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SYNTHESIS OF DESTOMIC AND *epi*-DESTOMIC ACID, AND THEIR C-6 EPIMERS

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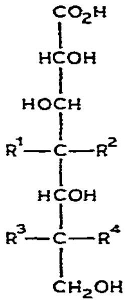
ABSTRACT

Four stereoisomers of 6-amino-6-deoxyheptonic acid, having the L-*glycero*-D-*galacto* (**1**), D-*glycero*-D-*galacto* (**2**), L-*glycero*-D-*gluco* (**3**), and D-*glycero*-D-*gluco* (**4**) configurations, were synthesized from D-*galacto*- (**8**) and D-*gluco*-dialdose (**23**) derivatives, respectively. Cyanomesylation of **8** and **23** gave two C-6 epimers, respectively, which were separately converted, *via* the corresponding 6,7-epimino derivatives, into 6-(benzyloxycarbonyl)amino-6-deoxy derivatives by reduction with lithium aluminum hydride, *N*-(benzyloxycarbonyl)ation, and acetolysis with acetic acid. After deprotection of each hemiacetal, the stereoisomers were oxidized with bromine, followed by total deprotection, to give **1**–**4**. Among these products, **1** and **3** proved to be identical with the naturally occurring destomic and *epi*-destomic acid obtained from antibiotic destomycins.

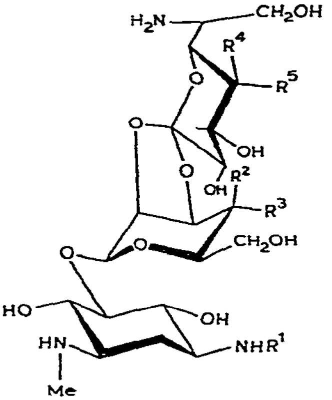
INTRODUCTIONS

Either destomic (**1**) or *epi*-destomic (**3**) acid can be one of the three components of a new type of aminocyclitol antibiotic: destomycin A (**5**) (ref. 1), B (**6**) (refs. 1b and 2), and C (**7**) (ref. 3), hygromycin B (ref. 4), SS-56C (ref. 5), and A-396-I (ref. 6) (SS-56D). These antibiotics show anthelmintic activity, and have unique, structural characteristics in two respects, namely, that (*a*) a deoxystreptamine unit is substituted by only one hexosyl residue, and (*b*) **1** or **3** is linked through an orthoester, *i.e.*, glycosylidene, linkage to the hexose moiety. The structures of **1** and **3** were first elucidated, by chemical conversion into *N*-(2,4-dinitrophenyl)-L-serine, to be (6*S*)-6-amino-6-deoxyheptonic acids[2,7], and later, by the coupling constants in the p.m.r. spectra of **5** and **6**, and the rotational value of the 1,5-lactone derivative of **3**, to have the D-*galacto* and D-*gluco* configuration, respectively[1b,2], for C-2–C-5. Recently, the structure proposed for **1** was confirmed by chemical synthesis, as reported in a preliminary communication[8], and also by X-ray analysis[9] conducted in our research division, where the configuration of the glycosylidene carbon atom was, for the first time, determined to be *R*.

Furthermore, the methods for preparation of glycosylidenediol derivatives, including orthoester-linked disaccharides, were also developed in our laboratory[10,11], and consequently, it should be significant to develop a method for the synthesis of **1** and **3**, and their C-6 epimers (**2** and **4**), not only for structural confirmation, but also for chemical synthesis of destomycin-group antibiotics.



	R^1	R^2	R^3	R^4
1	OH	H	NH_2	H
	(destomic acid)			
2	OH	H	H	NH_2
3	H	OH	NH_2	H
	(*epi*-destomic acid)			
4	H	OH	H	NH_2



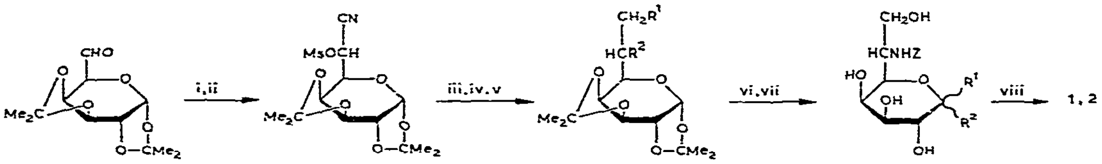
	R^1	R^2	R^3	R^4	R^5
5	H	OH	H	H	OH
6	Me	H	OH	OH	H
7	Me	OH	H	H	OH

RESULTS AND DISCUSSION

Two methods, nitromethane condensation and cyanotosylation, both followed by reduction, and appropriate ring-opening of the resulting 6,7-epimino derivatives, have been reported for the synthesis of 6-aminoheptose derivatives *via* the corresponding dialdoses. Recently, the former method was used in the synthesis of 2,6-diamino-2,3,4,6,7-pentadeoxy-L-*lyxo*-heptose (*epi*-purpurosamine)[12], and the latter, in the preparation of 6-amino-6-deoxy-D-*glycero*-D-*galacto*- and -L-*glycero*-D-*galacto*-heptose derivatives[13] from 1,2:3,4-di-*O*-isopropylidene-D-*galacto*-hexodialdo-1,5-pyranose (**8**), albeit in low yield.

As it was found that cyanomesylation, instead of cyanotosylation, gave an improved yield of the addition products in the case of **8**, this method was also chosen for the synthesis of **1**. The cyanomesylation of **8** was examined by two methods. In the first, a syrupy mixture of the corresponding cyanohydrins, obtained by treatment of **8** with potassium cyanide in methanol–water, was mesylated in pyridine, to afford, in 82% yield, a mixture of the D-*glycero*-D-*galacto*- (**9**) and L-*glycero*-D-*galacto*-heptononitrile (**10**) derivatives in the ratio of 2.8:1, whereas the cyanotosylation of **8** under similar reaction-conditions gave the corresponding products in ~25% yield[13]. In the second (and better) method, **8** was treated with hydrogen cyanide, followed by mesylation in pyridine; this also gave a mixture of **9** and **10**, but in the ratio of 1.7 : 1.0, in quantitative yield. The former compound could be obtained in the pure state by fractional recrystallization, but the latter, only by chromatography on a column of silica gel. For preparative purposes, however, separation of the two epimers is readily achieved, as **12** and **16**, after reduction with lithium aluminum hydride, followed by *N*-(benzyloxycarbonyl)ation.

The configuration of C-6 was determined by chemical conversion of one of the two isomers into an alanine derivative. The minor component, **10**, was reduced with

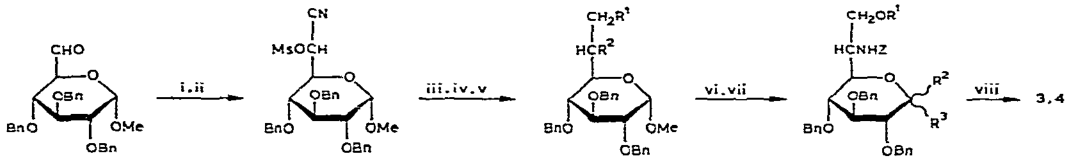


8

9
10 6-epimer of 6

11 R^1, R^2 = NH
12 R^1, R^2 = NZ
13 R^1 = OAc, R^2 = NHZ
14 R^1 = OH, R^2 = NHZ
15 6-epimer of 11
16 6-epimer of 12
17 6-epimer of 13
18 6-epimer of 14

19 R^1 = H, R^2 = OH
20 R^1, R^2 = O
21 6-epimer of 19
22 6-epimer of 20



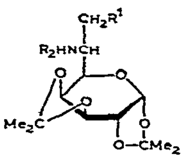
23

24
25 6-epimer of 24

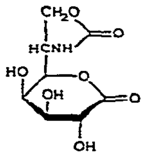
26 R^1, R^2 = NH
27 R^1, R^2 = NZ
28 R^1 = OAc, R^2 = NHZ
29 6-epimer of 26
30 6-epimer of 27
31 6-epimer of 28

32 R^1 = Ac, R^2 = H, R^3 = OAc
33 R^1, R^2 = H, R^3 = OH
34 R^1 = H, R^2, R^3 = O
35 6-epimer of 32
36 6-epimer of 33
37 6-epimer of 34

i, HCN–C_5H_5N or KCN–MeOH–H_2O; ii, MsCl–pyridine; iii, $LiAlH_4$–ether; iv, ZCl, $NaHCO_3$–1,4-dioxane–H_2O (for 11 and 15) or ZCl, Et_3N–benzene (for 26 and 29); v, AcOH; vi, Reaction sequences A for 13 and 17, and B for 28 and 31 (A: 1, MeONa–MeOH, 2, 0.5% H_2SO_4; B: 1, Ac_2O–H_2SO_4, 2, MeONa–MeOH; vii, Br_2–$BaCO_3$–H_2O (for 19 and 21) or Br_2–$BaCO_3$–1 4-dioxane–H_2O (for 33 and 36); viii, H_2–Pd–C–H_2O (for 20 and 22) or H_2–Pd–C–MeOH–H_2O (for 34 and 37).



