

Design and Synthesis of New 1,4-Diaminocyclitol Aminoglycosides: Use of Maltose as the Key Starting Material

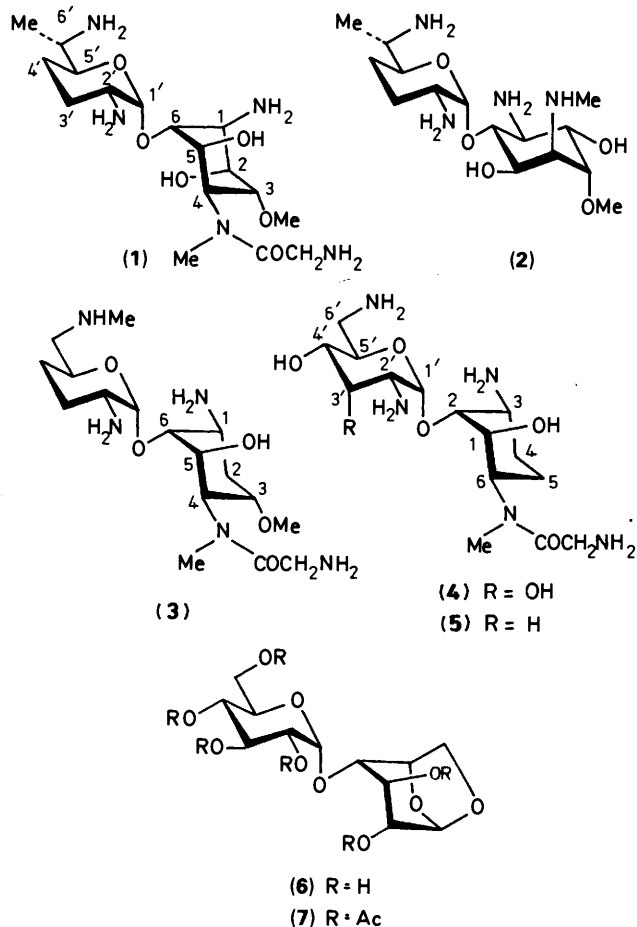
Nobuo Sakairi, Mitsuo Hayashida, Akihiro Amano, and Hiroyoshi Kuzuhara*
 RIKEN (The Institute of Physical and Chemical Research), Wako-shi, Saitama
 351-01, Japan

New antimicrobial aminoglycosides having a pseudodisaccharide structure, 1L-(1,6/2,3)-3-amino-2-(2,6-diamino-2,6-dideoxy- α -D-allopyranosyloxy)-6-[glycyl(methyl)amino]cyclohexanol (4) and its 3'-deoxy analogue (5) have been synthesized from 1,6-anhydro- β -maltose (6), utilizing its internal glycosidic linkage. This synthesis involves regio- and stereo-selective introduction of amino precursors, azido and methylamino groups, and transformation of the 1,6-anhydrohexopyranose moiety into a cyclitol moiety. The latter was accomplished by application of novel chemical devices, such as formation of phenyl 1-thioglycosides (32) and (39) by selective fission of 1,6-anhydro rings of disaccharides, and application of Ferrier's carbocyclization reaction to the thioglycosides.

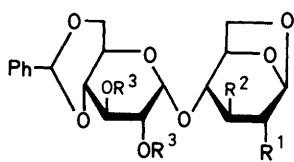
Since the discovery of fortimicin A (astromycin) (1) in 1977,¹ a series of similar novel aminoglycoside antibiotics has been isolated; istamycin B (3)² and sporaricin A³ among others. These antibiotics have attracted much attention for their antimicrobial activities against the strains resistant to known aminoglycoside antibiotics and their lower toxicity to both the auditory organs and the kidney. As exemplified by structures (1) and (3), these compounds are pseudodisaccharides which comprise 1,4-diaminocyclitols glycosylated with 2,6-diamino- α -D-pyranosyl residues. One of the amino groups of the aminocyclitol moieties is methylated without any exception and, in many cases, the methylamino groups are further aminoacylated with glycine or *N*-modified glycine. The most remarkable feature of these antibiotics is that the conformation of the aminocyclitol moieties is very flexible and can change depending on whether the methylamino group is acylated or not. For example, fortimicin B (2) having an unacylated methylamino group adopts the ⁴C₁ conformation, in contrast to the reverse conformation (¹C₄) taken by the other antibiotics carrying glycyated methylamino group.⁴ Interestingly, manifestation of the antimicrobial activities also require such a glycy (or *N*-modified glycy) moiety on the methylamino group, this being exemplified by the inactivity of compound (2).

Hitherto, total syntheses of some of these antibiotics have been achieved by conventional glycosidation reaction between appropriately protected aminocyclitols as glycosyl acceptors and amino sugars activated as glycosyl donors in such forms as glycosyl halide⁵ and acetate.⁶ Generally, preparations of those glycosyl donors and acceptors are rather laborious and the yields of the coupling reactions are not necessarily high. In past work on total syntheses of bioactive compounds [e.g., antithrombin III-binding site of heparin⁷ and α -D-glucosidase inhibitors, amylostatin (XG)⁸ and 'dihydroacarbose'⁹], we have often employed di- and tri-saccharides as key starting materials, utilizing their internal glycosidic linkages. As preliminarily communicated, we had also successfully applied such synthetic methodology in the preparation of novel 1,4-diaminocyclitol aminoglycoside, 1L-(1,6/2,3)-3-amino-2-(2,6-diamino-2,6-dideoxy- α -D-allopyranosyloxy)-6-[glycyl(methyl)amino]cyclohexanol (4), employing 1,6-anhydro- β -maltose (6) as the starting material.¹⁰ Here we describe the preparation of compound (4) in detail, as well as the synthesis of its 3'-deoxy analogue (5).

The target compounds, (4) and (5), were designed taking the

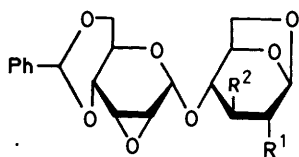


structure (3) as the model. Positions and configurations of all amino groups of the target molecules were the same as those of compound (3). It was interesting to know what would be the real conformation of compounds (4) and (5) when synthesized, because these compounds do not have an equatorial methoxy group corresponding to that present at C-3 of (3), which may be influencing the pyranosyloxy residue, the bulkiest substituent, to take an axial conformation. In spite of the apparently close



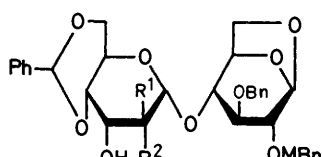
	R ¹	R ²	R ³
(8)	OH	OH	TIPS
(9)	OBz	OBz	TIPS
(10)	OBz	OBz	Ms
(11)	OCOCMe ₃	OH	Ms
(12)	OCOCMe ₃	OBn	Ms

TIPS = 1,1,3,3-tetraisopropylidisiloxane-1,3-diyl



(13) R¹: OH, R²: OBn

(14) R¹: OMBn, R²: OBn



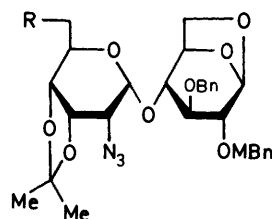
(15) R¹: N₃, R²: H

(16) R¹: H, R²: N₃

MBn = *p*-methoxybenzyl

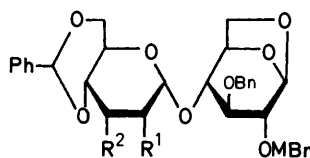
similarity of the molecular shapes between the target compounds and the starting material, the conversion of compound (6) into compound (4) or (5) actually required a number of well-organized specific chemical manipulations. The scheme employed involved (1) optimized discriminative protections of each hydroxy group of compound (6), (2) formation of the amino sugar moieties by introduction of two amino groups [and deoxygenation, for (5)], (3) construction of a cyclitol moiety from the 1,6-anhydrohexopyranose moiety in the disaccharide intermediates, (4) stepwise introductions of the amino and methylamino groups into the cyclitol moiety, and (5) acylation of the methylamino group and deprotection.

Preliminary Protections and Formation of Amino Sugar Moieties.—The conversion method of compound (6) into 1,6-anhydro-4',6'-*O*-benzylidene-2',3'-*O*-(1,1,3,3-tetraisopropylidisiloxane-1,3-diyl)- β -maltose¹¹ (8), which was practically the actual starting material, has been developed before by us;¹¹ after benzylation of compound (8) in the usual way, the resulting 2,3-dibenzoate (9) underwent de-*O*-silylation with fluoride anion in aqueous media¹¹ and subsequent treatment with methanesulphonyl chloride to give the 2',3'-bismethanesulphonate (10). For the present large-scale preparation of compound (9), the hexa-acetate of (6), compound (7), was used as the starting material and gave compound (9) in 58% overall yield after going through 4 continuous reaction steps without isolation of any intermediate. Since discrimination of the 2- and 3-hydroxy groups would become necessary for later methylation, *p*-methoxybenzyl and benzyl groups were chosen as their protecting group. For a preliminary protection of temporary nature, compound (10) was successively treated with a catalytic amount of sodium methoxide and pivaloyl chloride (1.2 mol equiv.) to give the 2-*O*-pivaloyl derivative (11) in 75% yield. Benzylation of the 3-hydroxy group of compound (11) without affecting alkali-labile pivaloyl and methanesulphonyl groups was achieved by employing phase-transfer benzylation¹² at a controlled temperature, giving the desired compound (12) in 84% yield. Subsequent treatment of



(17) R = OH

(18) R = N₃

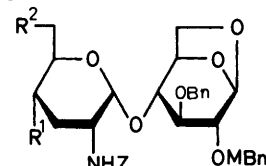


(19) R¹: N₃, R²: OCSOPh

(20) R¹: NHZ, R²: OH

(21) R¹: NHZ, R²: OCSOPh

(22) R¹: NHZ, R²: H



(23) R¹: R²: OH

(24) R¹: OH, R²: OTs

(25) R¹: OH, R²: N₃

(26) R¹: OBn, R²: N₃

Z = PhCH₂OCO

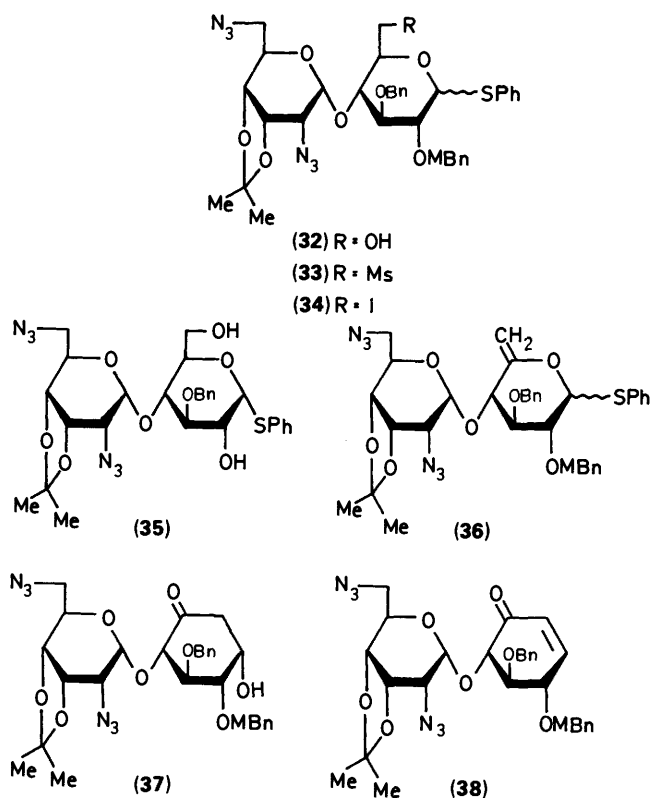
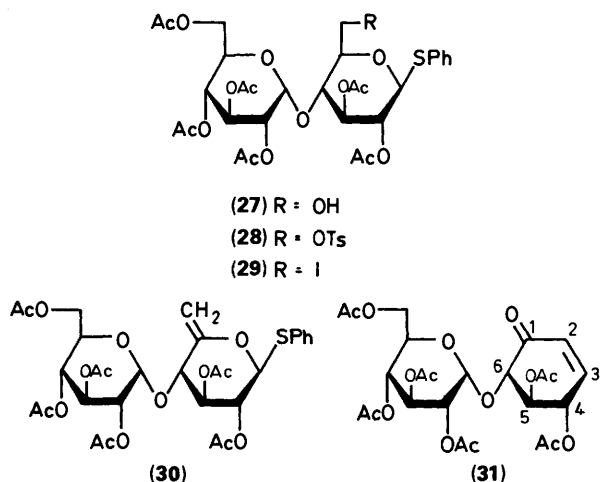
compound (12) with an excess of sodium methoxide gave a crystalline product (13) carrying the 2',3'-anhydro- α -D-allopyranosyl residue in 80% yield. Compound (13) smoothly underwent 2-*O*-*p*-methoxybenzylation by treatment with *p*-methoxybenzyl chloride-sodium hydride-tetrabutylammonium iodide, giving compound (14) in high yield. Introduction of an azido group to the 2'-position with α -orientation was conducted by application of a procedure established by Richardson *et al.* using the monosaccharide derivatives.¹³ Thus, nucleophilic opening of the epoxide ring of compound (14) with azido anion gave the 2'-azido-2'-deoxy- α -D-allopyranosyl derivative (15), which underwent dimethyl sulphoxide (DMSO) oxidation of the 3'-hydroxy group and subsequent reduction with sodium borohydride for inversion of the adjacent azido group to give the 2'-azido-2'-deoxy- α -D-allopyranosyl derivative (16) as desired. Compound (16) constituted the last common intermediate for preparation of compounds (4) and (5).

Introduction of the second azido group to the 6'-position was separately carried out towards both target molecules (4) and (5). The first step towards (4) was the removal of the 4',6'-*O*-benzylidene group of compound (16), which was followed by *O*-isopropylideneation with 2,2-dimethoxypropane-toluene-*p*-sulphonic acid (PTSA), giving the 3',4'-*O*-isopropylidene derivative (17) as a thermodynamically stable product. In the usual manner, another azido group was introduced to the 6'-position *via* the 6'-methanesulphonate intermediate, giving the 2',6'-diazido derivative (18).

On the other hand, deoxygenation at the 3'-position preceded introduction of the azido group to C-6' in the synthetic course directed towards compound (5). Thus, the 3'-phenoxythioformate (19) of compound (16) was treated with tributyltin hydride-azoisobutyronitrile (AIBN).¹⁴ However, this radical-initiated reaction failed, giving a complex mixture; this failure was probably ascribable to the presence of an azido group, which is liable to change into reactive species such as iminyl or triazenyl radicals¹⁵ under those conditions. Therefore, the azido group of compound (16) was first changed to the benzyloxycarbonylamino group by reduction with lithium aluminium hydride and treatment with benzyl chloroformate. The resulting compound (20) underwent *O*-phenoxythiocarbonylation at the 3'-position with phenyl chlorothioformate-4-(*N,N*-dimethylamino)pyridine (DMAP), giving compound (21)

in good yield. Deoxygenation of thioester (21) with tributyltin hydride–AIBN smoothly proceeded in toluene at 80 °C, giving the 3'-deoxy derivative (22) in quantitative yield. After removal of the benzylidene group from compound (22), the resulting diol (23) underwent selective toluene-*p*-sulphonation at the primary hydroxy group and subsequent replacement of this group with azido anion, giving the 6'-azido derivative (25) *via* the tosyl ester (24). Compound (25) was treated with benzyl bromide–barium oxide–barium hydroxide for benzylation of the 4'-hydroxy group to give compound (26). Thus, syntheses of a couple of important intermediates, (18) and (26), were completed.

