Carbohydrate Research, 250 (1993) 177–184
Elsevier Science Publishers B.V., Amsterdam

Note

Chemical modification of the sugar moiety of methyl acarviosin: synthesis and inhibitory activity of eight analogues containing a 1,6-anhydro bridge †

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(Received January 4th, 1993; accepted March 12th, 1993)

Methyl acarviosin[2] (**1**), which is a core structure of acarbose and related carba-oligosaccharidic alpha-amylase inhibitors[3], possesses a strong inhibitory activity against some glycoside hydrolases. In the course of studies of the elucidation of the structure–inhibitory activity relationship of this kind of inhibitor, we previously reported[4] that inversion of the conformation ($^4C_1 \rightarrow {}^1C_4$) of its sugar moiety by replacement of the methyl 4-amino-4,6-dideoxy-α-D-glucopyranoside residue with 4-amino-3,6-anhydro-4-deoxy-β-D-glucopyranoside (**2**) or 4-amino-1,6-anhydro-4-deoxy-α-D-glucopyranose (**3**) provided a new type of potent carba-disaccharide inhibitor of biological interest.

In this paper, further chemical modification of the 4-amino-1,6-anhydro-4-deoxy-β-D-glucopyranose residue of **3** has been carried out to prepare eight analogues (**4–11**), which has led to the discovery of strong inhibitors, the 2-deoxy **10** and the 2,3-dideoxy derivatives **11**, that are almost 10 times more potent against α-D-glucosidase than the parent **1** (Table II).

Synthesis of the analogues was carried out conventionally[5] by coupling of 1,6:3,4-dianhydro-β-D-hexopyranose derivatives (**13–16**) with di-*O*-isopropylidenevalienamine[6] (**17**) in 2-propanol in a sealed tube for several days at 120°C. The products were isolated and characterised as the totally acetylated derivatives (**18–22**), the structures of which were assigned mainly on the basis of the 270-MHz ^{1}H NMR spectra (Table I).

First, 1,6:3,4-dianhydro-β-D-talopyranose[7] (**13**) was converted into 1,6:3,4-dianhydro-2-azido-2-deoxy-[8] (**14**) and -2-deoxy-2-fluoro-β-D-galactopyranose[9] (**15**) in the standard manner. The thioether **16** was obtained from the intermediate trifluoromethanesulfonate of **13** by treatment with *p*-toluenethiol.

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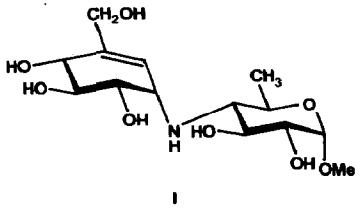
† Synthesis of Pseudo-oligosaccharide Glycosidase Inhibitors, Part XI. For Part X, see ref 1.



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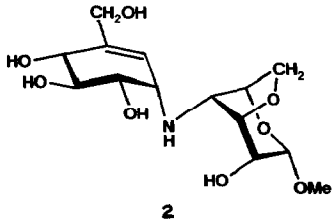

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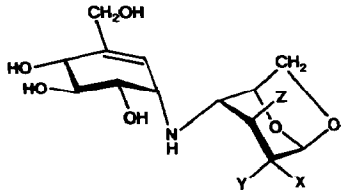


	X	Y	Z
3	H	OH	OH
4	OH	H	OH
5	H	N_3	OH
6	H	NH_2	OH
7	H	NHAc	OH
8	H	F	OH
9	H	p-MeC_6H_4S	OH
10	H	H	OH
11	H	H	H

Formule 1.

Coupling of a slight excess of **13** and **17** in 2-propranol in a sealed tube under an argon atmosphere for 10 days at 120°C afforded a single condensate, which was successively *O*-deisopropylidenated by treatment with aqueous 80% acetic acid at 60°C and acetylated with acetic anhydride in pyridine at room temperature, to give the crystalline hexa-acetyl derivative **18** of the carba-disaccharide **4** in 51% yield. The ^1H NMR spectrum of **18** supported the structure assigned (Table I).

