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Synthesis Studies of Structural Analogues of Tagetitoxin: 4-*O*-Acetyl-3-amino-1,6-anhydro-3-deoxy-D-gulose 2-Phosphate

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Abstract

Synthetic approaches to structural analogues of tagetitoxin (**1**) are described. The successful route to analogue **3** (X=O) has, as a key step, protection of the *cis*-vicinal amino alcohol moiety of compound **7** as an *N*-benzylated cyclic carbamate (**9**). X-Ray crystallographic analyses of the hydrochloride of compound **7** and of the hydroxyacid **56** are reported.

Keywords: Amines; Carbohydrate mimetics; Phosphoric acid and derivatives; X-Ray crystal structures.

Introduction

Tagetitoxin is a phytotoxin produced by the plant pathogenic bacterium *Pseudomonas syringae* pv. *tagetis* [1] and induces chlorosis in the apex of the host plant by specifically inhibiting chloroplast RNA polymerase [2]. The structure of tagetitoxin has yet to be proved unequivocally, but the bicyclic structure **1** is currently favoured [3] over the alternatives **2a,b** from analysis of nmr data, although the position of the amide group is still uncertain. The production of tagetitoxin from a selected *P. syringae* strain and its use as a plant growth regulator have been patented [4], and tagetitoxin is available commercially.[1] To our knowledge only preliminary synthetic studies have been reported [5,6].

The biological activity of tagetitoxin has led us to prepare substructures for evaluation as herbicides and plant growth regulators. Assuming the validity of structure **1**, we hypothesised that the acetate, amine and phosphate groups are important for activity, whilst the C-S-C bridge

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[1] Available as Tagetin™ Inhibitor from Epicentre Technologies, Madison, WI, USA

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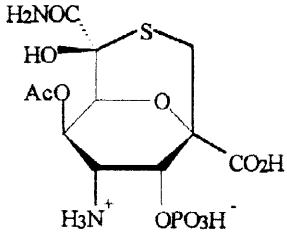
is present to impose the required geometry on the pyranoid ring. No information is available on the absolute configuration of tagetitoxin, but it was decided to make analogues derived from D-sugars, not just because these are more readily available, but because many 1,6-anhydro-D-hexose derivatives, which are structurally related to the illustrated enantiomer (**1**), show herbicidal activity [7]. This paper describes several approaches to analogues based on structures **3** and **4**. The work was designed to provide insight into stucture-activity relationships of tagetitoxin, and incidentally into the construction of carbohydrate-based vicinal *cis*-amino phosphates in general. While compounds of type **3** were made satisfactorily, unexpected problems were encountered with those of the [3.3.1] bicyclic type related to **4** (X=O,S).



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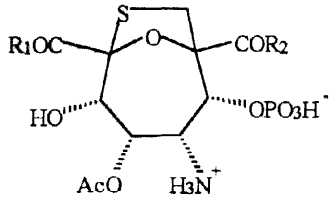
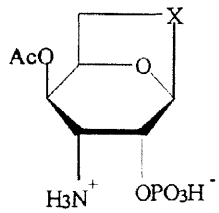


2a R^1=OH, R^2=NH_2
2b R^1=NH_2, R^2=OH



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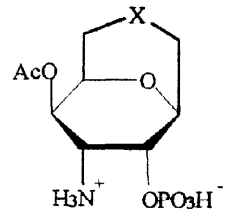

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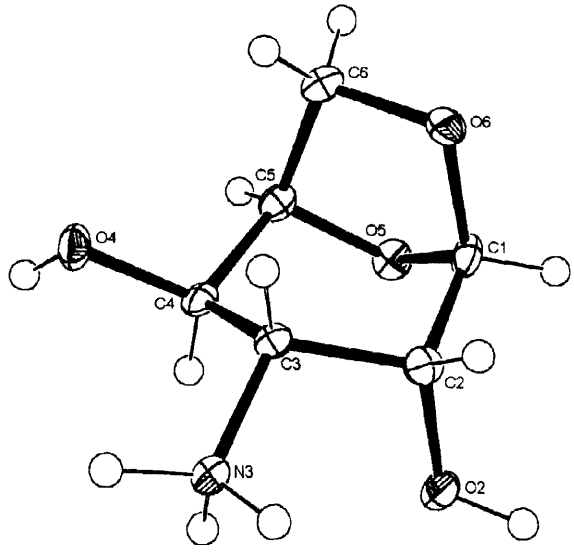
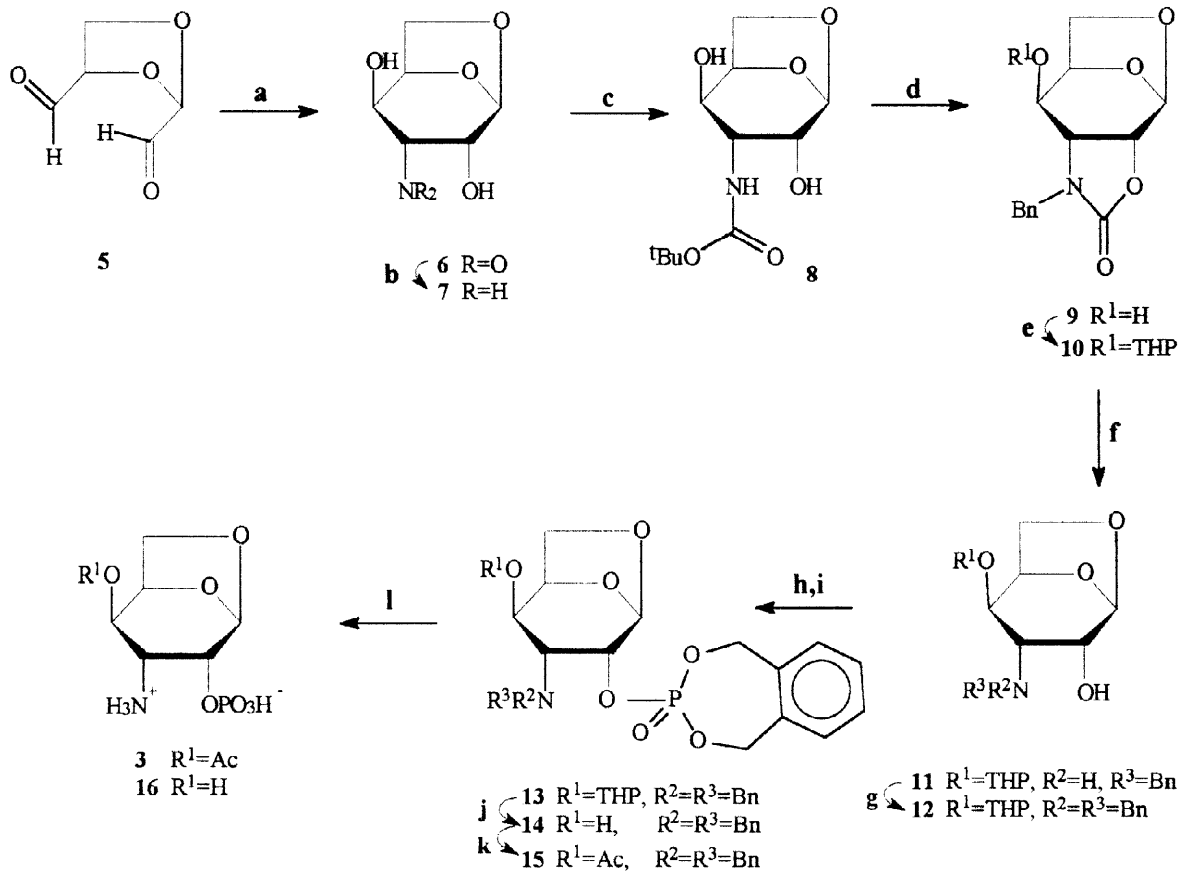
Results and Discussion

1,6-Anhydro-3-deoxy-3-nitro-D-gulose (**6**) is available (13.5%) by cyclisation with nitromethane of the dialdehyde **5** readily obtainable by periodate oxidation of levoglucosan (or any other 1,6-anhydro-D-hexopyranose), and fractional crystallisation of the mixed isomeric products (Scheme 1) [8]. Hydrogenolytic reduction of the nitro compound leads to the amine **7** [8], the D-*gulo*-configuration of which is supported by its large $^1H,^1H$ nmr coupling constant $J_{3ax,4ax}$ (9.9 Hz)

Fig1. Thermal ellipsoid plot (50% probability level) of compound **7.HCl** drawn using ORTEP [32,33].



and confirmed byX-ray analysis of its hydrochloride (Fig. 1). In an approach to compounds of type **3** it seemed desirable to exploit the *syn*-disposition of the C-2 and C-3 substituents in the anhydride **7** to permit esterification of the C-2 and C-4-hydroxyl groups selectively, and treatment of the *N*-Boc derivative **8** with bis(tributyltin) oxide (1.3 equiv), followed by tetrabutylammonium bromide [9] and benzyl bromide in refluxing toluene, led directly to the *N*-benzyl-protected cyclic carbamate **9** (96%). The position of the benzyl group was evident from the ^{13}C nmr chemical shift of the benzylic carbon atom (δ 46.6), and there was no evidence for the formation of 4-*O*-benzylated by-products. Conversion of compound **9** to the 4-*O*-tetrahydropyranyl derivative **10** and alkaline cleavage of the carbamate group led to the mono-ol **11**, which was specifically *N*-benzylated with dibutyltin oxide, followed by tetrabutylammonium bromide and benzyl bromide to give the tertiary amine **12**. Phosphitylation with *o*-xylylene *N,N*-diethylphosphoramidite and 1*H*-tetrazole, followed by peracid oxidation [10] were efficient processes, and removal of the 4-*O*-THP protecting group from the derived phosphate **13** gave alcohol **14**, which was acetylated to afford **15**. Hydrogenolysis of compounds **14** and **15** gave the salts **16** and **3** (X=O), respectively, in quantitative yield.

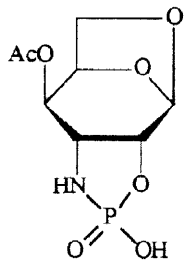


Scheme 1: **a**) $MeNO_2$, NaOMe, MeOH; **b**) H_2, Pd/C, 2M HCl, 50 p.s.i.; **c**) $(Boc)_2O$, Na_2CO_3, H_2O, THF; **d**) $(Bu_3Sn)_2O$, Bu_4NBr, BnBr, toluene; **e**) dihydropyran, TsOH; **f**) NaOH, EtOH; **g**) Bu_2SnO, Bu_4NBr, BnBr, toluene; **h**) *o*-xylylene-*N,N*-diethylphosphoramidite, 1*H*-tetrazole; **i**) MCPBA; **j**) 2M HCl; **k**) Ac_2O, pyr; **l**) H_2, Pd/C, 50 p.s.i., EtOH, AcOH.

The nmr spectra of products **16** and **3** (X=O) were fully consistent with the structures shown. In the ^{31}P spectrum of the latter, the sole resonance was at δ 0 relative to phosphoric acid. The phosphorus atom was coupled with H-2 ($^3J_{PH}$ = 8.3 ± 0.1 Hz) and H-3 ($^4J_{PH}$ =1.3 ± 0.1 Hz), and the retention of the *gulo*-configuration was indicated by the proton coupling constants $J_{1,2}$, $J_{2,3}$, $J_{3,4}$ of 2.4, 4.6 and 10.3 Hz, respectively. The elemental analyses ruled out the possible cyclic (dehydrated) phosphoramidate variant **17**.

These experiments have provided the tagetitoxin analogue **3** (X=O). Neither it nor its analogue (**16**) was active (applied at 1000 g/ha) against the following pre- or post-emergent agriculturally important weeds: *Avena fatua* (wild oat), *Setaria viridis* (green foxtail), *Amaranthus retroflexus* (redroot pigweed) or *Chenopodium album* (fat hen).

The route adopted has potential applicability to analogues with a carboxylic acid substituent at C-1 (hexose numbering), as found in tagetitoxin, since 2,7-anhydrosedoheptulose **18**, on periodate oxidation, gives a dialdehyde from which the required 4-deoxy-4-nitro-D-*gulo*-anhydride **19** is obtainable [11,12]. The above pathway to analogue **3** (X=O) illustrates a way of making carbohydrate *cis*-vicinal amine phosphates, by temporary protection of corresponding amino alcohols as *N*-benzyloxazolidinones.



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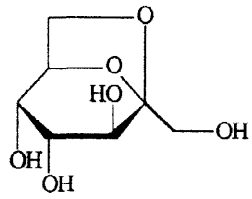

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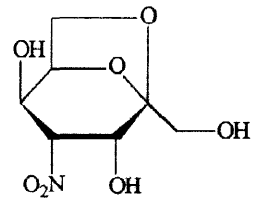

