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STUDIES ON ANHYDRO-OSAZONES. STRUCTURE AND ANOMERIC CONFIGURATION OF THE 3,6-ANHYDRO-OSAZONE DERIVATIVES OBTAINED FROM D-*galacto*-2-HEPTULOSE PHENYLOSAZONE

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ABSTRACT

Dehydration of D-*galacto*-2-heptulose phenylosazone with methanolic sulfuric acid afforded two 3,6-anhydro-osazone derivatives (**2** and **3**). Compound **2** was obtained as the preponderant isomer, without inversion at C-1 (C-3 of the starting osazone), and **3** was obtained with inversion. The anomeric configurations of **2** and **3** were determined by n.m.r. spectroscopy. Refluxing of **2** and **3** with copper sulfate afforded two *C*-nucleoside analogs, namely, 4-β- and 4-α-D-lyxofuranosyl-2-phenyl-1,2,3-triazole, **4** and **5**, respectively. The anomeric configurations of **4** and **5** were determined by n.m.r. and c.d. spectroscopy. Acetylation of **4** and **5** afforded the tri-*O*-acetyl derivatives. The mass spectra of these compounds were discussed.

INTRODUCTION

Monosaccharide 3,6-anhydro-osazones[1–3] are useful precursors for the synthesis of *C*-nucleoside analogs[4] needed for biochemical investigations. They are prepared by dehydrative cyclization of the hydroxyalkyl chain of monosaccharide osazones with methanolic sulfuric acid solution, but have not been extensively used for the synthesis of *C*-nucleosides, because of the uncertainty regarding the anomeric configuration, a matter of considerable importance in the field of nucleosides, as simultaneous formation of both anomers often occurs. The dehydrative cyclization process is stereospecific, and the anomeric configuration of the products is correlated to the configuration of the starting osazones by an empirical rule[5]. Atom C-3 of the 3,6-anhydro-osazone tends to have the same configuration as C-4, irrespective of the configuration of C-3 in the starting osazone. A mechanism for the dehydration process was suggested by El Khadem[6].

In a recent communication[7], a series of 3,6-anhydro-osazone derivatives of higher monosaccharides was studied, and an analogous correlation was observed. Higher monosaccharide osazones having *trans*-3,4-hydroxyl groups produce two anomeric 3,6-anhydro-osazones, the anomer having the bis(hydrazone) group trans to the 4-hydroxyl group preponderating. The present work describes the synthesis and separation of the two 3,6-anhydro-osazone derivatives obtained by

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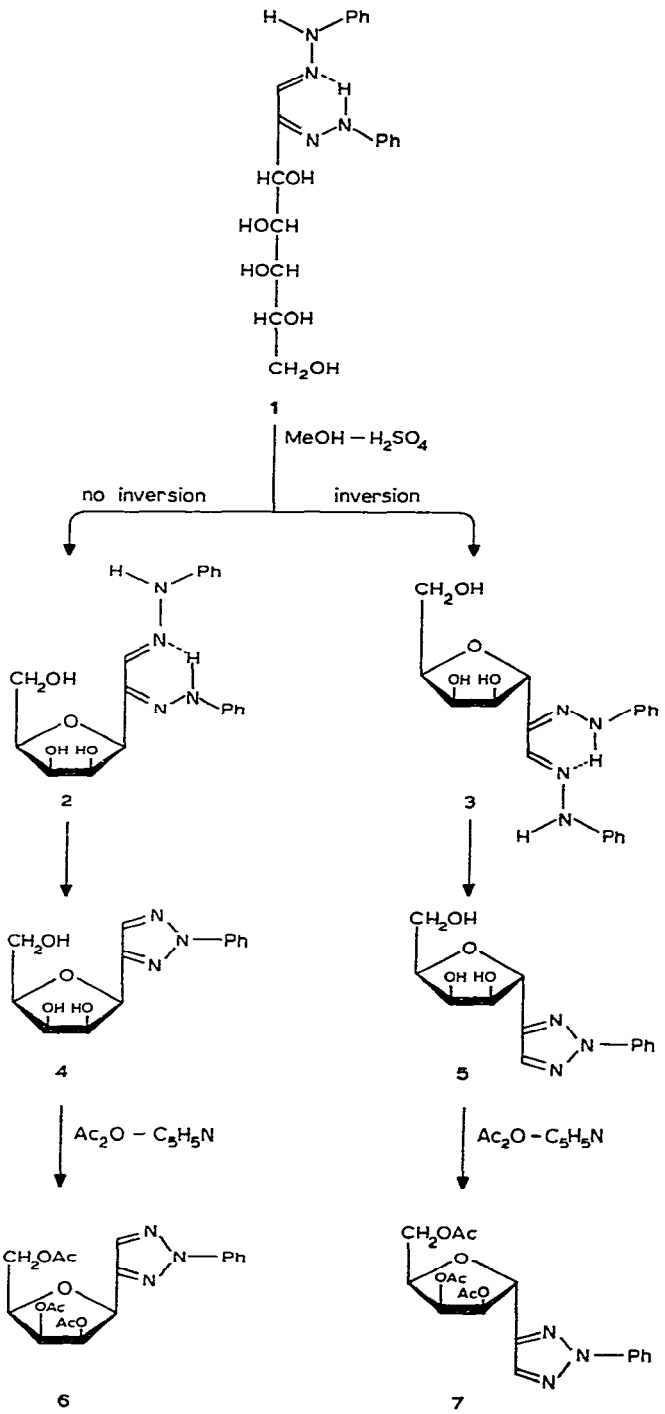


Scheme 1.

dehydrative cyclization of D-*galacto*-heptulose phenylosazone with methanolic sulfuric acid, where the preponderant anomer was the one having the bis(hydrazone) group cis to the 4-hydroxyl group (OH-2 on the furanoid ring).