Likewise, coupling of **14** and **17** gave a product which was *O*-deisopropylidenated and acetylated to afford the azide penta-acetate **19** in 61% overall yield. On the other hand, the azido group of the product was reduced with hydrogen sulfide, and subsequent *O*-deisopropylidenation gave the amine **6** in 86% yield. This compound was characterised by converting it into the hexa-*N*,*O*-acetyl derivative **20**.

Similar coupling of **15** with **17** afforded, however, a complex mixture of products, from which the desired product was isolated as the penta-acetate **21** in only 14% yield.

Coupling of **16** and **17** gave, after similar processing, the thioether **22** in 71% yield. A solution of **22** in acetone was desulfurised in the presence of Raney nickel T-4[10] at room temperature for 4 h to give, after chromatography on silica gel, the

TABLE I

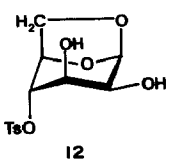
^{1}H NMR data (270 MHz, $CDCl_3$) for compounds **18–24**

Proton	**18**	**19**	**20**	**21**	**22**	**23**	**24**
Chemical shifts (δ)							
H-1	5.41bs	5.46bs	5.40s	5.51bd	5.61s	5.52s	5.48s
H-2	4.91bd	3.46bs	4.08bd	4.28d	3.14s	2.01bdd 1.81bd	1.53– 1.90m
H-3	5.29bd	4.94bs	4.59bs	5.02bd	5.25s	4.93bd	
H-4	2.86s	2.66bs	2.74s	2.63bs	~ 2.64bs	2.67s	2.57bs
H-5	4.51bd	4.56bd	4.47bd	4.59bd	4.59bd	4.46bd	4.41bd
H-6	4.19d	4.09d	4.11d	4.03d	4.12d	4.16d	3.85d
H-6	3.86dd	3.82dd	3.82dd	3.82bdd	3.82dd	3.79dd	3.81dd
H-1′	3.85bt	3.94bt	3.72bt	3.99bt	4.09bt	3.85bt	3.71bt
H-2′	6.05bd	6.06bd	6.09bd	6.08bd	6.15bd	6.07bd	5.97bd
H-4′ H-5′	5.54– 5.59m	5.64bd 5.69dd	5.42bd 5.47dd	5.66bd 5.70dd	5.70bd 5.81dd	5.58– 5.61m	5.61– 5.70m
H-6′	5.11dd	5.13dd	5.13dd	5.14bdd	5.20dd	5.08dd	5.06dd
H-7′	4.67bd	4.68bd	4.65bd	4.70d	4.69d	4.68d	4.69d
H-7′	4.39bd	4.38bd	4.40bd	4.37d	4.38d	4.39d	4.38d
NH			6.74bd				
Ac	2.13	2.11	2.09	2.11	2.11	2.09	2.08
	2.11	2.10	2.08	2.07	2.06	2.07	2.06 [b]
	2.08	2.06	2.07 [a]	2.06	2.05	2.06	2.04
	2.06	2.05	2.03	2.05	2.04	2.05	
	2.05	2.04		2.03	2.03	2.04	
	2.04						
Me					2.33		
Coupling constants (Hz)							
$J_{1,2}$	0	0	0	0	0	0	0
$J_{2,2}$						15.8	
$J_{2,3}$	5.5	0	0	0	0	5.5	
$J_{3,4}$	0	0	0	0	0	0	
$J_{4,5}$	0	0	0	0	0	0	
$J_{5,6}$	5.1	5.5	5.5	5.5	5.5	5.1	5.1
$J_{5,6}$	5.1	5.5					0
$J_{6,6}$	7.7	7.7	7.3	7.7	7.3	7.3	7.3
$J_{1',2'}$	5.1	5.5	5.1	5.1	4.8	5.1	5.5
$J_{4',5'}$		7.0	5.9	6.6	7.0		
$J_{5',6'}$	9.9	9.9	8.8	9.2	10.6	9.9	9.2
$J_{1',6'}$	5.1	4.0	4.4	4.8	4.4	4.4	5.1
$J_{7',7'}$	13.2		12.8	12.8	13.2	13.2	12.8
J_{1F}			1.1				
J_{2F}			44				
J_{3F}			15.8				

[a] Singlet for three methyl groups. [b] Singlet for two methyl groups.