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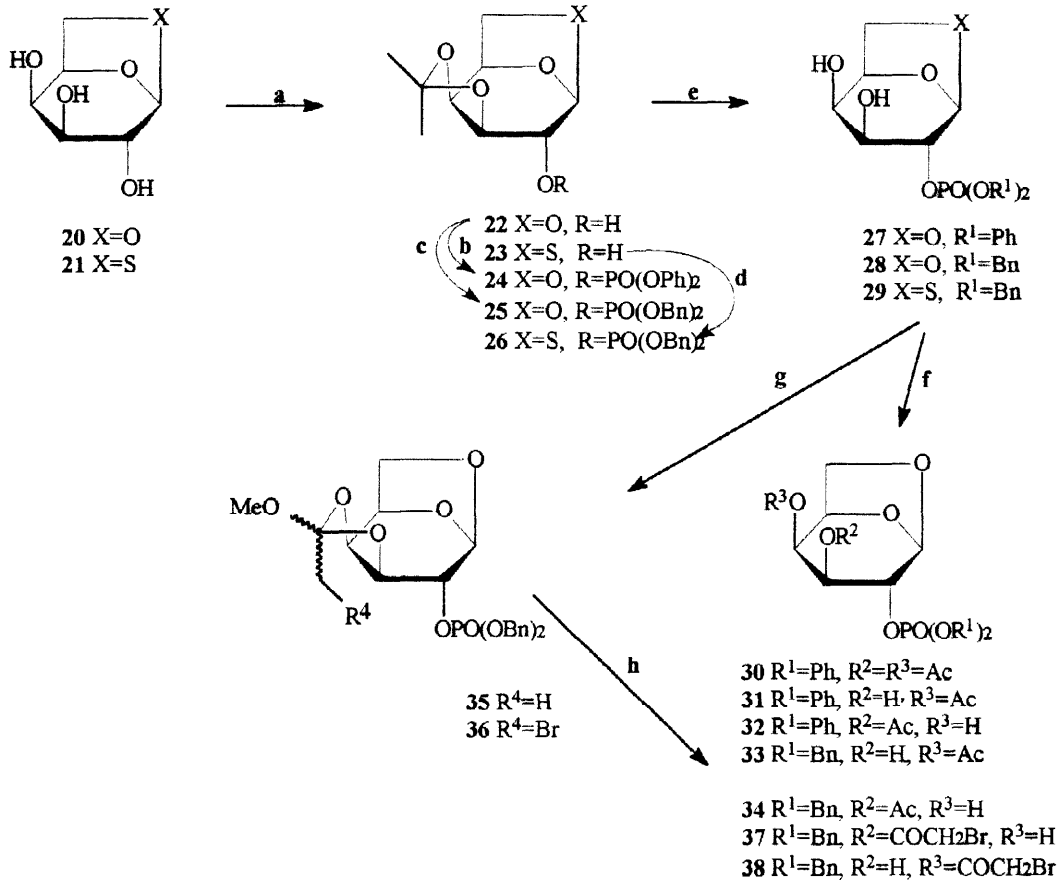
In a second approach to compounds based on structure **3** it was necessary to functionalise O-2 and O-4 of 1,6-anhydro-D-galactose **20** [13] differentially, and develop a good leaving group at C-3 for introduction of the amino function with configurational inversion. Treatment with acetic anhydride (1.3 equiv) in pyridine of the 2-phosphate **27**, prepared by the route **20**→**22**→**24**→**27** as indicated in Scheme 2 and used as a model compound, gave diacetate **30** (18%) and an inseparable mixture of the monoacetates **31** and **32** (64%). The mixture contained over 90% of the 4-ester **31** which, as expected, was derived by selective reaction of the more accessible equatorial hydroxyl group. That the acetate in the major product was located at C-4 was revealed by the $^1H,^1H$ COSY nmr spectrum and by the low-field H-4 triplet (J = 4.5 Hz) in the ^1H spectrum, consistent with H-4 being involved in two roughly equivalent axial-equatorial couplings. For the minor monoacetate **32**, the low field H-3 doublet of doublets ($J_{2,3}$ = 1.2, $J_{3,4}$ = 5.4 Hz) indicates one axial-equatorial and one smaller diequatorial coupling. With appropriate selective acetylation established for compound **27**

this approach was considered applicable to the closely related anhydrides **28** (Scheme 2, **22**→**25**→**28**) and **29** (Scheme 2, **21**→**23**→**26**→**29**). Attempts to work with the latter were however frustrated by the sensitivity of compound **26** to acid and its consequent failure to yield the required diol **29**. Presumably this sensitivity is due to the participation of the sulfur atom in reactions of carbocations generated under the conditions used.

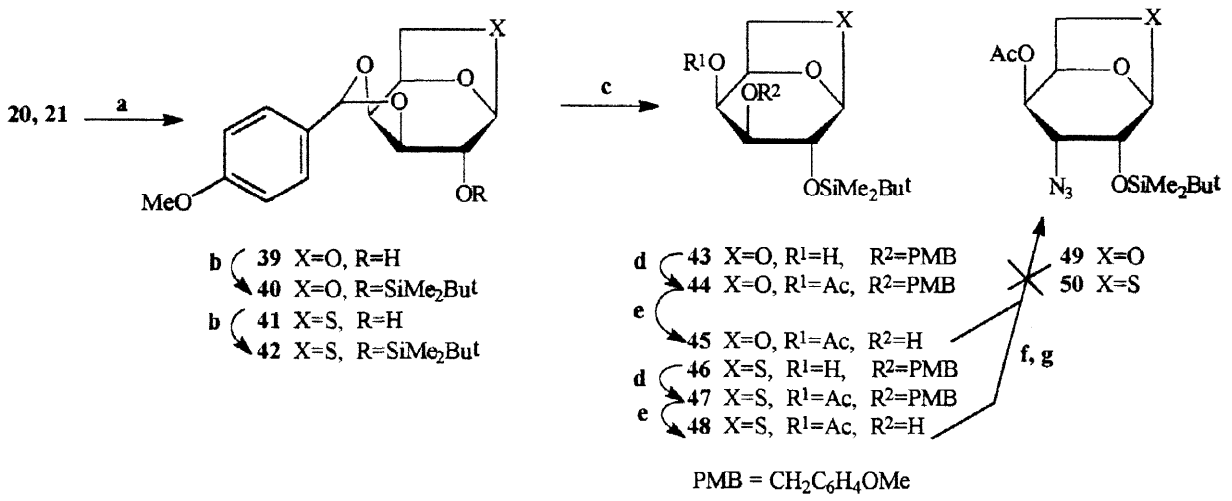


Scheme 2: a) $Me_2C(OMe)_2$, Me_2CO, TsOH; b) $ClPO(OPh)_2$, pyr; c) BuLi, $[(BnO)_2PO]_2O$; d) NaH, $[(BnO)_2PO]_2O$; e) 2M HCl; f) Ac_2O and (pyr or Bu_2SnO or $(Bu_3Sn)_2O$); g) for **35**: $MeC(OEt)_3$, TsOH; for **36**: $BrCH_2C(OEt)_3$, TsOH; h) AcOH, H_2O.

Acetylation of diol **28** with acetic anhydride and pyridine, or following reaction with dibutyltin oxide or bis(tributyltin) oxide, gave inseparable 1:1 mixtures of monoacetates **33** and **34**, in contrast with the selectivity observed for the model compound **27**. Reaction with dibutyltin oxide and the bulkier pivaloyl chloride also led to an unsuitable mixture of monoesters. It is not clear whether these reactions were inherently unselective, or victims of subsequent ester migration which can reduce initial selectivity, but a selective acetylation did occur when diol **28** was converted to the cyclic orthoacetates **35**, and subjected to mild hydrolysis. While this gave exclusively, and as expected

[14], the acetate **34** with the new ester group at the axial O-3 position, an attempt to turn this result to advantage was not successful: the brominated orthoesters **36**, which were expected to give an O-3 ester which could be removed in the presence of an acetate at C-4, did not hydrolyse selectively, but instead gave an inseparable mixture of bromoacetates **37** and **38**. Conceivably configurational inconsistences at the orthoester chiral centre could have led to this irregularity.

An alternative way of selectively functionalising anhydrides **20** and **21** was developed from a literature report [15] of the regioselective reductive cleavage of the *O*-benzyl and *O*-allyl derivatives of the *endo*-isomer of methoxybenzylidene acetal **39**. In like manner, reduction of the 2-*O*-silyl derivatives **40** and **42** (*endo*-isomers), derived from **39** and **41**, respectively, with $LiAlH_4$-$AlCl_3$ gave specifically the 3-*O*-*p*-methoxybenzyl ethers **43** and **46** (Scheme 3). Acetylation to give esters **44** and **47**, and cleavage of the *p*-methoxybenzyl ethers to give hydroxy acetates **45** and **48** was straightforward, but the derived 3-triflates, mesylates or tosylates all failed to afford the expected azides **49** and **50** on reaction with sodium azide in DMF, HMPA or DMSO. Presumably the path of the incoming nucleophile was impeded by the bulky substituent on O-2 and either no reaction or decomposition resulted.

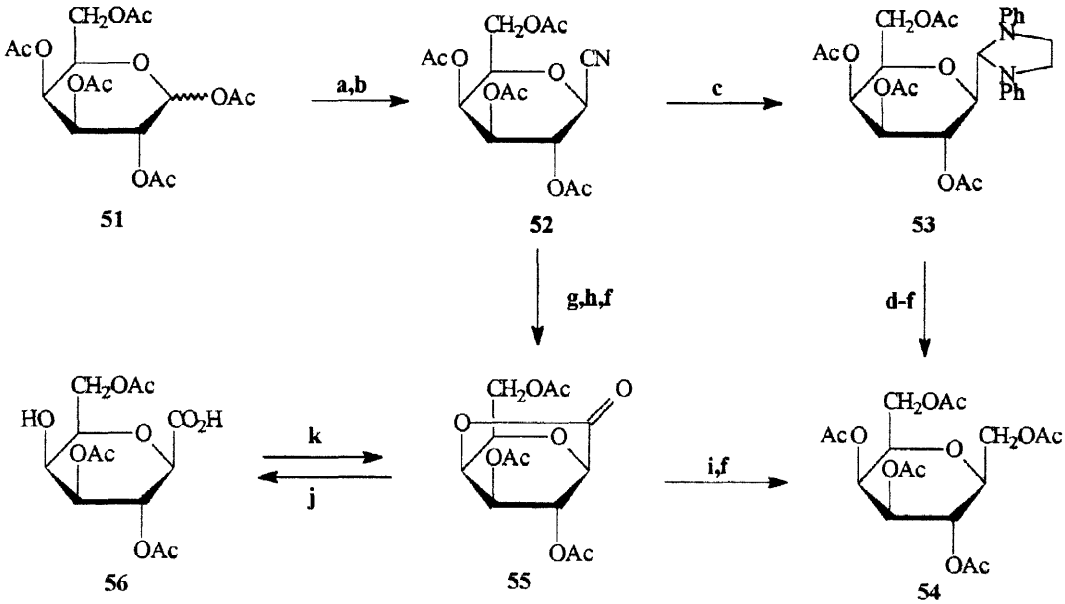


Scheme 3: a) $MeOC_6H_4CH(OMe)_2$, TsOH; b) Bu^tMe_2SiCl, imidazole, DMF; c) $LiAlH_4$, $AlCl_3$, THF; d) Ac_2O, pyr; e) DDQ, CH_2Cl_2, H_2O; f) Tf_2O, MsCl or TsCl, pyr; g) DMF, HMPA or DMSO, NaN_3.

With a route opened to tagetitoxin analogue **3** (X=O), attention was turned to more closely related anhydroheptitol compounds **4** (X=O,S), and it was envisaged that analogue **4** (X=S) could be made from D-galactopyranose by chain extension by one carbon atom at C-1, followed by a ring closure involving linking the new atom and C-7 through sulfur. Regiospecific phosphorylation and acetylation, and introduction of the amino function by an S_N2 process would give the D-*gulo*-

configured target.

D-Galactose pentaacetate **51** was therefore converted to the α-glycosyl bromide then treated with mercury(II) cyanide in nitromethane to give the β-nitrile **52** [16] (Scheme 4). Reductive hydrolysis with Raney nickel and trapping of the resultant, unstable aldehyde with 1,2-dianilinoethane gave the imidazolidine **53** [17,18]. This reduction step, however, gave variable yields and the elimination by-product **57** was sometimes observed. The aldehyde was regenerated by precipitation of 1,2-dianilinoethane as its *p*-toluenesulfonic acid salt; sodium borohydride reduction and acetylation gave the known pentaacetate **54** [19]. In an alternative procedure for the preparation of this acetate, nitrile **52** was deacetylated with sodium methoxide in methanol and then treated with refluxing aqueous sodium hydroxide (6 M). Acetylation of the crude hydrolysis product after neutralisation gave a syrupy lactone, rather than the carboxylic acid as expected [20]. However a sample of the lactone deposited a crystalline fraction on standing, X-ray structural analysis (Fig. 2) and nmr spectroscopy showing this to be the 5,1-hydroxy acid **56**.

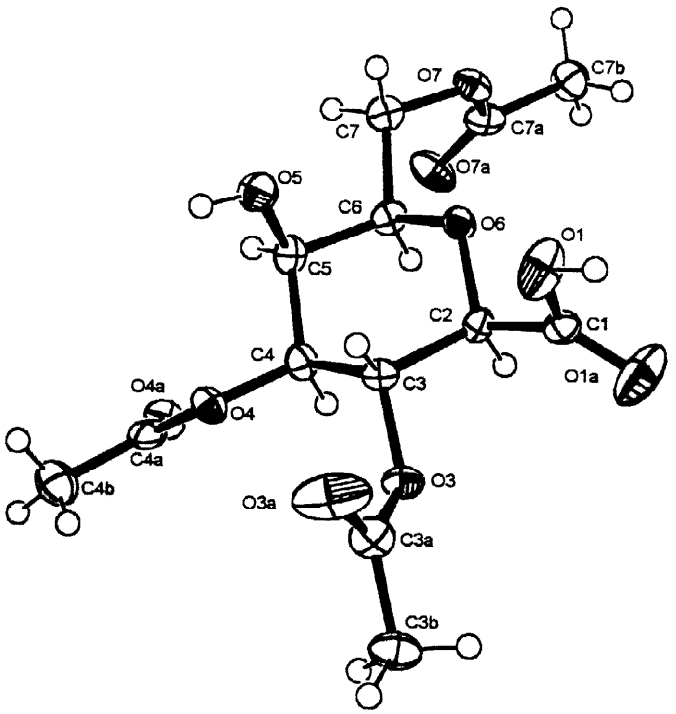


Scheme 4: **a)** HBr, HOAc; **b)** $Hg(CN)_2$, $MeNO_2$; **c)** Raney Ni, NaH_2PO_2, $PhHN(CH_2)_2NHPh$; **d)** TsOH, Me_2CO, CH_2Cl_2; **e)** $NaBH_4$; **f)** Ac_2O, pyr; **g)** MeONa, MeOH; **h)** 25% w/v NaOH; **i)** $LiAlH_4$; **j)** H_2O; **k)** Ac_2O, NaOAc.

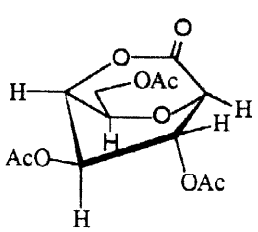
The lactone is therefore likely to be the 2,6-anhydroheptono-1,5-lactone ester **55**, although the isomer **59** could have led by hydrolysis to the 7,1-hydroxy acid **58**, and hence the observed compound **56** by acetyl migration. The likelihood of this having happened is, however, diminished by the finding that hydroxy acid **56**, on heating in acetic anhydride in the presence of sodium acetate, was cleanly reconverted to lactone **55**. Lithium aluminium hydride reduction of this lactone and peracetylation gave the desired pentaacetate **54**.

Unusually for a 6-membered ring compound, compound **55** shows very small $^{3}J_{H,H}$ values for all the ring protons which are more readily accommodated by the [2.2.2] bicyclic structure **55** in the twist boat conformation **55a** than by the [3.3.1] bicyclic **59**.

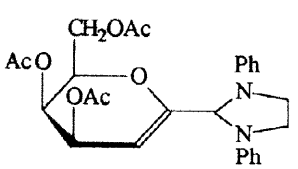
Fig. 2 Thermal ellipsoid plot (50% probability level) of compound 56 drawn using ORTEP [29,30].



Deacetylation of anhydride **54** gave pentaol **60** and selective tosylation at the primary centres afforded ditosylate **61**, the best yield (33%) being obtained by use of four equivalents of tosyl chloride, under which conditions the tritosylate **62** was also isolated (25%). Ditosylate **61** was converted to the acetonide **63** and attempts were made to bond C-1 and C-7 by way of a sulfur atom, but ring closure could not be achieved by treatment in DMF with either lithium sulfide or sodium sulfide (Scheme 5). The only product isolated was the thiol **64**; no evidence could be found for the formation of the cyclic sulfide **65** even under severe conditions.