DISCUSSION

Dehydration of D-*galacto*-2-heptulose phenylosazone by refluxing with methanolic sulfuric acid (with monitoring of the reaction by t.l.c.) afforded 3,6-anhydro-D-*galacto*-2-heptulose phenylosazone (**2**) and 3,6-anhydro-D-*talo*-2-heptulose phenylosazone (**3**) (see Scheme 1) in the ratio of 3:2; they were separated by column chromatography, and purified by fractional recrystallization or by preparative t.l.c. Unlike that of the osazones previously studied, the dehydration of D-*galacto*-2-heptulose phenylosazone afforded more of the anomer having the bis(hydrazone) group cis to OH-4 (OH-2 on the furanoid ring). The formation of two isomers has been explained by racemization at C-3 of the starting osazone at some stage of the reaction, and formation of the 2-phenylazo-2-ene intermediate[6,8], the different ratio of the two isomeric anhydro-phenylosazones depending on the relative stability of the isomers having cis and trans groups on C-3 and C-4.

Circular dichroism (c.d.) spectra of compounds **1**, **2**, and **3** (see Fig. 1) showed a multiple Cotton-effect. The configuration of C-3 of these compounds (C-1 of the aldosyl group formed) is manifested by the sign of the Cotton effect at the long-wavelength absorption[5,9]. As previously observed[5], a positive Cotton-effect indicates the L-*glycero* configuration of C-3, and *vice versa*. Compound **2** showed a positive

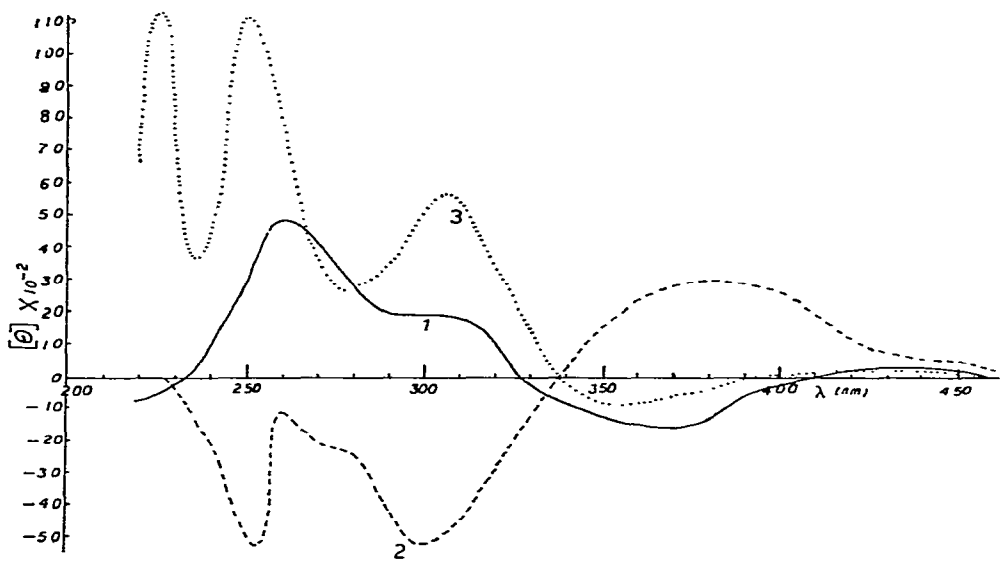


Fig. 1. C.d. spectra of (1) D-*galacto*-heptulose phenylosazone (——), (2) 3,6-anhydro-D-*galacto*-heptulose phenylosazone (– – –), and (3) 3,6-anhydro-D-*talo*-heptulose phenylosazone (····).

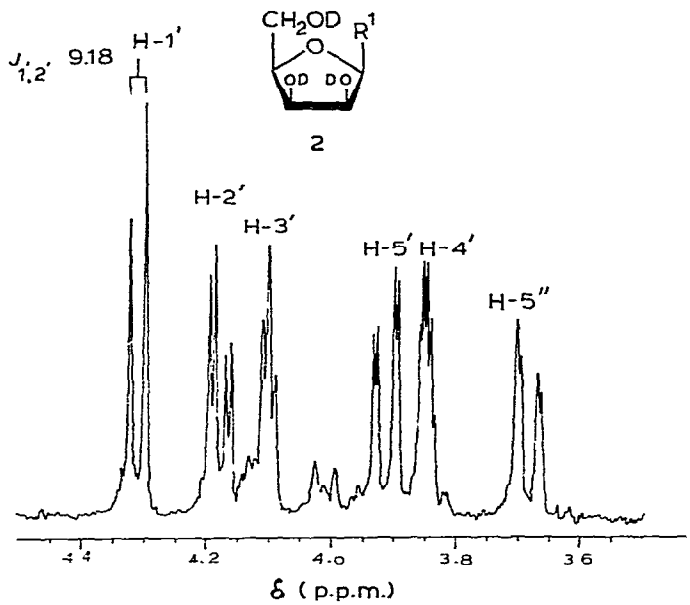


Fig. 2. N.m.r. spectrum, at 360 MHz, of 3,6-anhydro-D-*galacto*-heptulose phenylosazone (**2**) + CD_3CO_2D (high resolution, of the sugar moiety); R^1 = bis(phenylhydrazone) residue.

Cotton-effect at 340–440 nm, opposite in sign to that of the precursor osazone **1**. This suggested the D-*talo* configuration for **2**. On the other hand, compound **3** showed a negative Cotton-effect in the same region, suggesting the D-*galacto* configuration.

These chiroptical results were not consistent with the n.m.r.-spectral results. The high-resolution (360 MHz), n.m.r. spectrum of **2** (see Fig. 2) showed the anomeric proton as a doublet at δ 4.30 ($J_{1',2'}$ 9.18 Hz). This large coupling-constant is consistent[10] with a *cis* arrangement for H-1 and H-2 of a β-D-lyxofuranosyl group. The n.m.r. spectrum (80 MHz) of **3** showed the anomeric proton at δ 4.08 ($J_{1',2'}$ 1.0 Hz), in accord[10] with the trans arrangement of H-1 and H-2 (in an α-D-lyxofuranosyl group).