38 R^1 = H, R^2 = DNP
39 R^1, R^2 = O–C=O



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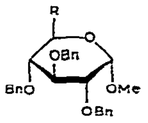
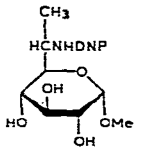


41 R = CH_2OH
42 R = $\underset{\text{MsO–C–H}}{\text{CONH}_2}$



43

Bn = $PhCH_2$, DNP = 2,4-dinitrophenyl,
Ms = methylsulfonyl, Z = $PhCH_2OCO$

lithium aluminum hydride, to afford the 6,7-epimino derivative (**15**), with inversion of configuration of C-6. Then, compound **15** was hydrogenolyzed in the presence of Raney nickel, to give, regioselectively, the 6-amino-6,7-dideoxy derivative, which was converted into the *N*-(2,4-nitrophenyl) derivative (**38**) with fluoro-2,4-dinitrobenzene. The amino acid derivative obtained by *O*-deisopropylidenation of **38** and periodate–permanganate oxidation of the product proved to be *N*-(2,4-dinitrophenyl)-D-alanine from its negative rotational value, indicating that part of the configuration of **10** was L-*glycero*. Therefore, **9** was the D-*glycero* isomer, *i.e.*, an appropriate starting compound for the synthesis of **1**.

Then, **9** was reduced with lithium aluminum hydride, to afford the 6,7-epimino derivative (**11**) in 94% yield. In this step, moisture should be carefully excluded, in order to avoid the epimerization at C-6 mentioned later. The imine **11** was converted, with benzyl chloroformate and sodium hydrogencarbonate in 1,4-dioxane–water, into its *N*-benzyloxycarbonyl derivative (**12**) in 54% yield. The slightly lower yield obtained here may be due to the lower basicity of the epimine, and also to undesired ring-opening with chloride ion formed during the reaction. The acetolysis product (**13**), obtained in quantitative yield by treatment of **12** with acetic acid at 40°, was deacetylated, to give **14** in 86% yield and this was *O*-deisopropylidenated, to afford 6-(benzyloxycarbonyl)amino-6-deoxy-L-*glycero*-D-*galacto*-heptose (**19**) in 82% yield. By bromine oxidation in the presence of barium carbonate, and catalytic reduction of the product in the presence of palladium–charcoal, compound **19** was converted, *via* the aldonolactone (**20**), into the corresponding 6-amino-6-deoxyheptonic acid (**1**) in 63% yield; this was identified as destomic acid by comparison of its physical data and chromatographic behavior with those of the natural product (see Table I).

An alternative oxidation of **19** with potassium hypoiodite[14] gave 6-*N*,7-*O*-carbonyl-6-deoxy-L-*glycero*-D-*galacto*-heptonolactone (**40**) in high yield. Similar

TABLE I

ANALYTICAL DATA FOR SYNTHETIC **1**–**4**, AND FOR DESTOMIC AND *epi*-DESTOMIC ACID

Compound	*M.p.* *(dec.)* *(°C)*	$[\alpha]_D$ (H_2O) *(degrees)*	*Retention time*[a] *(min)*
1	200–210	+4.7 (*c* 2)	127.5
2	203–213	+14.1 (*c* 0.5)	132.0
3	210–215	+17.8 (*c* 1)	140.2
4	111–113	+1.0 (*c* 1)	136.5
Destomic acid	207–209[b]	+1.9 (*c* 2)	127.5
epi-Destomic acid	216[c]	+3.7 (*c* 2)	—[d]

[a]Measured with a Hitachi amino acid analyzer Model 835-30; column (4 × 150 mm) packed with Hitachi custom No. 2619; elution mode, as for analysis of biological substances; elution rate: 225 μL/min. [b]Reported[7]. [c]Reported[2]. [d]Authentic sample could not be obtained.

oxazolinone-ring formation under alkaline conditions was previously observed in the case of benzyl 4-azido-2-(benzyloxycarbonyl)amino-2,4-dideoxy-β-L-ribopyranoside[15].

The C-6 epimer (**2**) of **1** was prepared from **10** by the reaction sequences described for **1**, namely, **10**→**15**→**16**→**17**→**18**→**21**→**22**→**2**. During this conversion, a slight difference was observed in the deacetylation step (from **17** to **18**), that is, an appreciable proportion (8.5%) of the 6-*N*,7-*O*-carbonyl derivative (**39**) was formed as a by-product.

For the synthesis of *epi*-destomic acid (**3**), *i.e.*, the 4-epimer of **1**, methyl 2,3,4-tri-*O*-benzyl-α-D-glucopyranoside (**41**) was selected as the starting material. Compound **41** was readily prepared from methyl 2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranoside by simultaneous acetolysis of the glycoside and the 6-benzyl ether group, followed by re-glycosidation, as well as from methyl 2,3-di-*O*-benzyl-4,6-*O*-benzylidene-α-D-glucopyranoside by reduction[16] with lithium aluminum hydride–aluminum chloride.

Oxidation of **41** with dimethyl sulfoxide and dicyclohexylcarbodiimide in the presence of pyridinium phosphate gave the corresponding dialdose (**23**) in 92% yield. As in the case of **8**, a mixture of D-*glycero*-D-*gluco*- (**24**) and L-*glycero*-D-*gluco* (**25**) -heptononitrile derivatives was obtained by cyanomesylation of **23** with hydrogen cyanide and mesyl chloride in pyridine, and this could be separated by fractional recrystallization from ether–hexane, followed by chromatography on a column of silica gel. The ratio of D-*glycero* (**24**) to L-*glycero* (**25**) isomer, obtained in total yield of 93%, was ~2.2 : 1.0. An alternative cyanation with potassium cyanide in methanol–water followed by mesylation proved unfavorable, owing to partial hydrolysis of the cyano group to give the corresponding amide (**42**), whose configuration at C-6 was presumed only by its rotational value. The yield of **42** reached 15% after 18 h.

The configuration of the cyanomesylation products was determined, as already described, by conversion of the preponderant isomer **24** into *N*-(2,4-dinitrophenyl)-L-alanine *via* the imine (**26**) prepared by reduction of **24** with lithium aluminum hydride. Successive hydrogenolytic ring-opening and *O*-debenzylation of **26**, respectively catalyzed by Raney nickel and palladium–charcoal, followed by *N*-(2,4-dinitrophenyl)ation, gave methyl 6,7-dideoxy-6-(2,4-dinitrophenyl)amino-L-*glycero*-D-*gluco*-heptopyranoside (**43**), which was further converted into *N*-dinitrophenyl-L-alanine by acid hydrolysis and periodate–permanganate oxidation, indicating that **24** has the D-*glycero* configuration at C-6.

The imine **26** was converted into **3** by reaction sequences similar to those described for the synthesis of **1**, *i.e.*, *N*-(benzyloxycarbonyl)ation, acetolysis with acetic acid, acetolysis with acetic anhydride–sulfuric acid, *O*-deacetylation, oxidation with bromine in the presence of barium carbonate in 1,4-dioxane–water, and finally hydrogenolytic removal of the *N*-(benzyloxycarbonyl) and *O*-benzyl groups; **24**→**26**→**27** (2 steps, 31%)→**28** (88%)→**32** (89%)→**33** (98%)→**34** (55–61%)→**3**.

Furthermore, the C-6 epimer (**4**) of **3** was also derived from **25**, *i.e.*, **25**→**29**→**30**→**31**→**35**→**36**→**37**→**4**.

