Simple syntheses of L-fucopyranose and fucosidase inhibitors utilizing the highly stereoselective methylation of an arabinofuranoside 5-urose derivative

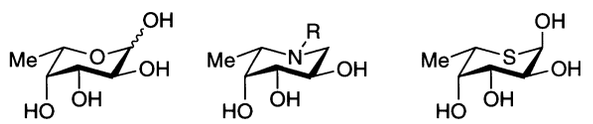
Shunya Takahashi* and Hiroyoshi Kuzuhara

The Institute of Physical and Chemical Research (RIKEN), Wako-shi, Saitama 351-01, Japan

The simple syntheses of L-fucopyranose 1 and its three analogues 2–4 are described. A key reaction is a stereocontrolled elongation by one carbon unit at the side chain of an α-D-*arabino*-pentodialdo-1,4-furanoside 9 with MeMgI–$ZnCl_2$ or Me_3Al. Diastereofacial selectivities of more than 92% were achieved.

Introduction

Fucoses are distributed in a wide variety of natural products. D-Fucose is mainly found in plants and in microbial substances such as antibiotics, whereas its L-enantiomer occurs in many bacterial and plant polysaccharides, the oligosaccharides of human milk, and many glycolipids and glycoproteins. The widespread occurrence of L-fucose suggests the diverse biological functions and importance of this sugar. For example, L-fucose is the immunodominant sugar of many complex carbohydrate antigens. Furthermore, its content in animal glycans is known to change under pathological conditions such as cancer.[1] Therefore, compounds that selectively inhibit L-fucosidases might be useful not only for the study of structure–function relationships of fucose-containing glycans, but also for leading to a new understanding of the respective disease due to a deficiency of the L-fucosidase. Interests derived from these considerations have prompted chemists to design and synthesize several L-fucosidase inhibitors which can be considered to act as a mimic of L-fucopyranose **1**. Based on the findings that polyhydroxypiperidine alkaloids, as represented by 1-deoxynojirimycin, could be powerful glycosidase inhibitors,[2] Fleet *et al*. designed an azasugar, 1,5-dideoxy-1,5-imino-L-fucitol **2**, as a L-fucosidase inhibitor and synthesized it from D-glucose in 1985.[3] Since then, several additional papers have appeared dealing with the synthesis of compound **2** from D-glucose[4] or 2-azidogalactose.[5] This azasugar **2** shows potent inhibitory activity against several α-L-fucosidases,[3,4] and its *N*-methoxycarbonylpentyl derivative **3** is used for preparing affinity ligands to purify these enzymes.[6] In addition, its *N*-methyl analogue, as well as ester **3**, have been found to inhibit human immunodeficiency virus (HIV) cytopathicity at concentrations which were non-cytotoxic.[7] Furthermore, a thiosugar analogue, 5-deoxy-5-thio-L-fucopyranose **4**, was found to possess remarkable inhibitory activity against fucosidases from bovine epididymis and kidney.[8] Sugar analogues having a phosphorus atom in the hemiacetal ring of compound **1** were also synthesized.[9] The synthetic examples reported so far, however, have relied mainly on the chemical manipulations of hexoses, which led to rather long synthetic routes, and are inconvenient for large-scale preparation of the L-fucosidase inhibitors. In this paper we describe the details of our work[10] on a simple synthesis of targets **1**, **2** and **4** utilizing a common pentose intermediate prepared from D-arabinose. Independently, Fleet *et al*.[11] and Hashimoto and Izumi[12] have reported the syntheses of compounds **2** and **4** from D-lyxonolactone and D-arabinose, respectively.