On being refluxed with copper sulfate, compounds **2** and **3** afforded *C*-nucleoside derivatives, namely, 4-β-D-lyxofuranosyl-2-phenyl-1,2,3-osotriazole (**4**) and 4-α-D-lyxofuranosyl-2-phenyl-1,2,3-osotriazole (**5**), which could readily be separated by fractional recrystallization. Their n.m.r. spectra (see Fig. 3) showed the anomeric proton shifted to lower field, far from the glycosyl protons, which facilitated the assignment of their anomeric configuration. The n.m.r. spectrum of **4** showed the anomeric proton as a doublet at δ 4.65 ($J_{1',2'}$ 9.6 Hz), and that of compound **5** showed the anomeric proton at δ 4.73 ($J_{1',2'}$ 1.1 Hz). Acetylation of **4** and **5** gave the triacetyl derivatives **6** and **7**, respectively. The n.m.r. spectrum of **6** showed the anomeric proton at δ 5.02 ($J_{1',2'}$ 8.4 Hz), and compound **7** showed the anomeric proton at δ 4.97 ($J_{1',2'}$ 1.0 Hz). The large coupling-constants ($J_{1',2'}$) observed for

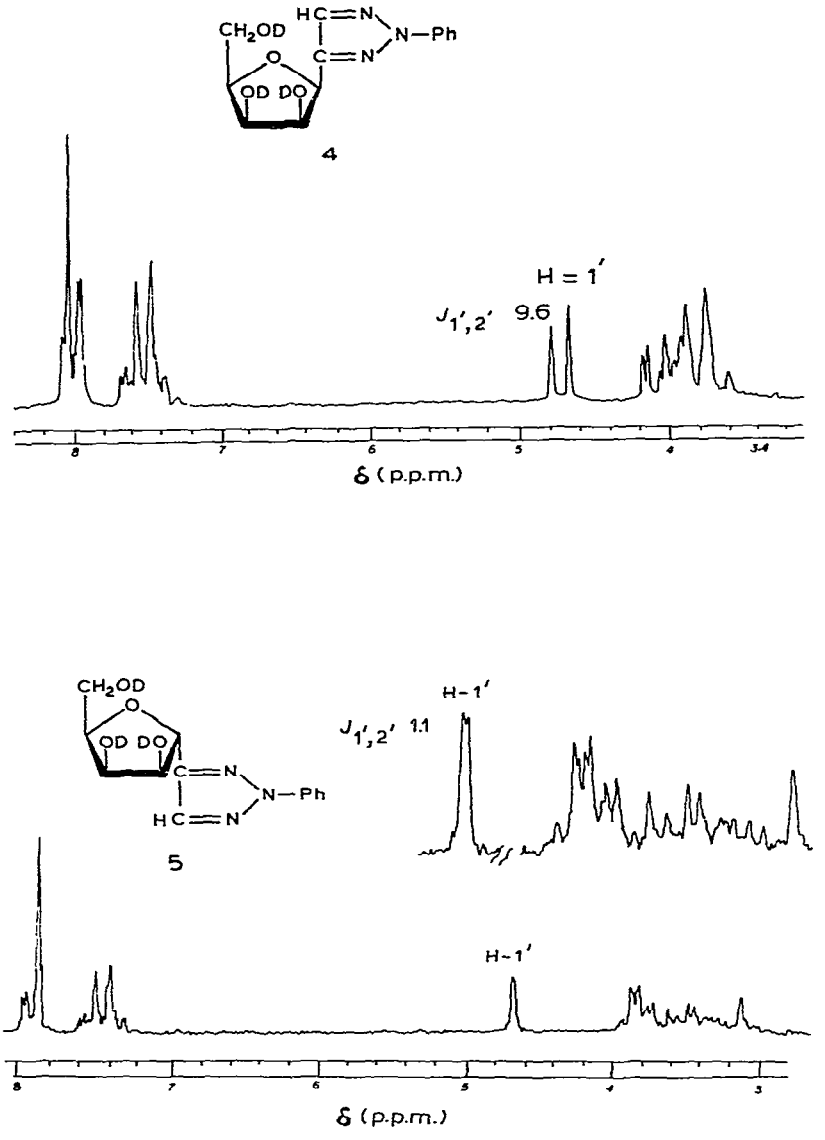


Fig. 3. N.m.r. spectra, at 80 MHz, of 4-β-D-lyxofuranosyl-2-phenyl-1,2,3-osotriazole (**4**), and 4-α-D-lyxofuranosyl-2-phenyl-1,2,3-osotriazole (**5**), after addition of CD_3CO_2D.

compounds **4** and **6** were consistent with the cis arrangement for H-1 and H-2 of the β-D-*lyxo* configuration of the glycosyl group. The small coupling-constant for **5** and **7** were in accord[10] with the trans arrangement for H-1 and H-2 of the α-D-*lyxo* configuration. The anomeric configuration of the *C*-nucleosides can be determined from the chemical shift of the anomeric proton[11–13], which shows the anomeric proton of the *cis*-H-1,H-2 anomer at lower field than that of the corresponding trans anomer. Compounds **4** and **5** showed an opposite relationship. However, the anomeric

