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The synthesis of 5-*C*-(6-deoxy-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranos-6-yl)-2,3-*O*-isopropylidene-D-*allo*-pentofuranose [deaminotri-*O*-isopropylidene tunicamine]*

Jan Ramza and Aleksander Zamojski†
Institute of Organic Chemistry, Polish Academy of Sciences, 01-224 Warsaw (Poland)

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ABSTRACT

Three approaches to the synthesis of deaminotunicamine and derivatives were developed. Tin tetrachloride condensation of 6-deoxy-1,2:3,4-di-*O*-isopropylidene-α-D-*galacto*-heptodialdo-1,5-pyranose with 2-(trimethylsilyloxy)furan gave a mixture of stereoisomeric precursors. Condensation of 1,2:3,4-di-*O*-isopropylidene-α-D-*galacto*-hexodialdo-1,5-pyranose with the phosphate carbanion obtained from diethyl (2-furyl)methoxymethyl phosphonate led to 6-deoxy-7-*C*-(2-furyl)-1,2:3,4-di-*O*-isopropylidene-L-*glycero*-α-D-galactoheptopyranose (**13**). This was converted, *via* the "$\Delta^{2'}$"-butenolide route, to a mixture of stereoisomeric 5-*C*-(6-deoxy-α-D-galactopyranos-6-yl)-pentono-1,4-lactones of the D-*allo* and D-*talo* configuration. In the third approach, **13** was transformed by the "enulose" approach to deamino-tri-(*O*-isopropylidene)tunicamine.

INTRODUCTION

The unusual carbohydrate constituent of antibiotics belonging to the tunicamycin[1], streptovirudin[2], and corynetoxin[3] families is tunicamine (**1**), a dialdoaminodideoxyundecose. Tunicamine may be viewed as a *C*-disaccharide, *i.e.*, 2-amino-2,6-deoxy-D-galactose linked with its C-6 atom to C-5 of D-*allo*-pentofuranose, which suggests a synthetic approach. In the first synthesis of **1**, Suami and assoc.[4,5] condensed a 2-amino-2-deoxy-D-*galacto*-dialdehyde derivative with a 5-nitro-D-ribofuranose derivative to obtain the 11-carbon atom precursor of tunicamine **2**; deoxygenation at C-6, followed by conversion of the nitro group into a hydroxyl group yielded a derivative of **1**. In the second synthesis of **1**, Danishefsky and Barbachyn[6] condensed the dialdehyde **3** with 1-benzoyloxy-2-(*tert*-butyldimethylsilyloxy)-4-methoxy-1,3-butadiene, to give **4** as the single product. Further steps converted the dihydropyranone part of **4** into the 2-amino-2-deoxy-D-galactose unit, thus successfully accomplishing the synthesis of **1** (*cf.* also ref. 7). In our approach to obtain **1**, the synthesis of deaminotunicamine (**5**) was first attempted starting from 1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose (**8**) and by elongating the carbon atom chain, if possible in a stereoselective way, with a C_5-unit having the D-allofuranose configuration.

* Dedicated to Professor Serge David on the occasion of his 70th birthday.
† To whom correspondence should be addressed.

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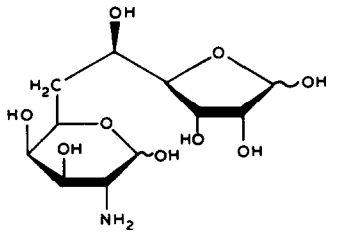

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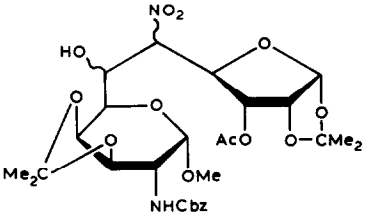

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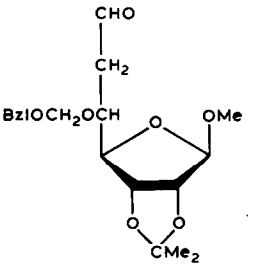

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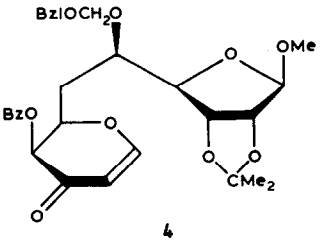

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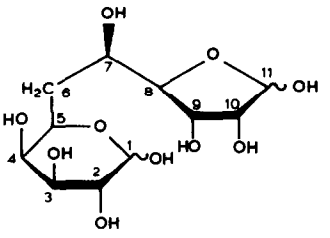
RESULTS AND DISCUSSION

At first, a simple approach to the synthesis of **5** was considered in (a) elongation of the chain of the aldehyde **7** (obtained from **6**) to give the C_7-aldehyde **9**, and (b) an Asaoka–Takei[8]-type condensation of **9** with 2-(trimethylsilyloxy)furan to give **10**. Further steps, *i.e.*, *cis*-hydroxylation of the double bond and reduction of the lactone carbonyl group with diisobutylaluminium hydride, would yield deaminotunicamine (**5**).