2-deoxy (**23**, 53%) and the 2,3-dideoxy derivative (**24**, 38%). The ratio of the products was rather variable, depending on the activity of the Raney nickel.

The free carba-disaccharides **4**, **5**, and **7–11** derived by Zemplén *O*-deacetylation or by treatment with ammoniacal methanol of the corresponding acetyl derivatives **18–24** were directly subjected to bioassay (Table II). Initially, the C-2



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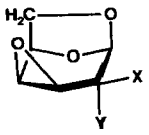
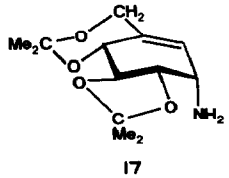
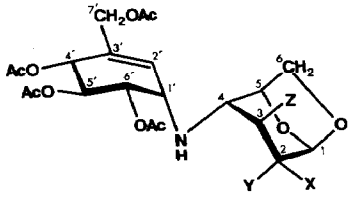


	X	Y
13	OH	H
14	H	N_3
15	H	F
16	H	*p*-MeC_6H_4S



17



	X	Y	Z
18	OAc	H	OAc
19	H	N_3	OAc
20	H	NHAc	OAc
21	H	F	OAc
22	H	*p*-MeC_6H_4S	OAc
23	H	H	OAc
24	H	H	H

Formule 2.

hydroxyl function of **2** or **3**, located in the 1,3-diaxial position to the C-4 imino group, seemed[4] to play a role in enhancing its binding to glycoside hydrolases. However, the present results suggest that the absence of a polar function or

Table II

Inhibitory activity IC_{50} (μg mL^{-1}) against α-D-glucosidase [a]

Compound	IC_{50}	
1	0.36	(1.1×10^{-3} mM)
2	1.45	(4.4×10^{-3} mM)
3	0.18	(5.6×10^{-4} mM)
4	0.50	(1.6×10^{-3} mM)
5	0.29	(8.4×10^{-4} mM)
6	2.2	(6.9×10^{-3} mM)
7	33	(9.2×10^{-2} mM)
8	0.10	(3.1×10^{-4} mM)
9	0.18	(4.2×10^{-4} mM)
10	0.032	(1.1×10^{-4} mM)
11	0.030	(1.0×10^{-4} mM)

[a] Yeast α-D-glucosidase, 0.66 mM *p*-nitrophenyl α-D-glucopyranoside, 100 mM phosphate buffered saline (pH 6.8).

introduction of a hydrophobic portion around the imino linkage is likely to increase their inhibitory activity.

EXPERIMENTAL

General methods.—Melting points were determined with a Mel–Temp capillary melting-point apparatus and are uncorrected. Optical rotations were measured with a Jasco DIP-370 polarimeter. ^{1}H NMR spectra were recorded for solutions in $CDCl_3$ (internal Me_4Si) with a Jeol JNM FX90A (90 MHz) or JNM GSX-270 (270 MHz) instrument. TLC was performed on Silica Gel 60 GF (E. Merck, Darmstadt) with detection by charring with H_2SO_4. Column chromatography was conducted on Wakogel C-300 (300 mesh). Organic solutions were dried over anhyd Na_2SO_4 and evaporated $< 50°C$ under diminished pressure.

*1,6 : 3,4-Dianhydro-2-azido-2-deoxy-β-*D*-galactopyranose* (**14**).—A solution of 1,6 : 3,4-dianhydro-β-D-talopyranose[7] (**13**; 392 mg, 2.72 mmol) in CH_2Cl_2 (1.1 mL) was treated with trifluoromethanesulfonic anhydride (0.55 mL, 3.26 mmol) for 5 min at −15°C. The mixture was poured into satd aq $NaHCO_3$, and extracted with CH_2Cl_2. The extract was evaporated and the residue was treated with sodium azide (0.88 g, 13 mmol) in DMF (10 mL) for 11 h at room temperature. The mixture was processed in the usual manner, and the product was crystallised from $CHCl_3$–petroleum ether to give **14** (0.22 g, 48%); mp 80–81°C; $[\alpha]_D^{23}$ −88° (*c* 1.0, $CHCl_3$) {lit.[8] mp 76.5–78°C, $[\alpha]_D^{20}$ −93° (*c* 2, $CHCl_3$)}.