From the synthetic point of view, the reaction sequences for the synthesis of **3** and **4** differed slightly from those for synthesis of **1** and **2** in two respects, that is,

TABLE II

EPIMERIZATION OF SOME 6-*O*-MESYL HEPTOPYRANOSIDURONONITRILES

Starting compound	*Time*[a] *(h)*	*Equilibrium mixture*[b]	*Cyanomesylation*[c]
9	20	**9** 0.80:1.0 **10**	**9** 1.7:1.0 **10**
	48	**9** 0.86:1.0 **10**	
24	20	**24** 2.05:1.0 **25**	**24** 2.2:1.0 **25**
25	20	**24** 2.00:1.0 **25**	

[a] The starting compound (0.2 mmol) in ether (7 mL) was heated under reflux with $LiAlH_4$ (10–15 mg) deactivated with 3 drops of water. [b] Ratios were determined by the n.m.r. signals of mesyl protons. [c] Obtained from cyanomesylation with HCN followed by MsCl in pyridine.

in the steps of *N*-(benzyloxycarbonyl)ation and *O*-deacetylation. In the former step, the reaction was conducted with benzyl chloroformate and triethylamine in benzene, because of the low solubility of **26** and **29** in 1,4-dioxane–water, resulting in lower yields of **27** and **30**. In the latter step, formation of 6-*N*,7-*O*-carbonate was not observed.

In order to examine in detail the epimerization at C-6 that is sometimes encountered during the reductive formation of 6,7-epimino derivatives, the cyanomesylated derivatives (**9**, **24**, and **25**) were treated with lithium aluminum hydride decomposed with water in ether; this apparently gave an equilibrium mixture, by epimerization at C-6, after 20 h (see Table II), as indicated in the case of **24** and **25**, where the ratios were of the same order as those of cyanomesylation. The difference observed in the case of **9** is not clear.

The identity of synthesized **3** with natural *epi*-destomic acid was also confirmed by comparison of some physical data and the liquid-chromatographic behavior (see Table I). The relatively large discrepancy in the optical rotational values may be attributed to contamination of the natural product by impurity.

EXPERIMENTAL

General methods. — Melting points were determined with a Mel-Temp melting-point apparatus and are not corrected. Optical rotations were measured in a 0.5-dm tube with a Carl Zeiss LEP-Al polarimeter at room temperature. I.r. spectra were recorded with a Hitachi Model EPI-G2 grating spectrometer. Amino acids were analyzed with a Hitachi 835 liquid chromatograph, using a column (4 × 150 mm) packed with Hitachi custom No. 2619. A standardized elution system for the analysis of biological body fluids was used. N.m.r. spectra were recorded at 100 MHz with a JEOL PS-100 spectrometer, for solutions in chloroform-*d*, using tetramethylsilane as the internal standard unless stated otherwise. The ^{1}H-n.m.r. data for **9–18**, **23–25**, **27**, **28**, **30**, **31**, **41**, and **42** are summarized in Table III.

*1,2;3,4-Di-O-isopropylidene-6-O-(methylsulfonyl)-α-*D*-*glycero-D-galacto*-heptopyranurononitrile* (**9**) *and its β-*L-glycero-D-galacto *isomer* (**10**). — *Method A.* To a stirred solution of[17] **8** (15 g, 58 mmol) in dry pyridine (35 mL) was added hydrogen cyanide (3.4 mL, 86.5 mmol) dropwise at 0°, and the mixture was kept for 2 h at 0° and for 10 h at room temperature. Then, the mixture was rechilled in an ice-water bath, methanesulfonyl chloride (6.8 mL, 88 mmol) was added, and the mixture was kept overnight at room temperature and poured into a cold, saturated solution of sodium hydrogencarbonate. The resulting mixture was extracted with chloroform, and the extract was dried, and evaporated, to give a crude, syrupy mixture of **9** and **10** (21.9 g) in the ratio of 1.7:1.0 (n.m.r. spectrum). Crystallization of the syrup from ethanol gave 5.65 g (27%) of **9**. The isomeric mixture obtained from the mother liquor was separated on a column of silica gel with 11:9 (v/v) hexane–ether, to give **10** (7.9 g, 37.5%) and a further crop of **9** (7.45 g, 35%) as faster- and slower-moving components, respectively. Compound **10** crystallized from ether–hexane.

Compound **9**: m.p. 124–125°, $[\alpha]_D$ −98.6° (*c* 1.0, chloroform).

Anal. Calc. for $C_{14}H_{21}NO_8S$: C, 46.28; H, 5.83; N, 3.85; S, 8.82. Found: C, 46.37; H, 5.89; N, 3.85; S, 8.84.

Compound **10**: m.p. 157–159.5°, $[\alpha]_D$ −46.8° (*c* 1.6, chloroform).

Anal. Found: C, 46.36; H, 5.83; N, 3.81; S, 8.60.

Method B. To an ice-cold solution of **8** (10.8 g, 41.8 mmol) in methanol (100 mL) was added dropwise a solution of potassium cyanide (10.9 g, 167 mmol) in water (50 mL), with stirring, during 1 h. The mixture was stirred overnight at room temperature, and extracted with chloroform. The extract was washed with water, dried, and evaporated, to give a syrup (12.5 g) which was methanesulfonylated in the conventional way, to afford a mixture of **9** and **10** in the ratio of 2.8:10 (total yield 82%).

*6,7-(*N*-Benzyloxycarbonyl)epimino-6,7-dideoxy-1,2;3,4-di-O-isopropylidene-β-*L-glycero-D-galacto*-heptopyranose* (**12**). — To a solution of **9** (1.0 g, 2.75 mmol) in dry ether (50 mL) was added lithium aluminum hydride (114 mg, 3.8 mmol), with stirring, at room temperature. The mixture was stirred for 1 h, slowly diluted with moist ether (to decompose the excess of the reagent), and filtered. The filtrate was washed with water, dried, and evaporated, to give a syrup of **11** (0.70 g, 2.6 mmol), which was characterized only by its ^{1}H-n.m.r. spectrum.

To a suspension of **11** and sodium hydrogencarbonate (0.76 g, 9.1 mmol) in 1,4-dioxane (15 mL)–water (17.5 mL) was added dropwise, with stirring, a solution of benzyl chloroformate (1.0 mL, 5.86 mmol) in 1,4-dioxane (1.0 mL) during 15 min at 30°. The mixture was stirred overnight at room temperature, shaken with chloroform (3 × 20 mL) and saturated sodium hydrogencarbonate (2 × 10 mL), and the organic layer washed with water, dried, and evaporated, to give a syrup, which was purified on a column of silica gel with 3:2 (v/v) hexane–water; yield 0.60 g (57%), m.p. 127–129°, $[\alpha]_D$ −120.7° (*c* 2.0, chloroform); ν_{max}^{KBr} 1725 cm^{-1} (urethan).

Anal. Calc. for $C_{21}H_{27}NO_7$: C, 62.21; H, 6.71; N, 3.46. Found: C, 61.92; H, 6.46; N, 3.72.

TABLE III

^{1}H-N.M.R. DATA MEASURED AT 100 MHz IN $CDCl_3$

Compound	*Chemical shifts (δ) and coupling constants (Hz)*											
	H-1 ($J_{1,2}$)	*H-2* ($J_{2,3}$)	*H-3* ($J_{3,4}$)	*H-4* ($J_{4,5}$)	*H-5* ($J_{5,6}$)	*H-6* ($J_{6,7}$)	*H-7* ($J_{6,7'}$)	*H-7′* ($J_{7,7'}$)	CCH_3^{a} (OCH_3)	OCH_2^{b}	*Ph*	*Others*
9	5.54(d) (4.8)	4.39(dd) (2.4)	4.70(dd) (7.6)	4.29(dd) (2.0)	4.14(dd) (7.9)	5.24(d)	—	—	1.56, 1.48 1.36	—	—	3.22 (Ms,s)
10	5.53(d) (4.8)	4.38(dd) (2.7)	4.70(dd) (8.1)	4.43(dd) (2.0)	4.12(dd) (8.8)	5.31(d)	—	—	1.55, 1.48 1.37, 1.35	—	—	3.19 (Ms,s)
11	5.55(d) (5.0)	4.30(dd) (2.1)	4.61(dd) (8.0)	4.27(dd) (1.9)	3.32(dd) (6.4)	2.35(dd) (6.0)	1.83(d) (3.5)	1.59(d) (0)	1.50, 1.38 1.33	—	—	—
12	5.57(d) (5.0)	4.28(dd) (2.4)	4.58(dd) (8.0)	4.18(dd) (2.0)	3.38(dd) (7.2)	2.87(dd) (6.2)	2.38(d) (4.0)	2.20(d) (0)	1.48, 1.33 1.31	5.09(s)	7.34	—
13	5.51(d) (5.0)	4.29(dd) (2.0)	4.58(dd) (8.0)	← H-4,5,6,7,7′; 3.8–4.3 →					1.48, 1.37 1.30, 1.28	5.09(s)	7.32	2.01 (Ac,s)
14	5.51(d) (5.0)	4.29(dd) (2.0)	4.60(dd) (8.0)	4.33(dd) (1.5)	4.09(dd)	← H-6,7,7′; 3.6–4.0 →			1.50, 1.42 1.32	5.09(s)	7.33	
15	5.51(d) (5.1)	4.29(dd) (2.3)	4.62(dd) (8.2)	4.38(dd) (1.8)	3.30(dd) (7.0)	2.39(dd) (5.9)	1.93(d) (3.5)	1.61(d) (0)	1.49, 1.38 1.33	—	—	—
16	5.49(d) (5.0)	4.27(dd) (2.1)	4.60(dd) (7.7)	4.40(dd) (1.7)	3.49(dd) (6.4)	2.88(dd) (6.4)	2.43(d) (4.0)	2.24(d) (0)	1.47, 1.45 1.37, 1.32	5.16(s)	7.36	—