Aldehyde **7** was condensed with the ylide obtained from methoxymethyl(diphenyl)phosphine oxide to yield the enol ether **8** in a 1:1 mixture of the *E* and *Z* stereoisomers. Hydrolysis of **8** gave the aldehyde **9** which was condensed with 2-(trimethylsilyloxy)furan at low temperature to yield the desired "Δ^{2}"-butenolide **10** as a mixture of all four diastereoisomers in a 18:14:7:2 proportion. The low stereoselectivity of this reaction and the difficulties in separating the mixture into pure components led us to abandon this pathway. Recently, however, Casiraghi *et al.*[9] found that a similar condensation with 2,3-*O*-isopropylidene-D-glyceraldehyde leads to only two stereoisomeric products in a 21:1 proportion. The low stereodiscrimination observed in our reaction is undoubtedly connected with the reduced, inductive influence of the center of chirality at C-5 of the aldehyde **9**.

In a second approach, aldehyde **7** was condensed with the phosphonate carbanion formed from diethyl (2-furyl)methoxymethyl phosphonate. The enol ether **11** obtained was hydrolyzed to give ketone **12**, which was reduced with potassium tri(*sec*-butyl)borohydride to afford the two stereoisomeric alcohols, **13** and **14**, in ~ 5:1



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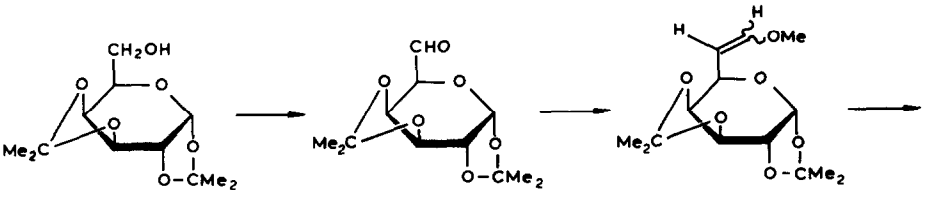

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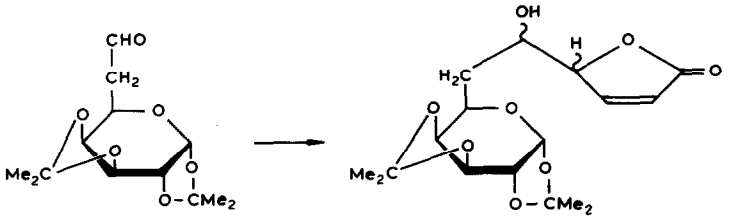

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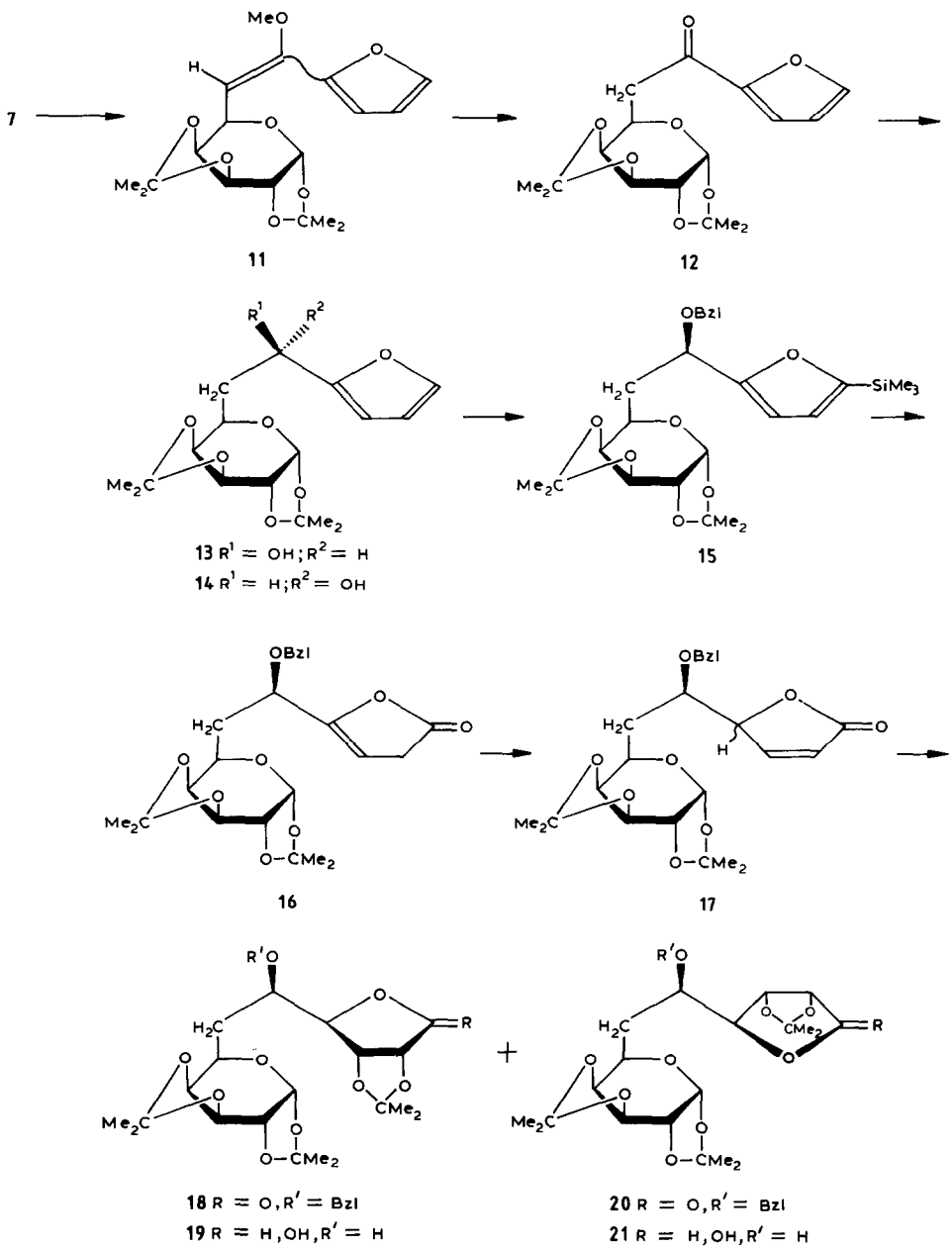
proportion[10]. X-Ray structural determination of the major product **13** indicated the desired *R* configuration[10] at C-7.