*1,6 : 3,4-Dianhydro-2-deoxy-2-fluoro-β-*D*-galactopyranose* (**15**).—The trifluoromethanesulfonate obtained from **13** (96 mg, 0.66 mmol) was treated with M tetrabutylammonium fluoride–THF (2 mL) in DMF (2 mL) for 20 h at room temperature. The usual work-up gave crude **15** (124 mg, ~ 100%). This compound was assigned on the basis of the ^{1}H NMR data (270 MHz, $CDCl_3$) reported[9], and then directly used in the next reaction.

*1,6 : 3,4-Dianhydro-2-thio-2-*S*-(*p*-tolyl)-β-*D*-galactopyranose* (**16**).—To a solution of the trifluoromethanesulfonate obtained from **13** (0.30 g, 2.1 mmol) in DMF (2 mL) was added a solution of *p*-toluenethiol (0.28 g, 2.3 mmol) in DMF (3 mL) previously treated with 60% NaH (0.11 g, 2.7 mmol) for 5 min at 0°C. After the usual work-up, the product was eluted from a column of silica gel (15 g) with 1 : 6 EtOAc–hexane, to give **16** (0.24 g, 46%) as a syrup; $[\alpha]_D^{23}$ −75°C (*c* 1.8, $CHCl_3$); ^{1}H NMR data (270 MHz, $CDCl_3$): δ 7.38 and 7.13 (2 m, each 2 H, Ph), 5.46 (bs, 1 H, H-1), 4.85 (bt, 1 H, $J_{4,5}$ 4.8, $J_{5,6}$ 5.1 Hz, H-5), 4.04 (d, 1 H, $J_{6,6}$ 6.2 Hz, H-6a), 3.61 (bt, 1 H, $J_{3,4}$ 4.4 Hz, H-4), 3.55 (dd, 1 H, H-6b), 3.39 (bs, 1 H, H-2), and 3.29 (bd, 1 H, H-3). Anal. Calcd for $C_{13}H_{14}O_3S$: C 62.38; H, 5.64. Found: C, 62.58; H, 5.66.

*2,3-Di-*O*-acetyl-1,6-anhydro-4-deoxy-4-[(1*S*)-(1,4,6/5)-4,5,6-triacetoxy-3-acetoxymethylcyclohex-2-enylamino]-β-*D*-mannopyranose* (**18**).—A mixture of **13** (19.4 mg, 0.135 mM) and (+)-4,7:5,6-di-*O*-isopropylidenevalienamine[6] (**17**; 28.7 mg, 0.112 mmol) in 2-propanol (0.5 mL) was heated in a sealed tube for 10 days at 120°C,

and then the solvent was evaporated. The residue was eluted from a column of silica gel (3 g) with 1:3 Me_2CO–PhMe, to give the condensate (33 mg, 74%), which was treated with aq 80% AcOH for 3 h at 60°C and then acetylated with Ac_2O in pyridine for 5 h at room temperature. The product was chromatographed on a column of silica gel (2 g) with 1:8 butanone–PhMe, to give **18** (24 mg, 51%); mp 160–161°C (from EtOH); $[\alpha]_D^{28}$ −13° (*c* 1.7, $CHCl_3$); ^1H NMR data are listed in Table I. Anal. Calcd for $C_{25}H_{33}NO_{14}$: C, 52.54; H, 5.82; N, 2.45. Found: C, 52.38; H, 5.70; N, 2.43.