17	5.49(d) (5.0)	4.30(dd) (2.0)	4.59(dd) (8.0)	← H-4,5,6,7,7′; 3.8–4.4 →					1.46, 1.45 1.31	5.09(s)	7.32	2.00 (Ac,s)
18	5.51(d) (5.0)	4.29(dd) (2.0)	4.60(dd) (8.0)	4.32(dd) (∼0.5)	← H-5,6,7,7′; 3.6–4.2 →				1.46, 1.31	5.09(s)	7.12	—
23[c]	4.58(d) (1.5)	3.39(dd) (5.0)	4.24(dd) (4.2)	3.52(dd) (5.0)	4.53(dd) (0.5)	9.51(d)	—	—	(3.06)	4.95, 4.69 4.47	7.0–7.4	—
24	4.66(d) (4.0)	3.57(dd) (9.2)	4.05(dd) (8.4)	3.62(dd) (9.6)	3.96(dd) (1.8)	5.60(d)	—	—	(3.45)	4.93, 4.87 4.72	7.2–7.4	3.22 (Ms,s)
25	4.63(d) (3.7)	3.57(dd) (9.6)	4.06(dd) (8.1)	3.5(dd) (9.9)	4.01(dd) (1.5)	5.33(d)	—	—	(3.38)	4.92, 4.78 4.71	7.2–7.4	3.07 (Ms,s)
27	4.49(d) (3.4)	3.45(dd) (9.7)	4.03(dd) (8.8)	3.37(dd) (9.7)	3.88(dd) (3.0)	2.78(dd) (3.4)	2.23(d) (6.3)	2.07(d) (0)	(3.32)	5.06, 4.90 4.79, 4.69	7.2–7.4	—
28	4.42(d) (3.7)	3.37(dd) (9.5)	4.09(dd) (8.2)	3.46(dd) (10.3)	3.91(dd) (3.0)	← H-6,7,7′; 4.1–4.5 →			(3.00)	5.05, 4.87 4.83, 4.49	7.0–7.4	1.65 (Ac,s)
30	4.59(d) (3.2)	3.53(dd) (9.8)	4.01(dd) (9.5)	← H-4,5; 4.4–4.8 →		2.94(dd) (0.2)	2.41(d) (4.2)	2.35(d) (0)	(3.36)	5.11, 4.91 4.84, 4.71	7.2–7.4	—
31	4.49(d) (4.0)	3.36(dd) (9.5)	(9.5)	3.53(dd) (9.5)	← H-3,5,6,7,7′; 3.7–4.3 →				(3.09)	5.11, 5.12 4.93, 4.55	7.0–7.4	1.63 (Ac,s)
41	4.57(d) (3.5)	3.49(dd) (4.8)	4.00(dd) (4.0)	← H-4,5,6; 3.4–3.8 →			—	—	(3.36)	4.91, 4.79 4.72	7.2–7.4	—
42	4.57(d) (3.3)	3.52(dd) (9.5)	4.07(dd) (8.6)	3.58(dd) (9.8)	4.23(dd) (1.5)	5.41(d)	—	—	(3.30)	4.91, 4.85 4.71	7.2–7.4	3.12 (Ms,s)

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[a] Singlet. [b] Centers of AB quartets having coupling constants of 9–12 Hz, unless stated otherwise. [c] Measured in benzene-d_6.

*7-O-Acetyl-6-(benzyloxycarbonyl)amino-6-deoxy-1,2;3,4-di-O-isopropylidene-β-*L-glycero-D-galacto-*heptopyranose* (**13**). — A solution of **12** (0.60 g, 1.5 mmol) in acetic acid (2 mL) was heated for 15 min at 40°, and then evaporated under diminished pressure at a bath temperature not exceeding 20°, to give a quantitative yield of syrupy **13**, $[\alpha]_D$ −47.8° (*c* 2.0, chloroform); ν_{max}^{NaCl} 1740 (ester), and 1730 and 1560 cm^{-1} (urethan).

Anal. Calc. for $C_{21}H_{31}NO_9$: C, 59.33; H, 6.72; N, 3.01. Found: C, 59.13; H, 6.65; N, 2.97.

*6-(Benzyloxycarbonyl)amino-6-deoxy-1,2;3,4-di-O-isopropylidene-β-*L-glycero-D-galacto-*heptopyranose* (**14**). — To a solution of **13** (0.69 g, 1.5 mmol) in methanol (5 mL) was added 0.22M methanolic sodium methoxide (1.5 mL). The mixture was kept for 1 h at room temperature, passed through a column of Dowex 50-W X-8 (H$^+$) resin (2 mL), and the effluent evaporated, to give **14** as a syrup; this was purified on a column of silica gel with 5:4 (v/v) ethyl acetate–hexane; yield, 0.54 g (86%), $[\alpha]_D$ −48.8° (*c* 2.0, chloroform); ν_{max}^{NaCl} 1680 and 1540 cm^{-1} (urethan).

Anal. Calc. for $C_{21}H_{29}NO_8$: C, 59.56; H, 6.90; N, 3.31. Found: C, 59.69; H, 7.34; N, 3.37.

*6,7-(N-Benzyloxycarbonyl)epimino-6,7-dideoxy-1,2;3,4-di-O-isopropylidene-α-*D-glycero-D-galacto-*heptopyranose* (**16**). — Treatment of **10** with lithium aluminum hydride followed by *N*-(benzyloxycarbonyl)ation, as described for **12**, gave **16** in 50% yield, m.p. 77–78° (ether–hexane), $[\alpha]_D$ −26.9° (*c* 2.0, chloroform); ν_{max}^{KBr} 1725 cm^{-1} (urethan). (The intermediate **15** was characterized only by ^{1}H-n.m.r. spectroscopy.)

Anal. Calc. for $C_{21}H_{27}NO_7$: C, 62.21; H, 6.71; N, 3.46. Found: C, 62.14; H, 6.62; N, 3.45.

Because of the difficulty in the separation of **9** and **10**, it is recommended that, for preparative purposes, the two epimers be separated after conversion into **12** and **16**, as shown in the following example. A syrupy mixture (1.635 g, 4.5 mmol) of **9** and **10** in the ratio of 4:1 was treated with lithium aluminum hydride, and the product was *N*-(benzyloxycarbonyl)ated, to give an epimeric mixture that was separated on a column of silica gel with 29:20:1 (v/v/v) benzene–hexane–acetone, to afford **12** (0.83 g, 45.5%) and **16** (0.15 g, 8.2%) as the faster- and slower-moving components, respectively.

*7-O-Acetyl-6-(benzyloxycarbonyl)amino-6-deoxy-1,2;3,4-di-O-isopropylidene-α-*D-glycero-D-galacto-*heptopyranose* (**17**). — A solution of **16** (0.305 g, 0.86 mmol) in acetic acid was heated for 2 h at 50°, cooled, and processed as described for **13**, to give syrupy **17**, which was purified by preparative t.l.c., and crystallized from ether–hexane; yield 0.30 g (86%), m.p. 104–105°, $[\alpha]_D$ −45.4° (*c* 2.0, chloroform); ν_{max}^{KBr} 1740 (ester), and 1720 and 1530 cm^{-1} (urethan).

Anal. Calc. for $C_{23}H_{31}NO_9$: C, 59.33; H, 6.72; N, 3.01. Found: C, 59.32; H, 6.62; N, 3.05.