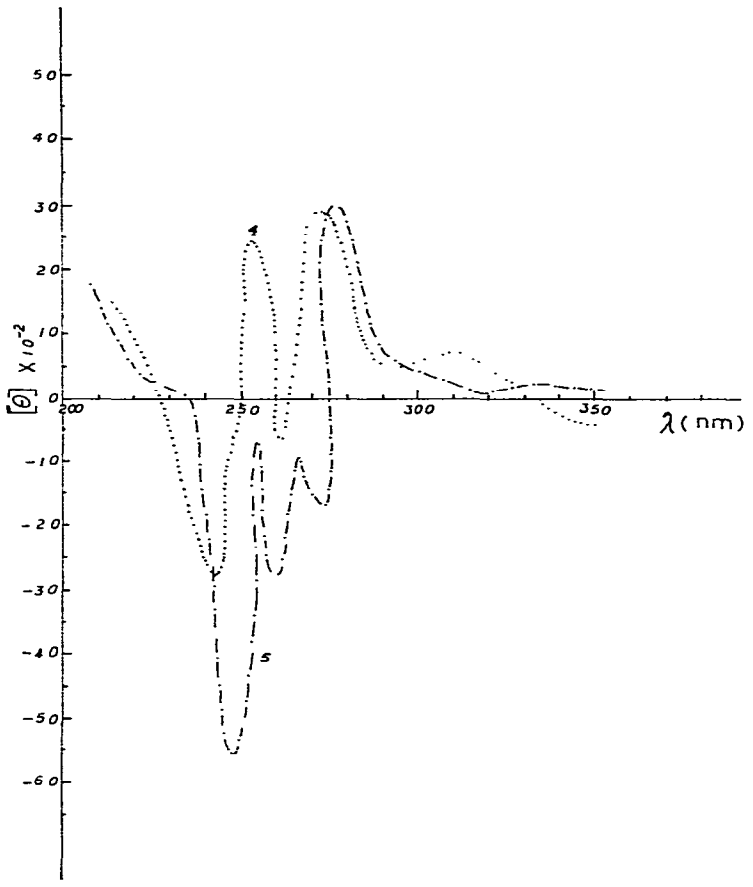


Fig. 4. C.d. spectra of 4-β-D-lyxofuranosyl-2-phenyl-1,2,3-osotriazole (**4**) (····), and 4-α-D-lyxofuranosyl-2-phenyl-1,2,3-osotriazole (**5**) (–·–·–).

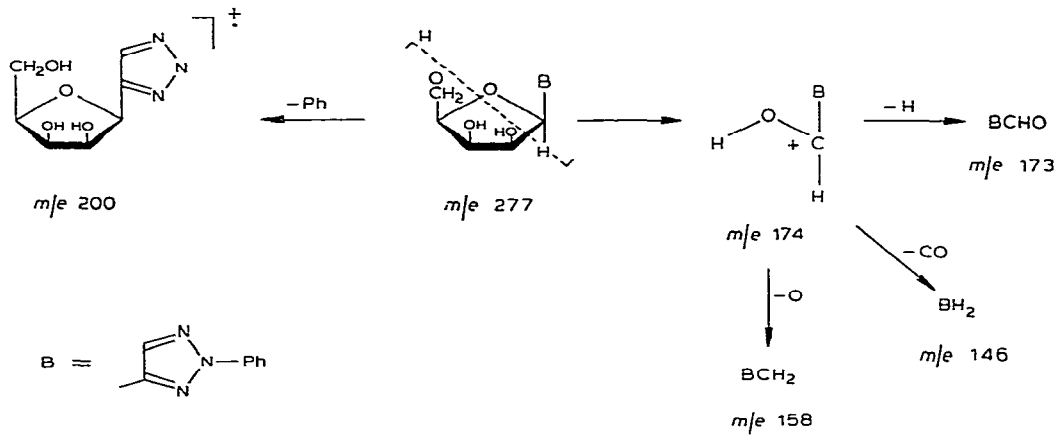
configuration of 2-phenyl-1,2,3-osotriazole *C*-nucleosides can be determined from the chemical shift of H-5 of the triazole moieties[4]. It was found that H-5 of a 1,2,3-osotriazole moiety appears as a sharp, well resolved signal in the aromatic region, at lower field for β-nucleosides than for the corresponding α anomers. Compounds **4** and **6** showed H-5 at δ 8.04 and 7.83, both at lower field than for their anomers, **5** and **7**, which appeared at δ 7.94 and 7.76, respectively. It is evident, therefore, that compounds **6**, **4**, and their 3,6-anhydro-osazone precursor **2** have the β-D-*lyxo* configuration, and that compounds **7**, **5**, and their 3,6-anhydro-osazone precursor **3** have the α-D-*lyxo* configuration, and not the anomeric configuration suggested from the c.d. spectra shown in Fig. 1.

Additional evidence supporting the n.m.r. assignment for the anomeric configuration of **4** and **5** was obtained from their c.d. spectra (see Fig. 4). Compound **4** showed a positive Cotton-effect at 275–250 nm, and compound **5**, a negative Cotton-effect in the same region. C.d. spectra of monosaccharide 2-phenyl-1,2,3-osotri-

azoles[14] having the D-*glycero* configuration of the carbon atom α to the osotriazole ring show a positive Cotton-effect in this region, and those having the L-*glycero* configuration show a negative Cotton-effect. Accordingly, compound **4** was given the D-*glycero* configuration at C-3 (C-1 of the aldosyl group formed), and **5** was given the L-*glycero* configuration. This was consistent with the optical properties at the D-line for compounds **4** and **5**. In accordance with the Hudson isorotation rule[15], compound **5** showed the larger (positive) specific rotation ($[\alpha]_D^{22}$ in methanol: **5**, +51°; **4**, +4.3°). These results strongly support the β-D-*lyxo* configuration for **4**, and the α-D-*lyxo* configuration for **5**. It is therefore evident that the preponderant isomer **2**, formed from **1** without inversion at C-3, is 3,6-anhydro-D-*galacto*-2-heptulose phenylosazone, and compound **3**, formed from **1** with inversion at C-3, is 3,6-anhydro-D-*talo*-2-heptulose phenylosazone (See Scheme 1). The conflicting c.d.-spectral results may be attributed to the mutarotation exhibited by the chelated-ring structure of osazones[16]. Compound **2** showed mutarotation, $[\alpha]_D^{22}$ +52.4 (initial value) → −20.7° (157 h; equilibrium value). It seems that the chiroptical properties of anhydro-osazones should not be used alone for the assignment of anomeric configuration, and must be supported by the n.m.r.-spectral results.