55a



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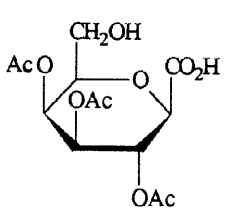

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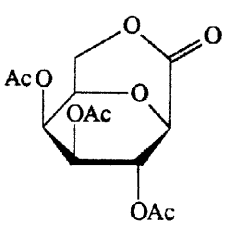

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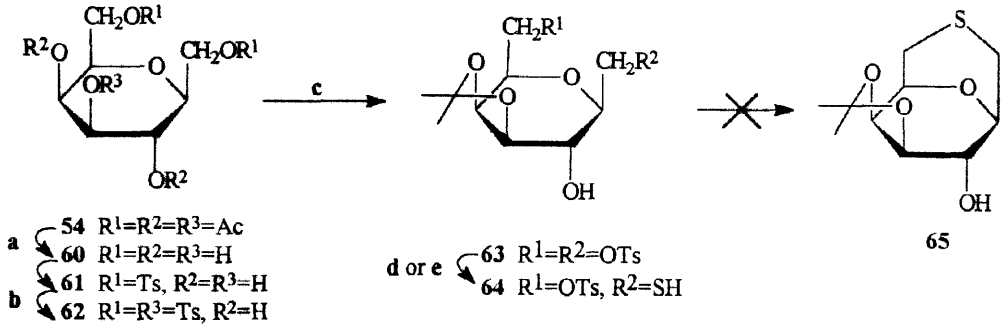
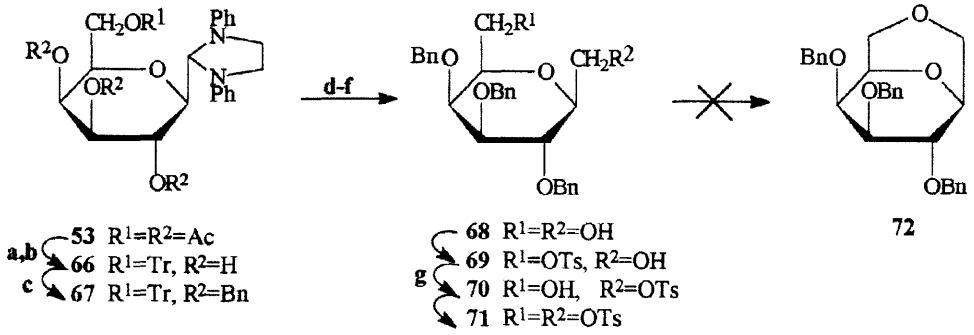


Scheme 5: a) MeONa, MeOH; b) TsCl, pyr; c) $Me_2C(OMe)_2$, TsOH; d) Na_2S, DMF; e) Li_2S, DMF.

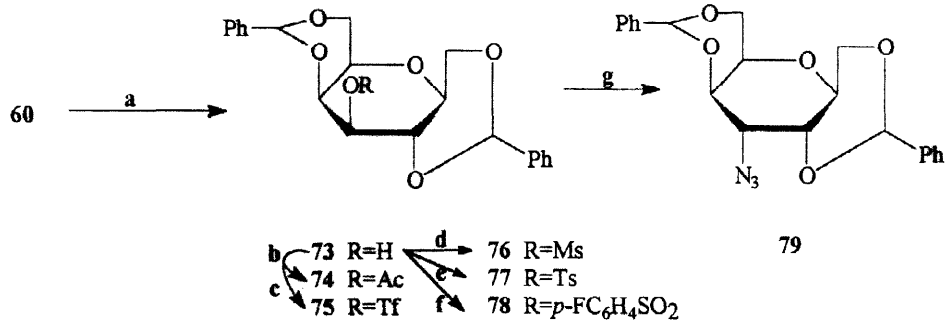
In order to remove any steric constraints placed on the ring closure by the isopropylidene protecting group in the ditosylate **63**, a modified substrate was chosen for attempts to form anhydride precursors for target compound **4** (X=O). Thus, deacetylation of **53** and tritylation of the primary alcohol gave **66** (Scheme 6). After perbenzylation to give **67**, unmasking of the aldehyde, borohydride reduction and detritylation gave the diol **68**. Treatment of the derived monotosylate **70** (obtained together with its isomer **69** and ditosylate **71**) with sodium hydride gave a complex mixture, from which none of the desired cyclic ether **72** could be isolated. Neither an acid-catalysed cyclodehydration of compound **68** in refluxing toluene, nor reaction with triphenylphosphine and diethyl azodicarboxylate [21] in 1,2-dichloroethane was successful, starting material being recovered in each case.



Scheme 6: a) MeONa, MeOH; b) TrCl, Et_3N; c) NaH, BnBr; d) TsOH, Me_2CO, CH_2Cl_2; e) $NaBH_4$; f) TsOH, MeOH; g) TsCl, pyr.

The merits of introducing the α-nitrogen-bonded substituent at C-4 prior to ring closure, thus removing any steric hindrance associated with a β-substituent at that position were also assessed. A suitable substrate would have a good leaving group at C-4, and therefore pentaol **60** was treated with benzaldehyde dimethyl acetal to give the diacetal **73** which was converted to the known acetate **74** [22] (Scheme 7). Several sulfonate esters were prepared from **73**: the triflate **75**, mesylate **76**, tosylate **77** and *p*-fluorobenzenesulfonate **78**, and a number of nucleophilic displacement reactions

were attempted with sodium azide or tetrabutylammonium nitrite in DMF or DMSO. At temperatures between r.t. and 180 °C either there was no reaction or the substrate decomposed. Reaction of the tosylate **77** with sodium azide in refluxing DMSO did give a small amount of the desired azide **79** (10%), but the efficiency of the reaction did not recommend its application.



Scheme 7: a) $PhCH(OMe)_2$, TsOH; b) Ac_2O, pyr; c) Tf_2O, pyr; d) MsCl, pyr; e) TsCl, DMAP, pyr; f) p-$FC_6H_4SO_2Cl$, DMAP, pyr; g) for **77**: NaN_3, DMSO, 180°.

In conclusion, the tagetitoxin analogue **3** was made as indicated in Scheme 1, but other approaches to this type of compound following the routes outlined in Schemes 2 and 3, were not successful. Likewise, the paths indicated in Schemes 4-6 did not provide access to compounds of the type represented by **4** which is a closer analogue of the natural product.

Experimental

Nmr spectra were recorded on a Bruker AC-300 F instrument at 300 MHz (^1H) or 75 MHz (^{13}C), in $CDCl_3$ (or on occasion DMSO-d_6) with internal tetramethylsilane as reference, or in D_2O with acetone as reference, (Λ CH_3 2.15, CH_3 32.8). Where the data refer to 500 MHz spectra, the instrument used was a Varian Unity 500. Where multiplicities are quoted for ^{13}C resonances, they refer to the results of DEPT experiments. The assignment of resonances relied on COSY experiments. Accurate mass determinations were performed by Dr Lawrence Porter at ESR Ltd on a VG70-250S mass spectrometer under EI or CI conditions. Elemental analyses were performed by the Campbell Microanalytical Laboratory, Dunedin, NZ. Melting points were determined on a Reichert hot stage microscope and are uncorrected. "Hexanes" refers to the fraction of light petroleum, b.p. 66-68 °C. Reactions were monitored by thin layer chromatography (tlc) on Merck Kieselgel 60 F_{254} sheets 0.2 mm thick. Flash chromatography was performed with Merck Kieselgel 60 (0.040 - 0.063 mm). The term "extractive workup" refers to partitioning of a reaction mixture between an organic solvent and water, washing the organic phase with acid, alkali, brine or water as appropriate, drying over magnesium sulfate, filtration, and concentration under vacuum.

1,6-Anhydro-3-deoxy-3-nitro-β-D-gulopyranose (6). The title compound **6** was prepared by the method of Richardson and Fischer [8] in 15% yield (lit. [8] 14%), m.p. *ca.* 150 °C (lit.[8] 163-164 °C, turned waxy at 150 °C). ^1H nmr (500 MHz) δ (D_2O) 3.77 (1H, dd, J=4.8, 8.5 Hz, H-6), 4.12 (1H, d, J=8.5 Hz, H-6'), 4.44 (1H, dd, J=2.4, 4.9 Hz, H-2), 4.70 (1H, t, J=4.6 Hz, H-5), 4.73 (1H, dd, J=4.3, 9.8 Hz, H-4), 4.86 (1H, dd, J=4.9, 9.8 Hz, H-3), 5.53, (1H, d, J=2.1 Hz, H-1). ^{13}C nmr δ (D_2O) 66.3, t, C-6; 66.7, d, C-4; 71.6, d, C-2; 76.7, d, C-5; 88.9, d, C-3; 103.5, d, C-1.

3-Amino-1,6-anhydro-3-deoxy-β-D-gulopyranose hydrochloride (7). The title compound **7** was prepared by hydrogenation at 50 psi of the nitro-sugar **6** (3 g) in hydrochloric acid (0.5 M, 60 mL) over palladium on charcoal, after the method of Richardson and Fischer [8]. The

pure hydrochloride salt (7.HCl) was obtained on evaporation of the filtered reaction mixture, and crystals suitable for X-ray structural analysis were obtained from methanol-acetone. For 7.HCl ^{1}H nmr (500 MHz) δ (D_2O) 3.42 (1H, dd, *J*=4.4, 10.2 Hz, H-3), 3.75 (1H, dd, *J*=5.1, 8.4 Hz, H-6), 4.01-4.04 (1H, m, H-2), 4.08 (1H, dd, *J*=4.1, 10.2 Hz, H-4), 4.13 (1H, d, *J*=8.4 Hz, H-6'), 4.62 (1H, t, *J*=4.5 Hz, H-5), 5.48 (1H, s, H-1). ^{13}C nmr δ (D_2O) 54.0, d, C-3; 65.7, t, C-6; 68.2, d, C-4; 69.3, d, C-2; 77.1, d, C-5; 103.0, d, C-1.

3-Amino-1,6-anhydro-3-*N*-*tert*-butoxycarbonyl-3-deoxy-β-D-gulopyranose (8). The crude amino-sugar hydrochloride 7.HCl (4.09 g, 21.4 mmol) was stirred with di-*tert*-butyl dicarbonate (7.0 g, 32 mmol) in a mixture of THF (50 mL), saturated aqueous sodium carbonate (30 mL) and water (30 mL) overnight. Extractive workup and crystallisation (dichloromethane-hexanes) gave the title compound **8** as a white powder (3.88 g, 70%), m.p. 185 °C (dec.), $[\alpha]_D^{25}$ -34 (*c*, 0.3, $CHCl_3$). Found: C, 50.5; H, 7.2; N, 5.4. $C_{11}H_{19}NO_6$ requires C, 50.6; H, 7.3; N, 5.4%]. ^{1}H nmr δ ($CDCl_3$ with D_2O exchange) 1.47 (9H, s), 3.6-3.8 (3 H, m, H-2,3,6), 3.83 (1H, dd, *J*=4.2, 8.8 Hz, H-4), 4.22 (1H, d, *J*=7.9 Hz, H-6'), 4.43 (1H, t, *J*=4.6 Hz, H-5), 5.39 (1H, d, *J*=2.0 Hz, H-1). ^{13}C nmr δ (DMSO-d_6) 29.5, q, CH_3; 53.0, d, C-3; 63.9, t, C-6; 68.0, 69.9, 75.8, all d, C-4, 2, 5; 79.0, s, CCH_3; 102.7, d, C-1; 156.5, s, C=O.

1,6-Anhydro-3-*N*-benzylamino-2-*O*,3-*N*-carbonyl-3-deoxy-β-D-gulopyranose (9). A suspension of *N*-Boc amino sugar **8** (1.24 g, 4.76 mmol) was heated with bis(tributyltin) oxide (3.68 g, 6.17 mmol) in refluxing toluene (25 mL) under argon and with azeotropic removal of water. The mixture quickly became homogeneous, and after 90 min, tlc showed the starting material to have been converted to a more polar material. The solution was cooled and treated with tetrabutylammonium bromide (1.30 g, 4.03 mmol) and benzyl bromide (1.5 mL, 13 mmol). Reflux was continued for 2.5 h, after which time the intermediate had been converted to a much less polar product. Cooling, evaporation, partitioning of the residue between wet acetonitrile and hexanes, and concentration of the acetonitrile phase gave a gum. Flash chromatography (2:3 hexanes:ethyl acetate) gave the title compound **9** as a white solid (1.27 g, 96%), m.p. (ethanol-hexanes) 145-146 °C; $[\alpha]_D^{25}$ -47 (*c*, 0.5, $CHCl_3$). [Found: C, 60.8; H, 5.4; N, 4.9. $C_{14}H_{15}NO_5$ requires C, 60.6; H, 5.5; N, 5.0%]. ^{1}H nmr δ 3.57 (1H, dd, *J*=6.0, 8.0 Hz, H-3), 3.63, (1H, dd, *J*=5.8, 7.8 Hz, H-6), 3.91-4.04, (3 H, m, H-4,6', OH), 4.20 (1H, d, *J*=8.2 Hz, H-2), 4.32, 4.77 (2 x 1H, 2d, both *J*=15.0 Hz, CH_2Ph), 4.43 (1H, t, *J*=5.3 Hz, H-5), 5.55 (1H, s, H-1), 7.33 (5H, s, Ph). ^{13}C nmr δ 46.6, t, OCH_2Ph; 56.8, d, C-3; 62.6, t, C-6; 70.8, d, C-4; 73.1, 73.2, both d, C-2,5; 97.4, d, C-1; 128.1, 128.4, 128.9, all d; 135.8, 157.5, both s.

1,6-Anhydro-3-*N*-benzylamino-2-*O*,3-*N*-carbonyl-3-deoxy-4-*O*-(2-tetrahydropyranyl)-β-D-gulopyranose (10). A solution of alcohol (**9**) (1.23 g, 4.42 mmol) was stirred with dihydropyran (0.8 mL, 9 mmol) and *p*-toluenesulfonic acid (5 mg) in dichloromethane (25 mL) for 60 min. Extractive workup and flash chromatography (2:1 hexanes:ethyl acetate) gave the syrupy title compound **10** as a mixture of diastereomers (1.41 g, 88%). [Found: m/z (CI) 362.1602. $C_{19}H_{24}NO_6$ $(MH)^+$ requires m/z 362.1604]. ^{13}C nmr δ 20.3, 21.3, 24.9, 25.1, 31.3, 31.5, 45.7, 46.8, all t; 54.3, 55.3, both d; 62.7, 63.1, 63.9, 65.6, all t; 70.0, 72.6, 72.7, 73.1, 73.6, 79.6, 97.6, 97.8, 98.4, 101.5, 127.8, 128.0, 128.5, 128.6, 128.8, all d; 136.1, 136.5, 156.7, 156.8, all s.