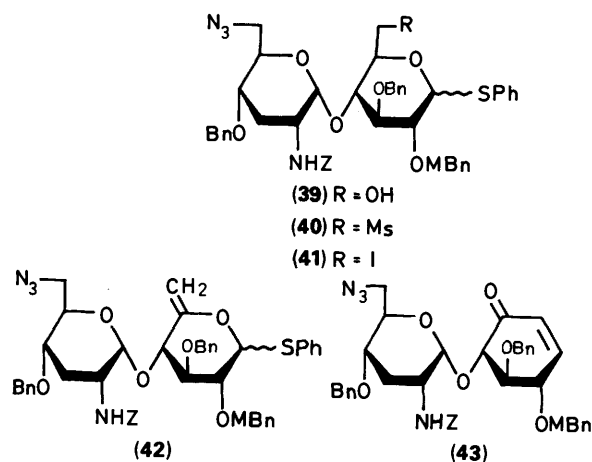
Construction of Aminocyclitol Moiety.—Conversion of the 1,6-anhydro- β -D-glucopyranose moiety in intermediates (18) and (26) into a cyclitol moiety was regarded as one of the key steps for total syntheses of compounds (4) and (5). Before proceeding, we developed a model synthetic route for such chemical transformation, employing 1,6-anhydro- β -maltose hexa-acetate (7) as a model substrate. When compound (7) was treated with Hanessian's reagent system,¹⁶ (phenylthio)trimethylsilane (PhSTMS)–zinc iodide, at room temperature, the 1,6-anhydro ring selectively reacted without any cleavage of the internal glycosidic linkage, giving the phenyl 1-thio- β -D-glucopyranoside *O*-silylated at the 6-position. After acidic hydrolysis of the trimethylsilyl ether, compound (27) was isolated in 78% yield. Compound (27) was changed to the 6-toluene-*p*-sulphonate (28), which was expected to give the 6-deoxy-6-iodo derivative (29) by the usual treatment. However, attempts to replace the toluene-*p*-sulphonyloxy group using iodide anion in acetone or *N,N*-dimethylformamide (DMF), with sodium iodide as the reagent, resulted in decomposition of the thioglycoside by the attack of liberated iodine. This problem was finally overcome by the use of lithium iodide in diethyl ether at room temperature and under argon atmosphere. Compound (29) thus obtained was immediately subjected to the next β -elimination reaction, without purification because of its instability. Thus, treatment of iodide (29) with 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) in toluene gave the 5-enopyranoside derivative (30) in an overall yield of 77% from compound (28). For the subsequent carbocyclization reaction, the method of Ferrier,^{17,18} using a mercury(II) salt that has been widely used for preparation of cyclohexanone derivatives from 5-enopyranoses, was applied, on the presumption that the soft acid [mercury(II) ion]–soft base (sulphur atom) affinity would promote the reaction. In fact, the reaction smoothly proceeded at lower temperature than in a similar reaction with the corresponding methyl *O*-glycoside derivative,¹⁷ when compound (30) was treated with mercury(II) chloride in aqueous acetone. The resulting unstable product



was quickly subjected to β -elimination by treatment with acetic anhydride–pyridine, giving the known pseudodisaccharide carrying the 4,5-acetoxycyclohex-2-enone moiety, *i.e.* compound (31).

Following the establishment of this model transformation procedure, intermediates (18) and (26) were processed. Unfortunately, partial deprotection was found to accompany the thiolysis of the 1,6-anhydro ring of these complex substrates; treatment of compound (18) with PhSTMS–zinc iodide caused de-*O*-isopropylidene and partial removal of the *p*-methoxybenzyl group as side reactions. The product was therefore re-isopropylideneated after de-*O*-silylation with acid, giving the desired phenyl 1-thioglycoside (32) (α : β 3:1) in 56% yield together with the 2,6-diol (35) in 31% yield. Similar treatment of intermediate (26) also brought about loss of the *N*-benzyloxycarbonyl group. Therefore, after treatment with aqueous sodium hydrogen carbonate, the product was again *N*-benzyloxycarbonylated to give the desired phenyl 1-thioglycoside (39) (α : β 7:3) in 58% yield. Conversion of thioglycosides (32) and (39) into the corresponding 5-enopyranoside derivatives (36) and (42) was achieved in good yield *via* the 6-methanesulphonates (33) and (40) and the 6-deoxy-6-iodo compounds (34) and (41), after the model reactions mentioned above. Ferrier reaction of compound (36) was also successful and gave the carbocyclic hydroxy ketone (37) in 67% yield. The ¹H NMR spectrum of the product revealed that a hydroxy group was generated through this reaction at C-5, but only with an α -configuration. This labile hydroxy group was readily removed by treatment with methanesulphonyl chloride–pyridine as the result of β -elimination, giving the cyclohex-2-enone derivative (38). In a similar way, the 3'-deoxy analogue (42) provided the corresponding cyclohex-2-enone derivative (43) in 61% overall yield.

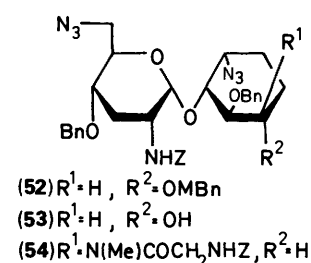
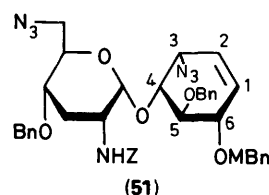
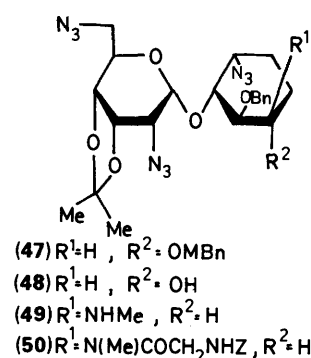
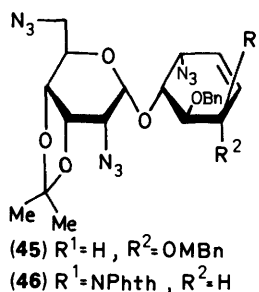
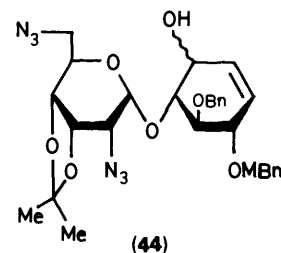
For introduction of an amino group into the allylic position of compound (38), application of the Mitsunobu reaction¹⁹ seemed attractive. In advance, the carbonyl group was selectively reduced in methanol at –78 °C by treatment with



sodium borohydride–cerium(III) chloride,²⁰ giving an inseparable epimeric mixture of allylic alcohols (44) and a small amount of the corresponding saturated alcohols. Without further purification, compound (44) was treated with hydrazoic acid–triphenylphosphine (TPP)–diethyl azodicarboxylate (DEAD) in toluene at -15°C followed by careful purification on a silica gel column, to give an allylic triazido compound in 64% yield. The configuration of the newly introduced azido group in this major product was uncertain at this stage but was recognized as being α , in correlation with the product obtained in a later step, which meant that this Mitsunobu reaction produced compound (45). For introduction of a methylamino group into the other allylic position, compound (45) was preliminarily examined by a series of reactions: *i.e.*, *de-O-p*-methoxybenzylation²¹ followed by replacement of the resulting hydroxy group with an amino function, and methylation of the amino group. Thus, compound (45) was treated with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) and then with phthalimide–TPP–DEAD in tetrahydrofuran (THF), giving the *N*-phthaloyl derivative (46) in 59% overall yield. Several attempts at methylation of the amino group produced by treatment of the phthalimide (46) with hydrazine hydrate failed, probably because the allylic azido system was too labile to survive the basic conditions employed. This failure drew our attention towards direct methylation preceded by selective reduction of the C–C double bond. After several unsuccessful attempts, selective reduction of the double bond of compound (45) was achieved by homogeneous hydrogenation in benzene employing Wilkinson's catalyst,²² without affecting the co-existing azido and *O*-benzyl groups which are very susceptible to general hydrogenation methods, and gave the saturated triazido derivative (47) in 71% yield. For removal of the *O-p*-methoxybenzyl group, compound (47) was oxidized with DDQ, giving the 3-hydroxy derivative (48). In the ^1H NMR spectrum of the product (48), signals appearing at δ 3.60 (br s), 3.74 (t), 3.79 (d d), and 4.07–4.09 (m) were assignable to the protons of C-1, C-2, C-3, and C-4, respectively. Their coupling constants, $J_{1,2} = J_{2,3} = 7.8$ Hz and $J_{3,4} = 2.9$ Hz, revealed the $^4\text{C}_1$ conformation of the cyclitol moiety and also determined the configuration of the azido group introduced at C-4 as being α . Direct introduction of the methylamino group and its glycylation was performed by three continuous reaction steps without isolation of intermediates, which was necessitated by limited sample quantities. Thus, compound (48) was oxidized with DMSO–trifluoroacetic anhydride (TFAA) at -78°C and the resulting ketone was subjected to reductive amination with methylamine–sodium cyanoborohydride at pH 6.2,²³ giving one product which was later confirmed to have the β -oriented methylamino group as in structure (49). Compound (49) was

acylated with the *N*-hydroxysuccinimide ester of *N*-benzyloxycarbonylglycine according to a literature method²⁴ to give the fully protected aminoglycoside (50). Finally, the *O*-isopropylidene group of compound (50) was removed in aqueous trifluoroacetic acid (TFA) and the hydrolysate was subjected to catalytic hydrogenolysis in methanol–hydrochloric acid with 10% palladium on carbon as the catalyst. The product was purified through a column of CM-Sephadex C-25 [NH_4^+ form] with aqueous ammonium hydroxide as eluant to give the aminoglycoside (4).

Compounds (43) and (38) have exactly the same cyclohexenone moiety, and therefore it was assumed that the manipulation of compound (43) towards the target compound (5) would also smoothly proceed by the same way as the conversion of intermediate (38) into aminoglycoside (4). Introduction of an azido group into the allylic position of compound (43) was successful [as for compound (38)] by 1,2-reduction of the enone group and successive Mitsunobu reaction, giving diazide (51). Quite unexpectedly, no reaction took place when compound (51) was subjected to homogeneous hydrogenation with Wilkinson's catalyst for selective reduction of the C=C double bond. This failure was probably ascribable to deactivation of the catalyst by the coexisting benzyloxycarbonylamino group. The selective hydrogenation desired was achieved by treatment with diimide generated from excess of potassium azodicarboxylate–acetic acid in acetonitrile,²⁵ giving compound (52) which was contaminated with a trace of unchanged compound (51). Crude compound (52) underwent *de-O-p*-methoxybenzylation with DDQ and subsequent careful purification with column chromatography, giving the pure 3-hydroxy derivative (53) in 54% overall yield from (51). Similarly



to the conversion of intermediate (48) into compound (4), intermediate (53) was subjected to a series of reactions including DMSO oxidation, reductive methylation, and *N*-glycylation to give compound (54). Catalytic hydrogenolysis of compound (54) and purification of the product by chromatography on CM-Sephadex C-25 [NH_4^+] with aqueous ammonia as eluant gave the target aminoglycoside (5).

The structure of the common cyclitol moiety of aminoglycosides (4) and (5) was unambiguously elucidated on the basis of their ^1H NMR spectra as shown in the Figure. The vicinal coupling constants, $J_{2,3} = J_{1,2} = J_{1,6} = J_{5_{\text{eq}},6} = \text{ca. } 3 \text{ Hz}$ and $J_{5_{\text{ax}},6} = \text{ca. } 12 \text{ Hz}$, strongly supported the $^1\text{C}_4$ conformation of the cyclitol moiety in compounds (4) and (5), which was the same as for natural aminoglycosides of this type bearing an equatorial methoxy group. Furthermore, the configuration of the methylamino group introduced by reductive amination was determined as being β on the basis of these ^1H NMR data.

Antimicrobial activities of aminoglycosides (4) and (5) against several micro-organisms were tested, being compared with commercial fortimicin A (1). Compounds (4) and (5) showed similar antimicrobial spectra and were 20–50% as active as compound (1).

Experimental

General Methods.—M.p.s were determined with a Yamato micro melting point apparatus, and are uncorrected. Optical rotations were determined with a Perkin-Elmer Model 241MC polarimeter. IR spectra were recorded with a Shimadzu IR-27 spectrophotometer, for potassium bromide disks or on KRS (thallium bromide iodide) for thin films. ^1H NMR spectra were recorded at 400 MHz or 500 MHz with JEOL JNM-GX 400 or

500 spectrometers, with tetramethylsilane as the internal standard for solutions in deuteriochloroform, unless otherwise noted. High-resolution mass spectra were recorded with a Hitachi M-80 spectrometer and secondary-ion (si) mass spectra were recorded with the same spectrometer in a glycerol matrix at an ionization voltage of 3 kV (primary ion of xenon) and 8–9 kV (secondary ion). All reactions were monitored by TLC, which was conducted on a precoated plate of silica gel 60F₂₅₄ (layer thickness 0.25 mm; E. Merck, Darmstadt, Germany), and spots were detected by UV light and by methanol-*p*-methoxybenzaldehyde-conc. sulphuric acid (85:10:5 v/v) spray followed by heating at 200 °C. Silica gel 60 (70–230 mesh and 230–400 mesh; E. Merck) was used for column chromatography and for flash column chromatography, respectively.

The procedure referred to as usual work-up in the following section was as follows: reaction mixture was poured into ice-water, stirred for several hours, and extracted with chloroform several times. The combined extracts were successively washed with *m*-hydrochloric acid, saturated aqueous sodium hydrogen carbonate, and brine, dried (Na_2SO_4), and evaporated under reduced pressure at a temperature below 40 °C.