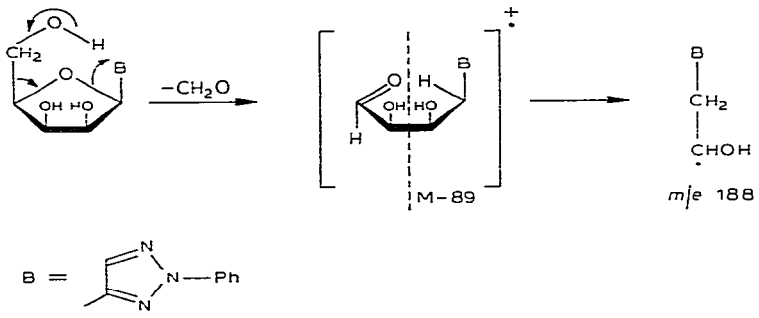
The mass spectra of **2** and **3** were identical, and showed the same type of fragmentation (see Experimental part). However, a little difference in intensity does occur; in particular, the molecular-ion peaks at *m/e* 370, 371, and 372, corresponding to M, M + 1, and M + 2. The base peak at *m/e* 93 corresponds to $PhNH_2$.

The mass spectra of the anomeric 2-phenyl-1,2,3-osotriazole *C*-nucleoside analogs **4** and **5** were studied, and used for the elucidation of the anomeric, carbon–carbon linkage in these compounds. Their mass spectra showed the same type of fragmentation. The molecular-ion peaks appeared at *m/e* 277, 278, and 279, corresponding to M, M + 1, and M + 2, respectively. The base peak appeared at *m/e* 174, which corresponds to the fragment B + 30 ($BCH{=}O^+H$), where B equals the 2-phenyl-1,2,3-osotriazole base moiety; this peak is characteristic for *C*-nucleosides[17,18],



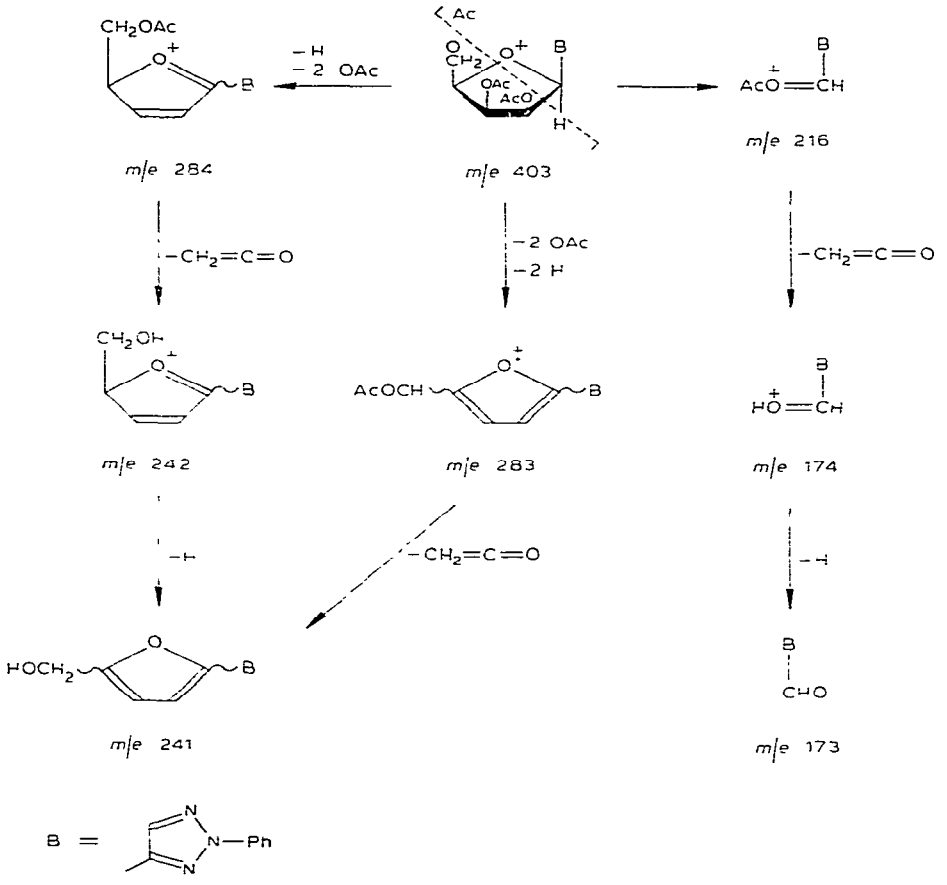
Scheme 2

and usually occurs as the predominant peak. In direct contrast, the predominant peaks for *N*-nucleosides[17,18] are normally B + 1, B + 2, and the glycosyl part. These very weak peaks were found at *m/e* 145, 146, and 133 for compounds **4** and **5**. The base peak at *m/e* 174 represents the triazole base moiety plus a protonated formyl group, which results from the fragmentation of the sugar part into C-1′, the ring-oxygen atom, and a rearranged hydrogen atom as shown in Scheme 2. The presence of this base peak at *m/e* 174, together with the low intensity of the peaks at *m/e* 145, 146, and 133 for compounds **4** and **5**, constitutes strong evidence for the carbon–carbon bond of the glycosyl linkage, which is not ruptured to any major extent under these conditions. The peak at *m/e* 174 may be considered to be M — 103, where M is the molecular weight of the *C*-nucleoside, and is an indication of the presence of a *C*-linked pentosyl structure; this would appear to be general for nucleosides that possess a sugar moiety attached to a heterocyclic base by a C–C bond. Another important peak for recognizing structural features of **4** and **5** appeared at *m/e* 188, corresponding to (M — 89), which retains the base (B), C-1′, and C-2′. A route for its formation is shown in Scheme 3.



Scheme 3

The mass spectra of saccharide phenylosotriazole acetates[19] have been used for determination of the sequence of monosaccharide units in oligosaccharides. The mass spectrum of the *C*-nucleoside triacetate **6** showed a fragmentation pattern characteristic for acetylated *C*-nucleosides[20]: molecular-ion peaks at *m/e* 403, 404, and 405, corresponding to M, M + 1, and M + 2, respectively; and the base peak at *m/e* 43, corresponding to CH_3CO. The peak B + 30, characteristic for *C*-nucleosides, was strong, and appeared at *m/e* 174, but with less intensity than that for compounds **4** and **5**. The peaks at *m/e* 146, 145, and 144, corresponding to B + 2, B + 1, and B, were very weak, indicating that fission of the carbon–carbon linkage between the base moiety and the glycosyl acetate part, is not favored. A peak at *m/e* 330, corresponding to rupture of the CH_2OAc tail, was also absent. This indicates that rupture at either side of the furanoid ring of *C*-nucleoside acetates is not feasible. The fragmentation pattern is shown in Scheme 4.