1,6-Anhydro-3-(*N*,*N*-dibenzylamino)-3-deoxy-4-*O*-(2-tetrahydropyranyl)-β-D-gulopyranose (12). A solution of cyclic carbamate **10** (1.38 g, 3.81 mmol) was heated with sodium hydroxide (1.4 g) in refluxing 85% ethanol (35 mL) for 20 min. Cooling, evaporation of solvent and extractive workup gave syrupy 3-amino-1,6-anhydro-3-*N*-benzyl-3-deoxy-4-*O*-(2-tetrahydropyranyl)-β-D-gulopyranose (**11**), as a mixture of diastereomers; $[\alpha]_D^{25}$ -14 (*c*, 0.5, $CHCl_3$). [Found: m/z (CI) 336.1796. $C_{18}H_{26}NO_5$ $(MH)^+$ requires m/z 336.1811]. In a separate experiment, the diastereomers were separated by flash chromatography (2:3 hexanes:ethyl acetate) to give the major diastereomer: ^{1}H nmr δ 1.4-1.9 (6 H, m), 2.90 (1H, dd, *J*=4.6, 9.5 Hz, H-3), 3.4-3.5 (1H, m), 3.6-3.8 (6H, m), 3.97 (1H, d, *J*=8 Hz), 4.6-4.7 (2 H, m), 5.49 (1H, d, *J*=2.2 Hz, H-1), 7.2-7.4 (5H, m). ^{13}C nmr δ 20.3, 25.1, 31.0, 51.1, all t; 56.7, d; 63.6, 64.0, both t; 67.0, 74.3, 77.2, 101.1, 102.0, 127.3, 128.0, 128.6, all d; 139.7, s; minor diastereomer: ^{1}H nmr δ 1.4-1.9, (6 H, m), 2.84 (1H, dd, *J*=4.7, 9.3 Hz, H-3), 3.4-3.5 (1H, m), 3.6-3.9 (6 H, m), 3.99 (1H, d, *J*=7.6 Hz), 4.4-4.5 (2 H, m), 5.52 (1H, d, *J*=2.2 Hz, H-1), 7.2-7.4 (5 H, m). ^{13}C nmr δ 21.2, 25.1, 31.4, 51.1, all t; 56.7, d; 63.8, 65.0, both t; 66.4, 73.0, 74.8, 100.1, 101.1, 127.1, 128.0, 128.5, all d; 139.6, s.

Isomers **11** were heated with dibutyltin oxide (1.34 g, 5.38 mmol) in refluxing toluene (25 mL), under argon and removal of water with a Dean-Stark apparatus. After 20 min, the mixture was cooled and treated with tetrabutylammonium bromide (1.22 g, 3.78 mmol) and benzyl bromide (1.8 mL, 15 mmol). Reflux was continued for 15 min, whereupon reaction was complete (tlc). Cooling, concentration, partitioning of the residue between wet acetonitrile and hexanes, and evaporation of the acetonitrile phase gave a gum, which was flash chromatographed (2:1 hexanes:ethyl acetate) to give a colourless foamy mixture of diastereomers identified as the title compound **12** (1.29 g, 80%). [Found: m/z (CI) 426.2290. $C_{25}H_{32}NO_5$ $(MH)^+$ requires m/z 426.2280]. Major diastereomer: ^{1}H nmr δ 1.5-2.0 (6 H, m), 2.30 (1H, br. s), 3.03 (1H, dd, *J*=4.2, 10.4 Hz, H-3), 3.44-3.52 (1H, m), 3.61 (1H, dd, *J*=5.2, 7.5 Hz), 3.71-3.81 (1H, m), 3.80 (2 H, d, *J*=13.9 Hz), 3.94 (1H, d, *J*=7.5 Hz), 4.06 (2 H, d, *J*=13.9 Hz), 4.21 (1H, dd, *J*=4.2, 10.4 Hz), 4.74-4.78 (2 H, m), 5.24 (1H, *J*=2.3 Hz, H-1), 7.1-7.4 (10 H, m).

^{13}C nmr δ 20.1, 25.2, 31.5, all t; 56.2, d; 56.2, 63.2, 64.0, all t; 72.9, 74.4, 75.8, 101.5, 101.7, 126.9, 128.3, 128.5, all d; 140.1, s. Minor isomer: ^{13}C nmr δ 20.3, 25.3, 31.6, all t; 55.8, d; 56.1, 63.4, 64.1, all t; 70.1, 71.7, 73.4, 96.7, 101.9, 126.8, 128.3, 128.6, all d; 140.6, s.

1,6-Anhydro-3-(*N*,*N*-dibenzylamino)-3-deoxy-4-*O*-(2-tetrahydropyranyl)-β-D-gulopyranose 2-(o-xylylene phosphate) (13). A mixture of compound **12** (915 mg, 2.15 mmol), 1*H*-tetrazole (453 mg, 6.47 mmol) and o-xylylene *N*,*N*-diethylphosphoramidite (815 mg, 3.41 mmol) was stirred in dichloromethane (5 mL) for 40 min, whereupon conversion to a less polar material was complete (tlc). Water (0.1 mL) was added, followed after 5 min by 85% *m*-chloroperbenzoic acid (530 mg, 2.6 mmol). After 5 min a more polar material had formed; extractive workup and flash chromatography (3:2 hexanes:ethyl acetate) gave the title compound **13** as a foamy mixture of diastereomers (1.184 g, 91%). [Found: m/z (CI) 608.2405. $C_{33}H_{39}NO_8P$ $(MH)^+$ requires m/z 608.2413]. Major diastereomer: ^{1}H nmr δ 1.5-2.0, (6 H, m), 3.15-3.21 (1H, m), 3.44-3.51 (1H; m), 3.60 (1H, dd, *J*=5.0, 7.5 Hz), 3.73-3.80 (1H, m), 3.80 (2 H, d, *J*=13.8 Hz), 3.89 (1H, d, *J*=7.7 Hz), 4.05 (2 H, d, *J*=14.4 Hz), 4.28 (1H, dd, *J*=4.1, 10.5 Hz), 4.60-4.64 (1H, m), 4.78-4.80 (2 H, m), 5.07 (2 H, d, *J*=16.0 Hz), 5.13-5.32 (2 H, m), 5.47 (1H , d, *J*=2.1 Hz), 7.1-7.5 (14 H, m). ^{13}C nmr δ 20.0, 25.2, 31.5, all t; 54.0, dd, J_{CP}=7.7 Hz; 56.2, 63.2, 64.3, 68.4, 68.4, 69.5, all t; 74.7, 75.7, both d; 79.0, dd, J_{CP} = 7.7 Hz; 56.0, 63.8, 64.1, 68.3, 68.4, 68.5, all t; 70.2, 72.0, both d; 79.9, dd; 96.6, 99.9, both d; aromatics.

1,6-Anhydro-3-(*N*,*N*-dibenzylamino)-3-deoxy-β-D-gulopyranose 2-(o-xylylene phosphate) (14). A solution of tetrahydropyranyl ether **13** (1.25 g, 2.06 mmol) in THF (10 mL) was stirred with 2 M hydrochloric acid (2 mL) for 2 d, after which time reaction was mostly complete (tlc). Extractive workup and flash chromatography (1:1 hexanes:ethyl acetate) gave the title compound **14** (622 mg, 58%), m.p. (chloroform:hexanes) 165-166 °C. [Found: m/z (CI) 524.1829. $C_{28}H_{31}NO_7P$ $(MH)^+$ requires m/z 524.1838]. ^{1}H nmr δ 2.64, (1H, s, OH), 2.91 (1H, dt, *J*=3.7, 10.5 Hz, H-3), 3.55 (1H, dd, *J*=4.8, 7.9 Hz, H-6), 3.65 (1H, d, *J*=7.9 Hz, H-6'), 3.79, 4.09 (4 H, 2d, *J*=13.8 Hz, CH_2Ph), 4.26 (1H, dd, *J*=4.1, 10.5 Hz, H-4), 4.53 (1H, t, *J*=4.3 Hz, H-5), 4.90-4.94 (1H, m, H-2), 5.19-5.39 (4 H, m, $CH_2C_6H_4CH_2$), 5.55 (1H, d, *J*=2.2 Hz, H-1),7.2-7.4 (14 H, m). ^{13}C nmr δ 54.3, t; 56.2, dd, $^3J_{CP}$=6.8 Hz, C-3; 63.8, t, C-6; 64.6, d, C-4; 68.6, 68.7, 68.7, 68.8, all d; 74.3, dd, $^2J_{CP}$=6.4 Hz, C-2; 74.7, d, C-5; 100.4, d, C-1; 127.4, 128.6, 128.8, 128.9, 129.0, 129.2, 129.4, all d; 134.9, 135.3, 139.4, all s.

4-*O*-Acetyl-1,6-anhydro-3-(*N*,*N*-dibenzylamino)-3-deoxy-β-D-gulopyranose 2-(*O*-xylylene phosphate) (15). A solution of alcohol **14** (397 mg, 0.758 mmol), pyridine (1 mL) and acetic anhydride (0.5 mL) in dichloromethane (2 mL) was kept for 2 d. Concentration and flash chromatography (3:2 hexanes:ethyl acetate) gave the title compound **15** as a colourless foam (402 mg, 94%). [Found: m/z 566.1939. $C_{30}H_{33}NO_8P$ $(MH)^+$ requires m/z 566.1944]. ^{1}H nmr δ 2.18 (3 H, s), 3.30 (1H, dt, *J*=3.9, 11.0 Hz, H-3), 3.59 (1H, dd, *J*=4.9, 7.9 Hz, H-6), 3.76 (1H, d, *J*=7.9 Hz, H-6'), 3.79, 3.95 (4 H, 2d, *J*=13.9 Hz); 4.56 (1H, t, *J*=4.4 Hz, H-5), 4.76-4.80 (1H, m, H-2), 5.1-5.6 (4 H, m), 5.52 (1H, dd, *J*=4.1, 11.1 Hz, H-4), 5.55 (1H, d, *J*=1.9 Hz, H-1), 7.1-7.4 (14 H, m). ^{13}C nmr δ 21.2, q; 53.0, dd, $^3J_{CP}$=7.3 Hz, C-3; 55.4, t; 64.3, t, C-6; 67.8, d, C-4; 68.6, 68.7, both t; 72.6, d, C-5; 77.4, dd, C-2; 100.0, d, C-1; 127.1, 128.3, 128.5, 128.8, 129.0, 129.1, 129.3, all d; 134.8, 135.2, 139.5, 169.9, all s.

3-Amino-1,6-anhydro-3-deoxy-β-D-gulopyranose 2-phosphate (16). A solution of the protected amino phosphate **14** (0.135 g, 0.258 mmol) in ethanol (2 mL) and acetic acid (0.5 mL) was added to 10% palladium on charcoal (50-100 mg), and hydrogenated at 50 p.s.i. in a Parr apparatus with shaking overnight. Filtration over Celite and trituration with ethanol gave the title compound **16** as a white powder (62 mg, 100%). The compound decomposed without melting at about 280 °C; $[\alpha]_D^{25}$ +36 (*c*, 1.0, H_2O). [Found: C, 29.8; H, 4.8; N, 5.7. $C_6H_{12}NO_7P$ requires C, 29.9; H, 5.0; N, 5.8%]. ^{1}H nmr (500 MHz) δ (D_2O) 3.41 (1H, ddd, $^4J_{HP}$=1.4, $^3J_{HH}$=4.6, 10.2 Hz, H-3), 3.64 (1H, dd, *J*=4.9, 8.2 Hz, H-6), 3.99-4.03 (2 H, m, H-4,6'), 4.26 (1H, ddd, $^3J_{HP}$ = 8.5 Hz, $^3J_{HH}$=2.5, 4.5 Hz, H-2), 4.51 (1H, t, *J*=4.4 Hz, H-5), 5.53 (1H, d, *J*=2.4 Hz, H-1). ^{13}C nmr δ (D_2O) 53.4, dd, $^3J_{CP}$=6.0 Hz, C-3; 65.9, t, C-6; 68.0, d, C-4; 72.7, dd, $^2J_{CP}$=5.1 Hz, C-2; 77.2, d, C-5; 101.5, d, C-1. ^{31}P nmr δ (D_2O) -0.1, d, J_{PH}=7.3 Hz.

4-*O*-Acetyl-3-amino-1,6-anhydro-3-deoxy-β-D-gulopyranose 2-phosphate (3, X=O). The *O*-acetylated amino phosphate **15** (0.28 g, 0.50 mmol) was treated as for alcohol **14** to give the title compound **3** (X=O) as a white powder (0.132 g, 94%) which decomposed without melting at about 280 °C; $[\alpha]_D^{25}$ +40 (*c*, 1.1, H_2O). Attempted recrystallisation from boiling water also caused some decomposition. [Found: C, 33.6; H, 5.1, N, 4.9. $C_8H_{14}NO_8P$ requires C, 33.9; H, 5.0; N, 5.0%]. ^{1}H nmr (500 MHz) δ (D_2O) 1.98 (3 H, s), 3.60 (1H, dd, *J*=4.8, 8.4 Hz, H-6), 3.70 (1H, ddd, $^4J_{HP}$=1.2 Hz, $^3J_{HH}$=4.6, 10.4 Hz, H-3), 4.00 (1H, d, *J*=8.7 Hz, H-6'), 4.28 (1H, ddd, $^3J_{HP}$=2.4, 4.7 Hz, H-2), 4.64 (1H, t, *J*=4.4 Hz, H-5), 5.03 (1H, dd, *J*=3.9, 10.4 Hz, H-4), 5.54 (1H, d, *J*=2.4 Hz, H-1). ^{13}C nmr δ (D_2O) 21.3, q; 49.5, dd, $^3J_{CP}$=6.6 Hz, C-3; 65.1, t, C-6; 68.9, d, C-4; 71.3, dd, $^2J_{CP}$=4.6 Hz, C-2; 72.6, d, C-5; 100.1, d, C-1; 173.5, s. ^{31}P nmr δ (D_2O) 0.0 (relative to H_3PO_4).

1,6-Anhydro-3,4-*O*-isopropylidene-6-thio-β-D-galactopyranose (23). A solution of 1,6-anhydro-6-thio-β-D-galactopyranose **(21)** [23] (457 mg, 2.56 mmol), which was made by adoption of a route developed for 1,6-anhydro-6-thio-β-D-mannopyranose [24], in dry acetone (5 mL) and 2,2-dimethoxypropane (2 mL) was stirred with *p*-toluenesulfonic acid monohydrate (5 mg) for 30 min. Filtration over silica gel (ethyl acetate), concentration and radial chromatography (1:1 hexanes:ethyl acetate) gave the title compound **23** as a white semi-solid (471 mg, 84%). [Found: m/z (CI) 219.0692. $C_9H_{15}O_4S$ $(MH)^+$ requires m/z 219.0691]. ^{1}H nmr δ 1.34, 1.35 (2 x 3H, 2s), 2.39 (1H br s, OH), 2.89 (1H, dd, *J*=6.6, 10.1 Hz, H-6), 3.36 (1H, d, *J*=10.1 Hz, H-6'), 3.98 (1H, s, H-2), 4.19 (1H, dd, *J*=0.9, 7.3 Hz, H-3), 4.41 (1H, t, *J*=7.1 Hz, H-4), 4.86 (1H, t, *J*=6.7 Hz, H-5), 5.42 (1H, s, H-1). ^{13}C nmr δ 24.1, 25.8, both q; 29.4, t, C-6; 69.0, d, C-4; 73.0, d, C-2; 76.8, d, C-3; 77.5, d, C-5; 82.8, d, C-1; 108.7, s, *C*-Me_2.