*6-(Benzyloxycarbonyl)amino-6-deoxy-1,2;3,4-di-O-isopropylidene-α-*D-glycero-D-galacto-*heptopyranose* (**18**). — Deacetylation of **17** as described for **14** gave **18** in 82% yield; m.p. 96–97°, $[\alpha]_D$ −44.6° (*c* 2.0, chloroform); ν_{max}^{KBr} 3550 (OH), 3370 (NH), and 1720 and 1515 cm^{-1} (urethan).

Anal. Calc. for $C_{21}H_{29}NO_8$: C, 59.56; H, 6.90; N, 3.31. Found: C, 59.52; H, 6.79; N, 3.42.

In this reaction, there was formed, as a by-product, 6-*N*,7-*O*-carbonyl-6-deoxy-1,2;3,4-di-*O*-isopropylidene-α-D-*glycero*-D-*galacto*-heptopyranose (**39**), yield 8.5%; m.p. 67–69°, $[\alpha]_D$ −85.3° (*c* 0.5, chloroform); ν_{max}^{NaCl} 1760 and 1630 cm^{-1} (cyclic carbamate); ^{1}H-n.m.r. (C_6D_6): δ 5.27 (d, 1 H, $J_{1,2}$ 5.0 Hz, H-1), 4.03 (dd, 1 H, $J_{2,3}$ 2.0 Hz, H-2), 4.33 (dd, 1 H, $J_{3,4}$ 7.5 Hz, H-3), 4.00 (dd, 1 H, $J_{4,5}$ 4.5 Hz, H-4), 4.26 (dd, 1 H, $J_{5,6}$ 7.5 Hz, H-5), 4.6–4.9 (m, 3 H, H-6,7,7′), 1.30, 1.11, and 0.95 (each s, total 12 H, 4 CCH_3), and 6.64 (broad s, 1 H, NH).

Anal. Calc. for $C_{14}H_{21}NO_7$: C, 53.32; H, 6.71; N, 4.44. Found: C, 53.19; H, 6.34; N, 4.58.

*6-(Benzyloxycarbonyl)amino-6-deoxy-*L-glycero-D-galacto-*heptopyranose* (**19**). — A suspension of **13** (0.51 g, 1.2 mmol) in 0.5% sulfuric acid (8 mL) was heated, with stirring, for 50 min at 86–89°, cooled, and the acid neutralized with barium carbonate. The insoluble material was filtered off, and the filtrate was passed through a column of Dowex 50-W X-8 (H$^+$) resin (2 mL). Evaporation of the effluent gave **14** (0.40 g, 96%); after recrystallization from water–methanol, this had m.p. 170–173° (dec.), $[\alpha]_D$ +52.9° (*c* 1.0, water); ν_{max}^{KBr} 1685 and 1545 cm^{-1} (urethan); ^{1}H n.m.r. (D_2O): δ 5.69 (d, 0.4 H, $J_{1,2}$ 1.5 Hz, H-1β), 4.97 (d, 0.6 H, $J_{1,2}$ 7 Hz, H-1α), 5.59 (s, 2 H, CH_2 in Z), and 7.93 (s, 5 H, Ph).

Anal. Calc. for $C_{15}H_{21}NO_8$: C, 52.47; H, 6.17; N, 4.08. Found: C, 52.65; H, 6.09; N, 4.01.

*6-(Benzyloxycarbonyl)amino-6-deoxy-*D-glycero-D-galacto-*heptopyranose* (**21**). — Hydrolysis of **18** as described for **19** gave **21** in 93% yield; m.p. 198–201° (dec.), $[\alpha]_D$ +32.8° (*c* 1.0, water); ν_{max}^{KBr} 1670 and 1535 cm^{-1} (urethan); ^{1}H-n.m.r. (D_2O): δ 5.69 (d, 0.4 H, $J_{1,2}$ 1 Hz, H-1α), 4.97 (d, 0.6 Hz, $J_{1,2}$ 6 Hz, H-1β), and 5.59 (s, 2 H, CH_2 in Z).

Anal. Calc. for $C_{15}H_{21}NO_8$: C, 52.47; H, 6.17; N, 4.08. Found: C, 52.86; H, 6.15; N, 4.05.

*6-Amino-6-deoxy-*L-glycero-D-galacto-*heptonic acid* (*destomic acid*, **1**). — To a suspension of **19** (2.5 g, 7.3 mmol) and barium carbonate (2 g, 10 mmol) in water (100 mL) was added bromine (1 mL, 19 mmol). After stirring for 6 h at room temperature, the excess of bromine was removed by bubbling air through, and the insoluble material was filtered off. The aqueous solution of **20** was hydrogenolyzed in the presence of 10% palladium–charcoal (2 g), the catalyst filtered off, the filtrate stirred with silver carbonate, the insoluble material filtered off, and the filtrate concentrated to ~5 mL. The aqueous solution was placed on a column of Dowex 50-W X-8 resin (H$^+$; 100 mL), and this was successively eluted with water (300 mL) and 2% aqueous ammonium hydroxide (300 mL). The fractions that showed a positive ninhydrin test were combined, and concentrated to ~5 mL, 28% aqueous ammonium hydroxide (0.1 mL) was added, the solution was kept for 20 h at room temperature (in order to convert the corresponding lactam, formed during processing, into **1**) and methanol (45 mL) was added, to give **1** (1.0 g, 63%). Some physical data, and the chromatographic behavior are given in Table I. Its n.m.r. spectrum was identical with that of an authentic sample.

Anal. Calc. for $C_7H_{15}NO_7$: C, 37.33; H, 6.71; N, 6.22. Found: C, 37.36; H, 6.81; N, 6.27.

6-Amino-6-deoxy-D-glycero-D-galacto-*heptonic acid* (**2**). — Oxidation of **21**, followed by hydrogenolytic de(benzyloxycarbonyl)ation, was conducted as described for **1**, to give **2** in 53% yield after recrystallization. Some physical and chromatographic data are given in Table I.

Anal. Calc. for $C_7H_{15}NO_7$: C, 37.33; H, 6.71; N, 6.22. Found: C, 36.95; H, 6.58; N, 6.13.

*Methyl 2,3,4-tri-O-benzyl-α-*D-gluco-*hexodialdo-1,5-pyranoside* (**23**). — To a stirred solution of **41** (50 g, 108 mmol) and dimethyl sulfoxide (93 mL, 1.3 mol) in benzene were added pyridine (5.6 mL, 69.2 mmol), phosphoric acid (1.3 mL, 24.2 mmol), and dicyclohexylcarbodiimide (70 g, 343 mmol) under cooling, and stirring was continued for 7 h at room temperature. The excess of the diimide was decomposed by addition of oxalic acid, and the 1,3-dicyclohexylurea that separated out was filtered off. Evaporation of the filtrate gave **23** as a syrup; this was purified on a column of silica gel with 25:1 (v/v) benzene–methanol; yield 46 g (92%); $[\alpha]_D$ +13.6° (*c* 2.6, chloroform); ν_{max}^{NaCl} 1745 cm^{-1} (aldehyde).

Anal. Calc. for $C_{28}H_{30}O_6$: C, 72.71; H, 6.54. Found: C, 72.35; H, 6.46.

*Methyl 2,3,4-tri-O-benzyl-6-O-(methylsulfonyl)-α-*D-glycero-D-gluco-*heptopyranurononitrile* (**24**) *and its β-*L-glycero-D-gluco *isomer* (**25**). — *Method A.* To a solution of **23** (40 g, 86.5 mmol) in dry pyridine (170 mL) was added hydrogen cyanide (17.1 mL, 435 mmol) at room temperature. The mixture was stirred for 3 h, and the product was methanesulfonylated, and the ester isolated as described for **9** and **10**. Crystallization of the product mixture from ether–hexane gave **24** (22 g, 45%), m.p. 110–111°, $[\alpha]_D$ +14.0° (*c* 2.0, chloroform).

Anal. Calc. for $C_{30}H_{33}NO_8S$: C, 63.47; H, 5.86; N, 2.47; S, 5.65. Found: C, 63.46; H, 5.79; N, 2.45; S, 5.85.

The syrupy mixture of **24** and **25** obtained by evaporation of the mother liquor was separated on a column of silica gel with 3:2 (v/v) hexane–ether, to give a further crop of **24** (8.8 g, total yield 63%) as the faster-moving component, and **25** (14.5 g, 29.5%), which had $[\alpha]_D$ +49.9° (*c* 2.4, chloroform).