Scheme 4

EXPERIMENTAL

General. — Melting points are uncorrected. Evaporations were performed under diminished pressure below 60°. Thin-layer chromatography (t.l.c.) was conducted on silica gel (Kiesel gel G, Merck) with solvent *A*, 3:1 benzene-ethanol; solvent *B*, 2:1:1 benzene–chloroform–ethanol; and solvent *C*, butanone saturated with water. U.v. absorption spectra were recorded with a Cary 17 instrument. Circular dichroism measurements were recorded with a Cary 60 spectropolarimeter, at a dynode voltage not >0.75 kV. N.m.r. spectra were recorded with Varian FT (80 MHz), Varian XL (100 MHz), and NTC (360 MHz) instruments, using tetramethylsilane as the internal, reference standard. Mass spectra were obtained with AEI MS 902 and Dupont MS 21-492B spectrometers. Combustion analyses were performed in the Department of Chemistry, Purdue University.

3,6-Anhydro-D-galacto-*2-heptulose phenylosazone* (**2**). — D-*galacto*-Heptulose

phenylosazone (5 g) was boiled under reflux with 0.05% methanolic sulfuric acid (600 mL) for 6 h, and the reaction was monitored by t.l.c.; after 6 h, t.l.c. (solvent *A*) revealed the absence of the starting osazone and the formation of two more-mobile spots in the ratio of 3:2, having R_F 0.44 and 0.37, respectively (solvent *A*). The solution was poured into hot water, and the methanol was evaporated under diminished pressure. The precipitate obtained was filtered off, washed with water, and dried: yield 3.5 g. The mixture (0.7 g) was purified by chromatography on a column (2 × 50 cm) of silica gel, with solvent *C* as the eluant. The yellow fractions were collected, and, upon concentration, gave yellow needles of **2**; yield 0.3 g. It was recrystallized from dilute methanol, to give chromatographically (t.l.c.) pure, yellow needles, m.p. 234–235°, having R_F 0.44 (solvent *A*), 0.48 (solvent *B*); $[\alpha]_D^{22}$ +52.4 (initial) →−20.7° (157 h, equil.; *c* 0.93, pyridine); ν_{max}^{KBr} 3350 (OH), 3240 (NH), and 1600 cm^{-1} (C=N): n.m.r. data (360 MHz; acetone-d_6): δ 3.642–4.167 (m, 3 OH and 6 sugar protons), 4.260 (d, 1 H, H-1′, $J_{1',2'}$ 9.31 Hz), 6.86–7.39 (m, 10 H, aromatic protons), 7.80–8.02 (d, 1 H, aldimino proton), 9.82 (s, 1 H, nonchelated NH of C-1 hydrazone residue), and 12.38 (s, 1 H, chelated NH of C-2 hydrazone residue). After addition of CD_3CO_2D, the two NH protons and the three OH protons disappeared: δ 3.68 (dd, 1 H, H-5″, $J_{4',5''}$ 1.92, $J_{5',5''}$ 11.92 Hz), 3.832–3.853 (m, 1 H, H-4′), 3.86 (dd, 1 H, H-5′, $J_{4',5'}$ 1.43 Hz), 4.10 (t, 1 H, H-3′, $J_{3',4'}$ 3.44 Hz), 4.174 (dd, 1 H, H-2′, $J_{2',3'}$ 3.01 Hz), and 4.31 (d, 1 H, H-1′, $J_{1',2'}$ 9.12 Hz); mass-spectral data (selected ions): *m/e* 372 (2, M + 2), 371 (16, M + 1), 370 (58, M), 353 (2, M + 1 − H_2O), 352 (M − H_2O), 314(3), 293 (M − Ph), 279 (9, M − PhN), 278 (9, M − PhNH), 264(4), 263 (8, M − PhNHNH), 262 (M − $PhNHNH_2$), 250(5), 249(9), 243(6), 238(5), 237(10), 189(5), 288(28), 187(9), 175(8), 174(25), 173(8), 158(14), 147(5), 146(5), 145(9), 137(6), 129(8), 123(8), 119(13), 112(9), 111(14), 109(10), 108(12), 105(11), 104 (12, PhCNH), 103 (5, PhCN), 99(7), 98(16), 97(28), 96(15), 95(18), 94(19), 93 (100, $PhNH_2$), 92 (61, PhNH), 91 (29, PhN), 85(19), 84(21), 83(31), 82(18), 81(18), 79(10), 78(10, PhH), 77 (56, Ph), 73 (18), 71(31), 70(12), 69(39), 68(12), 67(17), 66(20), 65 (39, cyclopentadiene ion), 61(10), 60(14), 57(57), 56(16), 55(43), 54(10), and 45(17): accurate measurement of the molecular-ion peak: Found 370.1639 (Calc. 370.1635); circular dichroism data in 1,4-dioxane (*c* 0.04 mg/mL) at 22°: 480 ([*θ*] 0), 374 (+3,000), 338 (0), 298 (−5,400), 240 (−2,100), and 230 (−300).

Anal. Calc. for $C_{19}H_{22}N_4O_4$: C, 61.6; H, 6.0; N, 15.1. Found: C, 61.6; H, 5.9; N, 15.4.