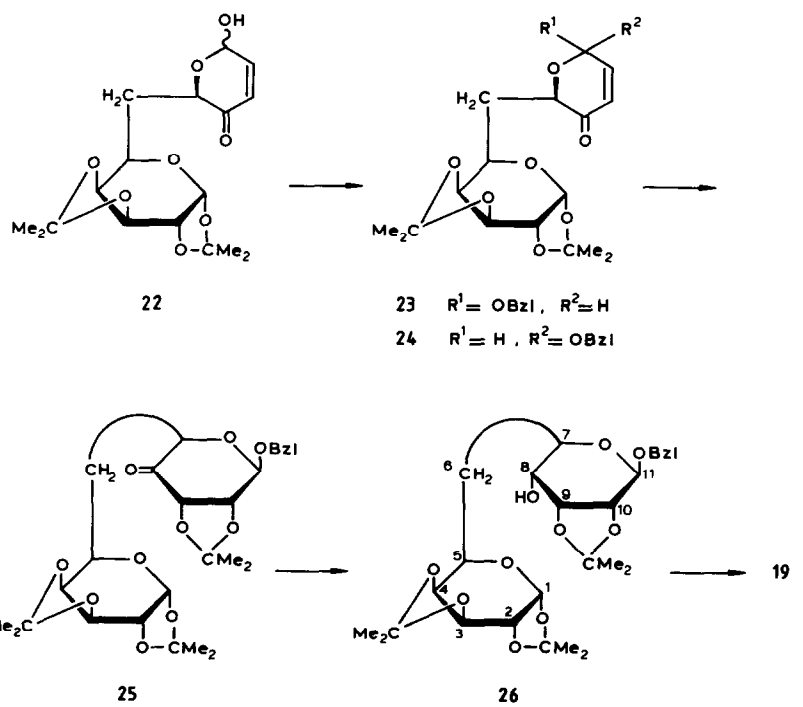
The hydroxyl group of **13** was protected with a benzyl group and C-5 in the furan ring was substituted with a trimethylsilyl group *via* metalation with lithium di(isopropyl)amide, followed by reaction with chlorotrimethylsilane. The resulting compound **15** was oxidized with peroxyacetic acid[11] to give the "Δ^{3}"-butenolide **16**, and isomerization of the double bond with triethylamine led to a mixture of the two stereoisomeric "Δ^{2}"-butenolides **17**. *Cis*-hydroxylation of **17** took place in the configuration *trans* to the C-8 substituent[12] to give the corresponding diols, which were protected with an isopropylidene group. The mixture was separated into the stereoisomeric lactones **18** and **20** obtained in a 1:1 proportion. The *ribo* configuration within the 1,4-lactone ring (from C-8 to C-11) was ascertained by ^{1}H-n.m.r. spectroscopy; $J_{8,9} < 0.5$ and $J_{9,10}$ 5.6 Hz for **18**, and <0.5 and 5.7 Hz for **20**, respectively (*cf.* $J_{3,4}$ 0 and $J_{2,3}$ 6.0 Hz for 5-bromo-5-deoxy-2,3-*O*-isopropylidene-D-ribono-1,4-lactone[13]). Reduction of both



lactones with diisobutylaluminium hydride, followed by hydrogenolysis of the benzyl group, afforded the furanose derivatives **19** and **21**; one of them was the desired deaminotunicamine derivative, but the proof was not convincing. Thus, a third approach to **5** was developed, which omitted the nonstereoselective step of isomerization of **16** into **17**; it was based on the approach by Achmatowicz and Grynkiewicz[14] to the

synthesis of the ribose structure. This method permits the stereochemical introduction of all hydroxyl groups.

