** and **10** produced by the reaction of **5** with **1**, thus establishing the relationships between **7** and **8**, and **9** and **10**. Azides **7** and **9** were converted into triazoles **11** and **13** in 92 and 89% yield, respectively, on treatment with dimethyl acetylenedicarboxylate for 16 h at 50°. The analytical and spectral data (see Experimental section) for **11** and **13** were in complete agreement with their assigned structures, and corroborated the original assignments for azides **6** and **7**.

Two other groups[10,12] converted 2,3-*O*-isopropylidene-5-*O*-trityl-D-ribofuranose into its glycosyl azide. However, only one anomer was produced, and, in each case, it was assigned the α configuration. Because we had both the β and α anomers, **7** and **9**, we converted them into their 5-*O*-trityl derivatives, **12** and **14**, respectively, in order to compare them to the azide previously assigned the α configuration **14**, and thus unambiguously confirm the configurational assignments. Deacylation of **7** and **9** with methanolic ammonia, followed by tritylation of the product with trityl chloride in pyridine, gave **12** and **14** in 79 and 71% yields, respectively. The n.m.r. spectrum of α anomer **14** was identical to those reported for



11 12



13 14

the azide previously assigned as the α anomer, whereas the n.m.r. spectrum of the β anomer **12** was quite different (an H-1 singlet at δ 5.48 for **12** *versus* an H-1 doublet at δ 5.25, $J_{1,2}$ 4 Hz for **14**). For other striking differences between the n.m.r. spectra of **12** and **14** (*e.g.*, the H-5a and H-5b resonances), see the Experimental section. Thus, the α configuration for the previously prepared **14** is firmly established.

The preponderance of the β anomers **7** and **8** over the α anomers **9** and **10** was to be expected as the isopropylidene group should shield the α faces of the presumed, intermediate oxonium ions from nucleophilic attack by **1**, relative to the β faces. Why **5** should give a higher β/α ratio than does **4** (2.3 *vs.* 1.2) is not readily apparent, but a similar dependence of β/α product-ratios on the nature of 6-*O*-acyl groups during the methanolysis of 6-*O*-acyl-2,3,4-tri-*O*-benzyl-D-glucopyranosyl bromides[22] and 6-*O*-acyltri-*O*-benzyl-1-*O*-*p*-tolylsulfonyl-D-glucopyranoses[23] has been observed. The latter effects are most certainly electronic, rather than steric, in nature, and it is presumed that the same applies in the present case, even though the results cannot yet be rationalized.

In conclusion, we have shown that (*1*) the azidotrimethylsilane route to glycosyl azides is applicable to 2,3-*O*-isopropylidene derivatives of D-ribose, (*2*) aluminum chloride, titanium tetrachloride, and boron trifluoride etherate are suitable alternatives to stannic chloride and trimethylsilyl trifluoromethanesulfonate as catalysts for the reaction of **1** with per-*O*-acylated sugars, and (*3*) the catalyst–solvent combination aluminum chloride–acetonitrile is the most versatile of those examined.

EXPERIMENTAL

General. — Dichloromethane and acetonitrile were dried by distillation from P_2O_5 and stored over 4A molecular sieves. Acetone was distilled from anhydrous $CuSO_4$ before use. Pyridine was dried by adding KOH pellets to freshly opened bottles thereof. All solvents were routinely removed by rotary evaporation at 40°. Melting points were obtained with a Thomas–Hoover capillary m.p. apparatus and are corrected. Optical rotations were measured with a Schmidt and Haensch polarimeter. Elemental analyses were performed by Galbraith Laboratories, Inc. Column chromatography was performed on Silica Gel 60 (E. Merck, 70–230 mesh), and t.l.c. was conducted on plates of Silica Gel 60 having a fluorescent indicator (E. Merck). I.r. spectra were recorded with a Perkin–Elmer Model 137 spectrophotometer. N.m.r. spectra were recorded at 90 MHz with a Varian EM390 spectrometer, with Me_4Si as the internal standard.