3,6-Anhydro-D-talo-*2-heptulose phenylosazone* (**3**). — This compound was isolated as a minor product, by fractional recrystallization, from the mother liquor of **2**, and purified by preparative t.l.c.; R_F 0.37 (solvent *A*), 0.45 (solvent *B*). It was recrystallized from dilute methanol, to give yellow needles, m.p. 249–250°; ν_{max}^{KBr} 3360 (OH), 3230 (NH), 1600 (C=N), 1490, and 730 cm^{-1} (Ph); n.m.r. data (80 MHz: Me_2SO-d_6): δ 3.10–4.00 (m, 8 H, 3 OH and 5 sugar protons), 4.08 (s, 1 H, H-1′), 6.52–6.75 (m, 10 H, aromatic protons), 7.87 (s, 1 H, aldimino proton), 10.70 (s, 1 H, nonchelated NH of C-1 hydrazone residue), and 12.28 (s, 1 H, chelated NH of

C-2 hydrazone residue); after addition of CD_3CO_2D, the NH and OH protons disappeared: δ 3.10–4.00 (m, 5 H, sugar protons), and 4.08 (s, 1 H, H-1', $J_{1',2'}$ 1.0 Hz); mass-spectral data (selected ions): *m/e* 372 (2, M + 2) 371 (11, M + 1), 370 (48, M), 353 (3, M − H_2O − H), 293 (5, M − Ph), 279 (6, M − PhN), 278 (8, M − PhNH), 264(5), 263 (10, M − PhNHNH), 262 (15, M − $PhNHNH_2$), 250(5), 249(8), 237 [10, bis(phenylhydrazone) residue], 188(27), 187(8), 175(7), 174(23), 173(7), 158(14), 147(4), 146(4), 145(8), 129(7), 123(7), 119(13), 111(14), 109(9), 108(11), 105(8), 104 (11, PhCNH), 103 (5, PhCN), 99(7), 98(15), 97(26), 96(12), 95(16), 94(18), 93 (100, $PhNH_2$), 92 (58, PhNH), 91 (27, PhN), 85(19), 84(20), 83(29), 82(17), 81(17), 79(6), 78 (10, PhH), 77 (53, Ph), 73(17), 71(29), 70(14), 69(37), 68(11), 67(17), 66(19), 65(37, cyclopentadiene ion), 61(10), 60(13), 57(49), 56(23), and 55(40); accurate measurement of the molecular-ion peak: Found 370.1640 (Calc. 370.1635); circular dichroism data in 1,4-dioxane (*c* 0.042 mg/mL) at 22°: 448([θ]0), 440 (+300), 390(0), 350(+900), 338(0), 305 (+4,600), 275(+2,600), 250 (+11,309), 240 (+5,000), 225 (+11,300), and 220 (+6,800).

*4-α-*D*-Lyxofuranosyl-2-phenyl-1,2,3-osotriazole* (**5**). — A suspension of a mixture of **2** and **3** (2 g) in water (50 mL) was boiled under reflux with stirring, and a solution of copper sulfate (1.6 g) in water (25 mL) was added dropwise; then 1-propanol (6 mL) was added, and the mixture was boiled for 6 h, cooled, filtered, and the filtrate stirred with Amberlite IR-MB cation–anion-exchange resin. The resin was filtered off, and washed thoroughly with methanol, and the filtrate and washings were combined, and evaporated to a syrup which crystallized from methanol, giving **4**; yield 80 mg. It was recrystallized from methanol, colorless needles, m.p. 204–206°, $[\alpha]_D^{22}$ +51° (*c* 0.4, methanol); ν_{max}^{KBr} 3300, 3400 (OH), 1590 (C=N), and 1490, 740 cm^{-1} (Ph); λ_{max}^{MeOH} 266 nm (log ε 4.3); n.m.r. data (80 MHz, Me_2SO-d_6 + CD_3CO_2D): δ 3.11–3.66 (m, 3 H, H-4',5',5''), 3.79 (m, 1 H, H-3'), 3.89 (dd, 1 H, H-2', $J_{2',3'}$ 3.2 Hz), 4.73 (d, 1 H, H-1', $J_{1',2'}$ 1.1 Hz), 7.36–7.68 (m, 3 H, meta and para protons of the phenyl group), 7.92–8.06 (m, 2 H, ortho protons of the phenyl group), and 7.94 (s, 1 H, H-5); mass-spectral data: *m/e* 279 (1, M + 2), 278 (5, M + 1), 277 (33, M), 188 (3, M − 89), 175 (16, B + 31), 174 (100, BCH=O$^+$H, where B = 2-phenyl-1,2,3-osotriazole moiety), 173 (5, BCHO), 159 (5), 158 (13, BCH_2), 146 (0.3, BH_2), 145 (0.2, BH), 144 (0.2, B), 118 (1, B − CN), 117 (1, B − HCN), 93 (1.3, $PhNH_2$), 92 (5, PhNH), 91 (13, PhN), 77 (10, Ph), 65(3), 60(13), 57(4), and 43(6); accurate measurement of the molecular-ion peak: Found 277.1063 (Calc. 277.1063); circular dichroism in methanol (*c* 0.07 mg/mL) at 22°: 350([θ]+150), 330 (+150), 320(0), 276(+3,000), 275(0), 272(−1,950), 268(−750), 260(−2,850), 248 (−5,700), 238(0), and 210(+1,500).

Anal. Calc. for $C_{13}H_{15}N_3O_4$: C, 56.30; H, 5.46; N, 15.16. Found: C, 56.53; H, 5.56; N, 15.04.