Found for **25**: C, 63.54; H, 5.94; N, 2.48; S, 5.86.

Method B. To a solution of **23** (2.0 g, 4.3 mmol) in methanol (15 mL) was added potassium cyanide (1.2 g, 18.4 mmol) in water (7 mL), with stirring, at room temperature, and stirring was continued for 4 h. The mixture was processed, and the resulting cyanohydrin methanesulfonylated, as described for **9** and **10** (Method B). The two isomers were separated as described in Method A, to give **24** and **25** in 57 and 24% yield, respectively.

When the reaction time allowed for cyanohydrin formation was prolonged to

18 h, the formation of methyl 2,3,4-tri-*O*-benzyl-6-*O*-(methylsulfonyl)-α-D-*glycero*-D-*gluco*-heptopyranuronamide (**42**) was confirmed. The amide crystallized readily from the syrupy mixture of products, and was recrystallized from methanol; yield ~15%; m.p. 195–197°, $[\alpha]_D$ +23.9° (*c* 1.0, chloroform).

Anal. Calc. for $C_{30}H_{35}NO_9S$: C, 61.52; H, 6.02; N, 2.39. Found: C, 61.80; H, 6.09; N, 2.30.

*Methyl 2,3,4-tri-*O*-benzyl-6,7-(*N*-benzyloxycarbonyl)epimino-6,7-dideoxy-β-*L-glycero-D-gluco-*heptopyranoside* (**27**). — To a stirred solution of **24** (14 g, 25 mmol) in dry ether (700 mL) was added lithium aluminum hydride (0.80 g, 21 mmol) in three portions at room temperature. The processing described for **12** gave crude epimino derivative (**26**). To a solution of **26** and triethylamine (5.2 mL, 37 mmol) in benzene (20 mL) was added benzyl chloroformate (3.0 mL, 18 mmol) in benzene (2.5 mL), with stirring, at 0°. After being stirred for 2 h at this temperature, the mixture was poured into a saturated, aqueous solution of sodium hydrogencarbonate, and extracted with chloroform. The extract was washed with water, dried, and evaporated, to give **27** as a syrup; this was purified on a column of silica gel with 13:7 (v/v) hexane–ether; yield 6.15 g (57%); $[\alpha]_D$ +49.3° (*c* 1.1, chloroform); ν_{max}^{NaCl} 1725 cm^{-1} (urethan).

Anal. Calc. for $C_{37}H_{39}NO_7$: C, 72.88; H, 6.45; N, 2.30. Found: C, 73.01; H, 6.40; N, 2.38.

*Methyl 7-O-acetyl-2,3,4-tri-O-benzyl-6-(N-benzyloxycarbonyl)amino-6-deoxy-β-*L-glycero-D-gluco-*heptopyranoside* (**28**). — A solution of **27** (5.0 g, 8.2 mmol) in acetic acid (10 mL) was heated for 1.5 h at 40°, and processed as described for **39**. Crystallization from ethanol, followed by preparative t.l.c. [7:2:1 (v/v/v) benzene–hexane–acetone] of the mother liquor gave **28** (5.4 g, 98%), m.p. 98–101°, $[\alpha]_D$ +11.4° (*c* 1.0, chloroform); ν_{max}^{KBr} 1740 (ester), and 1725 and 1525 cm^{-1} (urethan).

Anal. Calc. for $C_{39}H_{43}NO_9$: C, 69.94; H, 6.47; N, 2.09. Found: C, 69.58; H, 6.56; N, 2.27.

*Methyl 2,3,4-tri-O-benzyl-6,7-(*N*-benzyloxycarbonyl)epimino-6,7-dideoxy-α-*D-glycero-D-gluco-*heptopyranoside* (**30**). — Compound **30** was derived from **25**, *via* **29**, as described for **27**; yield 31%, syrup; $[\alpha]_D$ −12.9° (*c* 0.7, chloroform); ν_{max}^{NaCl} 1725 cm^{-1} (urethan).

Anal. Calc. for $C_{37}H_{39}NO_7$: C, 72.88; H, 6.45; N, 2.30. Found: C, 72.93; H, 6.39; N, 2.15.

*Methyl 7-O-acetyl-2,3,4-tri-O-benzyl-6-(*N*-benzyloxycarbonyl)amino-6-deoxy-α-*D-glycero-D-gluco-*heptopyranoside* (**31**). — Acetolysis of **30** with acetic acid as described for **28** gave syrupy **31** in 88% yield, $[\alpha]_D$ +4.8° (*c* 1.0, chloroform); ν_{max}^{NaCl} 1740 (ester), and 1730 and 1520 cm^{-1} (urethan).

Anal. Calc. for $C_{39}H_{43}NO_9$: C, 69.94; H, 6.47; N, 2.09. Found: C, 69.85; H, 6.56; N, 2.22.

*1,7-Di-O-acetyl-2,3,4-tri-O-benzyl-6-(*N*-benzyloxycarbonyl)amino-6-deoxy-*L-glycero-D-gluco-*heptopyranose* (**32**). — To a solution of **28** (5 g, 7.5 mmol) in chloroform (2 mL) and acetic anhydride (10 mL) was added concentrated sulfuric acid (0.1 mL) dropwise, with stirring. The mixture was kept for 2 h at room temperature, poured into ice–water, the acid neutralized with sodium hydrogencarbonate, and the mixture extracted with chloroform. The extract was washed with saturated aqueous sodium chloride, dried, and evaporated, to give syrupy **32**, which crystallized from ether–hexane; yield 4.8 g (92%); m.p. 75–78°, $[\alpha]_D$ +34.8° (*c* 1.0, chloroform); ν_{max}^{KBr} 1745 and 1735 (ester), and 1690 and 1525 cm^{-1} (urethan); ^{1}H-n.m.r.: δ 6.19 (d, 0.8 H, $J_{1,2}$ 3.5 Hz, H-1β), 5.51 (d, 0.2 H, $J_{1,2}$ 8.0 Hz, H-1α), 2.11 (s, 2.4 H, Ac-1β), 2.04 (s, 0.6 H, Ac-1α), and 1.95 (s, 3 H, Ac-7).

Anal. Calc. for $C_{40}H_{43}NO_{10}$: C, 68.85; H, 6.21; N, 2.01. Found: C, 68.60; H, 6.28; N, 2.06.

*2,3,4-Tri-O-benzyl-6-(N-benzyloxycarbonyl)amino-6-deoxy-*L-glycero-D-gluco-*heptopyranose* (**33**). — Deacetylation of **32** as described for **14** gave **33** in 96% yield; m.p. 159–163° (acetone–ethanol), $[\alpha]_D$ +15.5° (*c* 1.0, chloroform); ν_{max}^{KBr} 1685 and 1540 cm^{-1} (urethan).

Anal. Calc. for $C_{36}H_{39}NO_8$: C, 70.45; H, 6.41; N, 2.28. Found: C, 70.49; H, 6.38; N, 2.23.

*2,3,4-Tri-O-benzyl-6-(N-benzyloxycarbonyl)amino-6-deoxy-*L-glycero-D-gluco-*heptono-1,5-lactone* (**34**). — To a solution of **33** (3.0 g, 4.9 mmol) in 1,4-dioxane (80 mL) and water (45 mL) were added barium carbonate (6.0 g, 30 mmol) and bromine (1.5 mL, 29 mmol) in three portions, and the mixture was stirred overnight in the dark at room temperature. The excess of bromine was removed with sodium sulfite, and the insoluble material was filtered off. The filtrate was extracted with chloroform, and the extract was washed with water, dried, and evaporated, to give a syrup. Purification of the syrup on a column of silica gel with 13:7 (v/v) ethyl acetate–hexane gave **34** (1.82 g, 61%), $[\alpha]_D$ +113.4° (*c* 1.0, chloroform); ν_{max}^{NaCl} 1755 (lactone), and 1720 and 1520 cm^{-1} (urethan); ^{13}C-n.m.r.: 156.20 (urethan CO) and 168.61 p.p.m. (lactone CO).

Anal. Calc. for $C_{36}H_{37}NO_8$: C, 70.69; H, 6.10; N, 2.29. Found: C, 70.46; H, 6.30; N, 2.16.