1,6-Anhydro-2,3-di-*O*-benzoyl-4',6'-*O*-benzylidene-2',3'-*O*-(1,1,3,3-tetraisopropylidisiloxane-1,3-diyl)- β -maltose (9).—To an ice-cold solution of 1,6-anhydro-4',6'-*O*-benzylidene-2',3'-*O*-(1,1,3,3-tetraisopropylidisiloxane-1,3-diyl)- β -maltose¹¹ (8) (655 mg, 1 mmol) in pyridine (10 ml) was added dropwise benzoyl chloride (2 ml, 17 mmol), and the mixture was stirred at room temperature overnight. Usual work-up followed by column chromatography with benzene-EtOAc (97:3 v/v) as eluant gave the 2,3-dibenzoate (9) (783 mg, 91%) as an amorphous mass (Found: C, 62.45; H, 6.8. $\text{C}_{45}\text{H}_{58}\text{O}_{13}\text{Si}_2$ requires C, 62.6;

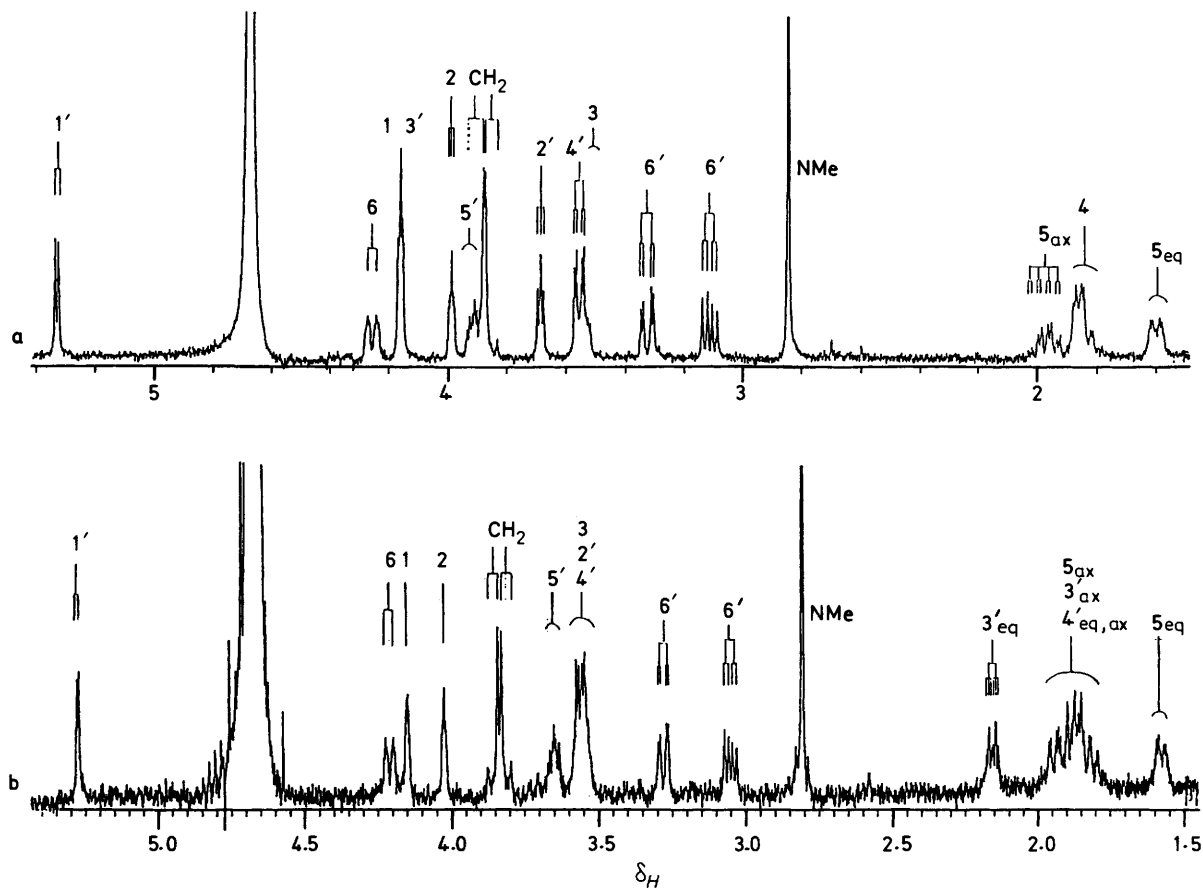


Figure. ^1H NMR spectra of compounds (4) (a) and (5) (b) for solution in $\text{DCI-D}_2\text{O}$ with tetramethylsilane as external standard.

H, 6.8%); $[\alpha]_D^{21} + 19.4^\circ$ (*c* 0.63 in CHCl_3); ν_{max} (film) 1720 cm^{-1} (C=O); δ_{H} (400 MHz) 3.55 (1 H, t, *J* 9.3 Hz, 4'-H), 3.71 (1 H, br s, 4-H), 3.83 (1 H, dd, *J* 3.9 and 9.0 Hz, 2'-H), 3.90 (1 H, dd, *J* 5.1 and 8.6 Hz, 6-H_a), 4.15 (1 H, t, *J* 9.0 Hz, 3'-H), 4.16 (1 H, d, *J* 8.6 Hz, 6-H_b), 4.89 (1 H, d, *J* 5.1 Hz, 5-H), 5.02 (1 H, br s, 2-H), 5.31 (1 H, br t, *J* 1.4 Hz, 3-H), 5.60 (1 H, s, *CH*Ph), 5.61 (1 H, br s, 1-H), and 5.09 (1 H, d, *J* 3.9 Hz, 1'-H).

For large-scale preparation, a pyridine solution of crude 1,6-anhydro-4',6'-*O*-benzylidene- β -maltose, which was prepared from 2,2',3,3',4',6'-hexa-*O*-acetyl-1,6-anhydro- β -maltose²⁶ (7) (120 g, 0.21 mmol) by de-*O*-acetylation with methanolic sodium methoxide followed by benzylation with α,α -dimethoxytoluene (43 ml, 0.28 mol),²⁷ was successively treated with 1,3-dichloro-1,1,3,3-tetraisopropylidensiloxane (70 ml, 0.22 mol) and benzoyl chloride (70 ml, 0.6 mol) at 0 °C to give compound (9) (104.8 g, 58% overall yield) without isolation of any intermediates.

1,6-Anhydro-2,3-di-*O*-benzoyl-4',6'-*O*-benzylidene-2',3'-di-*O*-methylsulphonyl- β -maltose (10).—To a solution of compound (9) (47.6 g, 55.1 mmol) and tetraethylammonium chloride (54.8 g, 0.33 mol) in acetonitrile–water (9:1; 500 ml) was added saturated aqueous potassium fluoride dihydrate (31.1 g, 0.33 mol). The mixture was stirred at room temperature for 6 h and extracted five times with chloroform. The combined extracts were washed with brine, dried, and evaporated to give a syrupy 2',3'-diol (41 g). To a stirred solution of the residual syrup in pyridine (275 ml) at 0 °C was added dropwise methanesulphonyl chloride (17.1 ml, 220 mmol). After 16 h at 0 °C, the mixture was poured into ice–water, and stirred for 3 h. The precipitate was filtered off and recrystallized from acetone–hexane to give the 2',3'-bismethanesulphonate (10) (39.7 g, 88%), m.p. 168–170 °C; Found: C, 54.1; H, 4.7; S, 8.3. $\text{C}_{35}\text{H}_{36}\text{O}_{16}\text{S}_2$ requires C, 54.35; H, 4.8; S, 8.1%; $[\alpha]_D^{19} + 40^\circ$ (*c* 0.37 in CHCl_3); δ_{H} (400 MHz) 2.87 and 2.99 (each 3 H, 2 × *s*, each MeSO_2), 3.77–3.85 (3 H, m, 4-H and 6'-H₂), 3.91 (1 H, dd, *J* 5.8, 7.8 Hz, 6-H_a), 4.14 (1 H, d, *J* 7.8 Hz, 6-H_b), 4.28–4.36 (2 H, m, 4'- and 5'-H), 4.77–4.81 (2 H, m, 5- and 2'-H), 5.14 (1 H, s, 2-H), 5.26 (1 H, t, *J* 9.5 Hz, 3'-H), 5.28 (1 H, s, 3-H), 5.58 (1 H, s, *CH*Ph), 5.66 (1 H, d, *J* 3.9 Hz, 1'-H), and 5.70 (1 H, s, 1-H).

1,6-Anhydro-4'-6'-*O*-benzylidene-2',3'-di-*O*-methylsulphonyl-2-*O*-pivaloyl- β -maltose (11).—To a stirred solution of compound (10) (74.1 g, 95.4 mmol) in THF–methanol (1:1 v/v; 800 ml) was added 28% methanolic sodium methoxide (4 ml; 20 mmol). After 1 h at room temperature, the mixture was neutralized with Amberlite IRC-45 (H^+), concentrated, and coevaporated with toluene three times to give a syrup (80 g). To a solution of the residue in dichloromethane–pyridine (6:1; 700 ml) at 0 °C was added dropwise pivaloyl chloride (20 ml, 110 mmol), and the mixture was stirred at 0 °C for 9 h. Usual work-up followed by column chromatography [benzene–EtOAc (from 9:1 to 3:1 v/v) as eluant] gave the 2-*O*-pivaloyl derivative (11) (74.7 g, 75%) as a white foam (Found: C, 48.0; H, 5.8; S, 9.0. $\text{C}_{29}\text{H}_{44}\text{O}_{17}\text{S}_2\cdot\text{EtOAc}$ requires C, 47.8; H, 6.1; S, 8.8%; $[\alpha]_D^{19} + 18^\circ$ (*c* 0.40 in CHCl_3); ν_{max} (KBr) 3500 (OH) and 1725 cm^{-1} (C=O); δ_{H} (400 MHz) 1.26 (9 H, s, 3 × *CMe*), 2.96 and 3.17 (each 3 H, 2 × *s*, each MeSO_2), 3.23 (1 H, d, *J* 4.9 Hz, OH), 3.68 (1 H, br s, 4-H), 3.73–3.80 (3 H, m, 6-H_a, 4'-H, and 6'-H_b), 3.90 (1 H, br s, 3-H), 4.09 (1 H, d, *J* 8.1 Hz, 6-H_b), 4.28–4.38 (2 H, m, 5'-H and 6'-H_b), 4.54 (1 H, br s, 2-H), 4.64 (1 H, dd, *J* 3.9, 9.8 Hz, 2'-H), 4.70 (1 H, d, *J* 4.9 Hz, 5-H), 5.08 (1 H, t, *J* 9.8 Hz, 3'-H), 5.40 (1 H, d, *J* 3.9 Hz, 1'-H), 5.40 (1 H, s, 1-H), and 5.56 (1 H, s, *CH*Ph).

1,6-Anhydro-3-*O*-benzyl-4',6'-*O*-benzylidene-2',3'-di-*O*-methylsulphonyl-2-*O*-pivaloyl- β -maltose (12).—To a vigorously stirred suspension of compound (11) (6.0 g, 9.2 mmol),

tetrabutylammonium hydrogen sulphate (5.0 g, 15 mmol), and benzyl bromide (20 ml, 170 mmol) in toluene (30 ml) at –10 to –15 °C was added dropwise 50% w/v aqueous sodium hydroxide (8 ml) during 2 h. The mixture was stirred vigorously at the same temperature overnight and was then partitioned between diethyl ether and water. The organic layer was washed with water, dried, and evaporated. Chromatography on a silica gel column with benzene–EtOAc–pyridine (190:10:1 v/v) as eluant gave the 3-*O*-benzyl derivative (12) (5.76 g, 84%) as a syrup (Found: C, 53.2; H, 5.65; S, 8.6. $\text{C}_{33}\text{H}_{42}\text{O}_{15}\text{S}_2$ requires C, 53.4; H, 5.7; S, 8.6%; $[\alpha]_D^{21} + 0.9^\circ$; $[\alpha]_{365\text{nm}}^{21} - 5.2^\circ$ (*c* 0.98 in CHCl_3); ν_{max} (KBr) 1720 cm^{-1} (C=O); δ_{H} (400 MHz) 1.26 (9 H, s, 3 × *CMe*), 2.94 and 3.12 (each 3 H, 2 × *s*, each MeSO_2), 3.63 (1 H, br s, 3-H), 3.70 (1 H, s, 4-H), 3.72–3.78 (3 H, m, 6-H_a, 4'-H, and 6'-H_b), 4.16 (1 H, d, *J* 7.6 Hz, 6-H_b), 4.34–4.44 (2 H, m, 5'-H and 6'-H_b), 4.61 (1 H, dd, *J* 3.9, 9.8 Hz, 2'-H), 4.63 and 4.79 (each 1 H, 2 × d, *J* 11.7 Hz, CH_2Ph), 4.73 (1 H, d, *J* 5.8 Hz, 5-H), 4.75 (1 H, s, 2-H), 5.05 (1 H, t, *J* 9.8 Hz, 3'-H), 5.24 (1 H, d, *J* 3.9 Hz, 1'-H), 5.42 (1 H, s, 1-H), and 5.55 (1 H, s, *CH*Ph).

1,6-Anhydro-4-*O*-(2,3-anhydro-4,6-*O*-benzylidene- α -D-allopyranosyl)-3-*O*-benzyl- β -D-glucopyranose (13).—To a solution of compound (12) (41.9 g, 56.4 mmol) in dichloromethane–methanol (1:1 v/v; 900 ml) was added 28% methanolic sodium methoxide (45 ml; 230 mmol). The mixture was stirred at 0 °C for 3 days, quenched with solid CO_2 , and concentrated. The residue was partitioned between chloroform and water. The organic layer was washed with water, dried, and evaporated to dryness. Crystallization from ethanol gave the 2',3'-epoxide (13) (14.1 g, 52%), and chromatography [with benzene–EtOAc (9:1 v/v) as eluant] of the filtrate gave a further crop of compound (13) (7.7 g, 28%); m.p. 163–164 °C (Found: C, 64.5; H, 5.8. $\text{C}_{26}\text{H}_{28}\text{O}_9$ requires C, 64.5; H, 5.8%; $[\alpha]_D^{21} + 58^\circ$ (*c* 0.60 in CHCl_3); ν_{max} (KBr) 3500 cm^{-1} (OH); δ_{H} (400 MHz) 3.42 (1 H, dd, *J* 2.9, 4.4 Hz, 2'-H), 3.51 (1 H, d, *J* 4.4 Hz, 3'-H), 3.61 (1 H, br s, 2-H), 3.65 (1 H, br s, 3-H), 3.67–3.71 (2 H, m, 4-H and 6'-H_a), 3.77 (1 H, dd, *J* 5.9, 7.3 Hz, 6-H_a), 3.95 (1 H, dd, *J* 1.2, 8.8 Hz, 4'-H), 4.15–4.23 (3 H, m, 6-H_b, 5'-H, and 6'-H_b), 4.56 and 4.71 (each 1 H, 2 × d, *J* 12.0 Hz, CH_2Ph), 4.59 (1 H, d, *J* 5.9 Hz, 5-H), 4.98 (1 H, d, *J* 2.9 Hz, 1'-H), 5.46 (1 H, s, 1-H), and 5.57 (1 H, s, *CH*Ph).

1,6-Anhydro-4-*O*-(2,3-anhydro-4,6-*O*-benzylidene- α -D-allopyranosyl)-3-*O*-benzyl-2-*O*-(*p*-methoxybenzyl)- β -D-glucopyranose (14).—To a stirred solution of compound (13) (6.6 g, 13.6 mmol), tetrabutylammonium iodide (5.0 g, 13.6 mmol), and *p*-methoxybenzyl chloride (10 ml, 73.8 mmol) in dry THF at 0 °C was added 60% sodium hydride (1 g; 42 mmol) in portions. After being stirred for 6 h at room temperature, the mixture was quenched by successive addition of methanol (2 ml) and water, and extracted with benzene. The extract was successively washed with aqueous sodium thiosulphate, aqueous sodium hydrogen carbonate, and brine (five times), and dried. After addition of pyridine (0.5 ml), the solvent was evaporated off to give a syrup, which was subjected to flash chromatography with toluene–EtOAc–pyridine (97:3:1 v/v) as eluant, giving the 2-*O*-*p*-methoxybenzyl derivative (14) (7.2 g, 88%) as a white amorphous solid (Found: C, 67.5; H, 6.1. $\text{C}_{34}\text{H}_{36}\text{O}_{10}$ requires C, 67.5; H, 6.0%; $[\alpha]_D^{21} + 32^\circ$ (*c* 0.21 in CHCl_3); δ_{H} (400 MHz) 3.34 (1 H, dd, *J* 2.9, 4.4 Hz, 2'-H), 3.37 (1 H, d, *J* 4.4 Hz, 2-H), 3.50 (1 H, d, *J* 4.4 Hz, 3'-H), 3.59 (1 H, dd, *J* 1.2, 6.0 Hz, 4-H), 3.62–3.68 (2 H, m, 3-H and 6-H_a), 3.79 (3 H, s, OMe), 3.86 (1 H, d, *J* 7.3 Hz, 6-H_b), 3.93 (1 H, dd, *J* 1.2, 8.8 Hz, 4'-H), 4.11–4.21 (2 H, m, 5'-H and 6'-H_b), 4.50 and 4.58 (each 1 H, 2 × d, *J* 11.9 Hz, CH_2Ar), 4.53 (1 H, d, *J* 7.1 Hz, 5-H), 4.59 and 4.68 (each 1 H, 2 × d, *J* 11.7 Hz, CH_2Ar), 5.08 (1 H, d, *J* 2.9 Hz, 1'-H), 5.41 (1 H, s, 1-H), and 5.55 (1 H, s, *CH*Ph).