*3-O-Acetyl-1,6-anhydro-2-azido-2,4-dideoxy-4-[(1S)-(1,4,6/5)-4,5,6-triacetoxy-3-acetoxymethylcyclohex-2-enylamino]-β-*D*-glucopyranose* (**19**).—A mixture of **14** (75 mg, 0.44 mmol) and **17** (94.5 mg, 0.37 mmol) in 2-propanol (1.5 mL) was heated in a sealed tube for 4 days at 120°C, and then the solvent was evaporated. The product was eluted from a column of silica gel (10 g) with 1:7 Me_2CO–PhMe, to give the condensate (110 mg, 70%), which was treated with aq 80% AcOH and then acetylated, as for the preparation of **18**, to give **19** (123 mg, 86%) as a syrup; $[\alpha]_D^{19}$ +13° (*c* 3.3, $CHCl_3$); ^1H NMR data are listed in Table I. Anal. Calcd for $C_{23}H_{30}N_4O_{12}$: C, 49.82; H, 5.45; N, 10.10. Found: C, 50.18; H, 5.42; N, 9.93.

*2-Amino-1,6-anhydro-2,4-dideoxy-4-[(1S)-(1,4,6/5)-4,5,6-trihydroxy-3-hydroxymethylcyclohex-2-enylamino]-β-*D*-glucopyranose* (**6**) *and 2-acetamido-3-O-acetyl-1,6-anhydro-2,4-dideoxy-4-[(1S)-(1,4,6/5)-4,5,6-triacetoxy-3-acetoxymethylcyclohex-2-enylamino]-β-*D*-glucopyranose* (**20**).—The condensate derived by coupling of **14** (75 mg) and **17** (95 mg) was reduced in aq 50% pyridine (5 mL) under a stream of H_2S gas for 2 h at room temperature. The solvents were evaporated and the residue was eluted from a column of silica gel (10 g) with PhMe → 1:5 EtOH–PhMe, to give the amine (98 mg), which was treated with aq 60% AcOH for 0.5 h at 60°C. The product was purified by elution from a column of Amberlite CG-50 (H^+) resin (10 mL) with H_2O → aq 2% NH_3 and then from a column of Amberlite IRA 400 (HO^-) resin (2 mL) with MeOH, to give **6** (71 mg, 86%) as a white solid; $[\alpha]_D^{23}$ +35° (*c* 0.52, MeOH); R_f 0.45 (2:2:1 $CHCl_3$–MeOH–aq 28% NH_3).

A 52-mg portion (0.16 mmol) of **6** was acetylated in the usual manner and the product was purified by chromatography on a column of silica gel (5 g) with 1:2 Me_2CO–PhMe, to give **20** (83 mg, 88%) as a syrup; $[\alpha]_D^{19}$ −11° (*c* 1.2, $CHCl_3$); ^1H NMR data are listed in Table I. Anal. Calcd for $C_{25}H_{34}N_2O_{13}$: C, 52.63; H, 6.01; N, 4.91. Found: C, 52.93; H, 6.03; N, 4.71.

*3-O-Acetyl-1,6-anhydro-2,4-dideoxy-2-fluoro-4-[(1S)-(1,4,6/5)-4,5,6-triacetoxy-3-acetoxymethylcyclohex-2-enylamino]-β-*D*-glucopyranose* (**21**).—A mixture of crude **15** (124 mg) and **17** (56 mg, 0.22 mmol) in 2-propanol (1.5 mL) was heated in a sealed tube for 7 days at 100°C, and then the solvent was evaporated. TLC (1:5 Me_2CO–PhMe) showed formation of several products. A mixture of the products was eluted from a column of silica gel (10 g) with 1:7 Me_2CO–PhMe, to give the major product (15 mg, 17%), which was *O*-deisopropylidenated and then acetylated. The product was eluted from a column of silica gel (2 g) with 1:6 Me_2CO–PhMe, to give **21** (16 mg, 84%) as a syrup; $[\alpha]_D^{22}$ +28° (*c* 0.62, $CHCl_3$); ^1H

NMR data are listed in Table I. Anal. Calcd for $C_{23}H_{30}FNO_{12}$: C, 51.98; H, 5.69; N, 2.64. Found: C, 52.15; H, 5.77; N, 2.49.