Thus, the alcohol **13** was converted with bromine in acetonitrile–water[15] into the enulose **22**. Glycosylation with benzyl bromide and silver oxide gave the *β*- (**23**) and *α*-glycoside (**24**) in a ~ 3:1 proportion. After separation, **23** was *cis*-hydroxylated to afford a single diol having both hydroxyl groups in *trans* configuration to the anomeric benzyloxy group. Isopropylidenation led to **25**, and sodium borohydride reduction of the ketone group gave the alcohol **26**, which has the required L-*allo* configuration (from C-10 to C-7), and debenzylation deprotected anomeric OH-11. Systems of this type may undergo a pyranose-to-furanose rearrangement, which results most probably from the lower, steric strain in the 2,3-*O*-isopropylidenefuranose structure, as compared to the 2,3-*O*-isopropylidenepyranose structure. Molecular modeling[17] of 6,7-dideoxy-2,3-*O*-isopropylidene-*β*-D-*allo*-hepto-furanose and -pyranose, has shown that the energy of the optimized conformation of the former is ~ 1 4 k*J* lower than that of the latter compound. Indeed, after hydrogenation, **26** spontaneously rearranged into the furanose form to yield **19**. Hydrogenation of **19** and **21** led to OH-7 free compounds: the one obtained from **19** was identical (t.l.c. and i.r. spectrum) with tri-*O*-isopropylidenedeaminotunicamine. Thus, the third synthetic route gave **19** from **7** in nine steps and a 6.4% overall yield.



EXPERIMENTAL

General methods. — Optical rotations were measured with a Jasco DIP-360 automatic polarimeter at 20 ± 2°. ^{1}H-N.m.r. spectra were recorded with a Bruker AM-500 (500 MHz) or Varian Gemini 200 (200 MHz) spectrometer for solutions in $CDCl_3$ (internal Me_4Si). T.l.c. was performed on aluminium plates precoated with silica gel (Merck) and column chromatography on silica gel (40–63 μ, Merck).

2-(Trimethylsilyloxy)furan was obtained from 2-buten-4-olide and chlorotrimethylsilane[18]. Diethyl (2-furyl)methoxymethylphosphonate was obtained by methylation (methyl iodide and Ag_2O in dichloromethane) of diethyl (2-furyl)hydroxymethylphosphonate[19] in 85% yield; ^{1}H-n.m.r. (60 MHz): δ 7.5 (s, 1 H, furan H-5), 6.5 (m, 2 H, furan H-3,4), 4.6 [d, 1 H, $J_{H,P}$ 17.0 Hz, (2-Fu)C*H*(OCH_3)], 4.1 (dq, 4 H, OCH_2CH_3), 3.3 (s, 3 H, OCH_3), and 1.2 (t, 6 H, OCH_2CH_3). 1,2:3,4-Di-*O*-isopropylidene-α-D-galactodialdo-1,5-pyranose (**7**) was prepared from 1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose (**6**) by Swern oxidation[20]. Compounds **11**–**14** were obtained as described by Krajewski *et al.*[10]. Replacement of potassium by lithium tri(*sec*-butyl)borohydride in the reduction of ketone **12** gave alcohols **13** and **14** in an improved 5:1 ratio and 78% yield. Reduction of **12** with sodium borohydride or lithium aluminium hydride was nonselective and led to mixtures of **13** and **14** in 72 or 82% yield, respectively. Both alcohols **13** and **14** could also be obtained in a ratio of 5:11 (with **14** preponderant) by condensation of aldehyde **9** with 2-lithiofuran in the presence[21] of $ZnBr_2$.

6-Deoxy-1,2:3,4-di-O-*isopropylidene*-α-D-galacto-*heptodialdo-1,5-pyranose* (**9**). — To a solution of diisopropylamine (0.85 mL, 6 mmol) in dry oxolane (100 mL) under Ar, was added butyllithium (4 mL of a 1.5M solution in hexane) at 0°, and the mixture was stirred for 15 min. Methoxymethyl(diphenyl)phosphine oxide[22] (1.47 g, 6 mmol) was added at 0° and stirring was continued for 30 min. The red solution was cooled to −78°, and a solution of aldehyde **7** (1.5 g, 5.5 mmol) in oxolane (15 mL) was slowly added while stirring. After 15 min, the mixture was allowed to attain room temperature. The mixture was poured into aq. NH_4Cl solution (100 mL) and extracted repeatedly with ether. Combined ether extracts were dried ($MgSO_4$), filtered, and the filtrate was concentrated to dryness. The remaining syrup was dissolved in oxolane (20 mL), NaH (300 mg) was added, and the mixture was stirred at room temperature. After 2 days, the solution was poured into aq. NH_4Cl solution and extracted with ether. The ether extract was dried, filtered, and concentrated to dryness to yield **8** (916 mg, 60%), a 1:1 mixture of *Z* [^{1}H-n.m.r.: δ 6.0 (d, 1 H, $J_{6,7}$ 5.5 Hz, H-7] and *E* [d, 1 H, $J_{6,7}$ 12.5 Hz, H-7] stereoisomers.