1,6-Anhydro-3,4-*O*-isopropylidene-β-D-galactopyranose 2-(diphenyl phosphate) (24). A stirred solution of 1,6-anhydro-3,4-*O*-isopropylidene-β-D-galactopyranose **(22)** (186 mg, 0.92 mmol) in dichloromethane (20 mL) and pyridine (2 mL) was treated with diphenyl chlorophosphoridate (0.3 mL, 1.4 mmol). After 2d, extractive workup and flash chromatography (2:1 hexanes:ethyl acetate) gave the title compound **24** as a colourless syrup (356 mg, 89%).; $[\alpha]_D^{25}$ -27 (*c*, 0.7, $CHCl_3$). The reaction was also performed with 11 g of compound **22** and a similar yield was obtained. [Found: m/z 435.1228. $C_{21}H_{24}O_8P$ requires m/z 435.1209)]. ^{1}H nmr δ 1.25, 1.51 (2 x 3H, 2s), 3.57 (1H, dd, *J*=5.4, 7.5 Hz, H-6), 4.10 (1H,d, *J*=7.6 Hz, H-6'), 4.19 (1H, d, *J*=7.3 Hz, H-3), 4.39 (1H, t, *J*=6.7 Hz, H-4), 4.51 (1H, t, *J*=5.6 Hz, H-5), 4.62 (1H, d, $^3J_{HP}$=10.0 Hz, H-2), 5.43 (1H, s, H-1), 7.2-7.4 (10 H, m). ^{13}C nmr δ 24.2, 25.7, both q; 63.3, t, C-6; 68.8, d, C-4; 72.1, d, C-5; 74.3, dd, $^3J_{CP}$=5.7 Hz, C-3; 75.7, dd, $^2J_{CP}$=6.7 Hz, C-2; 99.2, dd, $^3J_{CP}$=6.1 Hz, C-1; 109.0, s; 120.1, dd, $^3J_{CP}$=4.8 Hz; 125.6, 129.9, both d; 150.3, dd, $^2J_{CP}$=2.6 Hz; 150.4, dd, $^2J_{CP}$=2.4 Hz.

1,6-Anhydro-3,4-*O*-isopropylidene-β-D-galactopyranose 2-(dibenzyl phosphate) (25). To a stirred solution of the anhydrogalactose **22** (1.013 g, 5.01 mmol) in dry THF (40 mL), maintained at –40 °C under argon, was added 1.6 M butyllithium (1.3 equiv) in hexanes over 2 min. After 5 min, the temperature was lowered to –60 °C and a solution of tetrabenzyl diphosphate [25] (3.52 g, 6.54 mmol) in THF (20 mL) was added. The solution was allowed to reach r.t. gradually, and it was stirred for 2 d, during which time a thick precipitate formed. Extractive workup and flash chromatography (3:2 hexanes:ethyl acetate) gave the title compound **25** as a pale yellow syrup (1.67 g, 72%).; $[\alpha]_D^{25}$ -13 (*c*, 1.3, $CHCl_3$). ^{1}H nmr δ 1.25, 1.49 (2 x 3 H, 2s), 3.54 (1H, dd, *J*=5.4, 7.5 Hz, H-6), 4.07 (1H, d, *J*=7.6 Hz, H-6'), 4.19 (1H, d, *J*=7.2 Hz, H-3), 4.35 (1H, t, *J*=6.3 Hz, H-4), 4.38 (1H, d, $^3J_{HP}$=9.0 Hz, H-2), 4.47 (1H, t, *J*=5.6 Hz, H-5), 5.0-5.1 (4H, m, CH_2 Ph), 5.33 (1H, s, H-1) 7.34 (10 H, s). ^{13}C nmr δ 24.3, 25.7, both q; 63.3, t, C-6; 68.8, d, C-4; 69.6, 69.7, both td, $^2J_{CP}$=3.6 Hz; 72.0, d, C-5; 74.4, dd, $^3J_{CP}$=5.6 Hz, C-3; 74.6, dd, $^2J_{CP}$=6.0 Hz, C-2; 99.3 dd, $^3J_{CP}$=5.7 Hz, C-1; 108.9, s.

1,6-Anhydro-3,4-*O*-isopropylidene-6-thio-β-D-galactopyranose 2-(dibenzyl phosphate) (26). To a stirred solution of alcohol **23** (149 mg, 0.68 mmol) in dry DMF (5 mL), maintained under argon, was added 80 wt.% sodium hydride in mineral oil (25 mg, 0.83 mmol). After 2 min, tetrabenzyl diphosphate [25] (480 mg, 0.89 mmol) was added, and the resultant yellow solution was stirred for 3 h. Quenching with water, extractive workup and radial chromatography (7:3 hexanes:ethyl acetate) gave the title compound **26** (245 mg, 75%) as an unstable yellow gum. ^{1}H nmr δ 1.25, 1.51 (2 x 3H, 2s), 2.82 (1H, dd, *J*=6.6, 10.1 Hz, H-6), 3.31 (1H, d, *J*=10.1 Hz, H-6'), 4.13 (1H, dd, *J*=1.3, 7.6 Hz, H-3), 4.31 (1H, t, *J*=7.3 Hz, H-4), 4.49 (1H, d, $^3J_{HP}$=8.8 Hz, H-2), 4.83 (1H, t, *J*=6.7 Hz, H-5), 4.99-5.16 (4 H, m), 5.36 (1H, s, H-1), 7.35 (10H, s). ^{13}C nmr δ 24.2, 25.9, both q; 29.5, t, C-6; 68.8, d, C-4; 69.6, 69.7, both td, $^2J_{CP}$=3.4 Hz; 73.8, dd, $^3J_{CP}$=6.6 Hz, C-3; 77.4, d, C-5; 77.6, dd, $^2J_{CP}$=6.3 Hz, C-2; 81.2, dd, $^3J_{CP}$=4.3 Hz, C-1; 108.9, s; 128.1, 128.7, 128.7, all d; 135.5.s.

1,6-Anhydro-β-D-galactopyranose 2-(dibenzyl phosphate) (28) and 1,6-anhydro-β-D-galactopyranose 2-(diphenyl phosphate) (27). Acetonide **25** (1.55 g, 3.35 mmol) was heated with 2 M hydrochloric acid (5 mL) in refluxing THF (40 mL) until reaction was complete (tlc, 60 min). Evaporation of most of the solvent, extractive workup and flash chromatography (1:5 ethyl acetate:hexanes) gave white needles, m.p. 98.5-99.5 °C (ethyl acetate-hexanes) of phosphate **28** (702 mg, 50%); $[\alpha]_D^{25}$ -13 (*c*, 2, $CHCl_3$). [Found: C, 56.9; H, 5.5; P, 7.3. $C_{20}H_{23}O_8P$ requires C, 56.9; H, 5.5, P, 7.3%]. ^{1}H nmr δ ($CDCl_3$ with D_2O exchange) 3.59 (1H, dd, *J*=5.5, 7.0 Hz, H-6), 3.91 (1H, t, *J*=4.8 Hz, H-4), 3.99 (1H, dd, *J*=1.0, 5.0 Hz, H-3), 4.23 (1H, d, *J*=7.5 Hz, H-6'), 4.32 (1H, d, $^3J_{HP}$=8.9 Hz, H-2), 4.39 (1H, t, *J*=4.6 Hz, H-5), 4.96-5.08 (4H, m), 5.25 (1H, s, H-1), 7.30-7.35 (10 H, m). ^{13}C nmr 63.7, t, C-6; 64.0, d, C-4; 68.8, dd, $^3J_{CP}$ = 4.3 Hz, C-3; 69.9, 70.0, both t; 74.5, d, C-5; 76.2, dd, $^2J_{CP}$= 6.1 Hz, C-2; 99.4, dd, $^3J_{CP}$=6.2 Hz, C-1; 128.0, 128.1, 128.7, 128.7, 128.8, 128.8, all d; 135.3, dd, $^3J_{CP}$ = 6.0 Hz. Diphenyl phosphate **27** was obtained from **24** in a similar way, m.p. 93-94 °C. [Found: C, 54.7; H, 5.0; P, 7.6. $C_{18}H_{19}O_8P$ requires C, 54.8; H, 4.9; P, 7.9%]. ^{1}H nmr δ ($CDCl_3$ with D_2O exchange) 3.59 (1H, dd, *J*=5.4, 7.2 Hz, H-6), 3.91 (1H, t, *J*=4.9 Hz, H-4), 4.00 (1H, d, *J*=5.3 Hz, H-3), 4.23 (1H, d, *J*=7.6 Hz, H-6'), 4.39 (1H, t, *J*=4.6 Hz, H-5), 4.55 (1H, d, $^3J_{HP}$=9.0 Hz, H-2), 5.33 (1H, s, H-1), 7.2-7.4 (10 H, m). ^{13}C nmr δ 63.8, t, C-6; 64.0, d, C-4; 68.8, dd, $^3J_{CP}$=4.2 Hz, C-3; 74.5, d, C-5; 77.2, dd, $^2J_{CP}$=7.1 Hz, C-2; 99.3, dd,

$^3J_{CP}$=7.0 Hz, C-2; 99.3, dd, $^3J_{CP}$=7.0 Hz, C-1; 120.0, dd, J_{CP}=1.7 Hz; 120.1, dd, J_{CP}=2.0 Hz; 125.9, 130.0, both d; 150.2, dd, $^2J_{CP}$=7.4 Hz.

4-*O*-Acetyl-1,6-anhydro-β-D-galactopyranose 2-(diphenyl phosphate) (31) and 3,4-di-*O*-acetyl-1,6-anhydro-β-D-galactopyranose 2-(diphenyl phosphate) (30). A solution of phosphate **27** (1.60 g, 4.06 mmol), acetic anhydride (555 mg, 5.44 mmol) and pyridine (2 mL) in dichloromethane (20 mL) was stirred for 2 d. Evaporation of the solvent and excess of the reagents, followed by flash chromatography (2:3 hexanes:ethyl acetate), gave two products as colourless syrups. The more polar product was 4-acetate **31** (1.135 g, 64% containing 10% of the 3-acetate); $[\alpha]_D^{25}$ +6 (*c*, 2.0, $CHCl_3$). [Found: m/z (CI) 437.0997. $C_{20}H_{22}O_9P$ $(MH)^+$ requires m/z 437.1001]. ^{1}H nmr δ 2.07, (3 H, s), 3.5 (1H br.s), 3.63-3.67 (1H, m, H-6), 4.2-4.3 (1H, m, H-3), 4.40 (1H, d, *J*=7.4 Hz, H-6'), 4.49 (1H, t, *J*=4.3 Hz, H-5), 4.57 (1H, d, $^3J_{HP}$=9.1 Hz, H-2), 4.99 (1H, t, *J*=4.5 Hz, H-4), 5.41 (1H, s, H-1), 7.15-7.40 (10 H, m). ^{13}C nmr δ 20.8, q; 64.7, t, C-6; 66.9, d, C-4; 68.1, dd, $^3J_{CP}$=5.4 Hz, C-3; 72.2, d, C-5; 77.1, dd, C-2; 99.8, dd, $^3J_{CP}$=6.4 Hz, C-1; 120.1, 120.1, 120.2, 125.7, 129.9, 130.0, all d; 150.3, dd, $^2J_{CP}$=7.4 Hz; 169.6, s. The less polar product was identified as diacetate **30** (352 mg 18%). [Found: m/z (CI) 479.1092. $C_{22}H_{24}O_{10}P$ $(MH)^+$ requires m/z 479.1107]. ^{1}H nmr δ 2.02, 2.10 (2x 3 H, 2s), 3.70-3.74 (1H, m, H-6), 4.31 (1H, d, *J*=7.5 Hz, H-6'), 4.48-4.51 (2 H, m, H-2,5), 5.25 (1H, t, *J*=4.6 Hz, H-4), 5.38 (1H, d, *J*=5.2 Hz, H-3); 5.45, (1H, s, H-1), 7.2-7.4 (10 H, m). ^{13}C nmr δ 20.5, 20.6, both q; 64.5, d, C-4; 64.6, t, C-6; 67.8, dd, $^3J_{CP}$=6.8 Hz, C-3; 72.2, d, C-5; 75.2, dd, $^2J_{CP}$=6.4 Hz, C-2; 99.4, dd, $^3J_{CP}$=4.6 Hz, C-1; 120.1, 120.1, 120.2, 125.7, 129.9, 130.0, all d; 150.3, dd, $^2J_{CP}$=7.6 Hz; 169.1, 169.3 both s.

3-*O*-Acetyl-1,6-anhydro-β-D-galactopyranose 2-(dibenzyl phosphate) (34). A solution of phosphate **28** (51 mg, 0.12 mmol) and *p*-toluenesulfonic acid monohydrate (1 mg) was heated in refluxing triethyl orthoacetate (2 mL) under argon, until tlc indicated complete conversion to a less polar material. Extractive workup gave a gum, presumed to be the cyclic orthoester **35**, which was heated with 50% aqueous acetic acid (0.2 mL) in refluxing THF (2 mL) for 3 h. Extractive workup gave a colourless gum, identified as acetate **34** (46 mg, 83%). [Found: m/z (CI) 465.1316. $C_{22}H_{26}O_9P$ $(MH)^+$ requires m/z 465.1314]. ^{1}H nmr δ 2.10 (3H, s), 3.64 (1H, dd, *J*=5.4, 6.9 Hz, H-6), 4.13 (1H, t, *J*=4.9 Hz, H-4), 4.22-4.26 (2 H, m, H-2,6'), 4.39 (1H, t, *J*=4.4 Hz, H-5), 5.0-5.1 (4 H, m), 5.17 (1H, dd, *J*=1.4, 5.4 Hz, H-3), 5.35 (1H, s, H-1), 7.34 (10 H, s). ^{13}C nmr δ 20.9, q; 63.9, d, C-4; 63.9, t, C-6; 69.8, 69.9, 69.9, all t; 70.4, dd, $^3J_{CP}$=6.5 Hz, C-3; 74.2, d, C-2,5; 99.1, dd, $^3J_{CP}$=4.5 Hz, C-1; 128.1, 128.6, 128.7, all d; 135.4, dd, $^3J_{CP}$=6.4 Hz; 170.8, s.