1 **2** R = H **4**

3 R = $[CH_2]_5CO_2Me$

Results and discussion

Our synthetic strategy directed towards the fucosidase inhibitors included stereocontrolled elongation by one carbon unit at the side chain of the common pentose intermediate, methyl 2,3-di-*O*-(*tert*-butyldimethylsilyl)-α-D-*arabino*-pentodialdo-1,4-furanoside **9**. This key compound was prepared from readily accessible methyl α-D-arabinofuranoside tribenzoate **5**[13] by two different sequences with respect to protection (Scheme 1). Removal of the benzoyl groups in compound **5** with sodium methoxide gave a triol, which, without purification, was regioselectively pivaloylated or dimethoxytritylated at its 5-hydroxy group followed by silylation in a one-pot reaction, giving a pivaloylated or 4,4′-dimethoxytritylated disilyl derivative **6** or **7**, respectively, in 69 or 83% yield from **5**. We expected the bulky silyl protecting groups introduced at the oxygen functions would prevent unfavourable chelation of the C-2, -3 oxygens with a metal in the stereocontrolled one-carbon elongation reaction.[14] The pivaloyl group in compound **6** was removed cleanly under reductive conditions with lithium aluminium hydride without any silylmigration to give an alcohol **8** in 91% yield, while detritylation of compound **7** under mild acidic conditions was accompanied by a little desilylation as judged by TLC analysis, and provided compound **8** in 79% yield. The alcohol **8** was subjected to Swern oxidation using oxalyl dichloride[15] to give the key intermediate **9** in quantitative yield; this was used for the next step without thorough purification.

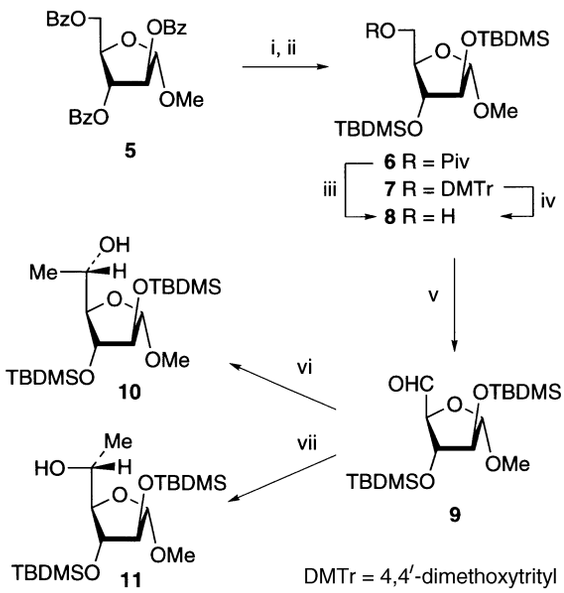
We needed both diastereomeric alcohols **10** and **11** with reversed configurations at their C-5 atoms for our synthetic goal. Attainment of efficient diastereofacially selective addition of a methyl unit to a carbonyl group in compound **9** would make it possible to obtain these diastereomers, but this was the toughest problem to be solved in the present synthesis. In 1962, Hanessian and Wolfrom suggested that an α-chelation-controlled addition of a methyl Grignard reagent to an aldehyde carbonyl group attached to a furanoside ring occurred preferentially from the less hindered site of the carbonyl group in tetrahydrofuran (THF)–diethyl ether.[16]

Therefore, under conditions similar to those for the α-chelation [Fig. 1(a)], compound **9** would be converted into an alcohol **10** with the *S* configuration at its C-5 position required for the synthesis of compound **1**. On the other hand, the addition of the methyl group to compound **9** under non-chelation-controlled conditions would produce compound **11** with the opposite *R*-configuration at C-5. Taking the chelation or non-chelation mode into account, we searched methyl organometallic reagents suitable for the conversion of substrate **9** into product **10** or **11**.

Table 1 Stereoselective methylation of compound **9**

Entry	Reagent	Solvent	Temp. (T/°C)	Ratio of diastereomers (**10**:**11**)[a]	Yield (%)
1	MeMgBr	THF	0	62:38	84
2	MeMgI	Et_2O	−20	71:29	76
3	MeMgBr, $ZnBr_2$[b]	THF	−20	67:33	83
4	MeMgI, $ZnCl_2$[b]	Et_2O	−20	93:7	73
5	MeMgI, $ZnCl_2$[b]	CH_2Cl_2–Et_2O	−78	97:3	68
6	Me_2CuLi	Et_2O	−78	92:8	70
7	$MeTi(OPr^i)_3$	Et_2O	−42	47:53	50
8	MeLi	Hexane	−78	33:67	66
9	MeLi	Et_2O	−110	24:76	76
10	MeLi	THF–HMPA	−78	17:83	37
11	MeLi, $BF_3{\cdot}Et_2O$[b]	Et_2O	−78	42:58	57
12	$MeCeCl_2$	THF	−78	25:75	88
13	Me_3Al	Hexane	−78	4:96	70

[a] Ratios were determined by NMR spectroscopy (500 or 400 MHz). [b] The aldehyde was precomplexed with the Lewis acid prior to addition of the organometallic reagent.