1,6-Anhydro-4-O-(2-azido-4,6-O-benzylidene-2-deoxy- α -D-allopyranosyl)-3-O-benzyl-2-O-(*p*-methoxybenzyl)- β -D-glucopyranose (15).—A suspension of compound (14) (6.3 g, 10.4 mmol), sodium azide (6.0 g, 92 mmol), and ammonium chloride (8 g, 150 mmol) in 90% aqueous ethanol (100 ml) was stirred at 80–90 °C for 11 h. The mixture was concentrated, diluted with chloroform, washed with water, dried, and evaporated. Chromatography with toluene–EtOAc (5:1 v/v) gave the 2'-azido-2'-deoxy derivative (15) (4.8 g, 71%) as a syrup (Found: C, 62.8; H, 5.9; N, 6.3. $C_{34}H_{37}N_3O_{10}$ requires C, 63.05; H, 5.8; N, 6.5%); $[\alpha]_D^{21} + 6.0^\circ$ (*c* 0.28 in $CHCl_3$); ν_{max} (film) 3 450 (OH) and 2 100 cm^{-1} (N_3); δ_H (400 MHz) 3.28 (1 H, br s, 2'-H), 3.40 and 3.49 (each 1 H, 2 \times br s, 2- and 4-H), 3.61 (1 H, dd, *J* 5.1, 7.3 Hz, 6-H_a), 3.68 (3 H, s, OMe), 3.70 (1 H, t, *J* 9.3 Hz, 4'-H), 3.75 (1 H, d, *J* 2.9 Hz, 3-H), 3.79 (1 H, dd, *J* 2.7, 10.3 Hz, 6'-H_a), 3.93 (1 H, d, *J* 7.3 Hz, 6-H_b), 4.05 (1 H, m, 3-H), 4.22 (1 H, dd, *J* 5.1, 10.3 Hz, 6'-H_b), 4.32–4.47 (5 H, m, 2 \times CH_2 Ar, 5'-H), 4.55 (1 H, d, *J* 5.1 Hz, 5-H), 4.74 (1 H, s, 1'-H), 5.33 (1 H, s, 1-H), and 5.53 (1 H, s, *CHPh*).

1,6-Anhydro-4-O-(2-azido-4,6-O-benzylidene-2-deoxy- α -D-allopyranosyl)-3-O-benzyl-2-O-(*p*-methoxybenzyl)- β -D-glucopyranose (16).—To a stirred solution of compound (15) (3.0 g, 4.6 mmol) in DMSO (50 ml) at 0 °C was added acetic anhydride (25 ml). After 12 h at room temperature, the mixture was poured into ice-cold aqueous sodium acetate, stirred for 3 h, and extracted with chloroform. The extract was washed successively with water, aqueous sodium hydrogen carbonate, and brine, dried, and evaporated to dryness to give an amorphous solid. To a solution of the residue in dichloromethane–ethanol–water (5:5:1 v/v; 110 ml) at 0 °C was added sodium borohydride (500 mg). The mixture was stirred for 30 min at 0 °C, quenched by successive addition of acetone and aqueous ammonium chloride, concentrated, and extracted with chloroform. The extract was washed with water, dried, and evaporated. Chromatography with toluene–EtOAc (9:1 v/v) gave the allopuranoside (16) (5.7 g, 49%), m.p. 140–141 °C (from Pr^iOH) (Found: C, 63.2; H, 6.0; N, 6.4. $C_{34}H_{37}N_3O_{10}$ requires C, 63.05; H, 5.8; N, 6.5%); $[\alpha]_D^{21} + 30^\circ$ (*c* 0.31 in $CHCl_3$); ν_{max} (film) 3 400 (OH) and 2 100 cm^{-1} (N_3); δ_H (400 MHz) 2.99 (1 H, t, *J* 3.2 Hz, 2'-H), 3.31 and 3.54 (2 H, 2 br s, 2- and 4-H), 3.43 (1 H, dd, *J* 2.7, 10.0 Hz, 4'-H), 3.60–3.74 (4 H, m, OH, 3-H, 6-H_a, and 6'-H_a), 3.69 (3 H, s, OMe), 4.04 (1 H, d, *J* 7.3 Hz, 6-H_b), 4.31–4.35 (2 H, m, 3'-H and 6'-H_b), 4.38–4.53 (4 H, m, 2 \times CH_2), 4.61 (1 H, dt, *J* 4.9, 10.0 Hz, 5'-H), 4.67 (1 H, d, *J* 5.1 Hz, 5-H), 4.99 (1 H, d, *J* 3.4 Hz, 1'-H), 5.36 (1 H, s, 1-H), and 5.52 (1 H, s, *CHPh*).

1,6-Anhydro-3-O-benzyl-4-O-(2-azido-2-deoxy-3,4-O-isopropylidene- α -D-allopyranosyl)-2-O-(*p*-methoxybenzyl)- β -D-glucopyranose (17).—A solution of compound (16) (3.2 g, 4.9 mmol) in 80% aqueous acetic acid (50 ml) was stirred at 80–90 °C for 3 h, evaporated, and coevaporated with toluene to give a syrup (2.9 g). A solution of the resulting syrup and PTSA monohydrate (30 mg) in acetone–2,2-dimethoxypropane (3:2 v/v; 50 ml) was stirred at room temperature for 2 days, poured into water (20 ml), and stirred for 15 min at room temperature. After addition of pyridine (2 ml), the resulting solution was evaporated to give a syrup, which was purified by chromatography with toluene–EtOAc (3:1 v/v), giving the 3',4'-O-isopropylidene derivative (17) (2.7 g, 91%) as a syrup (Found: C, 60.0; H, 6.2; N, 6.65. $C_{30}H_{37}N_3O_{10}$ requires C, 60.1; H, 6.2; N, 7.0%); $[\alpha]_D^{24} + 8.7^\circ$ (*c* 0.82 in $CHCl_3$); ν_{max} (film) 3 400 (OH) and 2 100 cm^{-1} (N_3).

1,6-Anhydro-3-O-benzyl-4-O-(2,6-diazido-2,6-dideoxy-3,4-O-isopropylidene- α -D-allopyranosyl)-2-O-(*p*-methoxybenzyl)- β -D-glucopyranose (18).—To a solution of monoazide (17) (814 mg, 1.35 mmol) in dichloromethane–pyridine (5:1 v/v; 12 ml) at

0 °C was added dropwise methanesulphonyl chloride (0.5 ml, 6.5 mmol), and the mixture was stirred at room temperature overnight. Usual work-up gave crude 6'-methylsulphonate (950 mg). A solution of the residue and sodium azide (880 mg) in hexamethylphosphoramide (10 ml) was stirred at 60–70 °C overnight. After cooling, the mixture was partitioned between diethyl ether and water. The organic layer was washed with water, dried, and evaporated. Flash chromatography with benzene–EtOAc (9:1 v/v) gave the 2',6'-diazido derivative (18) (700 mg, 84%) as a syrup (Found: C, 57.6; H, 5.85; N, 13.4. $C_{30}H_{36}N_6O_9$ requires C, 57.7; H, 5.8; N, 13.45%); $[\alpha]_D^{20} - 11.1^\circ$ (*c* 0.16 in $CHCl_3$); ν_{max} (film) 2 090 cm^{-1} (N_3); δ_H (400 MHz) 1.36 and 1.46 (each 3 H, 2 \times s, 2 \times Me), 3.18 (1 H, t, *J* 4.4 Hz, 2'-H), 3.34 (1 H, s, 4-H), 3.40 (1 H, dd, *J* 5.9, 13.2 Hz, 6'-H_a), 3.57 (1 H, dd, *J* 2.7, 13.2 Hz, 6'-H_b), 3.62 (1 H, s, 2-H), 3.72 (1 H, dd, *J* 5.9, 7.3 Hz, 6-H_a), 3.76 (1 H, br s, 3-H), 3.80 (3 H, s, OMe), 3.99 (1 H, dd, 4'-H), 4.05 (1 H, d, *J* 7.3 Hz, 6-H_b), 4.26 (1 H, dt, *J* 2.7, 5.9 Hz, 5'-H), 4.42 and 4.48 (each 1 H, 2 \times d, *J* 11.7 Hz, CH_2 Ar), 4.53 and 4.60 (each 1 H, 2 \times d, *J* 11.9 Hz, CH_2 Ar), 4.54 (1 H, t, *J* 4.6 Hz, 3'-H), 4.77 (1 H, d, *J* 5.9 Hz, 5-H), 5.42 (1 H, s, 1-H), and 5.50 (1 H, d, *J* 4.4 Hz, 1'-H).

1,6-Anhydro-3-O-benzyl-4-O-[4,6-O-benzylidene-2-(benzyl-oxycarbonylamino)-2-deoxy- α -D-allopyranosyl]-2-O-(*p*-methoxybenzyl)- β -D-glucopyranose (20).—To a suspension of lithium aluminium hydride (250 mg, 6.6 mmol) in dry diethyl ether (200 ml) at 0 °C was added dropwise a solution of the azide (16) (2.0 g, 3.1 mmol) in dry diethyl ether (50 ml) and the mixture was stirred at room temperature for 2 h. To the mixture were added successively (dropwise) water (0.5 ml) and aqueous sodium hydroxide (10%; 1 ml), and the mixture was filtered. The filtrate was evaporated, and the residue was dissolved in THF–methanol–saturated aqueous sodium hydrogen carbonate (10:1:4 v/v; 75 ml). Benzyl chloroformate (1.5 ml, 10.5 mmol) was added to the solution. The mixture was stirred at 0 °C for 2 h, quenched with aqueous ammonia, evaporated, and the residue was partitioned between chloroform and water. The organic layer was washed with water, dried, and concentrated. Chromatographic purification with toluene–EtOAc (5:1 v/v) followed by crystallization from EtOH gave the 2'-benzyl-oxycarbonylamino derivative (20) (1.85 g, 79%), m.p. 166–167 °C (Found: C, 66.5; H, 5.95; N, 1.65. $C_{42}H_{45}NO_{12}$ requires C, 66.75; H, 6.0; N, 1.85%); $[\alpha]_D^{23} - 24^\circ$ (*c* 0.31 in $CHCl_3$); ν_{max} (film) 3 420 and 3 470 (NH and OH) and 1 710 cm^{-1} (C=O); δ_H (400 MHz) 2.94 (1 H, d, *J* 8.6 Hz, OH), 3.32 (1 H, s, 4-H), 3.37 (1 H, s, 2-H), 3.53 (1 H, s, 3-H), 3.63 (1 H, dd, *J* 2.4, 9.1 Hz, 6'-H_a), 3.76 (4 H, m, OMe, 5'-H), 3.95–3.99 (1 H, m, 2'-H), 4.08 (1 H, d, *J* 7.0 Hz, 6-H_b), 4.25–4.28 (2 H, m, $CHAr$ and 3'-H), 4.33–4.46 (5 H, m, $\frac{3}{2}$ CH_2 Ar, 4'-H, and 6'-H_b), 4.60 (1 H, d, *J* 5.2 Hz, 5-H), 4.78 (1 H, d, *J* 3.6 Hz, 1'-H), 5.07 (2 H, s, CO_2CH_2Ph), 5.37 (1 H, s, 1-H), 5.60 (1 H, s, *CHPh*), and 5.96 (1 H, d, *J* 9.8 Hz, NH).

1,6-Anhydro-3-O-benzyl-4-O-[4,6-O-benzylidene-2-(benzyl-oxycarbonylamino)-2-deoxy-3-O-(phenoxylthiocarbonyl)- α -D-allopyranosyl]-2-O-(*p*-methoxybenzyl)- β -D-glucopyranose (21).—To a solution of compound (20) (1.76 g, 2.33 mmol) and DMAP (0.77 g, 6.3 mmol) in acetonitrile–pyridine (4:1 v/v; 20 ml) at 0 °C was added phenyl chlorothioformate (0.7 ml, 5.1 mmol) and the mixture was stirred at room temperature for 2 h. Usual work-up followed by chromatography [toluene–EtOAc (19:1) as the eluant] gave the 3'-thiocarbonate (21) (2.1 g, quant) as a white foam (Found: C, 65.9; H, 5.6; N, 1.6; S, 3.5. $C_{49}H_{49}NO_{13}S$ requires C, 66.0; H, 5.55; N, 1.55; S, 3.6%); $[\alpha]_D^{18} - 30^\circ$ (*c* 0.34 in $CHCl_3$); ν_{max} (film) 3 350 (NH) and 1 715 cm^{-1} (C=O).

1,6-Anhydro-3-O-benzyl-4-O-[4,6-O-benzylidene-2-(benzyl-oxycarbonylamino)-2,3-dideoxy- α -D-ribo-hexopyranosyl]-2-O-

(*p*-methoxybenzyl)- β -D-glucopyranose (**22**).—To a stirred solution of compound (**21**) (2.05 g, 2.3 mmol) in toluene (75 ml) at 80 °C under argon was added dropwise a solution of tributyltin hydride (4 ml, 15 mmol) and AIBN (0.2 g) in toluene (30 ml) during 1.5 h. The mixture was cooled, quenched with chloroform (40 ml), and evaporated to dryness. Crystallization of the residue from ethanol and chromatography of the filtrate with toluene–EtOAc (19:1) gave the 2',3'-dideoxy derivative (**22**) (1.63 g, 96%), m.p. 196.5–197.5 °C (Found: C, 68.0; H, 6.1; N, 1.9. $C_{42}H_{45}NO_{11}$ requires C, 68.2; H, 6.15; N, 1.9%); $[\alpha]_D^{23} -30^\circ$ (*c* 0.32 in $CHCl_3$); ν_{max} (KBr) 3 320 (NH) and 1 685 and 1 715 cm^{-1} (NHC=O); δ_H (500 MHz) 1.99 (1 H, q, *J* 11.7 Hz, 3'- H_{ax}), 2.03 (1 H, dt, *J* 4.1, 11.7 Hz, 3'- H_{eq}), 3.31 (1 H, s, 4-H), 3.55 (1 H, s, 2-H), 3.60–3.66 (2 H, m, 3- and 4'-H), 3.70–3.76 (2 H, m, 6- and 6'- H_a), 3.79 (3 H, s, OMe), 3.88 (1 H, br dt, *J* 4.9, 10.0 Hz, 5'-H), 3.96–4.03 (1 H, m, 2'-H), 4.09 (1 H, d, *J* 7.0 Hz, 6- H_b), 4.20–4.44 (5 H, m, 2 \times CH_2Ar and 6'- H_b), 4.59 (1 H, d, *J* 5.4 Hz, 5-H), 4.63 (1 H, d, *J* 3.4 Hz, 1'-H), 5.01 and 5.06 (each 1 H, 2 \times d, *J* 11.9 Hz, CO_2CH_2Ph), 5.37 (1 H, s, 1-H), 5.54 (1 H, s, *CHPh*), and 5.69 (1 H, d, *J* 9.5 Hz, NH).