1,6-Anhydro-*endo*-3,4-*O*-*p*-methoxybenzylidene-6-thio-β-D-galactopyranose (41). A solution of triol **21** (2.02 g, 11.3 mmol) and *p*-methoxybenzaldehyde dimethyl acetal (2.48 g, 13.6 mmol) in dry DMF (30 mL) was stirred with *p*-toluenesulfonic acid monohydrate (200 mg) for 3 h. Extractive workup and flash chromatography (1:1 hexanes:ethyl acetate) gave the title compound **41** as a white crystalline solid (2.71 g, 81%), m.p. 132 °C. [Found: C, 56.8; H, 5.7. $C_{14}H_{16}O_5S$ requires C, 56.7; H, 5.4%); m/z (CI) 297.0784. $C_{14}H_{17}O_5S$ (MH^+) requires m/z 297.0797]. ^{1}H nmr δ 2.81 (1H, dd, *J*=6.7, 10.1 Hz, H-6), 3.25 (1H, d, *J*=10.1 Hz, H-6'), 3.80 (3H, s), 4.09 (1H, s, H-2), 4.10 (1H, d, *J*=6.4 Hz, H-3), 4.45 (1H, t, *J*=7.1 Hz, H-4), 4.85 (1H, t, *J*=6.7 Hz, H-5), 5.42 (1H, s, H-1), 5.70 (1H, s, benzylidene [26]); 6.92, 7.47, (2x2H, 2d, *J*=8.7 Hz). ^{13}C nmr δ 30.0, t, C-6; 55.3, q; 69.4, d, C-4; 72.9, d, C-2; 77.5, d, C-3; 77.6, d, C-5; 83.0, d, C-1; 103.2, 114.0, 2x d; 127.8, s; 128.0, d; 160.6, s.

1,6-Anhydro-2-*O*-*tert*-butyldimethylsilyl-*endo*- and *exo*-3,4-*O*-*p*-methoxybenzylidene-β-D-galactopyranose (40) and 1,6-anhydro-2-*O*-*tert*-butyldimethylsilyl-*endo*-3,4-*O*-*p*-methoxybenzylidene-6-thio-β-D-galactopyranose (42). The requisite alcohol **39** [15] or **41** (*endo*-isomer) (9-21 mmol) was stirred with *tert*-butyldimethylsilyl chloride (1.4 equiv) and imidazole (2 equiv) in dry DMF (15-25 mL) for 2-3 h. Extractive workup and flash chromatography (8:1 hexanes:ethyl acetate) gave the respective title compound **40** or **42** (99-100%). For **40** (*endo*-isomer): [Found: m/z (CI) 395.1890 . $C_{20}H_{31}O_6Si$ $(MH)^+$ requires m/z 395.1890]. ^{1}H nmr δ 0.15 (6H, s), 0.93 (9H, s), 3.50 (1H, dd, *J*=5.9, 7.3 Hz, H-6), 3.82 (3H, s), 4.00 (1H, s, H-2), 4.07 (1H, d, *J*=6.6 Hz, H-3), 4.11 (1H, d, *J*=7.5 Hz, H-6'), 4.50-4.58 (2 H, m, H-4,5), 5.28 (1H, s, H-1), 5.75 (1H, s, benzylidene [26]), 6.92, 7.45 (2x2H, 2d, *J*=8.7 Hz). ^{13}C nmr δ -4.9, -4.8, 2x q; 18.2, s; 25.8, 55.3 2x q; 63.3, t, C-6; 69.5, 71.2, 72.1, 79.2, all d; 101.8, d, C-1; 102.7, 113.9, 127.7, all d; 127.9, 160.5, both s. In another experiment, using a mixture of *endo*- and *exo*-isomers of the starting material, the *exo*-isomer of **40** was isolated, m.p. 106-108 °C; $[\alpha]_D^{25}$ -35 (*c*, 0.8, $CHCl_3$). [Found: C, 60.7; H, 7.7. $C_{20}H_{30}O_6Si$ requires C, 60.9; H, 7.9%; m/z (CI) 395.1890. $C_{20}H_{31}O_8Si$ $(MH)^+$ requires m/z 395.1890]. ^{1}H nmr δ 0.06, 0.10 (2x3H, 2s), 0.87 (9H, s), 3.65-3.69, (1H, m, H-6), 3.81 (3H, s), 3.81-3.86 (1H, m), 3.95 (1H, s), 4.08 (1H, d, *J*=7.7 Hz, H=6'), 4.55-4.57 (2H, m), 5.27 (1H, s, H-1), 6.26 (1H, s, benzylidene [24]), 6.89, 7.33 (2x2H, 2 d, *J*=8.7 Hz). ^{13}C nmr δ -4.9, -4.9, 2x q; 18.2, s; 25.8, 55.3, 2x q; 63.7, t, C-6; 70.1, 71.2, 72.3, 76.0, all d; 101.7, d, C-1; 103.3, 113.8, 126.8, all d; 131.6, 160.0, 2x s. For the thio-compound **42** (*endo* isomer), m.p. 85 °C: [Found: C, 58.7; H, 7.6. $C_{20}H_{30}O_5SSi$ requires C, 58.5; H, 7.4%; m/z (CI), 411.1657. $C_{20}H_{31}O_5SSi$ $(MH)^+$ requires m/z 411.1661]. ^{1}H nmr δ 0.14, 0.15 (2x3H, 2s), 0.93 (9H, s), 2.80 (1H, dd, *J*=6.8, 10.1 Hz, H-6), 3.26 (1H, d, *J*=10.1 Hz, H-6'), 3.81 (3H, s), 4.03 (1H, br. d, *J*=7.6 Hz, H-3), 4.12 (1H, s, H-2), 4.48 (1H, t, *J*=7.1 Hz, H-4), 4.86 (1H, t, *J*=6.7 Hz, H-5) 5.35, (1H, s, H-1), 5.71 (1H, s,

benzylidene), 6.92, 7.49 (2x 2H, 2d, *J*=8.7 Hz). ^{13}C nmr δ -4.8, -4.7, 2x q; 18.1, s; 25.8, q; 29.9, t, C-6; 55.3, q; 69.5, d, C-4; 74.2, d, C-2; 77.1, d, C-5; 78.5, d, C-3; 83.8, d, C-1; 102.9, 113.9, 127.9, all d; 160.6, s.

4-*O*-Acetyl-1,6-anhydro-2-*O*-*tert*-butyldimethylsilyl-3-*O*-*p*-methoxybenzyl-β-D-galactopyranose (44) and 4-*O*-acetyl-1,6-anhydro-2-*O*-*tert*-butyldimethylsilyl-3-*O*-*p*-methoxybenzyl-6-thio-β-D-galactopyranose (47). The *p*-methoxybenzylidene acetal **40** (8.44 g, 21.4 mmol) in dry THF (30 mL) was added over 5 min to a stirred suspension of lithium aluminium hydride (2.60 g, 68.5 mmol) in THF (30 mL), maintained under argon. After 20 min, aluminium chloride (6.1 g, 46 mmol) was added portionwise with cooling. The mixture was kept at gentle reflux for 2 h, whereupon reaction was complete (tlc). Cooling, careful quenching with water, filtration over Celite, extractive workup and flash chromatography (4:1 hexanes:ethyl acetate) gave 1,6-anhydro-2-*O*-*tert*-butyldimethylsilyl-3-*O*-*p*-methoxybenzyl-β-D-galactopyranose **43** (4.76 g, 56%) as a nearly colourless gum. This material was heated with acetic anhydride (3 mL) in refluxing pyridine (10 mL) for 2 h. Cooling, extractive workup and flash chromatography (4:1 hexanes:ethyl acetate) gave the title compound **44** as a pale yellow gum (4.87 g, 92%); $[\alpha]_D^{25}$ -30 (*c*, 0.4, $CHCl_3$). [Found: m/z (CI) 456.2417. $C_{22}H_{38}NO_7Si$ $(MNH_4)^+$ requires m/z 456.2417]. ^{1}H nmr δ 0.00, 0.02, (2x3H, 2s), 0.86 (9H, s), 2.02 (3H, s), 3.60 (1H, m, H-6), 3.77 (3H, s), 3.76-3.80 (2H, m), 4.37-4.51 (4H, m), 5.05 (1H, t, *J*=4.5 Hz, H-4), 5.20 (1H, br. s, H-1), 6.84, 7.22 (2x2H, 2d, *J*=8.7 Hz). ^{13}C nmr δ -4.9, -4.8, both q; 18.0, s; 20.9, q, $OCOCH_3$; 25.7, q; 73.2, t; 77.3, d; 102.2, d, C-1; 113.8, 129.1, 2xd; 130.3, 159.3, 170.0, all s. In similar manner, title compound **47** was obtained as a pale yellow gum in 37% yield from **42**. [Found: m/z (CI) 455.1929. $C_{22}H_{35}O_6SSi$ $(MH)^+$ .equires m/z 455.1924]. ^{1}H nmr δ 0.03, 0.07, (2x3H, 2s), 0.89 (9H, s), 2.06 (3H, s), 2.98 (1H, dd, *J*=7.3, 9.5 Hz, H-6), 3.50 (1H, d, *J*=9.6 Hz, H-6'), 3.78-3.80 (1H, m, H-3), 3.80 (3H, s), 3.92 (1H, br. s, H-2), 4.40, 4.57 (2H, AB, *J*=11.4 Hz), 4.71, (1H, dd, *J*=4.6, 7.0 Hz, H-5), 5.04, (1H, t, *J*=4.7 Hz, H-4), 5.26 (1H, s, H-1), 6.87, 7.27 (2x 2H, 2d, *J*=8.1 Hz). ^{13}C nmr δ -4.8, -4.7, both q; 18.0, s; 21.0, q, $OCOCH_3$; 25.7, q; 31.3, t, C-6; 55.3, q; 68.7, d, C-4; 72.8, t; 73.2, d, C-2; 76.0, d, C-5; 77.3, d, C-3; 84.3, d, C-1; 113.8, 128.9, both d; 130.5, 159.2, 170.0, all s.

4-*O*-Acetyl-1,6-anhydro-2-*O*-*tert*-butyldimethylsilyl-β-D-galactopyranose (45) and 4-*O*-acetyl-1,6-anhydro-2-*O*-*tert*-butyldimethylsilyl-6-thio-β-D-galactopyranose (48). A solution of *p*-methoxybenzyl ether **44** (500 mg, 1.14 mmol) in dichloromethane (6 mL) was stirred with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (388 mg, 1.50 equiv) and water (2 mL) overnight. Filtration over Celite, washing of the organic phase with satd. sodium carbonate and water, drying, concentration and flash chromatography (3:2 hexanes:ethylacetate) gave the title compound **45** (362 mg, 99%) as a colourless gum which solidified on standing. [Found: m/z (CI) 319.1572. $C_{14}H_{27}O_6Si$ $(MH)^+$ requires m/z 319.1577]. ^{1}H nmr δ ($CDCl_3$ with D_2O exchange) 0.10 (6H, s), 0.90 (9H, s), 2.13 (3H, s), 3.64 (1H, dd, *J*=5.0, 7.3 Hz, H-6), 3.81 (1H, t, *J*=1.7 Hz, H-2), 3.96-3.98 (1H, m, H-3), 4.30 (1H, d, *J*=7.5 Hz, H-6'), 4.48 (1H t, *J*=4.1 Hz, H-5), 5.07 (1H, t, *J*=4.4 Hz, H-4), 5.29 (1H, br. s, H-1). ^{13}C nmr δ -4.9, q; 18.1, s; 20.9, q, $OCOCH_3$; 25.7, q; 64.3, t, C-6; 67.9, d, C-4; 70.7, d, C-3; 72.1, d, C-5; 73.0, d, C-2; 102.2, d, C-1; 159.8, s. In similar manner, title compound **48** was obtained as a pale yellow semisolid in 78% yield from **47**. [Found: m/z (CI) 335.1336. $C_{14}H_{27}O_5SSi$ $(MH)^+$ requires m/z 335.1348]. ^{1}H nmr δ 0.11, 0.12 (2x 3H, 2s), 0.91 (9H, s), 2.14 (3H, s), 3.02 (1H, dd, *J*=6.8, 10.2 Hz, H-6), 3.42 (1H, d, *J*=10.3 Hz, H-6'), 3.47 (1H d, *J*=10.0 Hz, OH), 3.92 (1H, br. s, H-2), 3.92-3.95 (1H, m, H-3), 4.83 (1H, t, *J*=5.7 Hz, H-5), 5.02 (1H, t, *J*=4.7 Hz, H-4), 5.34 (1H, t, *J*=1.7 Hz, H-1). ^{13}C nmr δ -4.9, -4.9, both q; 18.0, s; 20.9, q, $OCOCH_3$; 25.6, q; 31.0, t, C-6; 68.0, d, C-4; 70.6, 75.3, both d; 76.4, d, C-5; 83.8, d, C-1; 169.7, s.

2-(2,3,4,6-Tetra-*O*-acetyl-β-D-galactopyranosyl)-1,3-diphenyl-imidazolidine (53) and 2-(3,4,6-tri-O-acetyl-1,5-anhydro-2-deoxy-D-lyxo-hex-1-enitol-1-yl)-1,3-diphenyl-imidazolidine (57). The title compound **53** was prepared from the nitrile **52** according to the method of Dettinger, Kurz and Lehmann [18], m.p. 155 °C; $[\alpha]_D^{25}$ +13 (*c*, 1.7, $CHCl_3$); lit. [18] 153 °C; $[\alpha]_{578}^{22}$ +12 (*c*, 1, $CHCl_3$). ^{1}H nmr δ 1.88, 2.02, 2.02, 2.10 (4 x 3H, 4s), 3.44-3.72 (4H, m, H-4,5), 3.81 (1H, t, *J*=7.1 Hz, H-5'), 3.85 (1H, d, *J*=10.5 Hz, H-1'), 4.18 (2H, ABX, *J*=5.7, 7.1, 11.3 Hz, H-6',6''), 4.89 (H-1, dd, *J*=3.2, 9.7 Hz, H-3'), 5.22 (1H, t, *J*=9.8 Hz, H-2'), 5.30 (H-1, d, *J*=3.1 Hz, H-4'), 5.40 (1H, s, H-2), 6.7-7.3 (10H, m). ^{13}C nmr δ 20.4, 20.4, 20.5, 20.7, all q; 45.5, 47.0, both t, C-4,5; 68.0, t, C-6'; 66.9, d, C-2'; 67.5, d, C-4'; 73.1, d, C-3'; 74.0, d, C-5'; 76.4, d, C-2; 78.9, d, C-1'; 112.9, 113.5, 117.8, 118.0, 128.9, 129.2, all d; 144.9, 146.5, 168.3, 169.9, 170.0, 170.2, all s. A product slightly less polar than **53** was also isolated by flash chromatography (1:1 hexane:ethyl acetate) of the crude product mixture. Crystallisation from water gave alkene **57**, m.p. 125 °C; $[\alpha]_D^{25}$ -37 (*c*, 1.1, $CHCl_3$). [Found: C, 65.6; H, 6.3; N, 5.6. $C_{27}H_{30}N_2O_7$ requires C, 65.6; H, 6.1; N, 5.7%; m/z (CI) 495.2114. $C_{27}H_{31}N_2O_7$ $(MH)^+$ requires m/z 495.2131]; $[\alpha]_D$ - 40.3° (c=1.05, $CHCl_3$). ^{1}H nmr δ 1.80, 1.96, 2.01 (3 x 3H, 3s), 3.61-3.71 (4H, m, H-4,5), 3.92 (1H, dd, *J*=7.4, 11.5 Hz, H-6'), 4.04 (1H, dd, *J*=5.1, 11.5 Hz, H-6''), 4.10-4.14 (1H, m, H-5'), 5.00 (1H, dd, *J*=0.6, 1.8 Hz, H-2'), 5.21-5.23 (1H, m, H-4'), 5.44, 1H, td, *J*=0.6, 3.1 Hz, H-3'), 5.47 (1H, s, H-2), 6.72-6.91 (6H, m), 7.20-7.28 (4H, m). ^{13}C nmr δ 20.1, 20.5, 20.5, all q; 45.6, 45.7, both t, C-4,5; 61.5, t, C-6';63.4, d, C-4'; 64.5, d, C-3'; 72.7, d, C-5'; 74.5, d, C-2; 93.6, d, C-2'; 113.0, 113.8, 117.7, 117.9, 128.6, 128.9, all d; 144.8, 145.2, both s; 153.1, s, C-1'; 169.9, 170.1, both s.