2,3,5-Tri-O-benzoyl-β-D-ribofuranosyl azide (**6**). — To 252 mg (0.5 mmol) of 1-*O*-acetyl-2,3,5-tri-*O*-benzoyl-β-D-ribofuranose (**2**) in 3 mL of dichloromethane or acetonitrile was added 0.66 mL (2.5 mol) of azidotrimethylsilane (**1**) and 0.5 mmol of the Lewis acid, with stirring. After the reaction was complete under the conditions given in Table I, the solution was evaporated to dryness. The residue was then treated with water (10 mL) and extracted with chloroform (3 × 30 mL); the combined extracts were evaporated to a syrup which was chromatographed on a short column of silica gel (20 g) with chloroform, to give 231–239 mg (95–98%) of **6** as a homogeneous syrup; $[\alpha]_D^{25}$ −47.5° (*c* 3.11, $CHCl_3$) (lit.[5b] $[\alpha]_D^{22}$ −41.2° in $CHCl_3$); $\nu_{max}^{CHCl_3}$ 2150 cm^{-1} (N_3); n.m.r. data ($CDCl_3$): δ 4.43–4.92 (m, 3 H, H-4,5a,5b), 5.62 (dd, 1 H, $J_{2,3}$ 5, $J_{1,2}$ 1.5 Hz, H-2), 5.67 (d, 1 H, H-1), 5.85 (dd, 1 H, $J_{3,4}$ 6 Hz, H-3), 7.18–7.68 (m, 9 H, Ar H), and 7.82–8.25 (m, 6 H, Ar H).

5-O-Benzoyl-2,3-O-isopropylidene-β-D-ribofuranosyl azide. — To compound **6** (234 mg, 0.48 mmol) was added methanol (9 mL) presaturated with ammonia, and the solution was stirred for 5 h at 0° and evaporated; a solution of the residue in ethyl acetate was washed successively with small volumes of saturated aqueous $NaHCO_3$ and water, and evaporated, to give a pale-yellow syrup (115 mg). This material was then treated with acetone, 2,2-dimethoxypropane, and perchloric acid according to a procedure for the preparation of 5-*O*-benzoyl-2,3-*O*-isopropylidene-β-D-ribofuranosyl cyanide[17], to give 115 mg (88%) of the title compound as a homogeneous syrup; $[\alpha]_D^{25}$ −165.8° (*c* 3.1, $CHCl_3$); $\nu_{max}^{CHCl_3}$ 2125 cm^{-1} (N_3); n.m.r. data ($CDCl_3$): δ 1.33 and 1.52 (2 s, 6 H, CMe_2), 4.37–4.52 (m, 2 H, H-5a,5b), 4.56 (d, 1 H, $J_{2,3}$ 6 Hz, H-2), 4.65 (m, 1 H, H-4), 4.80 (d, 1 H, $J_{3,4}$ <1 Hz, H-3), 5.58 (s, 1 H, H-1), 7.28–7.72 (m, 3 H, Ar H), and 8.03–8.22 (m, 2 H, Ar H).

2,3-O-Isopropylidene-5-O-(p-nitrobenzoyl)-β- and -α-D-ribofuranosyl azides (**7** *and* **9**). — To 2,3-*O*-isopropylidene-1,5-di-*O*-(*p*-nitrobenzoyl)-β-D-ribofuranose[18] (**4**; 244 mg, 0.5 mmol) in acetonitrile (3 mL) were added **1** (0.66 mL, 2.5 mmol) and aluminum chloride (67 mg, 0.5 mmol). The mixture was heated at 55°, with stirring, and the reaction was monitored by n.m.r. spectroscopy. After 3 h, the reaction was complete, and the solvent was evaporated. The residue was treated with water (10 mL) and extracted with chloroform (3 × 30 mL). The extracts were combined and evaporated, and the residue was chromatographed on a column (1.5 × 40 cm) of silica gel with 1:1 (v/v) petroleum ether (b.p. 30–60°)–diethyl ether, to give 93 mg (51.5%) of crystalline β anomer **7**; m.p. 117–118°, $[\alpha]_D^{25}$ −152.4° (*c* 9.56, $CHCl_3$); $\nu_{max}^{CHCl_3}$ 2125 cm^{-1} (N_3); n.m.r. data ($CDCl_3$): δ 1.33 and 1.55 (2 s, 6 H, CMe_2), 4.40–4.72 (m, 4 H, H-2,4,5a,5b), 4.80 (d, 1 H, $J_{2,3}$ 6, $J_{3,4}$ <0.5 Hz, H-3), 5.62 (s, 1 H, H-1), 8.32 (s, 4 H, Ar H); and 75 mg (41.2%) of α anomer **9**; m.p. 132–133°, $[\alpha]_D^{25}$ −17.0° (*c* 2.8, $CHCl_3$); $\nu_{max}^{CHCl_3}$ 2100 cm^{-1} (N_3); n.m.r. data ($CDCl_3$): δ 1.37 and 1.63 (2 s, 6 H, CMe_2), 4.43–5.03 (m, 5 H, H-2,3,4,5a,5b), 5.13 (d, 1 H, $J_{1,2}$ 3 Hz, H-1), and 8.15–8.40 (m, 4 H, Ar H).