1,6-Anhydro-3-O-benzyl-4-O-[2-(benzyloxycarbonylamino)-2,3-dideoxy- α -D-ribo-hexopyranosyl]-2-O-(*p*-methoxybenzyl)- β -D-glucopyranose (**23**).—To a solution of compound (**22**) (1.29 g, 1.74 mmol) in acetic acid (20 ml) was added water (5 ml), and the solution was stirred at 60–70 °C for 2 h and evaporated to dryness. Chromatographic purification with chloroform–MeOH (99:1 v/v) as eluant gave a syrupy 4',6'-diol (**23**) (1.0 g, 88%) (Found: C, 63.7; H, 6.4; N, 2.1. $C_{35}H_{41}NO_{11} \cdot H_2O$ requires C, 63.65; H, 6.35; N, 2.1%); $[\alpha]_D^{24} -29^\circ$ (*c* 0.45 in $CHCl_3$); ν_{max} (film) 3 400 (NH, OH) and 1 705 cm^{-1} (C=O).

1,6-Anhydro-3-O-benzyl-4-O-[2-(benzyloxycarbonylamino)-2,3-dideoxy-6-O-(*p*-tolylsulphonyl)- α -D-ribo-hexopyranosyl]-2-O-(*p*-methoxybenzyl)- β -D-glucopyranose (**24**).—To a solution of the diol (**23**) (830 mg, 1.3 mmol) in pyridine (120 ml) was added toluene-*p*-sulphonyl chloride (360 mg, 1.9 mmol) and the mixture was stirred at room temperature for 60 h. Usual work-up followed by chromatographic purification with chloroform–MeOH (from 99:1 to 95:5 v/v) as eluant gave the 6'-toluene-*p*-sulphonate (**24**) (638 mg, 62%) and unchanged diol (**23**) (224 mg, 27%). Compound (**24**) had m.p. 141.5–142.5 °C (EtOH) (Found: C, 62.2; H, 5.9; N, 1.7; S, 4.0. $C_{42}H_{47}NO_{13}S \cdot \frac{1}{2}H_2O$ requires C, 62.25; H, 5.9; N, 1.75; S, 4.0%); $[\alpha]_D^{23} -23^\circ$ (*c* 0.45 in $CHCl_3$); ν_{max} (film) 3 420 (NH) and 1 705 cm^{-1} (NHC=O).

1,6-Anhydro-4-O-[6-azido-2-(benzyloxycarbonylamino)-2,3,6-trideoxy- α -D-ribo-hexopyranosyl]-3-O-benzyl-2-O-(*p*-methoxybenzyl)- β -D-glucopyranose (**25**).—A solution of compound (**24**) (50 mg, 0.05 mmol) and sodium azide (50 mg, 0.8 mmol) in DMF was heated at 100 °C for 22 h. The mixture was diluted with chloroform, washed with water, dried and evaporated. Chromatographic purification with toluene–EtOAc (2:1 v/v) gave the 6'-azido derivative (**25**) (32 mg, 91%) as an amorphous solid (Found: C, 62.1; H, 6.0; N, 8.1. $C_{35}H_{40}N_4O_{10}$ requires C, 62.1; H, 5.95; N, 8.3%); $[\alpha]_D^{22} -33^\circ$ (*c* 0.64 in $CHCl_3$); ν_{max} (film) 1 660 and 1 710 cm^{-1} (CONH), 3 350 (NH, OH), 2 070 (N_3); δ_H (400 MHz) 1.78 (1 H, q, *J* 11.7 Hz, 3'- H_{ax}), 1.93 (1 H, d, *J* 8.6 Hz, OH), 2.25 (1 H, dt, *J* 4.1, 11.7 Hz, 3'- H_{eq}), 3.31 (2 H, 2 s, 2- and 4-H), 3.40 (1 H, dd, *J* 6.8, 13.2 Hz, 6'- H_a), 3.54 (1 H, dd, *J* 2.4, 13.1 Hz, 6'- H_b), 3.61 (1 H, m, 4'-H), 3.65 (1 H, s, 3-H), 3.72 (1 H, t, *J* 7.3 Hz, 6- H_a), 3.76–3.88 (1 H, m, 5'-H), 3.80 (3 H, s, OMe), 3.86–3.88 (1 H, m, 2'-H), 4.11 (1 H, d, *J* 7.3 Hz, 6- H_b), 4.27 and 4.38 (each 1 H, 2 \times d, *J* 12.2 Hz, OCH_2Ar), 4.29 and 4.41 (each 1 H, 2 \times d, *J* 13.1 Hz, OCH_2Ar), 4.58 (1 H, d, *J* 9.1 Hz, 5-H), 4.59 (1 H, d, *J* 3.7 Hz, 1'-H), 5.01 and 5.05 (each 1 H, 2 \times d, *J* 12.2 Hz, CO_2CH_2Ph), 5.35 (1 H, s, 1-H), and 5.64 (1 H, d, *J* 9.2 Hz, NH).

1,6-Anhydro-4-O-[6-azido-4-O-benzyl-2-(benzyloxycarbonylamino)-2,3,6-trideoxy- α -D-ribo-hexopyranosyl]-3-O-benzyl-2-O-(*p*-methoxybenzyl)- β -D-glucopyranose (**26**).—A mixture of compound (**25**) (2.2 g, 3.25 mmol), barium hydroxide octahydrate (0.8 g), barium oxide (2.8 g), and benzyl bromide (1 ml) in DMF (50 ml) was stirred at room temperature overnight, quenched with conc. ammonium hydroxide (1 ml), and diluted with diethyl ether. Usual work-up followed by flash chromatography with 19:1 benzene–EtOAc gave the 3,4'-*di*-O-benzyl derivative (**26**) (1.85 g, 74%), m.p. 133–134 °C (EtOH) (Found: C, 65.8; H, 6.1; N, 7.3. $C_{42}H_{46}N_4O_{10}$ requires C, 65.8; H, 6.05; N, 7.3%); $[\alpha]_D^{23} -5.8^\circ$ (*c* 0.20 in $CHCl_3$); δ_H (500 MHz) 1.78 (1 H, q, *J* 11.2 Hz, 3'- H_{ax}), 2.48 (1 H, m, 3'- H_{eq}), 3.30 and 3.32 (each 1 H, 2 \times br s, 2- and 4-H), 3.35 (1 H, dd, *J* 7.0, 13.4 Hz, 6'- H_a), 3.44 (1 H, dt, *J* 4.0, 10.1 Hz, 4'-H), 3.50 (1 H, dd, *J* 2.1, 13.2 Hz, 6'- H_b), 3.64 (1 H, br s, 3-H), 3.70 (1 H, t, *J* 6.1 Hz, 6- H_a), 3.79 (3 H, s, OMe), 3.81–3.91 (2 H, m, 2'- and 5'-H), 4.24–4.43 (5 H, m, $\frac{1}{2} \times CH_2Ar$), 4.54 (1 H, br d, *J* 5.9 Hz, 5-H), 4.59 (1 H, d, *J* 3.7 Hz, 1'-H), 4.64 (1 H, d, *J* 11.3 Hz, $CHAr$), 5.0 (each 1 H, 2 \times d, *J* 11.9 Hz, CH_2Ph), 5.35 (1 H, s, 1-H), and 5.63 (1 H, br d, *J* 8.9 Hz, NH).

Phenyl 2,3-Di-O-acetyl-4-O-(2,3,4,6-tetra-O-acetyl- α -D-glucopyranosyl)-1-thio- β -D-glucopyranoside (**27**).—To a solution of 2,2',3,3',4',6'-hexa-O-acetyl-1,6-anhydro- β -maltose²⁷ (**7**) (0.288 mg, 0.5 mmol) and PhSTMS (0.38 ml, 2 mmol) in 1,2-dichloroethane (20 ml) at 0 °C was added zinc iodide (890 mg, 2 mmol). The suspension was stirred at room temperature for 4.5 h, filtered, and extracted with 1,2-dichloroethane. The extract was washed successively with aqueous sodium hydrogen carbonate and brine, dried, and evaporated. The solution of the residue in 0.1M-hydrochloric acid–methanol (9:1 v/v; 2 ml) was stirred at 0 °C for 10 min, poured into aqueous sodium hydrogen carbonate, and extracted with dichloromethane. The extract was washed successively with aqueous sodium hydrogen carbonate and brine, dried, and evaporated. Flash chromatography with toluene–EtOAc (2:1 v/v) gave the *thioglycoside* (**27**) (0.27 g, 78%), m.p. 169–170 °C (from EtOH) (Found: C, 52.4; H, 5.5; S, 4.5. $C_{30}H_{38}O_{16}S$ requires C, 52.5; H, 5.6; S, 4.7%); $[\alpha]_D^{21} +53^\circ$ (*c* 0.32, $CHCl_3$); ν_{max} (KBr) 3 450 (OH) and 1 740 cm^{-1} (C=O); δ_H (400 MHz; $CDCl_3$) 1.96, 1.97, 1.99, 2.02, 2.04, and 2.06 (each 3 H, 6 \times s, 6 \times Ac), 3.51 (1 H, m, 6- H_a), 3.77 (1 H, dt, *J* 3.6 and 9.05 Hz, 5-H), 3.91–3.97 (2 H, m, 6- and 5'-H), 4.06 (1 H, dd, *J* 2.2, 12.5 Hz, 6'-H), 4.07 (1 H, t, *J* 9.0 Hz, 4-H), 4.23 (1 H, dd, *J* 4.2, 12.5 Hz, 6'-H), 4.73–4.80 (3 H, m, 1-, 2-, and 2'-H), 4.99 (1 H, t, *J* 10.0 Hz, 4'-H), 5.28 (1 H, t, *J* 8.8 Hz, 3-H), 5.32 (1 H, t, *J* 9.5 Hz, 3'-H), and 5.41 (1 H, d, *J* 4.2 Hz, 1'-H).

Phenyl 2,3-Di-O-acetyl-4-O-(2,3,4,6-tetra-O-acetyl- α -D-glucopyranosyl)-6-O-(*p*-tolylsulphonyl)-1-thio- β -D-glucopyranoside (**28**).—To a solution of compound (**27**) (0.10 g, 0.15 mmol) in pyridine (3 ml) was added toluene-*p*-sulphonyl chloride (0.19 g, 1 mmol). The mixture was stirred at room temperature overnight, quenched with ice-water, and extracted with dichloromethane. Usual work-up followed by flash chromatography with toluene–EtOAc (3:2 v/v) gave the 6-toluene-*p*-sulphonate (**28**) (0.105 g, 83%) (Found: C, 52.9; H, 5.8; S, 7.5. $C_{37}H_{44}O_{18}S_2$ requires C, 52.85; H, 5.3; S, 7.6%); $[\alpha]_D^{22} +35^\circ$ (*c* 0.21, $CHCl_3$); δ_H (400 MHz; $CDCl_3$) 1.97, 2.00, 2.01, 2.03, 2.05, and 2.10 (each 3 H, 6 \times s, 6 \times Ac), 2.36 (3 H, s, Me), 3.58–3.62 (1 H, m, 5-H), 3.93–3.97 (2 H, m, 4- and 5'-H), 4.12 (1 H, d, *J* 2.1, 12.8 Hz, 6- H_a), 4.30–4.40 (3 H, m, 6- H_b and 6'- H_2), 4.62 (1 H, d, *J* 9.8 Hz, 1-H), 4.66 (1 H, dd, *J* 8.6, 10.0 Hz, 2'-H), 5.06 (1 H, t, *J* 10.1 Hz, 4'-H), 5.21 (1 H, t, *J* 10.4 Hz, 3'-H), and 5.38 (1 H, d, *J* 4.0 Hz, 1'-H).

Phenyl 2,3-Di-O-acetyl-4-O-(2,3,4,6-tetra-O-acetyl- α -D-glucopyranosyl)-6-deoxy-1-thio- β -D-xylo-hexo-5-enopyranoside

(30).—A solution of compound (28) (0.86 g, 1 mmol) and lithium iodide (2.0 g, 15 mmol) in diethyl ether (50 ml) was stirred for 1 day in the dark at room temperature under argon. The mixture was diluted with diethyl ether, washed successively with aqueous sodium thiosulphate and brine, dried, and evaporated. Flash chromatography with benzene–diethyl ether (2:1 v/v) gave the unstable iodide (29) (0.67 g, 83%).

A solution of compound (29) (0.66 g, 0.84 mmol) and DBU (0.4 g, 2.6 mmol) in toluene was stirred for 5 h at 75–80 °C under argon. After cooling, the mixture was diluted with diethyl ether and washed successively with aqueous ammonium chloride, aqueous sodium thiosulphate, and brine, dried, and evaporated. Flash chromatography with benzene–EtOAc (2:1 v/v) gave the 5-enopyranoside (30) (0.52 g, 93%) as a syrup (Found: C, 53.7; H, 5.4; S, 4.8. C₃₀H₃₆O₁₅S requires C, 53.9; H, 5.4; S, 4.8%); $[\alpha]_D^{25} + 31^\circ$ (c 0.17, in CHCl₃); δ_H (400 MHz; CDCl₃) 2.01, 2.02, 2.04, 2.05, 2.07, and 2.13 (each 3 H, 6 × s, 6 × Ac), 4.07 (1 H, dd, *J* < 2, 11.9 Hz, 6'-H_a), 4.12 (1 H, m, 5'-H), 4.17 (1 H, dd, *J* 4.6, 11.9 Hz, 6'-H_b), 4.21 (1 H, d, *J* 7.0 Hz, 4-H), 4.81 (1 H, dd, *J* 3.7, 10.4 Hz, 2'-H), 4.94 and 4.96 (each 1 H, 2 × s, 6-H₂), 5.02 (1 H, d, *J* 7.5 Hz, 1-H), 5.03 (1 H, t, *J* 9.5 Hz, 4'-H), 5.07 (1 H, t, *J* 7.3 Hz, 2-H), 5.14 (1 H, t, *J* 6.7 Hz, 3-H), 5.34 (1 H, d, *J* 4.0 Hz, 1'-H), and 5.46 (1 H, t, *J* 10.1 Hz, 3'-H).

4D-(4,6/5)-4,5-Diacetoxy-6-(2,3,4,6-tetra-O-acetyl- α -D-glucopyranosyloxy)cyclohex-2-enone (31).—To a solution of compound (30) (90 mg, 0.13 mmol) in acetone (3 ml) was added mercury(II) chloride (110 mg) in water (1.5 ml). The mixture was stirred for 2 days at room temperature and filtered. The precipitate was washed with acetone. The combined filtrate and washings were diluted with chloroform, washed with water, dried, and evaporated. To a solution of the residue in pyridine (2 ml) was added acetic anhydride (1 ml), and the mixture was stirred for 1 day at 0 °C and poured into ice–water. Usual work-up followed by flash chromatography with toluene–EtOAc (2:1 v/v) gave the enone (31) (38 mg, 52%), m.p. 177.5–179 °C (EtOH); $[\alpha]_D^{24} + 115^\circ$ (c 0.12, EtOH) {lit.²⁸ m.p. 178–179 °C; $[\alpha]_D^{22} + 117^\circ$ (c 0.10, EtOH)}.

Phenyl 3-O-Benzyl-4-O-(2,6-diazido-2,6-dideoxy-3,4-O-isopropylidene- α -D-allopyranosyl)-2-O-(*p*-methoxybenzyl)-1-thio-D-glucopyranoside (32).—To a stirred solution of compound (18) (1.60 g, 2.6 mmol) in 1,2-dichloroethane (30 ml) at 0 °C were successively added zinc iodide (3.2 g, 10 mmol) and PhSTMS (2.7 ml, 14 mmol). After 3 h at room temperature, the mixture was treated with 80% aqueous acetic acid (50 ml). The mixture was stirred at 60–70 °C for 2 h, poured into water, and extracted with chloroform. The extract was washed successively with water, 1M-aqueous sodium hydroxide, 1M-hydrochloric acid, aqueous sodium hydrogen carbonate, and brine, dried, and evaporated. The residual syrup was treated with 2,2-dimethoxypropane (40 ml), PTSA monohydrate (100 mg), and acetone (40 ml) in the same way as for the preparation of compound (17). Chromatographic separation of the products with toluene–EtOAc (19:1 v/v) gave an anomeric mixture (α : β 3:1) of the thioglycoside (32) (1.05 g, 56%), of which repeated chromatography with toluene–EtOAc (24:1 v/v) gave pure anomers.