Compound **8** was dissolved in 1,4-dioxane (10 mL), and water (2 mL) and pyridinium 4-toluenesulfonate (100 mg) were added. The mixture was refluxed for 1.5 h, and then cooled, poured into water, and extracted with ether. The extract was dried, filtered, and concentrated to dryness. The residue was chromatographed with 4:1 hexane–ethyl acetate to give **11** as a colorless syrup (534 mg, 59%), $[\alpha]_D$ −35° (*c* 0.7, chloroform); ν_{max}^{film} 3010, 1720, and 1070 cm^{-1}; ^{1}H-n.m.r.: δ 8.7 (bs, 1 H, H-7), 5.5 (d, 1 H, $J_{1,2}$ 5.0 Hz, H-1), 4.63 (dd, 1 H, $J_{3,4}$ 7.6 Hz, H-3), 4.33 (dd, 1 H, $J_{2,3}$ 2.5 Hz, H-2), 4.30–4.20

(m, 2 H, H-4,5), 2.7 (m, 2 H, H-6a,6b), 1.57, 1.46, 1.35, and 1.34 (4 s, 12 H, 2 CMe_2).

*7-C-(2-Buten-4-olid-4-yl)-6-deoxy-1,2:3,4-di-O-isopropylidene-*DL-glycero-α-D-galacto-*heptopyranose* (**10**). — A solution of aldehyde **9** (200 mg, 0.73 mmol) in abs. dichloromethane (20 mL) was cooled to −78°, 2-(trimethylsilyloxy)furan (198 mg, 1 mmol) and $ZnCl_2$ (5 mg) were added. The mixture was stirred at this temperature for 1 h, and then was allowed to attain slowly room temperature; t.l.c. showed disappearance of **9** after ~ 3 h. The mixture was poured into diluted $NaHCO_3$ solution and extracted repeatedly with dichloromethane, and the extract was washed with water and dried. Concentration of the solution gave the mixture of diastereoisomers **10** as a thick syrup. Chromatography with 4:1 hexane–ethyl acetate gave two fractions, each containing two products. The first to be eluted was a mixture of **10c** and **10d** (29 mg) in 7:2 ratio (^{1}H-n.m.r.); the second was a mixture of **10a** and **10b** (106 mg) in 6:5 ratio (^{1}H-n.m.r.); overall yield, 52%; ν_{max}^{film} 3600, 1770, 1395, and 1115 cm^{-1}; ^{1}H-n.m.r.: see Table I.

Anal. Calc. for $C_{17}H_{24}O_8$: C, 57.30; H, 6.79. Found: C, 57.07; H, 6.57.

*7-O-Benzyl-6-deoxy-1,2:3,4-di-O-isopropylidene-7-C-(5-trimethylsilyl-2-furyl)-*L-glycero-α-D-galacto-*heptopyranose* (**15**). — To a solution of **13** (3.4 g, 10 mmol) in abs. oxolane (50 mL), cooled to 0°, was added NaH (288 mg, 12 mmol) while stirring. After 30 min, benzyl bromide (2.05 g, 12 mmol) was added and the mixture was stirred at room temperature for 12 h. The solution was poured into saturated NH_4Cl solution (100 mL) and extracted with ether. The ether extract was dried, concentrated to dryness, and the remaining thick oil was purified by chromatography with 4:1 hexane–ether to yield the benzyl ether of **16** (3.74 g, 87%), $[\alpha]_D$ −17° (*c* 0.25, chloroform); ν_{max}^{film} 3010, 1080, and 900 cm^{-1}.

To a solution of the benzyl ether (2.5 g, 5.8 mmol) in absolute oxolane (50 mL), cooled to 0°, was added butyllithium (2.8 mL of a 2.5M solution in oxolane, 7 mmol). The mixture was stirred at this temperature for 1.5 h, chlorotrimethylsilane (0.76 g, 7 mmol) was added, and stirring was continued. After 1 h, t.l.c. showed disappearance of the starting material. The mixture was diluted with saturated NH_4Cl solution (100 mL) and extracted with ether. The extract was dried, filtered, and concentrated to dryness. Column chromatography (9:1 hexane–ether) of the residue gave **15** (2.15 g, 74%), $[\alpha]_D$ −19.5° (*c* 0.2, chloroform); ν_{max}^{film} 3000, 1070, and 900 cm^{-1}.

*7-O-Benzyl-7-C-(but-3-en-4-olid-4-yl)-6-deoxy-1,2:3,4-di-O-isopropylidene-*L-glycero-α-D-galacto-*heptopyranose* (**16**) *and 7-O-benzyl-7-C-(but-2-en-4-olid-4-yl)-6-deoxy-1,2:3,4-di-O-isopropylidene-*L-glycero-α-D-galacto-*heptopyranose* (**17**). — A solution of **15** (200 mg, 0.4 mmol) in dichloromethane (10 mL), cooled to 0°, was treated with 40% peroxyacetic acid (5 mL) and sodium acetate (1 g). The mixture was stirred at 0° for 3 days (until disappearance of the substrate; t.l.c. in 1:1 hexane–ether). The mixture was poured into water and extracted with dichloromethane. The extract was washed with water, dried, and concentrated to dryness (<20°). The residue was immediately chromatographed with 9:1 hexane–acetone to yield **16** (74 mg, 40%), unstable, colorless oil; ^{1}H-n.m.r.: see Table I.