1,5-Di-O-acetyl-2,3-O-isopropylidene-β-D-ribofuranose (**5**) was prepared from 2,3-*O*-isopropylidene-D-ribofuranose[19] essentially as reported[20]. However, we did not detect any of the α anomer of **5**, which was previously found (~5%) in addition to **5**. Pure **5** was isolated in 95% yield as a homogeneous syrup; n.m.r. data ($CDCl_3$): δ 1.33 and 1.50 (2 s, 6 H, CMe_2), 2.07 and 2.10 (2 s, 6 H, 2 OAc), 4.08 and 4.10 (overlapping doublets, 2 H, $J_{4,5a}$ 6, $J_{4,5b}$ 8 Hz, H-5a,5b), 4.42 (dd, 1 H, H-4), 4.75 (s, 2 H, H-2,3), and 6.26 (s, 1 H, H-1).

5-O-Acetyl-2,3-O-isopropylidene-β- and -α-D-ribofuranosyl azide (**8** *and* **10**). — Treatment of **5** with **1** according to the procedure used for **4** gave β anomer **8** and α anomer **10** as homogeneous syrups in 69.8 and 29.8% yield, respectively.

For **8**: $[\alpha]_D^{25}$ −228.8° (*c* 5.44, $CHCl_3$); $\nu_{max}^{CHCl_3}$ 2100 cm^{-1}; n.m.r. data ($CDCl_3$): δ 1.33 and 1.47 (2 s, 6 H, CMe_2), 2.09 (s, 3 H, OAc), 4.19 and 4.21 (overlapping doublets, 2 H, $J_{4,5a}$ 7, $J_{4,5b}$ 5 Hz, H-5a,5b), 4.48 (td, 1 H, $J_{3,4}$ 1.5 Hz, H-4), 4.51 (d, 1 H, $J_{2,3}$ 6 Hz, H-2), 4.70 (dd, 1 H, H-3), and 5.56 (s, 1 H, H-1).

For **10**: $[\alpha]_D^{25}$ −16° (*c* 3.74, $CHCl_3$); $\nu_{max}^{CHCl_3}$ 2100 cm^{-1} (N_3); n.m.r. data

($CDCl_3$): δ 1.37 and 1.60 (2 s, 6 H, CMe_2), 2.09 (s, 3 H, OAc), 4.20 (d, 2 H, $J_{4,5}$ 4.5 Hz, H-5a,5b), 4.45 (td, 1 H, $J_{3,4}$ 1.5 Hz, H-4), 4.65–4.87 (m, 2 H, H-2,3), and 5.06 (d, 1 H, $J_{1,2}$ 3 Hz, H-1).