For α -anomer of (32) (Found: C, 58.8; H, 5.8; N, 11.1; S, 4.3. C₃₆H₄₂N₆O₉S requires C, 58.8; H, 5.8; N, 11.4; S, 4.4%); $[\alpha]_D^{21} + 140^\circ$ (c 0.80 in CHCl₃); ν_{max} (film) 3 450 (OH) and 2 070 cm⁻¹ (N₃); δ_H (400 MHz) 1.36 and 1.52 (each 3 H, 2 × s, CMe₂), 2.29 (1 H, t, *J* 6.6 Hz, OH), 3.28 (1 H, t, *J* 4.4 Hz, 2'-H), 3.35 (1 H, dd, *J* 5.6, 12.9 Hz, 6'-H_a), 3.63 (1 H, dd, *J* 2.2, 12.9 Hz, 6'-H_b), 3.73 (1 H, ddd, *J* 2.7, 6.6, 12.2 Hz, 6-H₂), 3.78 (3 H, s, OMe), 3.80–4.03 (6 H, m, 2-, 3-, 4-, 5-, 4'-H, and 6-H_b), 4.23 (1 H, m, 5'-H), 4.25 (1 H, dd, *J* 4.4, 5.9 Hz, 3'-H), 4.59 and 4.67 (each 1 H, 2 × d, *J* 11.5 Hz,

CH₂Ar), 4.72 and 5.08 (each 1 H, 2 × d, *J* 11.2 Hz, CH₂Ar), 5.47 (1 H, d, *J* 4.4 Hz, 1'-H), and 5.58 (1 H, d, *J* 5.4 Hz, 1-H).

For β -anomer of (32) (Found: C, 59.0; H, 5.9; N, 11.1; S, 4.4%); $[\alpha]_D^{21} + 67^\circ$ (c 0.24 in CHCl₃); ν_{max} (film) 3 400 (OH) and 2 100 cm⁻¹ (N₃); δ_H (400 MHz) 1.34 and 1.55 (each 3 H, 2 × s, CMe₂), 2.25 (1 H, t, *J* 7.1 Hz, OH), 3.19 (1 H, t, *J* 4.6 Hz, 2'-H), 3.37 (1 H, dd, *J* 4.9, 13.2 Hz, 6'-H_a), 3.44 (1 H, ddd, *J* 2.9, 7.1, 9.5 Hz, 6-H₂), 3.53 (1 H, dd, *J* 8.5, 9.8 Hz, 4-H), 3.62 (1 H, dd, *J* 2.2, 13.2 Hz, 6'-H_b), 3.78 (3 H, s, OMe), 4.27 and 4.89 (each 1 H, 2 × d, *J* 9.8 Hz, CH₂Ar), 4.74 (1 H, d, *J* 10.0 Hz, 1-H), 4.77 and 5.07 (each 1 H, 2 × d, *J* 11.4 Hz, CH₂Ar), and 5.50 (1 H, d, *J* 4.6 Hz, 1'-H).

Further elution of the column with toluene–EtOAc (9:1 v/v) gave the 2,6-hydroxy derivative (35) (490 mg, 31%) as a powder by trituration with methanol (Found: C, 53.6; H, 5.6; N, 12.7; S, 5.2. C₂₈H₃₄N₆O₈S·CH₃OH requires C, 53.85; H, 5.9; N, 13.0; S, 4.95%); ν_{max} (film) 3 450 (OH) and 2 050 cm⁻¹ (N₃); δ_H (400 MHz) 1.37 and 1.54 (each 3 H, 2 × s, CMe₂), 2.41 (1 H, br s, OH), 3.34–3.39 (2 H, m, 2'-H and 6'-H_a), 3.65 (1 H, dd, *J* 2.4, 13.2 Hz, 6'-H_b), 3.78 (1 H, t, *J* 9.3 Hz, 4-H), 3.83 (1 H, m, 2-H), 3.94 (1 H, t, *J* 9.0 Hz, 3-H), 4.25 (1 H, t, *J* 2.9, 9.8 Hz, 5-H), 4.28 (1 H, dd, *J* 4.6, 5.9 Hz, 3'-H), 4.79 and 5.08 (each 1 H, 2 × d, *J* 11.2 Hz, CH₂Ph), 5.47 (1 H, d, *J* 4.6 Hz, 1'-H), and 5.59 (1 H, d, *J* 4.7 Hz, 1-H).

Phenyl 3-O-Benzyl-4-O-(2,6-diazido-2,6-dideoxy-3,4-O-isopropylidene- α -D-allopyranosyl)-2-O-(*p*-methoxybenzyl)-6-O-methylsulphonyl-1-thio-D-glucopyranoside (33).—An anomeric mixture of compound (32) (390 mg, 0.53 mmol) was treated with methanesulphonyl chloride (0.25 ml, 3.2 mmol) in dichloromethane–pyridine (5:1 v/v; 6 ml) at 0 °C for 2 days. Usual work-up followed by chromatography with toluene–EtOAc (19:1) gave the 6-methanesulphonate (33) (380 mg, 88%) as a syrup (Found: C, 53.5; H, 5.4; N, 9.7; S, 8.1. C₃₇H₄₄N₆O₁₁S₂·H₂O requires C, 53.4; H, 5.6; N, 10.1; S, 8.1%); ν_{max} (film) 2 100 cm⁻¹ (N₃); δ_H (400 MHz) 1.35 and 1.52 (each 3 H, 2 × s, CMe₂), 2.82 (3 H, s, MeSO₂), 3.31 (1 H, t, *J* 4.6 Hz, 2'-H), 3.35 (1 H, dd, *J* 4.5, 13.2 Hz, 6'-H_a), 3.64 (1 H, dd, *J* 2.5, 13.2 Hz, 6'-H_b), 3.72 (1 H, t, *J* 9.8 Hz, 4-H), 3.79 (3 H, s, OMe), 3.87 (1 H, dd, *J* 5.4, 9.3 Hz, 2-H), 3.97, 3.97, (1 H, t, *J* 9.3 Hz, 3-H), 4.01–4.07 (2 H, m, 4'- and 5'-H), 4.22 (1 H, t, *J* 4.6 Hz, 3'-H), 4.37 (1 H, dd, *J* 5.6, 11.7 Hz, 6-H_a), 4.49–4.53 (2 H, m, 5-H and 6-H_b), 4.60 and 4.69 (each 1 H, 2 × d, *J* 11.5 Hz, CH₂Ar), 4.72 and 5.08 (each 1 H, 2 × d, *J* 11.2 Hz, CH₂Ar), 5.39 (1 H, d, *J* 4.4 Hz, 1'-H), and 5.54 (1 H, d, *J* 5.4 Hz, 1-H).

Phenyl 3-O-Benzyl-6-deoxy-4-O-(2,6-diazido-2,6-dideoxy-3,4-O-isopropylidene- α -D-allopyranosyl)-2-O-(*p*-methoxybenzyl)-1-thio-D-xylo-hexo-5-enopyranoside (36).—A solution of anomeric mixture of compound (33) (180 mg, 0.22 mmol) and lithium iodide (0.5 g, 3.7 mmol) in diethyl ether (30 ml) was stirred under argon atmosphere in the dark at room temperature overnight. The mixture was diluted with diethyl ether, washed successively with aqueous sodium thiosulphate and brine, dried, and evaporated to give unstable 6-iodo derivative (34) (190 mg) as a syrup.

A solution of the crude product (34) and DBU (1 ml) in toluene (30 ml) was stirred under argon at 90–100 °C for 7 h. The mixture was diluted with diethyl ether, washed successively with aqueous ammonium chloride and brine, dried, and evaporated. Flash chromatography with toluene–EtOAc (97:3 v/v) gave unstable 5-enopyranoside (36) (110 mg, 70%) (Found: C, 58.8; H, 5.8; N, 11.1; S, 4.3. C₃₆H₄₀N₆O₈S·H₂O requires C, 58.8; H, 5.8; N, 11.4; S, 4.4%); ν_{max} (film) 2 100 cm⁻¹ (N₃); δ_H (400 MHz) 1.39 and 1.54 (each 3 H, 2 × s, CMe₂), 3.29 (1 H, t, *J* 4.6 Hz, 2'-H), 3.31 (1 H, dd, *J* 6.1, 12.9 Hz, 6'-H_a), 3.41 (1 H, dd, *J* 2.7, 12.9 Hz, 6'-H_b), 3.79 (3 H, s, OMe), 4.48 (1 H, t, *J* 5.1 Hz, 3'-H), 4.91 (0.25 H, d, *J* 8.8 Hz, 1-H of β -anomer), 5.48 (0.25 H, d, *J* 4.6 Hz, 1'-H of β -anomer), 5.55 (0.75 H, d, *J* 4.6 Hz, 1'-H of α -anomer), and 5.63 (0.75 H, d, *J* 5.1 Hz, 1-H of α -anomer).

2L-(2,4,5/3)-3-Benzoyloxy-2-(2,6-diazido-2,6-dideoxy-3,4-O-isopropylidene- α -D-allopyranosyloxy)-5-hydroxy-4-(p-methoxybenzyloxy)cyclohexanone (37).—A mixture of solution of (36) (100 mg, 0.14 mmol) in acetone (20 ml) and a solution of mercury(II) chloride (100 mg) in water (10 ml) was stirred at room temperature for 2 days. The mixture was diluted with chloroform, washed with brine, dried, and evaporated to dryness. Chromatography with toluene–EtOAc (3:1 v/v) as eluant gave syrupy 5-hydroxycyclohexanone (37) (59 mg, 67%) (Found: C, 57.7; H, 5.9; N, 13.4. $C_{30}H_{36}N_6O_9$ requires C, 57.7; H, 5.8; N, 13.45%); $[\alpha]_D^{25} + 32^\circ$ (c 0.18 in $CHCl_3$); ν_{max} (film) 3 450 (OH), 2 070 (N_3), and 1 720 cm^{-1} (C=O); δ_H (400 MHz) 2.26 (1 H, s, OH), 2.48 (1 H, d, *J* 14.4 Hz, 6- H_b), 2.71 (1 H, dd, *J* 2.9, 14.4 Hz, 6- H_b), 3.29–3.38 (4 H, m, 5- and 2'-H, and 6'- H_2), 3.81 (3 H, s, OMe), 3.84 (1 H, dd, *J* 9.5, 2.7 Hz, 4-H), 3.91 (1 H, dd, *J* 4.6, 9.5 Hz, 4'-H), 4.17 (1 H, t, *J* 9.5 Hz, 3-H), 4.23 (1 H, d, *J* 9.8 Hz, 2-H), 4.57 (1 H, t, *J* 4.6 Hz, 3'-H), 4.65–4.71 (3 H, m, 5'-H and CH_2Ar), 4.91 and 5.00 (1 H, d, *J* 10.5 Hz, CH_2Ar), and 5.24 (1 H, d, *J* 6.4 Hz, 1'-H).

4D-(4,6/5)-5-Benzoyloxy-6-(2,6-diazido-2,6-dideoxy-3,4-O-isopropylidene- α -D-allopyranosyloxy)-4-(p-methoxybenzyloxy)cyclohex-2-enone (38).—To an ice-cold solution of compound (37) (115 mg, 0.19 mmol) in pyridine–dichloromethane (5:1 v/v; 12 ml) at 0°C was added methanesulphonyl chloride (0.05 ml, 0.7 mmol). The mixture was stirred at room temperature overnight. Usual work-up followed by flash chromatography with benzene–EtOAc (19:1 v/v) gave the cyclohexenone (38) (101 mg, 90%) as a powder by trituration with methanol (Found: C, 58.0; H, 5.9; N, 12.9. $C_{31}H_{38}N_6O_9 \cdot MeOH$ requires C, 58.3; H, 6.0; N, 13.15%); $[\alpha]_D^{25} + 114^\circ$ (c 0.31 in $CHCl_3$); ν_{max} (film) 2 100 (N_3) and 1 690 cm^{-1} (C=O_{conj}); δ_H (400 MHz) 3.26 (1 H, t, *J* 4.6 Hz, 2'-H), 3.36 (1 H, dd, *J* 5.6, 13.2 Hz, 6'- H_2), 3.36 (1 H, dd, *J* 2.7, 13.2 Hz, 6'- H_b), 3.74 (3 H, s, OMe), 3.92 (1 H, dd, *J* 4.6, 9.7 Hz, 4'-H), 4.05 (1 H, dd, *J* 8.1, 11.0 Hz, 5-H), 4.19 (1 H, d, *J* 11.0 Hz, 6-H), 4.33 (1 H, dt, *J* 2.2, 8.1 Hz, 4-H), 4.51 (1 H, t, *J* 4.6 Hz, 3'-H), 4.62 (2 H, s, CH_2Ar), 4.83 (1 H, ddd, *J* 2.7, 5.6, 9.7 Hz, 5'-H), 4.88 and 4.96 (each 1 H, 2 \times d, *J* 10.5 Hz, CH_2Ar), 5.31 (1 H, d, *J* 4.6 Hz, 1'-H), 5.97 (1 H, dd, *J* 2.2, 10.3 Hz, 2-H), and 6.77 (1 H, dd, *J* 2.2, 10.5 Hz, 3-H).

Phenyl 4-O-[6-Azido-4-O-benzyl-2-(benzyloxycarbonylamino)-2,3,6-trideoxy- α -D-ribo-hexopyranosyl]-3-O-benzyl-2-O-(p-methoxybenzyl)-1-thio-D-glucopyranoside (39).—Compound (26) (770 mg, 1.0 mmol) was treated with PhSTMS (1.5 ml) and zinc iodide (700 mg) in 1,2-dichloroethane (20 ml) as described for the preparation of compound (32). The reaction mixture was poured into aqueous sodium hydrogen carbonate, stirred overnight, extracted with chloroform, and the extract was evaporated to dryness. To a stirred solution of the residue in THF – methanol – saturated aqueous sodium hydrogen carbonate (2:3:1 v/v; 60 ml) at 0°C was added benzyl chloroformate (0.5 ml, 3.5 mmol). The solution was stirred at 0°C for 1 h, then quenched with butylamine (0.5 ml). Usual work-up followed by flash chromatography with toluene–EtOAc (9:1 v/v) as eluant gave an anomeric mixture (α : β = 7:3) of the phenyl thioglycoside (39) (510 mg, 58%) (Found: C, 65.45; H, 6.1; N, 6.25; S, 3.5. $C_{48}H_{52}N_4O_{10}$ requires C, 65.7; H, 6.0; N, 6.4; S, 3.7%); δ_H ($CDCl_3$; 500 MHz) 1.51 (1 H, q, *J* 12.2 Hz, 3'- H_{ax}), 2.00 (0.7 H, t, *J* 6.4 Hz, OH), 2.15 (0.3 H, t, *J* 6.0 Hz, OH), 2.35 (1 H, m, 3'- H_{eq}), 3.77 (3 H, s, OMe), 5.17 (0.3 H, d, *J* 3.4 Hz, 1'-H of β -anomer), 5.28 (0.7 H, d, *J* 3.4 Hz, 1'-H of α -anomer), 5.53 (0.7 H, d, *J* 4.3 Hz, 1-H of α -anomer), and 5.60 (1 H, m, NH).