1,3,4,5,7-Penta-*O*-acetyl-2,6-anhydro-L-*glycero*-L-*galacto*-heptitol (54). A. From imidazolidine **(53)** - A stirred solution of **(53)** (1.19 g, 2.15 mmol) in dichloromethane (25 mL) and acetone (10 mL) was treated with *p*-toluenesulfonic acid monohydrate (0.90 g, 4.7 mmol). A precipitate formed rapidly and after 20 min the mixture was filtered. The filtrate was evaporated and the residue dissolved in methanol (20 mL). To the stirred solution was added sodium borohydride (50 mg, 1.3 mmol) and after 20 mins extractive workup gave a syrup which was stirred with pyridine (5 mL) and acetic anhydride (5 mL) overnight. Concentration and radial chromatography (3:2 hexanes:ethyl acetate) gave the chromatographically homogeneous title compound **54** (287 mg, 34%) as a syrup (lit. [20] m.p. 55-57 °C). ^{1}H nmr δ 1.98, 2.04, 2.05, 2.09, 2.16 (5 x 3H, 5 s), 3.70 (1H, ddd, *J*=2.5, 5.5, 9.8 Hz, H-6), 3.95 (1H, t, *J*=6.6 Hz, H-2), 4.12 (2H, d, *J*=7.2 Hz, H-1,1'), 4.12 (1H, m, H-7), 4.25 (1Hz, dd, *J*=5.5, 12.3 Hz, H-7'), 5.07 (1H, dd, *J*=3.4, 10.0 Hz, H-4), 5.23 (1H, t, *J*=10.0 Hz, H-5), 5.42 (1H, d, *J*=3.3 Hz, H-3). ^{13}C nmr δ 20.4, 20.5, 20.5, 20.5, 20.6, all q; 61.5, 62.6, both t; 66.0, 67.5, 71.9, 74.2, 76.3, all d; 169.5, 169.9, 170.1, 170.2, 170.5, all s.

B. From nitrile **52** - A stirred suspension of nitrile **52** (57.1 g, 160 mmol) in methanol (150 mL) was treated with sodium hydride (0.2 g), and after 18 h the resultant solution was evaporated to dryness. The residue was dissolved in aqueous sodium hydroxide (100 mL, 25% w/v) and heated under reflux. After 6 h ammonia evolution had ceased. The dark brown solution was then cooled and carefully acidified (conc. hydrochloric acid). The solution was concentrated to dryness and the residue was stirred with pyridine (100 mL) and acetic anhydride (100 mL) overnight. Acidification and extractive workup gave an oil which was flash chromatographed (7:3 hexane:ethyl acetate) to give a further oil presumed (see discussion) to be the tri-*O*-acetyl-2,6-anhydroheptono-1,5-lactone **55** (20.8 g, 41%). [Found: m/z (CI) 334.1135. $C_{13}H_{20}NO_9$ $(MNH_4)^+$ requires m/z 334.1137]. ^{1}H nmr δ 2.09, 2.15, 2.16 (3 x 3H, 3 s), 4.09 (1H, dd, *J*=6.3, 10.8 Hz, H-7), 4.22 (1H, dd, *J*=5.5, 6.2 Hz, H-6), 4.29 (1H, dd, *J*=5.4, 10.8 Hz, H-7'), 4.50 (1H, d, *J*=2.1 Hz, coupled to the signal at δ 5.02), 4.87 (1H, br. s), 4.91 (1H, br. s), 5.02 (1H, br. s). ^{13}C nmr δ 20.6, q; 61.7, t, C-7; 70.1, d, C-6; 71.0, d, C-4; 72.3, d, C-2; 73.4, d, C-3; 74.4, d, C-5; 166.3, 169.3, 169.7, 170.3, all s. IR (film) 1791, 1748 cm^{-1}. All of the lactone was dissolved in dry THF (300 mL) and to the cooled solution lithium aluminium hydride (7.5 g, 197 mmol) was cautiously added. The suspension was heated at gentle reflux for 2 h, and then acetic acid was added dropwise to the cooled mixture until the excess of reagent had been destroyed. Evaporation of the solvents gave a grey solid, which was broken up under pyridine (100 mL) and acetic anhydride (100 mL). The resultant suspension was stirred overnight and extractive workup and flash chromatography gave the title compound **54** (21.2 g, 80%, nmr data identical to those of the sample obtained by method A).

3,4,7-Tri-*O*-acetyl-2,6-anhydro-D-*glycero*-L-*manno*-heptonic acid (56). On standing, lactone **55** deposited crystals which on recrystallisation from propan-2-ol (x2) gave pure hydroxyacid **56**, mp 153-154°C; $[\alpha]_D^{25}$ +32 (*c*, 0.4,$CHCl_3$). [Found: C, 46.6; H 5.6. $C_{13}H_{18}O_{10}$ requires C, 46.7; H, 5.4%]. ^{1}H nmr δ (19:1 $CDCl_3$:d_6-Me_2SO) 2.03, 2.07, 2.10 (3 x 3H, 3 s), 3.79 (1H, t, *J*=6.0 Hz, H-6), 3.94 (1H, d, *J*=10.0 Hz, H-2), 4.09 (1H, d, *J*=2.7 Hz, H-5), 4.30 (2H, d, *J*=6.1 Hz, H-7,7'), 4.95 (1H, dd, *J*=3.1, 10.1 Hz, H-4), 5.51 (1H, t, *J*=10.1 Hz, H-3). ^{13}C nmr δ 21.0, 21.2, 21.25, all q; 63.4, t, C-7; 66.9, d, C-3; 67.5, d, C-5; 74.4, d, C-4; 76.4, d, C-6; 77.1, d, C-2; 169.5, 170.1, 170.7, 171.1, all s. X-Ray diffraction analysis see Fig. 2.

2,6-Anhydro-1,7-di-*O*-(*p*-toluenesulfonyl)-L-*glycero*-L-*galacto*-heptitol (61) and 2,6-anhydro-1,4,7-tri-*O*-(*p*-toluenesulfonyl)-L-*glycero*-L-*galacto*-heptitol (62). A stirred solution of pentaacetate **54** (430 mg, 1.09 mmol) in methanol (20 mL) was treated with 2% w/v methanolic sodium methoxide (1.0 mL). After 20 h, the solvent was evaporated and the residue was dissolved in water and filtered over a mixed bed resin, then freeze dried to give 2,6-anhydro-L-*glycero*-L-*galacto*-heptitol [19] **60** as an oil (180 mg, 85%). ^{1}H nmr δ (D_2O) 3.41-3.47 (1H, m), 3.63 (2H, t, *J*=9.5 Hz), 3.69-3.85, (4H, m), 3.97-4.03 (2H, m). ^{13}C nmr δ (D_2O) 64.2, 64.3, both t; 70.1, 71.9, 76.8, 81.2, 87.8, all d. Compound **61** (163 mg, 0.84 mmol) and *p*-toluenesulfonyl chloride (640 mg, 3.36 mmol) were stirred in dry pyridine (5 mL) under argon for 6 h. Extractive workup and radial chromatography (1:1-1:4 hexanes: ethyl acetate) gave two products. The more polar was a syrup identified as di-*p*-toluenesulfonate **61** (141 mg, 33%). [Found: m/z (CI) 331.0863. $C_{14}H_{19}O_7S$ $(M + H - TsOH)^+$ requires m/z 331.0852]. ^{1}H nmr δ 2.38, (2 x 3H, 2s), 3.32 (1H, m, H-6); 3.56-3.72 (3H, m, H-2,4,5), 3.95 (1H, br. s, H-3), 4.04 (1H, dd, *J*=6.8, 10.4 Hz, H-7), 4.10-4.19 (2H, m, H-1), 4.26 (1H, dd, *J* = 4.7, 11.0 Hz, H-7'), 7.27, 7.29 (2 x 2H, 2d, *J*=8.1 Hz), 7.74 (4H, d, *J*=8.1 Hz). ^{13}C nmr δ 21.6, 21.6, both q; 66.9, d; 68.5, t; 68.8, d; 69.3, t; 74.4, 75.5, 77.3, 127.9, 128.0, 130.0, 130.0, all d; 132.4, 132.5, 145.1, 145.1, all s. The less polar product was the syrupy 1,4,7-tri-*p*-toluenesulfonate **62** (140 mg, 25%). ^{1}H nmr δ 2.40, 2.42, 2.42 (3 x 3H, 3s), 2.92, 3.05 (2H, 2 br. s, 2 OH), 3.35 (1H, dt, *J*=3.3, 9.7 Hz, H-6), 3.64 (1H, t, *J*=6.2 Hz, H-2), 3.88-4.10 (4H, m, H-1,1,3,5), 4.20 (2H, d, *J*=3.3 Hz, H-7'), 4.35 (1H, dd, *J*=3.1, 9.4 Hz, H-4), 7.29, 7.32, 7.33, 7.73, 7.74, 7.82, (6 x 2H, 6d, *J*=8.3 Hz). ^{13}C nmr δ 21.5, q; 64.2, d, C-5; 67.4, d, C-3; 67.7, t, C-1; 68.5, t, C-7; 75.0, d, C-2; 77.2, d, C-6; 83.8, d, C-4.

2,6-Anhydro-3,4-di-*O*-isopropylidene-7-thio-1-*O*-*p*-toluenesulfonyl-L-*glycero*-L-*galacto*-heptitol (64). Di-*p*-toluenesulfonate **61** (314 mg, 0.62 mmol) was converted to the acetonide **63** with 2,2-dimethoxypropane and *p*-toluenesulfonic acid by standard procedures.

Crude product **63** was stirred with lithium sulfide (35 mg, 0.76 mmol) in dry *N,N*-dimethylformamide (2 mL) under argon, for 18 h at 20 °C and then 5 h at 80 °C. Extractive workup and radial chromatography (3:7 hexanes:ethyl acetate) gave a solid, identified as thiol **64** (160 mg, 64%) [Found: m/z (CI) 422.1325. $C_{17}H_{28}NO_7S_2$ $(MNH_4)^+$ requires m/z 422.1307]. ^{1}H nmr δ 1.28, 1.45, 2.45, (3H, 3 s), 2.90 (2H, ABX, *J*=3.0, 7.0, 14.4 Hz, H-7,7'), 3.31 (1H, ddd, *J*=2.9, 6.8, 9.7 Hz, H-6), 3.62 (1H, t, *J*=8.2 Hz, H-5), 3.96-4.29 (5 H, m, H-1,1',2,3,4), 7.35, 7.80 (2 x 2H, 2d, *J*=8.2 Hz). ^{13}C nmr δ 21.6, 26.3, 28.1, all q; 34.2, t, C-1; 69.1, t, C-7; 72.0, 73.3, 73.7, 79.4, 79.6, all d; 110.2, s; 128.0, 129.9, both d; 144.9, s.

1,3-Diphenyl-2-(6-*O*-triphenylmethyl-β-D-galactopyranosyl)-imidazolidine (66). A stirred solution of tetraacetate **53** (2.28 g, 4.11 mmol) in methanol (40 mL) was treated with 2% w/v methanolic sodium methoxide (3 mL). After 3 h the solvent was evaporated and the residue was dissolved in dichloromethane (30 mL). Triphenylmethyl chloride (1.20 g, 4.3 mmol) and triethylamine (0.60 mL, 4.3 mmol) were added, and the resultant solution was stirred overnight. Extractive workup and radial chromatography (1:1 hexanes:ethyl acetate) gave the title compound **66** (1.93 g, 74%). [Found: m/z (CI) 629.3026. $C_{40}H_{41}N_2O_5$ $(MH)^+$ requires 629.3015]. ^{1}H nmr δ 3.23-3.31 (2H, m), 3.35-3.38 (1H, m), 3.42-3.47 (1H, m), 3.52-3.66 (5H, m), 3.70-3.79 (2H, m), 5.63, (1H, s, H-2), 6.7-7.5, (25H, m). ^{13}C nmr δ 46.4, 47.1, 64.1, all t; 68.6, 70.2, 75.6, 75.6, 77.1, 80.2, all d; 87.0, s; 113.1, 113.4, 117.5, 117.8, 127.2, 127.9, 128.6, 129.3, all d; 143.7, 146.4, 146.5, all s.

1,3-Diphenyl-2-(2,3,4-tri-*O*-benzyl-6-*O*-triphenylmethyl-β-D-galactopyranosyl)-imidazolidine (67). A stirred solution of triol **66** (1.93 g, 3.06 mmol) in dry DMF (20 mL), kept at 0 °C under argon, was treated with sodium hydride (60 wt % in oil, 1.0 g, 25 mmol) and benzyl bromide (3.0 mL, 25 mmol). The suspension was allowed to reach r.t. during 1 h, then was stirred overnight. Quenching with water, extractive workup and flash chromatography (9:1 hexanes:ethyl acetate) gave the chromatographically pure title compound **67** (2.53 g, 92%). ^{1}H nmr δ 3.14 (1H, dd, *J*=4.8, 9.5 Hz, H-6'), 3.34-3.72 (9 H, m, H-4,5,1',3'-5',6''), 3.86 (1H, t, *J*=9.3 Hz, H-2'), 4.33-4.65 (4H, m), 4.77 (1Hz, d, *J* = 11.8 Hz), 5.03 (1H, d, *J* = 12.0 Hz), 5.46 (1H, s, H-2), 6.7-7.5 (40H, m). ^{13}C nmr δ 45.6, 47.2, both t, C-4,5; 64.1, t, C-6'; 72.1, 74.0, 74.0, all t; 74.4, d, C-4'; 75.1, d, C-2'; 77.5, d, C-5'; 77.5, d, C-2; 80.4, d, C-1'; 86.0, d, C-3'; 87.0, s; 112.9, 113.8, 117.2, 117.3, 126.6, 127.1, 127.2, 127.3, 127.8, 127.9, 128.0, 128.1, 128.3, 128.5, 128.9, 129.5, all d; 138.1, 139.1, 139.7, 144.2, 145.8, 147.3, all s.