To a solution of **16** in abs. toluene (25 mL) was added triethylamine (0.25 mL), and the mixture was kept at room temperature. After 1 h, the solution was concentrated

TABLE I

^{1}H-N.m.r. data for compounds: **5**, **10**, **12d**, **15–18**, **20**, and **23–26**

Comp.	*H-1* ($J_{1,2}$)	*H-2* ($J_{2,3}$)	*H-3* ($J_{3,4}$)	*H-4* ($J_{4,5}$)	*H-5* ($J_{5,6a}$) ($J_{5,6b}$)	*H-6a* ($J_{6a,7}$)	*H-6b* ($J_{6b,7}$) ($J_{6a,6b}$)
5	5.54 (5.1)	4.32 (2.3)	4.60 (7.9)	4.12 (1.7)	4.09 (10.4) (3.3)	1.97 (3.4)	1.86 (9.4) (14.6)
10a	5.51 (5.0)	4.31 (2.4)	4.61 (7.9)	4.17–4.0[a] [a]	4.17–4.0 [a]	2.01–1.89 [a]	2.01–1.89 [a]
10b	5.53 (5.2)	4.33 (2.4)	4.62 (7.8)	4.17–4.0 [a]	4.17–4.0 [a]	2.01–1.89 [a]	2.01–1.89 [a]
10c	5.51 (5.2)	4.32 (2.4)	4.61 (7.8)	4.16–4.02 [a]	4.16–4.02 [a]	2.05–1.87 [a]	2.05–1.87 [a]
12d	5.50 (5.2)	4.32 (2.4)	4.61 (7.9)	4.16–4.02 [a]	4.16–4.02 [a]	2.05–1.87 [a]	2.05–1.87 [a]
15	5.55 (5.0)	4.29 (2.3)	4.58 (7.9)	4.12 (1.8)	4.18 (10.4) (2.5)	2.17 (2.8)	2.04 (10.9) (14.7)
16	5.55 (5.1)	4.30 (2.4)	4.59 (7.9)	4.11 (1.9)	4.14 (10.2) (2.5)	2.04 (2.7)	1.98 (10.4) (14.6)
17a	5.57 (5.2)	4.32 (2.3)	4.60 (7.9)	4.11–3.98 [a]	4.11–3.98 [a]	1.97 [a]	1.73 [a] (14.6)
17b	5.57 (5.20)	4.31 (2.3)	4.59 (7.8)	4.11–3.98 [a]	4.11–3.98 [a]	1.91 [a]	1.66 [a] (14.4)
18	5.59 (5.3)	4.33 (2.3)	4.62 (7.9)	4.13 (2.0)	3.98 (10.4) (2.5)	1.98 (4.1)	1.80 (8.8) (14.7)
20	5.60 (5.3)	4.33 (2.3)	4.60 (7.9)	4.11 (2.0)	3.90 (4.1) (8.7)	2.08 (10.6)	1.95 (3.0) (14.9)
23	5.56 (5.1)	4.32 (2.3)	4.59 (7.9)	4.02 (1.9)	4.12 (11.0) (2.2)	2.48 (2.45)	1.86 (10.9) (14.8)
24	5.59 (5.2)	4.34 (2.4)	4.63 (7.9)	4.12 (2.0)	4.14 (11.3) (2.4)	2.63 (2.8)	1.67 (11.1) (14.9)
25	5.57 (5.2)	4.34 (2.3)	4.63 (7.9)	4.11 (1.9)	4.14 (11.3) (2.5)	2.42 (2.7)	1.79 (10.9) (15.0)
26	5.57 (5.2)	4.32 (2.2)	4.61 (7.9)	4.14 (1.9)	4.11	2.19	1.95 (15.0)

[a] Not determined.