Phenyl 4-O-[6-Azido-4-O-benzyl-2-(benzyloxycarbonylamino)-2,3,6-trideoxy- α -D-ribo-hexopyranosyl]-3-O-benzyl-2-O-(p-methoxybenzyl)-6-O-methylsulphonyl-1-thio-D-glucopyranoside (40).—Compound (39) (400 mg, 0.45 mmol) was

treated with methanesulphonyl chloride (0.2 ml, 2.5 mmol) as described for the preparation of compound (33), and the product was chromatographed with toluene–EtOAc (19:1 v/v) to give the 6-methanesulphonate (40) (370 mg, 85%) (Found: C, 61.2; H, 5.7; N, 5.7; S, 7.0. $C_{49}H_{54}N_4O_{12}S_2 \cdot \frac{1}{2}H_2O$ requires C, 61.6; H, 5.7; N, 5.9; S, 6.7%); ν_{max} (film) 3 300 (NH), 2 100 (N_3), and 1 715 cm^{-1} (C=O); δ_H (500 MHz) 1.65 (1 H, q, *J* 10.8 Hz, 3'- H_{ax}), 2.30–2.36 (1 H, m, 3'- H_{eq}), 2.83 (3 H, s, $MeSO_2$), 3.77 (3 H, s, OMe), 4.93 and 4.96 (each 1 H, 2 \times d, *J* 12.2 Hz, CH_2Ph), 5.12 (1 H, d, *J* 4.1 Hz, 1'-H), 5.52 (1 H, d, *J* 4.9 Hz, 1-H), and 5.65 (1 H, br d, *J* 8.3 Hz, NH).

Phenyl 4-O-[6-Azido-4-O-benzyl-2-(benzyloxycarbonylamino)-2,3,6-trideoxy- α -D-ribo-hexopyranosyl]-3-O-benzyl-6-deoxy-2-O-(p-methoxybenzyl)-1-thio-D-xylo-hex-5-enopyranoside (42).—Compound (40) (350 mg, 0.37 mmol) was treated with lithium iodide (400 mg, 3.0 mmol) and DBU (0.3 ml, 2 mmol) as described for the preparation of compound (36). Flash chromatography with toluene–EtOAc (97:3 v/v) gave unstable enopyranoside (42) (230 mg, 72%) (Found: C, 66.7; H, 6.3; N, 6.25; S, 4.0. $C_{48}H_{50}N_4O_9S$ requires C, 67.1; H, 5.9; N, 6.5; S, 3.7%); ν_{max} (film) 3 300 (NH), 2 080 (N_3) and 1 720 cm^{-1} (C=O); δ_H (500 MHz) 1.62–1.67 (1 H, m, 3'- H_{ax}), 2.27–2.30 (1 H, m, 3'- H_{eq}), 3.75 (3 H, s, OMe), 5.29 (0.3 H, d, *J* 3.7 Hz, 1'-H of β -anomer), 5.35 (0.7 H, d, *J* 3.9 Hz, 1'-H of α -anomer), 5.51 (0.7 H, d, *J* 4.6 Hz, 1-H of α -anomer), and 5.62 (1 H, br s, NH).

4D-(4,6/5)-6-[6-Azido-4-O-benzyl-2-(benzyloxycarbonylamino)-2,3,6-trideoxy- α -D-ribo-hexopyranosyloxy]-5-benzoyloxy-4-(p-methoxybenzyloxy)cyclohex-2-enone (43).—A mixture of compound (42) (210 mg, 0.24 mmol) in acetone (20 ml) and an aqueous solution (10 ml) of mercury(II) chloride (200 mg) was stirred at room temperature for 3 days, and then partitioned between chloroform and water. The organic layer was washed successively with aqueous sodium hydrogen carbonate and brine, dried, and evaporated to dryness. The residue was dissolved in pyridine (10 ml) and methanesulphonyl chloride (0.1 ml) was added dropwise to the solution at –15°C. The mixture was stirred at room temperature overnight. Usual work-up followed by flash chromatography with toluene–EtOAc (9:1 v/v) gave the cyclohexenone (43) (110 mg, 61%) as a syrup (Found: C, 66.1; H, 6.1; N, 7.4. $C_{42}H_{44}N_4O_9 \cdot H_2O$ requires C, 65.8; H, 6.05; N, 7.3%); $[\alpha]_D^{25} + 78^\circ$ (c 0.12 in $CHCl_3$); δ_H (500 MHz) 1.81 (1 H, q, *J* 11.3 Hz, 3'- H_{ax}), 2.38 (1 H, m, 3'- H_{eq}), 3.35–3.49 (3 H, m, 2'-H and 6'- H_2), 3.80 (3 H, s, OMe), 3.90 (1 H, dd, *J* 7.9, 10.3 Hz, 5-H), 3.95–3.99 (1 H, m, 4'-H), 4.30 (1 H, d, *J* 11.0 Hz, 6-H), 4.36 (1 H, dt, *J* 1.9, 7.9 Hz, 4-H), 4.40–5.00 (9 H, m, 4 \times CH_2Ar and 5'-H), 5.16 (1 H, d, *J* 3.4 Hz, 1'-H), 5.24 (1 H, br d, *J* 9.7 Hz, NH), 6.04 (1 H, dd, *J* 2.1, 10.4 Hz, 3-H), and 6.78 (1 H, dd, *J* 2.0, 10.3 Hz, 2-H).

3L-(3,4,6/5)-3-Azido-5-benzoyloxy-4-(2,6-diazido-2,6-dideoxy-3,4-O-isopropylidene- α -D-allopyranosyloxy)-6-(p-methoxybenzyloxy)cyclohexene (45).—To a stirred solution of compound (38) (190 mg, 0.31 mmol) and cerium(III) chloride heptahydrate (370 mg) in methanol–THF (9:1 v/v; 10 ml) at –78°C was added sodium borohydride (37 mg). The mixture was stirred at –78°C for 6 h, quenched with acetone (0.5 ml), warmed to room temperature, and partitioned between aqueous ammonium chloride and chloroform. The organic layer was washed with brine, dried, and evaporated to give a syrup (180 mg). To a solution of the syrup which had been coevaporated with dry toluene, and TPP (260 mg, 1 mmol) in toluene (5 ml) was added a 2.5M-benzene solution of hydrazoic acid²⁹ (1.5 ml), and the solution was stirred at 15°C. To the stirred solution at –15°C was added dropwise DEAD (0.3 ml, 1.8 mmol) during 30 min. The mixture was stirred at room temperature for 4 h, quenched with methanol, and diluted with chloroform. The

organic layer was washed with aqueous sodium hydrogen carbonate, dried, and evaporated. Flash chromatography with benzene-EtOAc (24:1 v/v) gave syrupy 2',3,6'-triazide (45) (125 mg, 64%) (Found: C, 57.2; H, 5.6; N, 19.5. $C_{30}H_{35}N_9O_7$ requires C, 56.85; H, 5.55; N, 19.9%); $[\alpha]_D^{22} + 4.7^\circ$ (c 0.56 in $CHCl_3$); ν_{max} (film) 2 050 cm^{-1} (N_3); δ_H (400 MHz) 3.33 (1 H, dd, J 7.3, 13.2 Hz, 6'-H), 3.45 (1 H, t, J 4.6 Hz, 2'-H), 3.51 (1 H, dd, J 2.3, 13.2 Hz, 6'-H_b), 3.80 (3 H, s, OMe), 3.92–3.97 (2 H, m, 4- and 4'-H), 4.05 (1 H, dd, J 7.3, 10.3 Hz, 5-H), 4.11 (1 H, br d, J 7.1 Hz, 6-H), 4.19 (1 H, dt, J 2.3, 7.2, 7.3 Hz, 5'-H), 4.25 (1 H, t, J 4.9 Hz, 3-H), 4.39 (1 H, dd, J 4.6, 5.9 Hz, 3'-H), 4.58 and 4.62 (each 1 H, 2 × d, J 11.2 Hz, CH_2 Ar), 4.87 and 4.95 (each 1 H, 2 × d, J 11.0 Hz, CH_2 Ar), 5.33 (1 H, d, J 4.6 Hz, 1'-H), 5.80 (1 H, ddd, J 1.7, 4.9, 9.8 Hz, 2-H), and 5.91 (1 H, dd, J 2.2, 9.8 Hz, 1-H).

3L-(3,4/5,6)-3-Azido-5-benzyloxy-4-(2,6-diazido-2,6-dideoxy-3,4-O-isopropylidene- α -D-allopyranosyloxy)-6-phthalimido-cyclohexene (46).—To a solution of compound (45) (120 mg, 0.19 mmol) in methanol (3 ml) was added DDQ (100 mg, 0.44 mmol). The mixture was stirred at room temperature for 7 h, diluted with chloroform, washed successively with aqueous sodium thiosulphate and brine, dried ($MgSO_4$), and evaporated to dryness. To a solution of the residue that had been coevaporated with dry toluene, TPP (120 mg, 0.45 mmol), and phthalimide (100 mg, 0.68 mmol) in THF (2 ml) was dropwise added DEAD (0.2 ml, 1.3 mmol). The mixture was stirred at room temperature overnight, poured into water, and extracted with chloroform. The extract was washed successively with saturated aqueous sodium hydrogen carbonate and brine, dried ($MgSO_4$), and evaporated. The residue was chromatographed with benzene-EtOAc (19:1 v/v) to give the phthalimide derivative (46) (72 mg, 59%) (Found: C, 56.2; H, 4.6; N, 21.6. $C_{30}H_{30}N_{10}O_7$ requires C, 56.1; H, 4.7; N, 21.8%); $[\alpha]_D^{24} + 25^\circ$ (c 0.72, $CHCl_3$); δ_H (400 MHz) 1.40 and 1.49 (each 3 H, 2 × s, 2 × Me), 3.29 (1 H, t, J 4.4 Hz, 2'-H), 3.35 (1 H, dd, J 6.3, 13.2 Hz, 6'-H_a), 3.46 (1 H, dd, J 2.4, 13.2 Hz, 6'-H_b), 3.93 (1 H, dd, J 4.8, 9.3 Hz, 4'-H), 3.96–4.02 (1 H, m, 5'-H), 4.52 (1 H, t, J 4.8 Hz, 3'-H), 4.56 (1 H, ddd, J 1.7, 3.7, 8.5 Hz, 3-H), ca. 4.6 (2 H, m, 4- and 5-H), 4.63 and 4.68 (each 2 H, 2 × d, J 11.5 Hz, CH_2 Ph), 5.22 (1 H, d, J 4.4 Hz, 1'-H), 5.55 (1 H, dd, J 4.0, 9.5 Hz, 6-H), 5.80 (1 H, td, J 1.7, 10.0 Hz, 1-H), and 6.11 (1 H, dd, J 3.7, 10.0 Hz, 2-H).

1L-(1,2,4/3)-1-Azido-2-(2,6-diazido-2,6-dideoxy-3,4-O-isopropylidene- α -D-allopyranosyloxy)-3-benzyloxy-4-(p-methoxybenzyloxy)cyclohexane (47).—To a solution of compound (45) (42 mg, 66 μ mol) in degassed benzene (10 ml) was added a solution of chlorotris(triphenylphosphine)rhodium(i) (50 mg) in degassed benzene (5 ml). The mixture was shaken under hydrogen for 5 h at 1 atm, and then applied to a column of aluminium oxide. The column was washed successively with benzene, diethyl ether, and ethyl acetate. The fractions that were eluted with ethyl acetate were collected and concentrated. The residual syrup was chromatographed on a silica gel column with benzene-EtOAc (97:3 v/v) to give the saturated 1,2',6'-triazido derivative (47) (31 mg, 71%) (Found: C, 56.4; H, 5.6; N, 19.7. $C_{30}H_{37}N_9O_7$ requires C, 56.7; H, 5.85; N, 19.8%); $[\alpha]_D^{22} + 60^\circ$ (c 0.75 in $CHCl_3$); ν_{max} (film) 2 050 cm^{-1} (N_3); δ_H (400 MHz) 1.24 and 1.38 (each 3 H, 2 × s, CM_e_2), 1.60–1.75, 1.82–1.90 (each 2 H, m, 5-H₂ and 6-H₂), 3.34–3.46 (3 H, m, 2'-H and 6'-H₂), 3.75 (1 H, dd, J 4.6, 11.0 Hz, 4'-H), 3.80 (3 H, s, OMe), 3.88–3.91 (3 H, m, 1-, 2-, and 3-H), 4.04 (1 H, m, 4-H), 4.14 (1 H, br t, J 11.0 Hz, 5'-H), 4.37 (1 H, t, J 4.6 Hz, 3'-H), 4.53 and 4.61 (each 1 H, 2 × d, J 11.0 Hz, CH_2 Ar), 4.77 and 5.02 (each 1 H, 2 × d, J 11.0 Hz, CH_2 Ar), and 5.34 (1 H, d, J 4.6 Hz, 1'-H).

1D-(1,3,4/2)-4-Azido-2-benzyloxy-3-(2,6-diazido-2,6-dideoxy-3,4-O-isopropylidene- α -D-allopyranosyloxy)cyclohexanol (48).—A suspension of compound (47) (42 mg, 60 μ mol) and DDQ (60

mg) in 95% aqueous dichloromethane (5 ml) was stirred at room temperature for 1 h. The mixture was diluted with dichloromethane, washed successively with aqueous sodium thiosulphate, aqueous sodium hydrogen carbonate, and brine, dried, and evaporated. Flash chromatography with benzene-EtOAc (5:1 v/v) as eluant gave the hydroxy derivative (48) (25 mg, 74%) [m/z , 500.199 4. $C_{21}H_{26}N_9O_6$ requires m/z 500.200 41 ($M - CH_3$)]; $[\alpha]_D^{21} + 67^\circ$ (c 0.18 in $CHCl_3$); ν_{max} (film) 3 400 (OH) and 2 060 cm^{-1} (N_3); δ_H (400 MHz) 1.37 and 1.56 (each 3 H, 2 × s, CM_e_2), 1.55–1.61 (1 H, m, 5-H_{ax}), 1.67–1.76 (1 H, m, 6-H_{ax}), 1.82 (1 H, dq, J 4.6, 13.3 Hz, 6-H_{eq}), 1.92 (1 H, dq, J 4.6, 13.9 Hz, 5-H_{eq}), 2.48 (1 H, br s, OH), 3.38 (1 H, dd, J 6.8, 13.2 Hz, 6'-H_a), 3.53 (1 H, d, J 2.4, 13.2 Hz, 6'-H_b), 3.57 (1 H, t, J 4.4 Hz, 2'-H), 3.60 (1 H, br s, 1-H), 3.74 (1 H, t, J 7.8 Hz, 2-H), 3.79 (1 H, dd, J 2.9, 7.8 Hz, 3-H), 3.99 (1 H, dd, J 5.6, 9.3 Hz, 4'-H), 4.07–4.09 (1 H, br d, J ca. 3.7 Hz, 4-H), 4.23 (1 H, ddd, J 4.6, 6.8, 9.3 Hz, 5'-H), 4.44 (1 H, dd, J 4.4, 9.3 Hz, 3'-H), 4.76 and 4.89 (each 1 H, 2 × d, J 11.2 Hz, CH_2 Ph), and 5.18 (1 H, d, J 4.4 Hz, 1'-H).