2,6-Anhydro-3,4,5-tri-*O*-benzyl-L-*glycero*-L-*galacto*-heptitol (68). A stirred solution of imidazolidine **67** (2.92 g, 3.23 mmol) in dichloromethane (100 mL) and acetone (30 mL) was treated with *p*-toluenesulfonic acid monohydrate (1.25 g, 6.57 mmol). After 3 min a precipitate which had formed was filtered off. The filtrate was concentrated and the residue was suspended in methanol (40 mL). To the stirred suspension was added sodium borohydride (0.5 g). After 1 h the suspension had cleared; quenching with water and extractive workup gave a syrup, which was stirred in methanol (50 mL) with *p*-toluenesulfonic acid monohydrate (0.25 g) for 2 h. Extractive workup and radial chromatography (ethyl acetate) gave the syrupy title compound **68** (895 mg, 60%). [Found: m/z (CI) 465.2288. $C_{28}H_{32}O_6(MH)^+$ requires m/z 465.2244). ^{1}H nmr δ 2.78 (2H, br. s, OH), 3.32-3.45 (3 H, m, H-2,6,7), 3.58-3.91 (6 H, m, H-1,1',3,4,5,7), 4.71 (2H, AB, *J* = 11.3 Hz), 4.77 (2H, AB, *J* = 10.1 Hz), 4.74 (2 H, s), 7.26 - 7.38 (15 H, m). ^{13}C nmr δ 62.4, t, C-1; 62.7, t, C-7; 72.7, t; 74.3; d, C-3; 74.4, 75.3, both t; 75.3, d, C-5; 78.7, d, C-2; 80.0, d, C-6; 84.7, d, C-4; 127.6, 127.8, 128.0, 128.1, 128.4, 128.5, 128.5, all d; 138.2, 138.2, 138.3, all s.

***p*-Toluenesulfonylation of Diol 68.** A solution of diol **68** (300 mg, 0.65 mmol) in dichloromethane (10 mL) was stirred with pyridine (0.5 mL) and *p*-toluenesulfonyl chloride (140 mg, 0.73 mmol) for 4 d. Extractive workup and radial chromatography (7:3 hexanes:ethyl acetate) gave starting material **68** (97 mg, 32%) and three products. The least polar product was identified as the syrupy di-*p*-toluenesulfonate **71**, (85 mg, 17%). [Found: m/z (CI) 790.2741. $C_{42}H_{48}NO_{10}S_2$, $(MNH_4)^+$ requires m/z 790.2719]. ^{1}H nmr δ 2.37, 2.47 (2 x 3H, 2s), 3.32-3.37 (1H, m, H-6), 3.48-3.55 (2 H, m, H-2,4), 3.75 (1H, t, *J*=9.5 Hz, H-5), 3.88 (1H, s, H-3), 3.89 (2H, d, *J*=6.8 Hz, H 1,1'), 4.14 (2H, ABX, *J*=1.5, 5.6, 10.7 Hz, H-7,7'), 4.47, 4.91 (2H, AB, *J*=11.2 Hz), 4.50, 4.85 (2H, AB, *J*=10.8 HMz), 4.70 (2H, AB, *J*=11.6 Hz), 7.17-7.40 (19 H, m), 7.71 (4H, t, *J*=7.8 Hz). ^{13}C nmr δ 21.6, q; 67.7, t, C-1; 69.0, t, C-7; 72.5, t; 73.0, d, C-3; 74.0, d, C-5; 74.5, 75.2, both t; 75.3, d, C-2; 77.2, d, C-6; 84.2, d, C-4; 127.0, 127.6, 127.7, 127.9, 128.0, 128.0, 128.1, 128.3, 128.4, 128.5, 129.7, 130.0, all d; 132.6, 133.0, 137.7, 137.8, 138.2, 144.6, 145.1, all s. The product of intermediate polarity was identified as syrupy mono-*p*-toluenesulfonate **69** (49 mg, 12%). [Found: m/z (CI) 636.2612. $C_{35}H_{42}NO_8S$ $(MNH_4)^+$ requires m/z 636.2630]. ^{1}H nmr δ 2.42, (3 H, s), 3.23-3.30 (1H, m, H-6), 3.58-3.65 (3 H, m, H-2,4,7), 3.76 (1H, ABX, *J*=2.7, 11.8 Hz, H-7'), 3.89 (1H, t, *J* = 9.5 Hz, H-5), 3.89 (1H, s, H-3), 3.95, 4.08 (2H, ABX, *J*=6.0, 6.5, 10.1 Hz, H-1, 1'), 4.51, 4.94 (2H, AB, *J*=11.3 Hz), 4.63, 4.89 (2H, AB, *J*=10.9 Hz), 4.72, 4.77 (2H, AB, *J*=11.7 Hz), 7.22-7.41 (17 H, m), 7.74 (2H, d, *J*=8.3 Hz). ^{13}C nmr δ 21.7, q; 62.3, t, C-7; 68.6, t, C-1; 72.8, t; 73.4, d, C-3; 74.6, t; 74.9, d, C-5; 75.4, t; 75.6, d, C-2; 79.8, d, C-6; 84.4, d, C-4; 127.7, 127.9, 128.1, 128.2, 128.4, 128.5, 128.6, 130.0, all d; 132.8, 138.1, 138.2, 145.1, all s. The most

polar product was identified as syrupy mono-*p*-toluenesulfonate **70** (115 mg, 29%). [Found: m/z (CI) 636.2641. $C_{35}H_{42}NO_8S$ $(MNH_4)^+$ requires m/z 636.2630]. ^{1}H nmr δ 2.37 (3 H, s), 3.31-3.46 (3 H, m, H-1,2,6), 3.57 (1H, dd, *J*=2.7, 9.3 Hz, H-4), 3.64 (1H, dd, *J*=6.8; 10.9 Hz, H-1), 3.80 (1H, t, *J*=9.5 Hz, H-5), 3.84 (1H, s, H-3), 4.16, 4.27 (2H, ABX, *J*=1.7, 5.8, 10.7 Hz, H-7), 4.54, 4.89 (2H, AB, *J*=10.9 Hz), 4.59, 4.92 (2H, AB, *J*=11.7 Hz), 4.67, 4.74, (2H, AB, *J*=11.7 Hz), 7.19-7.33, (17 H, m), 7.73 (2H, d, *J*=8.3 Hz). ^{13}C nmr δ 21.5, q; 62.0, t, C-1; 69.3, t, C-7; 72.4, t; 73.3, d, C-3; 74.2, t; 74.3, d, C-5; 75.1, t; 77.2, d, C-2; 78.6, d, C-6; 84.6, d, C-4; 127.5, 127.7, 127.9, 128.0, 128.1, 128.3, 128.4, 129.6, all d; 133.0, 137.8, 137.9, 138.2, 144.6, all s.

2,6-Anhydro-1,3:5,7-di-*O*-benzylidene-4-*O*-*p*-toluenesulfonyl-L-*glycero*-L-*galacto*-heptitol (77). A stirred solution of alcohol **73** [22] (16.3 g, 44.0 mmol), *p*-toluenesulfonyl chloride (12.5 g, 65.5 mmol) and 4-(dimethylamino)pyridine (1.0 g) in pyridine (100 mL) was kept at 70 °C for 3 h. Extractive workup and flash chromatograph (1:1 hexanes:ethyl acetate) gave the title compound **77** (16.8 g, 73%). [Found: m/z (CI) 525.1587. $C_{28}H_{29}O_8S$ $(MH)^+$ requires m/z 525.1583]. ^{1}H nmr δ 2.28, (3H, s), 3.43 (1H, dt, *J*=5.0, 9.8 Hz, H-6), 3.49 (1H, d, *J*=0.6 Hz, H-2), 3.82 (1H, t, *J*=10.3 Hz, H-7), 3.98 (1H, dd, *J*=1.5, 12.6 Hz, H-1), 4.15-4.27 (3H, m, H-1',5,7'), 4.52 (1H, d, *J*=3.3 Hz, H-3), 4.70 (1H, dd, *J*=3.6, 10.0 Hz, H-4), 5.42, 5.49 (2H, 2s), 7.02 (2H, d, *J*=8.1 Hz), 7.2 – 7.5 (10H, m), 7.73 (2H, d, *J*=8.3 Hz). ^{13}C nmr δ 21.7, q; 68.4, t, C-7; 69.1, t, C-1; 70.5, d, C-2; 71.5, d, C-6; 75.0, d, C-5; 75.4, d, C-3; 78.9, d, C-4; 100.9, d; 101.5, d; 126.2, 126.2, 128.0, 128.1, 128.2, 129.0, 129.1, 129.5, all d; 133.5, 136.9, 137.4, 144.6, all s.

2,6-Anhydro-4-azido-1,3:5,7-di-*O*-benzylidene-4-deoxy-L-*glycero*-L-*gluco*-heptitol (79). A solution of *p*-toluenesulfonate **77** (2.08 g, 3.96 mmol) and sodium azide (1.5 g, 23 mmol) was heated in refluxing dimethylsulfoxide (10 mL) under argon for 1 h. Cooling, extractive workup and flash chromatography gave starting material (0.53 g, 25%) and two products. The more polar product was identified as alcohol **73** (0.73 g, 50%), and the less polar product was a crude pale yellow syrup identified as the azide **79** (0.16 g); $[\alpha]_D^{25}$ +56 (*c*, 1.0, $CHCl_3$). [Found: m/z (CI) 396.1541. $C_{21}H_{22}N_3O_5$ $(MH)^+$ requires m/z 396.1559]. ^{1}H nmr δ 3.66 (1H, d, *J*=1.3 Hz, H-2), 3.86 (1H, t, *J*=10.2 Hz, H-7), 3.99-4.08 (3H, m, H-3,5,6), 4.19 (1H, t, *J*=3.2 Hz, H-4), 4.22-4.25 (1H, m, H-1), 4.27 (1H, dd, *J*=1.3, 11.4 Hz, H-1'), 4.33 (1H, dd, *J*=4.9, 10.3 Hz, H-7'), 5.55, 5.60 (2x1H, 2s), 7.31-7.56 (10H, m). ^{13}C nmr δ 59.6, d, C-4; 66.6, d; 67.0, d, C-2; 69.1, t, C-7; 69.6, t, C-1; 75.8, 76.6, 101.3, 102.2, 126.1, 128.3, 128.3, 129.1, 129.2, all d, 137.2, 137.4, both s. IR (film) 2110 cm^{-1}.

X-ray Single Crystal Analysis.[1] The intensity data were collected on a Nicolet R3m diffractometer using graphite-monochromatised Mo-Kα radiation (λ = 0.71073 A°) at low temperature by the ω scanning method. Preliminary refinement of the cell parameters was carried out using 24 reflections centred automatically in the $6.5 \leq 2\theta \leq 33°$ range. Crystal and experimental details are summarized in Table 1. Crystal and diffractometer stability were monitored using the intensities of three reflections every 100 reflections. For both crystals, the relative intensities of the standard reflections varied less than 0.5%. Equivalent reflections were averaged and corrected for Lorentz and polarisation factors [27]. No absorption corrections were applied.

The structures were solved by direct methods using programmes SHELXS [28] and subsequent difference Fourier syntheses for the hydrogen atoms. Conventional full matrix least refinements using all data were performed using programme SHELXL-96 [29]. All non-hydrogen and hydrogen atoms were refined with anisotropic and isotropic thermal parameters respectively. For compound **7.HCl** the normal parameters for H-2 and H-4 were constrained to 1.2 times the equivalent parameters of the carbon atoms to which they were bonded. All hydrogen atoms for compound **56** were also refined in this way. The weighting scheme on F_o^2 for each reflection was $[\sigma^2(Fo)^2 + (P_1M)^2 + P_2M]^{-1}$, where P_1, P_2 are given in Table 1 and M is [Maximum $(F_o^2,0) + 2F_c^2]/3$.

Comments pertaining to the X-ray crystallographic analysis of compounds **7.HCl** and **56** are as follows:

In the unit cell the independent molecules of the anhydro-compound **7.HCl** (Fig. 1) have each of their ammonium hydrogen atoms bonded to a chloride counter ion [N-3—H—Cl-1, 2.22 (6), 2.24 (4) and 2.28 (6) Å]; the hydroxyl group hydrogen atoms are also bonded to an adjacent chloride anion [O-2—H—Cl-1, 2.38 (5) Å] and O-6 of an adjacent molecule [O-4—H—O-6, 2.03 (4) Å]. The 5-membered ring is in the °E conformation [φ 351.4 (6)°] [30] with mean plane deviations for C-5, C-6, O-6 and C-1 ±0.03 Å from the plane and O-5 0.629 (5) Å out of the plane. The pyranoid ring adopts a slightly flattened $^1C_4$ chair [θ 160.9 (4)°,Q 0.636 (4) Å] [30] with C-3 and O-5 0.547 (5) Å and -0.827 (5) Å respectively, out of the plane through C-1, C-2, C-4 and C-5 [mean deviation ±0.007 (2) Å].

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[1] Structural factors, atom parameters and thermal parameters are available on request from the Director of the Cambridge Crystallographic Data Centre, University Chemical Laboratory, Lensfield Road, Canbridge CB2 IEW. Any request should be accompanied by the full literature citation for this paper.

For the hydroxy acid **56** (Fig. 2) the hydroxyl group hydrogen atoms are hydrogen bonded intermolecularly to the ring oxygen atom and to an ester carbonyl group: O-5—H—O-6, 2.05(5) Å and O-1—H—O-3a, 1.86 (4) Å. The pyranoid ring is close to a perfect $^4C_1$ chair [θ 3.6 (4)°, Q 0.602 (4) Å] [30] with C-3, C-6 0.684 (6) and –0.719 (5) Å from the plane through C-4, C-5, C-2 and O-6 [mean deviation ± 0.006 (2) Å].

The more constrained pyranoid geometry of the ammonium compound **7** HCl is reflected in its ring dihedral angles: C-1—C-2—C-3—C-4, C-1—O-5—C-5—C-4 are 42.6 (4)° and -75.7 (3)° compared with 55.1(4)° and 64.7(5)° for the corresponding angles in the hydroxy acid **56**. All dimensions in the two molecules are normal [31].

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