Scheme 1 *Reagents and conditions:* i, NaOMe, MeOH (quant.), room temp.; ii, pivaloyl chloride (1.1 mol equiv.), CH_2Cl_2–pyridine, −20 ⟶ 0 °C or 4,4′-dimethoxytrityl chloride (1.1 mol equiv.), pyridine, −20 ⟶ 0 °C; then *tert*-butyldimethylsilyl chloride (6.0 mol equiv.), imidazole (8.0 mol equiv.), 0 °C ⟶ room temp. (69% for **6** or 83% for **7**); iii, $LiAlH_4$, Et_2O, 0 °C (91%); iv, AcOH–THF–water (7:7:2), room temp. (79%); v, oxalyl dichloride, DMSO, CH_2Cl_2, −70 °C; then Et_3N (quant.); vi, MeMgI, $ZnCl_2$, CH_2Cl_2–Et_2O, −78 °C (68%); vii, Me_3Al, hexane, −78 °C (70%)

Methylmagnesium halides, methyllithium, lithium dimethylcuprate,[17] organotitanium reagents,[18] organocerium reagents,[19] and organoaluminium reagents[20] were tested under a variety of reaction conditions. The ratios of products **10** and **11** formed from these reactions were determined by the integrated intensity of each 6-methyl signal in the ^{1}H NMR (400 and 500 MHz) spectra and are summarized in Table 1. These data revealed that the stereoselectivity of the addition reactions varied over a wide range depending on the kind of reagent employed, whereas the chemical yields were moderately good in all entries except for entry 10. The diastereoselectivities for the reaction of substrate **9** with the Grignard reagents were modest to low, while the use of zinc chloride as an additive dramatically increased the selectivity up to 97:3 (entry 5). The reaction of lithium dimethylcuprate[17] also showed good selectivity (entry 6). The stereoselective formation of compound **10** in these cases would result from α-chelation control.

On the other hand, the reversed diastereofacial selectivity was observed when the methyllithium, organocerium, organotitanium or organoaluminium reagent was employed (entries 7–13). In spite of our expectation that the bulkiness of the $MeTi(OPr^i)_3$ reagent[18] coupled with its weak Lewis acidity would enhance the non-chelation control, this reagent showed the lowest stereoselectivity (entry 7) among the reagents tested. Reaction of compound **9** with methyllithium or methylcerium[19] gave compound **11** in modest diastereofacial selectivity. Highly stereoselective production of compound **11** (92% de) was realized by using Me_3Al in hexane (entry 13).[20] In this case it would be reasonable to assume a transition state as shown in Fig. 1(b), although the highly oxygenated functionality as well as the presence of the bulky protecting groups in compound **9** interfere with simple rationalization of the mechanism. These isomers (**10** and **11**) could be separated by silica gel column chromatography, and their configurations were later confirmed by conversion of these diastereomers into the respective known compounds **1**–**4** (*vide infra*).

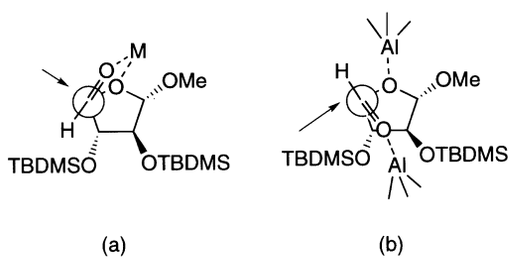


Fig. 1

A route to L-fucose **1** from compound **10** was straightforward and simple to manipulate (Scheme 2). Thus, acetolysis of substrate **10** followed by hydrolysis of the resulting acetates **12** gave L-fucose **1**, which was identical with an authentic sample.