1-[2,3-O-Isopropylidene-5-O-(p-nitrobenzoyl)-β-D-ribofuranosyl]-4,5-di-(methoxycarbonyl)-1,2,3-triazole (**11**). — A solution of **7** (93 mg, 0.25 mmol) in dimethyl acetylenedicarboxylate (1 mL) was heated for 16 h at 50° (the infrared band for azide had then disappeared). The excess of the reagent was removed under high vacuum, and the residue was chromatographed on a column (1.5 × 40 cm) of silica gel with 1:1 (v/v) petroleum ether (b.p. 30–60°)–diethyl ether, to give **11** as a homogeneous syrup (119 mg, 92%); $[\alpha]_D^{25}$ −80.2° (*c* 2.2, $CHCl_3$); $\nu_{max}^{CHCl_3}$ 1750 cm^{-1} (CO_2Me); n.m.r. data ($CDCl_3$): δ 1.43 and 1.60 (2 s, 6 H, CMe_2), 3.97 (s, 3 H, OMe), 4.05 (s, 3 H, OMe), 4.32 and 4.34 (overlapping doublets, 2 H, $J_{4,5a'}$ 5, $J_{4,5b'}$ 7.5 Hz, H-5a',5b'), 4.60–4.83 (m, 1 H, H-4'), 5.15 (dd, 1 H, $J_{2',3'}$ 6, $J_{3',4'}$ 3 Hz, H-3'), 5.75 (d, 1 H, H-2'), 6.67 (s, 1 H, H-1'), 8.16 (d, 2 H, J_{AB} 9 Hz, Ar H), and 8.30 (d, 2 H, Ar H).

Anal. Calc. for $C_{21}H_{22}N_4O_{11}$: C, 49.80; H, 4.35; N, 11.07. Found: C, 49.61; H, 4.50; N, 10.93.

1-[2,3-O-Isopropylidene-5-O-(p-nitrobenzoyl)-α-D-ribofuranosyl]-4,5-di-(methoxycarbonyl)-1,2,3-triazole (**13**) was prepared, according to the procedure for **11**, as a homogeneous syrup in 89% yield, 9:1 (v/v) chloroform–ethanol being used as the eluant for column chromatography; $[\alpha]_D^{25}$ −28.5° (*c* 2.6, $CHCl_3$); $\nu_{max}^{CHCl_3}$ 1725 cm^{-1} (CO_2Me); n.m.r. data ($CDCl_3$): δ 1.00 and 1.27 (2 s, 6 H, CMe_2), 4.00 (s, 6 H, 2 OMe), 4.69 and 4.70 (overlapping doublets, 2 H, $J_{4,5a'}$ 4, $J_{4',5b'}$ 5.5 Hz, H-5a',5b'), 4.97 (dd, 1 H, $J_{2',3'}$ 6, $J_{3',4'}$ 3 Hz, H-3'), 5.13–5.33 (m, 2 H, H-2',4'), 6.85 (d, 1 H, $J_{1',2'}$ 5 Hz, H-1'), 8.23 (d, 2 H, J_{AB} 9 Hz, Ar H), and 8.32 (d, 2 H, Ar H).

Anal. Calc. for $C_{21}H_{22}N_4O_{11}$: C, 49.80; H, 4.35; N, 11.07. Found: C, 49.84; H, 4.43; N, 10.92.

2,3-O-*Isopropylidene-5-O-trityl-β-D-ribofuranosyl azide* (**12**). — A solution of **7** (91 mg, 0.25 mmol) in methanol (10 mL) presaturated with ammonia was stirred for 10 h at 0° and evaporated, and the residual syrup was extracted with chloroform (3 × 10 mL). Evaporation of the combined extracts gave 51 mg (95%) of 2,3-*O*-isopropylidene-β-D-ribofuranosyl azide[21] as a homogeneous syrup; $[\alpha]_D^{25}$ −206.5° (*c* 4.46, $CHCl_3$); $\nu_{max}^{CHCl_3}$ 2150 cm^{-1} (N_3); n.m.r. data ($CDCl_3$): δ 1.33 and 1.50 (2 s, 6 H, CMe_2), 3.72 and 3.75 (overlapping doublets, 2 H, $J_{4,5a}$ 4, $J_{4,5b}$ 4.5 Hz, H-5a,5b), 4.42 (t, 1 H, H-4), 4.53 (d, 1 H, $J_{2,3}$ 6 Hz, H-2), 4.79 (dd, 1 H, $J_{3,4}$ <1 Hz, H-3), and 5.55 (s, 1 H, H-1).