*1,7-Di-O-acetyl-2,3,4-tri-O-benzyl-6-(N-benzyloxycarbonyl)amino-6-deoxy-*D-glycero-D-gluco-*heptopyranose* (**35**). — Acetolysis of **31** with acetic anhydride and concentrated sulfuric acid as described for **32** gave syrupy **35** in 89% yield after purification on a column of silica gel with 13:7 (v/v) hexane–ether; $[\alpha]_D$ +34.1° (*c* 1.0, chloroform); ν_{max}^{NaCl} 1750 (ester), and 1725 and 1510 cm^{-1} (urethan); ^{1}H-n.m.r.: δ 6.18 (d, 0.9 H, $J_{1,2}$ 4.0 Hz, H-1α), 5.54 (d, 0.1 H, $J_{1,2}$ 8.0 Hz, H-1β), 3.56 (dd, 0.9 H, $J_{2,3}$ 9.5 Hz, H-2α), 3.44 (t, 0.9 H, $J_{3,4} = J_{4,5} = 9.5$ Hz, H-4α), 2.12 (s, *J* 2.7 Hz, Ac-1α), 2.00 (s, 0.3 H, Ac-1β), and 1.93 (s, 3 H, Ac-7).

Anal. Calc. for $C_{40}H_{43}NO_{10}$: C, 68.85; H, 6.21; N, 2.01. Found: C, 68.92; H, 6.23; N, 2.14.

*2,3,4-Tri-O-benzyl-6-(N-benzyloxycarbonyl)amino-6-deoxy-*D-glycero-D-gluco-*heptopyranose* (**36**). — Deacetylation of **35** as described for **14** gave **36** in 99% yield; m.p. 117–119° (ethanol), $[\alpha]_D$ +10.7° (*c* 1.3, chloroform); ν_{max}^{KBr} 1710 and 1615 cm^{-1} (urethan).

Anal. Calc. for $C_{36}H_{39}NO_8$: C, 70.45; H, 6.41; N, 2.28. Found: C, 70.60; H, 6.30; N, 2.39.

*2,3,4-Tri-O-benzyl-6-(N-benzyloxycarbonyl)amino-6-deoxy-*D-glycero-D-gluco-*heptono-1,5-lactone* (**37**). — Oxidation of **36** as described for **34** gave **37** as a syrup in 58% yield; $[\alpha]_D$ +87.4° (*c* 1.0, chloroform); ν_{max}^{NaCl} 1760 (lactone), and 1720 and 1530 cm^{-1} (urethan); ^{13}C-n.m.r.: 156.60 (urethan CO) and 168.66 p.p.m. (lactone CO).

Anal. Calc. for $C_{36}H_{37}NO_8$: C, 70.69; H, 6.10; N, 2.29. Found: C, 70.64; H, 6.02; N, 2.05.

*6-Amino-6-deoxy-*L-glycero-D-gluco-*heptonic acid* (epi-*destomic acid*, **3**). — Compound **34** (1.84 g, 3.0 mmol) was hydrogenolyzed in methanol (100 mL) and water (40 mL) in the presence of 10% palladium–charcoal (3 g) and acetic acid (5 mL) under atmospheric pressure for 3 days at room temperature. The catalyst was filtered off, and the filtrate was evaporated to give a syrup, which was suspended in water (100 mL) and rehydrogenolyzed in the presence of 10% palladium–charcoal (1 g) and acetic acid (3 mL) for 24 h. After removal of the catalyst, the filtrate was evaporated, to give a crystalline residue which was purified as described for **1**, to give **3** in 81% yield. Some physical and chromatographic data are given in Table I.

Anal. Calc. for $C_7H_{15}NO_7$: C, 37.33; H, 6.71; N, 6.22. Found: C, 37.22; H, 6.62; N, 6.35.

*6-Amino-6-deoxy-*D-glycero-D-gluco-*heptonic acid* (**4**) — Hydrogenolysis of **37** as described for **3** gave **4** in 71% yield. Some physical and chromatographic data are given in Table I.

Anal. Calc. for $C_7H_{15}NO_7$: C, 37.33; H, 6.71; N, 6.22. Found: C, 36.91; H, 7.03; N, 6.50.

*6-N,7-O-Carbonyl-6-deoxy-*L-glycero-D-galacto-*heptonolactone* (**40**). — To a solution of **19** (66 mg, 0.19 mmol) in water (0.3 mL) and methanol (1 mL) were added iodine (115 mg, 0.45 mmol) and barium iodide (120 mg, 0.28 mmol) in methanol (5 mL). The mixture was warmed at 35–37°, with stirring, and then 5% methanolic potassium hydroxide (2.5 mL) was added dropwise. After being stirred for 10 min, the mixture was cooled to room temperature, and the insoluble material was filtered off. The filtrate was passed through a column of Dowex 50-W X-8 (H^+) resin, and the effluent was evaporated, to give **40**, which was recrystallized from methanol; yield 40 mg (89%), m.p. 189–191° (dec.), $[\alpha]_D$ −133.2° (*c* 1.0, water); ν_{max}^{KBr} 1740 and 1730 cm^{-1} (carbonate and lactone); ^1H-n.m.r. [4:1 (v/v) CD_3OD–D_2O]: δ 4.47 (d, 1 H, $J_{2,3}$ 1.5 Hz, H-2), 4.04 (dd, 1 H, $J_{3,4}$ 9.5 Hz, H-3), 3.91 (dd, 1 H, $J_{4,5}$ 5.0 Hz, H-4), and 4.71 (dd, 1 H, $J_{5,6}$ 1.5 Hz, H-5); ^{13}C-n.m.r. (D_2O): 177.83 (s, carbonate CO), and 162.33 p.p.m. (s, lactone CO).

Anal. Calc. for $C_8H_{11}NO_7 \cdot H_2O$; C, 38.25; H, 5.22; N, 5.58. Found: C, 38.24; H, 5.18; N, 5.69.

*Methyl 2,3,4-tri-O-benzyl-α-*D-*glucopyranoside* (**41**). — Methyl 2,3-di-*O*-benzyl-4,6-*O*-benzylidene-α-D-glucopyranoside was reduced with lithium aluminum hydride–aluminum chloride under reaction conditions similar to those reported by Lipták *et al.*[18], to give **41** in quantitative yield; m.p. 62–65° (previously reported[16] as a syrup), $[\alpha]_D$ +22.7° (*c* 2.0, chloroform); lit.[16] $[\alpha]_D$ +20° (*c* 0.55, chloroform).

Anal. Calc. for $C_{28}H_{32}O_6$: C, 72.39; H, 6.94. Found: C, 72.41; H, 6.90.

Conversion of **10** *into* N-*(2,4-dinitrophenyl)*-D-*alanine*. — Treatment of **10** (437 mg, 1.2 mmol) with lithium aluminum hydride as described for **12** gave **15** (295 mg) as a syrup. A solution of **15** (270 mg, 1.0 mmol) in methanol (20 mL) was placed in an autoclave, and Raney nickel (0.3 g) was added. Hydrogen at a pressure of 35 kg/cm^2 was introduced into the autoclave. The suspension was vigorously agitated for 2 days, and the insoluble material was filtered off. The filtrate was evaporated, to give 6-amino-6,7-dideoxy-1,2;3,4-di-*O*-isopropylidene-*β*-L-*glycero*-D-*galacto*-heptopyranose as a syrup; this was purified by preparative t.l.c. with 4:1 (v/v) benzene–methanol, yield, 143 mg (53%); ν_{max}^{NaCl} 3400 cm^{-1} (NH$_2$); ^{1}H-n.m.r.: δ 5.52 (d, 1 H, $J_{1,2}$ 4.9 Hz, H-1), 4.29 (dd, 1 H, $J_{2,3}$ 2.3 Hz, H-2), 4.61 (dd, 1 H, $J_{3,4}$ 7.5 Hz, H-3), 4.43 (dd, 1 H, $J_{4,5}$ 1.5 Hz, H-4), 3.38 (dd, 1 H, $J_{5,6}$ 7.8 Hz, H-5), 3.15 (m, 1 H, $J_{6,7}$ 6.3 Hz, H-6), 1.21 (d, 3 H, H-7), 2.44 (broad s, 2 H, NH$_2$), and 1.53, 1.45, 1.36, and 1.34 (each s, each 3 H, 4 C-CH$_3$).