*4-β-*D*-Lyxofuranosyl-2-phenyl-1,2,3-osotriazole* (**4**). — (*a*) This compound was isolated, by fractional recrystallization, from the mother liquor of **5**; yield 125 mg. It was recrystallized from butanone–hexane: colorless needles, m.p. 125–126°, $[\alpha]_D^{22}$ +4.3° (*c* 2.4, methanol); ν_{max}^{KBr} 3300 (OH), 1590 (C=N), 1490, and 745 cm^{-1}

(Ph); λ_{max}^{MeOH} 265 nm (log ε 4.4); n.m.r. data (80 MHz, Me_2SO-d_6); δ 3.44–4.07 (m, 5 H, sugar protons), 4.64 (d, 2 H, H-1′ and OH), 4.99 (broad s, 2 H, 2 OH), 7.30–7.68 (m, 3 H, meta and para protons of the phenyl group), 7.95–8.07 (m, 2 H, ortho protons of the phenyl group), and 8.04 (s, 1 H, H-5); after addition of CD_3CO_2D: δ 3.65 (broad s, 2 H, H-5′,5″), 3.78–3.93 (m, 2 H, H-3′,4′), 4.03 (dd, 1 H, H-2′, $J_{2',3'}$ 2.4 Hz), and 4.65 (d, 1 H, H-1′, $J_{1',2'}$ 9.6 Hz); mass-spectral data: *m/e* 279 (1, M + 2), 278 (6, M + 1), 277 (28, M), 188 (5, M − 89), 187(5), 175 (18, B + 31), 174 (100, $BCH{=}O^+H$, where B = 2-phenyl-1,2,3-osotriazole moiety), 173 (2, BCHO), 159(6), 158 (16, BCH_2), 146 (1, BH_2), 145 (0.4, BH), 144 (0.4, B), 133 (0.2, D-lyxofuranosyl part), 118 (2, B − CN), 117 (2, B − HCN), 93 (2, $PhNH_2$), 92 (10, PhNH), 91 (24, PhN), 77 (17, Ph), 65(7), 60(18), 51(8), and 43(8); accurate measurement of the molecular-ion peak: Found 277.1054 (Calc. 277.1062); circular dichroism data in methanol (*c*, 0.47 mg/mL) at 22°: 350 ([θ] − 480), 330(0), 310 [+720 (sh)], 290(+480), 270(+2,880), 263(0), 252(+2,400), 250(0), 242(−2,880), 227(0), and 220(+960).

Anal. Calc. for $C_{13}H_{15}N_3O_4$: C, 56.30; H, 5.45; N, 15.16. Found: C, 56.28; H, 5.56; N, 15.06.

(*b*) Compound **4** was also obtained by refluxing a pure sample of **2** with copper sulfate, and treating as in (*a*): m.p. and mixed m.p. 125°; same R_F as the sample obtained by method (*a*).

*2-Phenyl-4-(2,3,5-tri-*O*-acetyl-β-*D*-lyxofuranosyl)-1,2,3-osotriazole* (**6**). — A solution of **4** (70 mg) in pyridine (2 mL) was treated with acetic anhydride (2 mL), and kept for 24 h at room temperature. The mixture was evaporated to a syrup, and traces of pyridine were removed by repeatedly evaporating with toluene. The dry residue was crystallized from ether–hexane, to give colorless needles, m.p. 131–133°; ν_{max}^{KBr} 1735 cm^{-1} (OAc); n.m.r. data (80 MHz, $CDCl_3$): δ 1.96, 2.16, 2.17 (t, 9 H, 3 CH_3CO), 3.96–4.19 (dd, 2 H, H-5′,5″, $J_{4',5'}$ 2.4, $J_{4',5''}$ 2.6, $J_{5',5''}$ 13 Hz), 4.31–5.07 (m, 2 H, H-1′,4′), 5.47–5.69 (m, 2 H, H-2′,3′); INDOR experiments revealed δ 5.0 (m, H-4′, $J_{3',4'}$ 4.8 Hz), 5.02 (d, H-1′, $J_{1',2'}$ 8.4 Hz), 5.52 (t, H-3′, $J_{2',3'}$ 3.1 Hz), 5.63 (dd, H-2′), 7.14–7.79 (m, 3 H, meta and para protons of the phenyl group), 7.83 (s, 1 H, H-5), and 7.88–8.17 (m, 2 H, ortho protons of the phenyl group); mass-spectral data: *m/e* 405 (0.4, M + 2), 404 (1, M + 1), 403 (2, M), 285 (1, M − 2 Ac), 284 (8, M − H − 2 Ac), 283 (41, M − 2 H − 2 Ac), 259 (0.4, M − B, where B = 2-phenyl-1,2,3-osotriazole moiety), 258 (1, M − H − B), 243 (11, M − 2 Ac − $CH_2{=}C{=}O$), M − 2 Ac − H − $CH_2{=}C{=}O$), 240(8), 187 (7, BCHO), 186 (10, BCO), 185(5), 174 (12, $BCH{=}O^+H$), 158 (4, BCH_2), 146 (0.3, BH_2), 145 (1, BH), 144 (0.4, B), 93 (1, $PhNH_2$), 92 (3, PhNH), 91 (9, PhN), 83 (14), 77 (8, Ph), 47(5), and 43 (100, CH_3CO); accurate measurement of the molecular-ion peak: Found 403.139 (Calc. for $C_{19}H_{21}N_3O_7$, 403.139).

*2-Phenyl-4-(2,3,5-tri-*O*-acetyl-α-*D*-lyxofuranosyl)-1,2,3-osotriazole* (**7**). — Compound **5** (25 mg) was acetylated with pyridine and acetic anhydride as described for **4**. The product was recrystallized from ether–hexane: colorless needles, m.p. 114–115°: ν_{max}^{KBr} 1740 cm^{-1} (OAc); n.m.r. data (100 MHz, $CDCl_3$): δ 2.03, 2.04, 2.08

(t, 9 H, 3 CH_3CO), 3.38–3.59 (m, 1 H, H-5″, $J_{4',5''}$ 10.2 Hz), 4.27–4.43 (m, 1 H, H-5′, $J_{4',5'}$ 5.1 Hz, $J_{5',5''}$ 11.5 Hz), 4.97 (d, 1 H, H-1′, $J_{1',2'}$ 1.0 Hz), 5.16–5.26 (m, 1 H, H-3′), 5.31–5.36 (m, 1 H, H-4′, $J_{3',4'}$ 9.5 Hz), and 5.75–5.78 (dd, 1 H, H-2′, $J_{2',3'}$ 2.8 Hz). The chemical shifts of H-3′ and H-4′, and $J_{3',4'}$, were obtained from INDOR experiments; accurate measurement of the molecular-ion peak: Found 403.139 (Calc. for $C_{19}H_{21}N_3O_7$, 403.139).

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