3-O-Acetyl-1,6-anhydro-4-deoxy-2-thio-2-S-(p-tolyl)-4-[(1S)-(1,4,6/5)-4,5,6-triacetoxy-3-acetoxymethylcyclohex-2-enylamino]-β-D-glucopyranose (**22**).—A mixture of **16** (143 mg, 0.57 mmol) and **17** (91 mg, 0.36 mmol) in 2-propanol (2 mL) was heated in a sealed tube at 120°C for 3 days, and then the solvent was evaporated. The product was eluted from a column of silica gel (20 g) with 1:8 Me_2CO–PhMe, to give the condensate (146 mg, 81%), which was *O*-deisopropylidenated and then acetylated as for the preparation of **18**, to give, after elution from a column of silica gel (7 g) with 1:10 Me_2CO–PhMe, **22** (62 mg, 88%) as a syrup; $[\alpha]_D^{23}$ −77° (*c* 1.2, $CHCl_3$); ^1H NMR data are listed in Table I. Anal. Calcd for $C_{30}H_{37}NO_{12}S$: C, 56.68: H, 5.87; N, 2.20. Found: C, 56.84; H, 6.10; N, 2.03.

3-O-Acetyl-1,6-anhydro-2,4-dideoxy-4-[(1S)-(1,4,6/5)-4,5,6-triacetoxy-3-acetoxymethylcyclohex-2-enylaminol]-β-D-arabino-hexopyranose (**23**) *and 1,6-anhydro-2,3,4-trideoxy-4-[(1S)-(1,4,6/5)-4,5,6-triacetoxy-3-acetoxymethylcyclohex-2-enylamino]-β-D-erythro-hexopyranose* (**24**).–A solution of **22** (66 mg, 0.11 mmol) in Me_2CO (1 mL) was vigorously agitated, after addition of Raney nickel T-4 (0.5 mL), for 4 h at room temperature. The mixture was filtered, the filtrate was evaporated and the residue was eluted from a column of silica gel (2 g) with 1:8 Me_2CO–PhMe, to give **23** (28 mg, 53%), $[\alpha[_D^{23}$ + 1.4° (*c* 0.3, $CHCl_3$); and **24** (18 mg, 38%), $[\alpha]_D^{22}$ +22° (*c* 0.84, $CHCl_3$), as a syrup. ^1H NMR data are listed in Table I. Anal. For **23**: Calcd for $C_{23}H_{31}NO_{12}$: C, 53.80; N, 6.08; N, 2.73. Found: C, 54.03; H, 6.19; N, 2.55. For **24**: Calcd for $C_{21}H_{29}NO_{10}$: C, 55.38; H, 6.42; N, 3.08. Found: C, 55.52; H, 6.40; N, 2.97.

1,6-Anhydro-4-deoxy-4-[(1S)-(1,4,6/5)-4,5,6-trihydroxy-3-hydroxymethylcyclohex-2-enylamino]-β-D-mannopyranose (**4**).—Compound **18** (11 mg, 20 μmol) was treated in MeOH (0.5 mL) with methanolic M NaOMe (1 mL) for 2 h at room temperature. The product was purified on columns of Dowex 50W-X2 (H^+) resin and Amberlite IRA-400 (HO^-) resin, as described for the isolation of **6**, to give **4** (3.2 mg, 50%) as a syrup; R_f 0.41 (1:1 MeOH–$CHCl_3$); $[\alpha]_D^{21}$ +23° (*c* 0.80, MeOH).

1,6-Anhydro-2-azido-2,4-dideoxy-4-[(1S)-(1,4,6/5)-4,5,6-trihydroxy-3-hydroxymethylcyclohex-2-enylamino]-β-D-glucopyranose (**5**).—Compound **19** (37 mg, 67 μmol) was *O*-deacetylated as described for the preparation of **4**, and the product was similarly purified to give **5** (15 mg, 67%) as a syrup; $[\alpha]_D^{23}$ +12° (*c* 2.0, MeOH).

2-Acetamido-1,6-anhydro-2,4-dideoxy-4-[(1S)-(1,4,6/5)-4,5,6-trihydroxy-3-hydroxymethylcyclohex-2-enylamino]-β-D-glucopyranose (**7**).—Compound **20** (40 mg, 71 μmol) was similarly *O*-deacetylated to give **7** (25 mg, 98%) as a syrup; $[\alpha]_D^{23}$ +28° (*c* 0.85, MeOH).