A solution of the 5-unprotected azide (54 mg, 0.25 mmol) and trityl chloride (77 mg, 275 mol) in dry pyridine (3 mL) was kept overnight at room temperature with exclusion of atmospheric moisture. The solution was then heated for 1 h at 60°, cooled to room temperature, treated with ice–water (5 mL), and extracted with chloroform (3 × 20 mL). The extracts were combined and evaporated, and the residual syrup was chromatographed on a column (1.5 × 25 cm) of silica gel

with 1:1 (v/v) petroleum ether (b.p. 30–60°)–diethyl ether, to give crystalline **12** (95 mg, 83%); $[\alpha]_D^{25}$ −98.0° (*c* 2.74, $CHCl_3$); $\nu_{max}^{CHCl_3}$ 2113 cm^{-1} (N_3); n.m.r. data ($CDCl_3$): δ 1.27 and 1.47 (2 s, 6 H, CMe_2), 3.25 and 3.27 (overlapping doublets, 2 H, $J_{4,5a}$ 5, $J_{4,5b}$ 7 Hz, H-5a,5b), 4.37 (d, 1 H, $J_{2,3}$ 6 Hz, H-2), 4.50 (m, 1 H, H-4), 4.57 (dd, 1 H, $J_{2,3}$ 6, $J_{3,4}$ <1 Hz, H-3), 5.48 (s, 1 H, H-1), and 7.23–7.60 (m, 15 H, Ar H).

*2,3-O-Isopropylidene-5-O-trityl-α-*D*-ribofuranosyl azide* (**14**). — Treatment of **9** with methanolic ammonia as for **7** gave 2,3-*O*-isopropylidene-α-D-ribofuranosyl azide as a homogeneous syrup in 87% yield; $[\alpha]_D^{25}$ −55.8° (*c* 3.36, $CHCl_3$); $\nu_{max}^{CHCl_3}$ 2150 cm^{-1} (N_3); n.m.r. data ($CDCl_3$): δ 1.38 and 1.62 (2 s, 6 H, CMe_2), 3.55–3.97 (m, 2 H, H-5a,5b), 4.25–4.42 (m, 1 H, H-4), 4.65–4.87 (m, 2 H, H-2,3), and 5.17 (d, 1 H, $J_{1,2}$ 1.5 Hz, H-1).

Tritylation of the 5-unprotected azide produced **14** as a homogeneous syrup in 82% yield; $[\alpha]_D^{25}$ +1.3° (*c* 2.66, $CHCl_3$) (lit.[12] $[\alpha]_D^{23}$ +8° in $CHCl_3$); $\nu_{max}^{CHCl_3}$ 2120 cm^{-1} (N_3); n.m.r. data† ($CDCl_3$): δ 1.32 and 1.57 (2 s, 6 H, CMe_2), 3.13 (dd, 1 H, $J_{5a,5b}$ 10.5, $J_{4,5a}$ 3 Hz, H-5a), 3.43 (dd, 1 H, $J_{4,5b}$ 3.5 Hz, H-5b), 4.30 (br t, 1 H, H-4), 4.65 (dd, 1 H, $J_{2,3}$ 6, $J_{3,4}$ 1 Hz, H-3), 4.82 (dd, 1 H, $J_{1,2}$ 4 Hz, H-2), 5.25 (d, 1 H, H-1), and 7.30 (br s, 15 H, Ar H).

*Acetylation of 2,3-*O*-isopropylidene-β- and -α-*D*-ribofuranosyl azide.* — Acetylation of both 2,3-*O*-isopropylidene-β- and -α-D-ribofuranosyl azide, prepared from **7** and **9**, with acetic anhydride in pyridine produced **8** and **10**, identical in all respects with **8** and **10** produced by the action of **1** on **5**.

Treatment of **4** *and* **5** *with boron trifluoride etherate.* — Treatment of both **4** and **5** with **1**, in either dichloromethane or acetonitrile, in the presence of boron trifluoride etherate, according to the procedure used for **2**, resulted in a 92% recovery of **4** and **5**. None of the corresponding azides were detected.

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†Essentially identical to those previously reported[12].

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