1L-(1,2/3,4)-1-Azido-3-benzyloxy-4-{[N-(benzyloxycarbonyl)glycyl](methylamino)}-2-(2,6-diazido-2,6-dideoxy-3,4-O-isopropylidene- α -D-allopyranosyloxy)cyclohexane (50).—To a solution of DMSO (0.3 ml) in dichloromethane (10 ml) at $-78^\circ C$ was added dropwise TFAA (0.15 ml) and the mixture was stirred for 30 min. To the mixture at $-78^\circ C$ was added dropwise a solution of compound (48) (24 mg, 47 μ mol) in dichloromethane (5 ml), and the mixture was stirred at $-78^\circ C$ for 1 h. After addition of triethylamine (0.3 ml), the mixture was warmed to room temperature, and stirred for 1 h. Usual work-up gave a pale yellow syrup (24 mg), which was coevaporated with toluene several times. To a stirred solution of the syrup in methanol-THF (4:1; 10 ml) at $-15^\circ C$ were successively added molecular sieves 3Å (0.2 g), 40% methanolic methylamine (1 ml), acetic acid to adjust the pH 6.2–6.5, and sodium cyanoborohydride (12 mg). The suspension was stirred at $-15^\circ C$ for 1 h, and filtered. The filtrate was diluted with chloroform, washed with brine, dried (K_2CO_3), and evaporated to give crude methylamino derivative (49) (20 mg).

A mixture of the residue that had been coevaporated with toluene, *N*-[N-(benzyloxycarbonyl)glycyl]succinimide (40 mg), and triethylamine (0.1 ml) in 1,4-dioxane (10 ml) was stirred under argon at $60^\circ C$ for 8 h,²⁴ and then evaporated under reduced pressure. The residue was dissolved in chloroform, washed successively with *m*-hydrochloric acid, aqueous sodium hydrogen carbonate, and brine, dried ($MgSO_4$), and evaporated. Flash chromatography with benzene-EtOAc (4:1 v/v) as eluant gave the title compound (50) (11 mg, 45%) (Found: M^+ , 719.3117. $C_{33}H_{41}N_{11}O_8$ requires M , 719.3137); $[\alpha]_D^{24} + 67^\circ$ (c 0.56 in $CHCl_3$); ν_{max} (film) 3 300 (NH), 2 060 (N_3), 1 710 (NCO_2), and 1 635 cm^{-1} ($NC=O$); δ_H (400 MHz) 1.39 and 1.56 (each 3 H, 2 × s, CM_e_2), 1.56–1.79, 1.97–2.17 (each 2 H, m, 5-H and 6-H₂), 2.85 (3 H, s, NMe), 3.39 (1 H, t, J 4.6 Hz, 2'-H), 3.46 (1 H, dd, J 6.3, 14.2 Hz, 6'-H_a), 3.51 (1 H, dd, J 2.7, 14.2 Hz, 6'-H_b), 3.75 and 3.88 (each 1 H, 2 × dd, J 4.2, 16.2 Hz, $COCH_2NH$), 4.02–4.05 (3 H, m, 1-, 3-, and 4'-H), 4.10–4.14 (1 H, m, 2-H), 4.38 and 4.58 (each 1 H, 2 × d, J 11.7 Hz, CH_2 Ph), 4.38–4.50 (1 H, m, 5'-H), 4.62 (1 H, t, J 4.6 Hz, 3'-H), 4.76 (1 H, dt, J 4.0, 11.7 Hz, 4-H), 5.09–5.17 (3 H, m, CO_2CH_2Ph and 1'-H), and 5.85 (1 H, br t, J 4.2 Hz, NH).

1L-(1,6/2,3)-3-Amino-2-(2,6-diamino-2,6-dideoxy- α -D-allopyranosyloxy)-6-[glycyl(methylamino)]cyclohexanol (4).—A solution of compound (50) (11 mg, 15 μ mol) in THF (0.5 ml) was added to 90% aqueous TFA (1 ml) at $0^\circ C$. The mixture was stirred at $0^\circ C$ for 1 h, evaporated under reduced pressure, and coevaporated with ethanol at $0^\circ C$. The residue was dissolved in 0.01M-hydrochloric acid-MeOH (1:4 v/v; 5 ml), and the

solution was shaken with 10% palladium on carbon (5 mg) under hydrogen at 1 atm at room temperature overnight. The mixture was filtered through a millipore filter (0.22 μm) and the filtrate was evaporated to dryness. The residue was dissolved in 0.01M-hydrochloric acid (10 ml) and the solution was shaken again with 10% palladium on carbon (7 mg) in the same way as above. The residual syrup obtained on evaporation was chromatographed on a column (9 \times 50 mm) of CM-Sephadex C-25 [NH_4^+] with aqueous ammonia (from 0 to 0.5M) as eluant. The fractions which showed a spot at R_f 0.17 on TLC (MeOH-chloroform-17% aqueous ammonia, 8:1:3 v/v) were collected, and evaporated to dryness. The residue was dissolved in water, neutralized with 1mM-hydrochloric acid, and lyophilized to give compound (4) (2.4 mg) as an amorphous solid (Found: C, 34.4; H, 6.8; N, 12.5. $\text{C}_{15}\text{H}_{31}\text{N}_5\text{O}_6 \cdot 3\text{HCl} \cdot \text{H}_2\text{CO}_3 \cdot 0.5\text{H}_2\text{O}$ requires C, 34.45; H, 6.7; N, 12.55%); $[\alpha]_D^{25} + 87^\circ$ (c 0.11 in water); ν_{max} (film) 3350 (NH, OH) and 1640 cm^{-1} (NC=O); δ_{H} (400 MHz; D_2O containing 1 drop of 20% solution of DCl in D_2O ; TMS as the external standard) 1.58–1.62 (1 H, m, 5- H_{eq}), 1.81–1.87 (2 H, m, 4- H_2), 1.97 (1 H, qd, J 4.6, 11.9 Hz, 5- H_{ax}), 2.85 (3 H, s, NMe), 3.11 (1 H, dd, J 7.1, 13.4 Hz, 6'- H_a), 3.32 (1 H, dd, J 3.2, 13.4 Hz, 6'- H_b), 3.52 (1 H, m, 3-H), 3.55 (1 H, dd, J 3.2, 10.0 Hz, 4'-H), 3.69 (1 H, t, J 4.0 Hz, 2'-H), 3.87 and 3.89 (each 1 H, 2 \times d, J 17.2 Hz, COCH_2N), 3.91 (1 H, ddd, J 3.2, 7.1, 10.0 Hz, 5'-H), 3.99 (1 H, t, J 3.2 Hz, 2-H), 4.15–4.17 (2 H, m, 1- and 3'-H), 4.26 (1 H, dt, J 3.0, 12.0 Hz, 6-H), and 5.33 (1 H, d, J 4.0 Hz, 1'-H); m/z (si-ms) 378 ($M + \text{H}$).

3L-(3,4,6/5)-3-Azido-4-[6-azido-4-O-benzyl-2-(benzyloxy-carbonylamino)-2,3,6-trideoxy- α -D-ribo-hexopyranosyloxy]-5-benzyloxy-6-(p-methoxybenzyloxy)cyclohexene (51).—Compound (43) (140 mg, 0.17 mmol) was treated as described for the preparation of compound (45). Flash chromatography with benzene-EtOAc (19:1 v/v) gave the 3,6'-diazido derivative (51) (118 mg, 91%) as a syrup (Found: m/z , 747.3242. $\text{C}_{42}\text{H}_{45}\text{N}_5\text{O}_8$ ($M - \text{N}_2^+$) requires m/z 747.3265); $[\alpha]_D^{22} + 8.5^\circ$ (c 0.43, in CHCl_3); ν_{max} (film) 3400 (NH), 2100 (N_3), and 1720 cm^{-1} (C=O); δ_{H} (500 MHz) 1.64 (1 H, q, J 11.6 Hz, 3'- H_{ax}), 2.36–2.39 (1 H, m, 3'- H_{eq}), 3.33 (1 H, dd, J 5.8, 13.1 Hz, 6'- H_a), ca. 3.4 (1 H, m, 2'-H), 3.45 (1 H, dd, J 1.8, 12.8 Hz, 6'- H_b), 3.71 (3 H, s, OMe), 4.88 (1 H, d, J 3.3 Hz, 1'-H), 5.66 (1 H, dd, J 2.1, 13.4 Hz, 2-H), 5.76 (1 H, br d, J 13 Hz, 1-H), and 5.88 (1 H, br d, J 8.5 Hz, NH).

1D-(1,3,4/2)-4-Azido-3-[6-azido-4-O-benzyl-2-(benzyloxy-carbonylamino)-2,3,6-trideoxy- α -D-ribo-hexopyranosyloxy]-2-benzyloxy-cyclohexanol (53).—To a vigorously stirred yellow suspension of compound (51) (55 mg, 71 μmol) and potassium azodicarboxylate (1 g, 10 mmol) in acetonitrile (20 ml) was added dropwise an acetonitrile solution (10 ml) of acetic acid (1.5 ml, 25 mmol) during 3 h at room temperature. The pale yellow suspension was stirred overnight, evaporated, and the residue partitioned between ethyl acetate and water. The organic layer was washed successively with aqueous sodium hydrogen carbonate and brine, dried, and evaporated. Repeated treatment of the residue with the same amount of potassium azodicarboxylate and acetic acid afforded the crude cyclohexane derivative as a syrup, of which the ^1H NMR spectrum showed traces of olefinic protons.

To a solution of the residual syrup (46 mg) in dichloromethane (10 ml) that contained water (1 drop) was added DDQ (60 mg, 0.26 mmol). The mixture was stirred at room temperature for 3 h, quenched with aqueous sodium thiosulphate, and partitioned between dichloromethane and water. The organic layer was washed successively with aqueous sodium thiosulphate and brine, dried, and evaporated. Chromatography of the residue with chloroform gave the saturated alcohol (53) (25 mg, 54%) as a syrup (Found: M^+ ,

657.2890. $\text{C}_{34}\text{H}_{39}\text{N}_7\text{O}_7$ requires M , 657.2908); $[\alpha]_D^{20} + 69^\circ$ (c 0.21 in CHCl_3); ν_{max} (film) 3350 (NH, OH), 2080 (N_3), and 1715 cm^{-1} (C=O); δ_{H} (500 MHz) 1.61–1.98 (5 H, m, 5- H_2 , 6- H_2 , and 3'- H_{ax}), 2.39 (1 H, m, 3'- H_{eq}), 3.38–3.54 (4 H, m, 4- and 4'-H, and 6'- H_2), 3.62 (1 H, t, J 8.4 Hz, 2-H), 3.78 (1 H, dd, J 2.0, 8.8 Hz, 3-H), 3.95–3.98 (2 H, m, 2'- and 5'-H), 4.07 (1 H, br s, 1-H), 4.41 and 4.81 (each 1 H, 2 \times d, J 11.6 Hz, CH_2Ph), 4.63 and 4.81 (each 1 H, 2 \times d, J 11.3 Hz, CH_2Ph), 4.89 and 5.01 (1 H, d, J 12.2 Hz, $\text{CO}_2\text{CH}_2\text{Ph}$), 5.05 (1 H, d, J 3.0 Hz, 1'-H), and 5.40 (1 H, br s, NH).

1L-(1,2/3,4)-1-Azido-2-[6-azido-4-O-benzyl-2-(benzyloxy-carbonylamino)-2,3,6-trideoxy- α -D-ribo-hexopyranosyloxy]-3-benzyloxy-4-{[N-(benzyloxy-carbonyl)glycyl](methylamino)-cyclohexane (54).—Compound (53) (15 mg, 22 μmol) was treated as described for the preparation of compound (50). Chromatography with benzene-EtOAc (9:1 v/v) gave the title compound (54) (10 mg, 55%) (Found: M^+ , 861.3834. $\text{C}_{45}\text{H}_{51}\text{N}_9\text{O}_9$ requires M , 861.3806); $[\alpha]_D^{22} + 66^\circ$ (c 0.3 in CHCl_3); δ_{H} (500 MHz) 1.73 (1 H, q, J 11.3 Hz, 3'- H_{ax}), 1.83 (1 H, br q, J 11.3 Hz, 6- H_{ax}), 1.92–1.94 (2 H, m, 5- and 6- H_{eq}), 2.04 (1 H, br q, J 11.0 Hz, 5- H_{ax}), 2.18 (1 H, m, 3'- H_{eq}), 2.80 (3 H, s, NMe), 3.45 (1 H, dd, J 4.9, 13.1 Hz, 6'- H_a), 3.52 (1 H, dd, J 2.5, 13.1 Hz, 6'- H_b), 3.58 (1 H, m, 2'-H), 3.70 (1 H, br s, 3-H), 3.72 (1 H, br d, J 11.0 Hz, 1-H), 3.83 (1 H, br s, 2-H), 3.92 (2 H, m, CH_2NH), 4.07 (1 H, m, 5'-H), 4.30 and 4.43 (each 1 H, 2 \times d, J 11.3 Hz, CH_2Ph), 4.45 and 4.63 (each 1 H, 2 \times d, J 10.9 Hz, CH_2Ph), 4.74 (1 H, d, J 11.0 Hz, 4-H), 5.02–5.16 (5 H, m, 2 \times CH_2Ph and 1'-H), 5.65 (1 H, br s, NH), and 6.25 (1 H, br d, J 6.0 Hz, NH).

1L-(1,6/2,3)-3-Amino-2-(2,6-diamino-2,3,6-trideoxy- α -D-ribo-hexopyranosyloxy)-6-[glycyl(methylamino)cyclohexanol (5).—A solution of compound (54) (9 mg, 10 μmol) and 10% palladium on carbon (5 mg) in methanol-0.05M-hydrochloric acid (5:1 v/v) was shaken under hydrogen at room temperature for 15 h and filtered through a millipore filter (0.22 μm). The concentrated filtrate, in 0.05M-hydrochloric acid, was hydrogenated with the same catalyst (7 mg) for 18 h and the mixture was filtered. The filtrate was evaporated, coevaporated twice with water, and lyophilized. The residue was chromatographed on a column (9 \times 80 mm) of CM-Sephadex C-25 [NH_4^+ form] with aqueous ammonia (from 0 to 0.3M) as eluant. The fractions which showed a spot at R_f 0.71 on TLC [methanol-chloroform-17% ammonium hydroxide; 8:1:3 v/v] were collected and evaporated. The residue was dissolved in water, neutralized with 1mM-hydrochloric acid, and lyophilized to give compound (5) (3.8 mg, 75%) as an amorphous solid (Found: C, 32.8; H, 6.9; N, 12.8. $\text{C}_{15}\text{H}_{31}\text{N}_5\text{O}_5 \cdot 4\text{HCl} \cdot 2\text{H}_2\text{O}$ requires C, 33.2; H, 7.2; N, 12.9%); $[\alpha]_D^{24} + 104^\circ$ (c 0.14, in water); δ_{H} (500 MHz; D_2O containing 1 drop of 20% solution of DCl in D_2O ; TMS as the external standard) 1.55–1.58 (1 H, m, 5- H_{eq}), 1.78–1.95 (4 H, m, 5- H_{ax} , 6- H_2 , and 3'- H_{ax}), 2.15 (1 H, dt, J 4.3, 11.6 Hz, 3'- H_{eq}), 2.80 (3 H, s, NMe), 3.04 (1 H, dd, J 7.3, 13.4 Hz, 6'- H_a), 3.27 (1 H, dd, J 3.4, 13.4 Hz, 6'- H_b), 3.52–3.57 (3 H, m, 3-, 2'-, and 4'-H), 3.64 (1 H, ddd, J 3.4, 7.0, 9.8 Hz, 5'-H), 3.80 and 3.85 (each 1 H, 2 \times d, J 16.5 Hz, COCH_2N), 4.02 (1 H, t, J 3.0 Hz, 2-H), 4.14 (1 H, br s, 1-H), 4.19 (1 H, dt, J 2.8, 11.9 Hz, 6-H), and 5.26 (1 H, d, J 3.7 Hz, 1'-H).

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