1,6-Anhydro-2,4-dideoxy-2-fluoro-4-[(1S)-(1,4,6/5)-4,5,6-trihydroxy-3-hydroxymethylcyclohex-2-enylamino]-β-D-glucopyranose (**8**).—Compound **21** (15 mg, 28 μmol) was treated with MeOH (1 mL) saturated with NH_3 at 0°C. The product was purified, as described for the isolation of **6**, to give **8** (5.8 mg, 67%) as a syrup; $[\alpha]_D^{22}$ +41° (*c* 0.63, MeOH).

*1,6-Anhydro-4-deoxy-2-thio-2-*S*-(*p*-tolyl)-4-[(1*S*)-(1,4,6/5)-4,5,6-trihydroxy-3-hydroxymethylcyclohex-2-enylamino]-β-*D*-glucopyranose* (**9**).—Compound **22** was *O*-deacetylated as described for the preparation of **4**, to give **9** as a syrup; $[\alpha]_D^{21}$ −41° (*c* 0.70, MeOH).

*1,6-Anhydro-2,4-dideoxy-4-[(1*S*)-(1,4,6/5)-4,5,6-trihydroxy-3-hydroxymethylcyclohex-2-enylamino]-β-*D*-arabino-hexopyranose* (**10**).—Compound **23** was *O*-deacetylated as described for the preparation of **4**, to give **10** as a syrup; $[\alpha]_D^{21}$ +62° (*c* 0.20, MeOH).

*1,6-Anhydro-2,3,4-trideoxy-4-[(1*S*)-(1,4,6/5)-4,5,6-trihydroxy-3-hydroxymethylcyclohex-2-enylamino]-β-*D*-erythro-hexopyranose* (**11**).—Compound **24** was *O*-deacetylated as described for the preparation of **4**, to give **11** as a syrup; $[\alpha]_D^{21}$ +53° (*c* 0.26, MeOH).

Without further purification, compounds **4**–**11**, after rough characterisation by their ^{1}H NMR spectra (270 MHz, D_2O), were subjected to bioassay (Table II).

ACKNOWLEDGEMENTS

We thank Mr. E. Hata for elemental analyses, Drs. S. Inouye and T. Machinami (Meiji Seika Kaisha, Yokohama) for bioassay, and Yamakawa Chemical Industry Co., Ltd. (Tokyo) for providing us with optically resolving reagent. The work was supported, in part, by a grant from the Asahi Glass Foundation for the contribution to industry technology.

REFERENCES

1 Y. Shibata, Y. Kosuge, T. Mizukoshi, and S. Ogawa, *Carbohydr. Res.*, 228 (1992) 377–398.
2 B. Junge, F.R. Heiker, J. Kurz, L. Müller, D.D. Schmidt, and C. Wunsche, *Carbohydr. Res.*, 128 (1984) 235–268.
3 E. Truscheit, W. Frommer, B. Junge, L. Müller, D.D. Schmidt, and W. Wingender, *Angew. Chem. Int. Ed. Engl.*, 20 (1981) 744–761.
4 S. Ogawa, Y. Shibata, Y. Kosuge, K. Yasuda, T. Mizukoshi, and C. Uchida, *J. Chem. Soc., Chem. Commun.*, 1990, 1387–1388.
5 S. Ogawa, H. Sugizaki, Y. Iwasawa, and T. Suami, *Carbohydr. Res.*, 140 (1985) 325–331.
6 Y. Shibata and S. Ogawa, *Carbohydr. Res.*, 189 (1989) 309–322.
7 R.M. Hann and C.S. Hudson, *J. Am. Chem. Soc.*, 64 (1942) 925–928.
8 H. Paulsen and H. Koebernick, *Chem. Ber.*, 109 (1976) 104–111.
9 J. Pacák, J. Podešva, Z. Točík, and M. Černý, *Collect. Czech. Chem. Commun.*, 37 (1972) 2589–2599.
10 S. Nishimura, *Bull. Chem. Soc. Jpn.*, 32 (1959) 61–64.