H-7 ($J_{7,8}$)	*H-8* ($J_{8,9}$)	*H-9* ($J_{9,10}$)	*H-10* ($J_{10,11}$)	*H-11*	*Others*
4.02 (2.0)	4.27 (<0.2)	4.82 (5.9)	4.55 (<0.2)	5.34	1.54, 1.48, 1.46, 1.34, 1.33, 1.31 (3 × CMe_2), 4.91, 3.51 (2 × OH)
4.17–4.0 (4.9)	4.99 (1.6)	7.48 (5.8)	6.19		1.51, 1.45, 1.34, 1.32 (2 × CMe_2)
4.17–4.0 (5.9)	5.05 (1.5)	7.63 (5.8)	6.19		1.52, 1.46, 1.35, 1.33 (2 × CMe_2)
4.16–4.02 (5.2)	5.20 (1.5)	7.72 (5.8)	6.17		1.52, 1.46, 1.35, 1.33 (2 × CMe_2)
4.16–4.02 (5.2)	5.20 (1.5)	7.58 (5.8)	6.17		1.52, 1.47, 1.35, 1.34 (2 × CMe_2)
4.70		6.52 (3.1)	6.23		1.42, 1.41, 1.32, 1.30 (2 × CMe_2) 0.24 ($SiMe_3$), 4.48, 4.42 (AB, q, CH_2Ph)
4.35		5.37 (2.30)	3.17 ($J_{9,10b}$) (1.7)		1.45, 1.39, 1.34, 1.31 (2 × CMe_2) 4.65, 4.57 (AB, q, CH_2Ph)
4.11–3.98 (3.8)	5.12 (1.6)	7.45 (5.8)	6.17 ($J_{8,10a}$) (2.0)		1.46, 1.37, 1.34, 1.31 (2 × CMe_2) 4.75, 4.67 (AB, q, CH_2Ph)
4.11–3.98 (4.6)	5.01 (1.7)	7.39 (5.8)	6.143 ($J_{8,10a}$) (2.0)		1.45, 1.35, 1.34, 1.31 (2 × CMe_2) 4.79, 4.69 (AB, q, CH_2Ph)
4.02 (1.9)	4.61 (<0.2)	4.60 (5.7)	4.72		1.47, 1.45, 1.37, 1.35, 1.33, 1.30 (3 × CMe_2), 4.75, 4.52 (AB, q, CH_2Ph)
3.96 (1.7)	4.52 (<0.2)	4.19 (5.6)	4.55		1.46, 1.41, 1.35, 1.33, 1.29, 1.22 (3 × CMe_2), 4.87, 4.56 (AB, q, CH_2Ph)
4.39		6.16 (10.3)	6.89 (1.7)	5.48 ($J_{9,11}$) (1.6)	1.58, 1.46, 1.34, 1.32 (2 × CMe_2) 4.98, 4.70 (AB, q, CH_2Ph)
4.80		6.10 (10.2)	6.88 (3.6)	5.32 ($J_{9,11}$) (0.2)	1.55, 1.49, 1.36, 1.30 (2 × CMe_2) 5.13, 4.55 (AB, q, CH_2Ph)
4.28		4.42 (7.3)	4.58 (2.0)	4.92	1.55, 1.51, 1.45, 1.39, 1.34, 1.33 (3 × CMe_2), 4.89, 4.75 (AB, q, CH_2Ph)
3.68–3.61 [a]	3.64 (5.6)	4.21 (6.1)	4.16 (2.8)	4.81	1.61, 1.51, 1.46, 1.40, 1.35, 1.32, (3 × CMe_2), 4.95, 4.77 (AB, q, CH_2Ph), 2.74 (OH)

(< 20°) to dryness, and the remaining syrup was purified by chromatography to yield **17** (45 mg, 60%) as a mixture of two stereoisomers; ν_{max}^{film} 1745, 1270, and 1175 cm^{-1}; ^1H-n.m.r. of **17a** and **17b**: see Table I.

Anal. Calc. for $C_{24}H_{30}O_8$: C, 64.56; H, 6.77. Found: C, 64.27; H, 6.84.

5-O-Benzyl-5-C-(6-deoxy-1,2:3,4-di-O-isopropylidene-α-D-galactopyranos-6-yl)-2,3-O-isopropylidene-D-allo-pentano-1,4-lactone (**18**) *and* -D-talo-*pentano-1,4-lactone* (**20**). — To a solution of **17** (16 mg, 0.035 mmol) in dichloromethane (5 mL), cooled to −78°, were added $KMnO_4$ (7 mg) and crown ether 18-C-6 (one crystal), and the mixture was stirred until disappearance of the starting material (12 h, t.l.c. in 1:1 hexane–ethyl acetate). The mixture was diluted with dichloromethane (20 mL) and aq. $Na_2S_2O_3$ (10 mL) was added. The organic layer was dried and concentrated to dryness. The remaining syrup was dissolved in abs. acetone (5 mL) and to the solution were added dimethoxypropane (0.2 mL), 4-toluenesulfonic acid (one crystal), and anhydrous $CuSO_4$ (50 mg); the mixture was stirred at room temperature. After 18 h, the acid was neutralized with triethylamine, the mixture filtered, and the filtrate concentrated to dryness. The residue was chromatographed with 9:1 hexane–ethyl acetate to give first **20** (5 mg, 27.5%), $[\alpha]_D$ +38° (*c* 0.1, chloroform); ν_{max}^{film} 1720 cm^{-1}; ^1H-n.m.r.: see Table I.

The second compound to be eluted was **18** (5 mg, 27.5%), $[\alpha]_D$ +14° (*c* 0.15, chloroform); ν_{max}^{film} 1715 cm^{-1}; ^1H-N.m.r.: see Table I.

Both compounds **18** and **20** were reduced with diisobutylaluminium hydride (1.2 equiv. −78°, toluene solution. The products obtained were hydrogenolyzed in the presence of 5% Pd–C catalyst to afford compounds **19** and **21**, respectively. These compounds were compared by t.l.c. in 1:1 hexane–ether, 1:1 hexane–ethyl acetate, and 5:5:1 hexane–ether–methanol with the tri-*O*-isopropylidene derivative of **5**. Compound **19** was indistinguishable from this derivative, whereas **21** showed spots having different R_F values; the i.r. spectrum of **19** was identical with that of the tri-*O*-isopropylidene derivative of **5**.