To a suspension of the 6-amino-6,7-dideoxy derivative (143 mg, 0.52 mmol) and sodium hydrogencarbonate (155 mg, 1.85 mmol) in ethanol (0.5 mL) was added a solution of fluoro-2,4-dinitrobenzene (157 mg, 0.84 mmol) in ethanol (0.2 mL). After being stirred for 2 h in the dark at room temperature, the mixture was evaporated to dryness. An aqueous solution of the residue was washed with ether (4 × 10 mL) the pH adjusted with M hydrochloric acid to 2.0, and the solution extracted with ethyl acetate (5 × 8 mL). The extract was dried, and evaporated, to give the corresponding 6-(2,4-dinitrophenyl)amino derivative (**38**) as a syrup; this was purified by preparative t.l.c. with 20:1 (v/v) benzene–methanol; yield, 119 mg (52%); ^{1}H-n.m.r.: δ 5.55 (d, 1 H, $J_{1,2}$ 4.9 Hz, H-1), 4.36 (dd, 1 H, $J_{2,3}$ 2.1 Hz, H-2), 4.67 (dd, 1 H, $J_{3,4}$ 8.2 Hz, H-3), 4.48 (dd, 1 H, $J_{4,5}$ 1.5 Hz, H-4), 3.88 (dd, 1 H, $J_{5,6}$ 7.5 Hz, H-5), 4.2 (m, 1 H, $J_{6,7}$ 6.9 Hz, H-6), 1.46 (d, 3 H, H-7), 1.56 and 1.37 (each s, each 6 H, C-CH$_3$), and 9.1–8.2 (m, 3 H, aromatic protons).

O-Deisopropylidenation of **38** (108 mg, 0.25 mmol) was achieved in 90% trifluoroacetic acid (1 mL) for 30 min at room temperature. Then, the solution was evaporated, to give a syrup (105 mg) of 6,7-dideoxy-6-(2,4-dinitrophenyl)amino-D-*glycero*-D-*galacto*-heptopyranose, which, without purification, was subjected to the following oxidation. The syrup was dissolved in water (67 mL) and, after addition of potassium carbonate (141 mg, 1.0 mmol), sodium periodate (74 mg, 0.32 mmol), and potassium permanganate (4 mg, 25 μmol), the solution was kept in the dark for 3 h at room temperature. The resulting, blackish-brown precipitate was filtered off, and the filtrate was acidified with 10% sulfuric acid to pH ~2, and extracted with ethyl acetate (3 × 25 mL). The extracts were combined, dried, and evaporated, to give a residue which was purified by preparative t.l.c. with 5:4:1 (v/v/v) acetone–ethyl acetate–water, to give *N*-(2,4-dinitrophenyl)-D-alanine (15 mg, 20%); $[\alpha]_D$ −101.7° (*c* 0.035, M NaOH); ν_{max}^{NaCl} 3350 cm^{-1}; ^{1}H-n.m.r. (CD$_3$OD): δ 8.93, 8.24, and 7.03 (ABX, each 1 H, aromatic protons), 4.54 (q, 1 H, *J* 7.0 Hz, CH) and 1.63

(d, 3 H, CH_3). The n.m.r. spectrum coincided with that of an authentic sample having $[\alpha]_D$ −133.7° (*c* 0.8, M NaOH).

Conversion of **27** *into* N-*(2,4-dinitrophenyl)*-L-*alanine*. — A solution of **27** (2.78 g, 4.56 mmol) in methanol (220 mL) and water (10 mL) was placed in an autoclave, Raney nickel (3.0 g) was added, and a hydrogen pressure of 90 kg/cm^2 was applied. After vigorous agitation for 4 days, the insoluble material was filtered off, and the filtrate was evaporated, to give the corresponding 6-amino-6,7-dideoxy derivative; this was further hydrogenolyzed in methanol (120 mL) and water (20 mL) in the presence of 10% palladium–charcoal (1.0 g) and acetic acid (10 mL). The catalyst was filtered off, and the filtrate was evaporated, to give a crude syrup of methyl 6-amino-6,7-dideoxy-β-L-*glycero*-D-*gluco*-heptopyranoside, whose ^{1}H-n.m.r. spectrum revealed no aromatic protons.

Then, the syrup was *N*-(2,4-dinitrophenyl)ated as already described, to give the corresponding 6-(2,4-dinitrophenyl)amino derivative (**43**), which was purified on a column of silica gel with ethyl acetate; yield 0.3 g (18%); ν_{max}^{NaCl} 3350 cm^{-1}; ^{1}H-n.m.r. (CD_3OD): δ 8.98, 8.26, and 7.16 (ABX, each 1 H, aromatic protons) and 1.34 (d, 3 H, H-7).

Compound **43** was suspended in 0.34M sulfuric acid, and the suspension was boiled under reflux overnight. After neutralization of the acid with barium carbonate, the insoluble material was filtered off, and the filtrate was evaporated, to give a syrup of 6,7-dideoxy-6-(2,4-dinitrophenyl)amino-L-*glycero*-D-*gluco*-heptopyranose. Oxidation of the syrup as already described gave *N*-(2,4-dinitrophenyl)-L-alanine, which was purified by preparative t.l.c.; yield, 27 mg (11%); $[\alpha]_D$ +84.4° (*c* 0.13, M NaOH); ^{1}H-n.m.r. (CD_3OD): δ 8.96, 8.23, and 7.00 (ABX, each 1 H, aromatic protons), 4.4 (m, 1 H, CH), and 1.60 (d, 3 H, CH_3). The rotational value, lower than that expected, may be due to partial epimerization during the treatment with lithium aluminum hydride.

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REFERENCES

1 (a) S. Kondo, E. Akita, and M. Koike, *J. Antibiot., Ser. A*, 19 (1966) 139–140; (b) S. Kondo, K. Iinuma, H. Naganawa, M. Shimura, and Y. Sekizawa, *J. Antibiot.*, 28 (1975) 79–82.

2 M. Shimura, Y. Sekizawa, K. Iinuma, H. Naganawa, and S. Kondo, *Agric. Biol. Chem.*, 40 (1976) 611–618.

3 M. Shimura, Y. Sekizawa, K. Iinuma, H. Naganawa, and S. Kondo, *J. Antibiot.*, 28 (1975) 83–84.

4 N. Neuss, K. F. Koch, B. B. Molloy, W. Day, L. L. Huckstep, D. E. Dorman, and J. D. Roberts, *Helv. Chim. Acta*, 53 (1970) 2314–2319.

5 S. Inouye, T. Shomura, H. Watanabe, K. Totsugawa, and T. Niida, *J. Antibiot.*, 26 (1973) 374–385.

6 J. SHOJI AND Y. NAKAGAWA, *J. Antibiot.*, 23 (1970) 569–571.
7 S. KONDO, E. AKITA, AND M. SEZAKI, *J. Antibiot., Ser. A*, 19 (1966) 137–138.
8 H. HASHIMOTO, K. ASANO, F. FUJII, AND J. YOSHIMURA, *Chem. Lett.*, (1980) 1439–1440. The structural formula of **1** and **2** therein was erroneously drawn with reversed configurations for C-2 and C-4.
9 S. HORITO, Y. OHASHI, N. GASSNER, J. YOSHIMURA, AND Y. SASADA, *Bull. Chem. Soc. Jpn.*, 54 (1981) 2147–2150.
10 (a) J. YOSHIMURA AND M. TAMARU, *Carbohydr. Res.*, 72 (1979) c9–c11; (b) M. TAMARU, S. HORITO, AND J. YOSHIMURA, *Bull. Chem. Soc. Jpn.*, 53 (1980) 3687–3690.
11 J. YOSHIMURA, S. HORITO, AND H. HASHIMOTO, *Chem. Lett.*, (1981) 375–376.
12 T. SUAMI, Y. HONDA, AND T. KATO, *Chem. Lett.*, (1978) 1125–1128.
13 H. SAEKI AND E. OHKI, *Chem. Pharm. Bull.*, 18 (1970) 789–802.
14 P. ANDREWS, L. HOUGH, AND J. M. PICKEN, *Biochem. J.*, 94 (1965) 75–80.
15 H. HASHIMOTO, K. ARAKI, AND J. YOSHIMURA, *Bull. Chem. Soc. Jpn.*, 52 (1979) 3051–3059.
16 A. LIPTÁK, I. JODÁL, AND P. NÁNÁSI, *Carbohydr. Res.*, 44 (1975) 1–11.
17 D. HORTON, M. NAKADATE, AND J. M. J. TRONCHET, *Carbohydr. Res.*, 7 (1968) 56–65.
18 A. LIPTÁK, P. FÜGEDI, AND P. NÁNÁSI, *Carbohydr. Res.*, 68 (1979) 151–154.