Benzyl 5-C-(6-deoxy-1,2:3,4-di-O-isopropylidene-D-galactopyranos-6-yl)-2,3-dideoxy-β- (**23**) *and* -α-D-glycero-*hex-2-enopyranosid-4-ulose* (**24**). — To a solution of **13** (2.5 g, 7.6 mmol) in acetonitrile (50 mL) and water (10 mL), cooled to 0°, was slowly added Br_2 (1.23 g, 7.7 mmol) while stirring. After 10 min, t.l.c. (1:1 hexane–ethyl acetate) showed disappearance of the starting material. The mixture was poured into cold water and extracted thoroughly with ethyl acetate. The extract was dried and concentrated (< 20°) to dryness. Syrupy **22** was dried additionally by azeotropic distillation with toluene (< 20°). The dry product was dissolved in dichloromethane, and AgO (2.7 g, 11.4 mmol) and benzyl bromide (1.95 g, 11.4 mmol) were added, and the mixture was stirred at room temperature in the dark. After 12 h, the mixture was filtered, the filtrate was concentrated, and the residue was chromatographed with 9:1 hexane–ethyl acetate. The first compound to be eluted was **24** (0.57 g, 17%), $[\alpha]_D$ −48° (*c* 0.9, chloroform); ν_{max}^{film} 1705, 1390, and 1070 cm^{-1}; ^1H-n.m.r.: see Table I.

Anal. Calc. for $C_{24}H_{30}O_8 \cdot H_2O$: C, 62.05; H, 6.94. Found: C, 62.05; H, 7.12.

The second compound to be eluted was **23** (1.7 g, 50%), $[\alpha]_D$ −33° (*c* 1.35, chloroform); ν_{max}^{film} 1705, 1390, and 1070 cm^{-1}; ^1H-n.m.r.: see Table I.

Anal. Calc. for $C_{24}H_{30}O_8 \cdot H_2O$: C, 62.05; H, 6.94. Found: C, 62.05; H, 7.04.

*Benzyl 5-C-(6-deoxy-1,2:3,4-di-*O*-isopropylidene-α-*D*-galactopyranos-6-yl)-2,3-*O*-isopropylidene-β-*D*-ribo-pentopyranosid-4-ulose* (**25**). — To a solution of **23** (1.95 g, 4.4 mmol) in oxolane (40 mL) were added $AgClO_3$ (1.01 g, 5.3 mmol), OsO_4 (5 mg), and water (10 mL); the mixture was stirred at room temperature until disappearance of the starting material (48 h: t.l.c. in 1:1 hexane–ethyl acetate). Ethyl acetate (50 mL) was added, and the solution was filtered through a silica gel pad. The filtrate was poured into water and the mixture was extracted with ethyl acetate (3 × 50 mL). Combined extracts were dried, filtered, and concentrated to dryness. The remaining syrup was dissolved in acetone (30 mL), and dimethoxypropane (1 mL), $CuSO_4$ (2 g), and 4-toluenesulfonic acid (15 mg) were added, and the mixture was stirred overnight at room temperature. The acid was neutralized with triethylamine, the mixture filtered, and the filtrate concentrated. The residue was chromatographed with 9:1 hexane–ethyl acetate, to yield **25**, colorless syrup (1.15 g, 50%), $[\alpha]_D$ −15° (*c* 0.15, chloroform); ν_{max}^{film} 1725, 1390, and 1075 cm^{-1}; ^{1}H-n.m.r.: see Table I.

Anal. Calc. for $C_{27}H_{36}O_{10}\cdot 2H_2O$: C, 58.26; H, 7.24. Found: C, 58.74; H, 7.44.

*Benzyl 5-C-(6-deoxy-1,2:3,4-di-*O*-isopropylidene-α-*D*-galactopyranos-6-yl)-2,3-*O*-isopropylidene-β-*D*-allo-pentopyranoside* (**26**). — To a cooled (−78°) solution of **25** (1 g, 1.9 mmol) in oxolane (25 mL), was added $NaBH_4$ (76 mg, 1.2 mol. equiv.). The solution was stirred for 2 h, and then poured into aq. NH_4Cl solution (50 mL) and extracted with ether. The extract was dried, filtered, and concentrated to dryness. The residue was purified by chromatography with 4:1 hexane–ethyl acetate to yield **26**, colorless oil (0.754 g, 76%), $[\alpha]_D$ −59° (*c* 0.55, chloroform); ν_{max}^{film} 3600, 1395, and 1180 cm^{-1}; ^{1}H-n.m.r.; see Table I.

Anal. Calc. for $C_{27}H_{38}O_{10}\cdot H_2O$: C, 59.99; H, 7.46. Found: C, 59.80; H, 7.65.

*5-C-(6-Deoxy-1,2:3,4-di-*O*-isopropylidene-α-*D*-galactopyranos-6-yl)-2,3-*O*-isopropylidene-D-allo-pentofuranose* (**19**). — To a solution of **26** (600 mg, 1.15 mmol) in ethanol (25 mL) was added 5% Pd–C catalyst (200 mg), and the suspension was intensively shaken in an H_2 atmosphere overnight. The suspension was filtered and the filtrate was concentrated to dryness. The residue was purified by chromatography with 2:1 hexane–ethyl acetate to yield **19** (457 mg, 92%), $[\alpha]_D$ −36° (*c* 1.05, chloroform); ν_{max}^{film} 3420, 1395, 1210, and 1080 cm^{-1}; ^{1}H-n.m.r.: see Table I.

Anal. Calc. for $C_{20}H_{32}O_{10}$: C, 55.54; H, 7.46. Found: C, 55.44; H, 8.03.

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