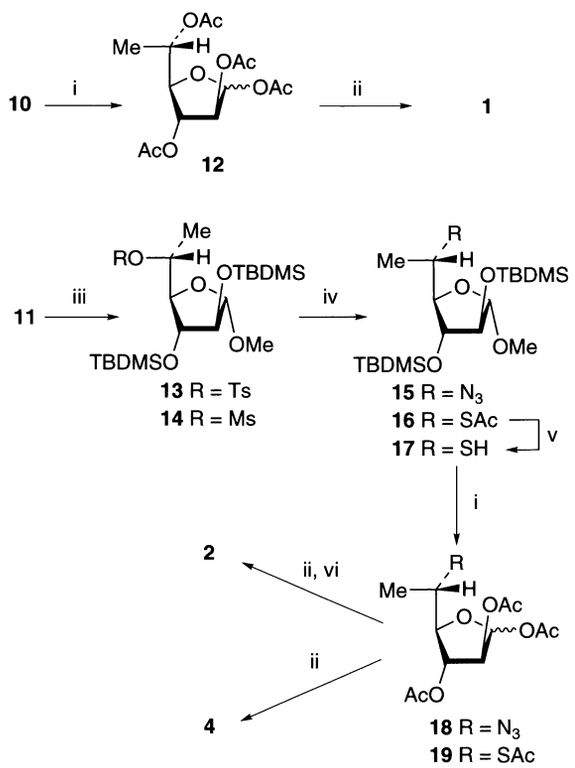
For the synthesis of analogues **2**–**4**, the introduction of an azido or a thio functionality to C-5 in compound **11** was required. First, substrate **11** was submitted to tosylation under standard conditions. The reaction, however, proceeded very sluggishly, but furnished the desired tosyl derivative **13** in good yield. On the other hand, mesylation of compound **11** gave, in a short reaction time, 5-*O*-mesyl ester **14** quantitatively. The corresponding trifluoromethanesulfonate derivative prepared by the conventional method was revealed to be unstable toward further manipulations.

The substitution reactions of the sulfonates with sodium azide and with potassium thioacetate were examined in three different solvents, dimethylformamide (DMF), dimethyl sulfoxide (DMSO) and hexamethylphosphoric triamide (HMPA). The results are shown in Table 2. An azide **15** was produced in 85% yield either from sulfonate ester **13** or from sulfonate ester **14** when DMSO was used as the solvent, while the best yield (74%) of a thioacetate **16** was obtained from substrate **13** in

Table 2 S_N2 substitution reaction of the sulfonate **13** or **14**

Reagent	Solvent	Temp. (T/°C)	Time (t/h) From **13**	Time (t/h) From **14**	Product	Yield (%) From **13**	Yield (%) From **14**
NaN_3	DMF	80	10	13	**15**	84	85
	DMSO		8	5.5		85	85
	HMPA		3.5	1.2		69	73
KSAc	DMF	85	12	24	**16**	43 (19)[a]	48 (5)
	DMSO		12	24		46 (16)	42
	HMPA		4	22		74	68

[a] The values in parentheses denote the amount of recovered starting material.



Scheme 2 *Reagents and conditions:* i, AcOH–Ac_2O–H_2SO_4 (15 : 15 : 1), 0 °C ⟶ room temp. (90–97%); ii, NaOMe, MeOH (quant.), room temp.; iii, TsCl (2.0 mol equiv.), pyridine, room temp. or MsCl (1.5 mol equiv.), pyridine, −10 °C ⟶ room temp. (99% for **13** or 98% for **14**); iv, NaN_3 (3.0 mol equiv.), DMSO, 80 °C or KSAc (4.0 mol equiv.), HMPA, 85 °C (85% for **15** from **14** or 74% for **16** from **13**); v, $LiAlH_4$, Et_2O, 0 °C (96%); vi, 10% Pd–C, H_2, MeOH–water, room temp. (83%)

HMPA. Acetolysis of azide **15** gave triacetates **18** in high yield. After removal of all acetyl groups in compound **18** with base, the resulting triol was hydrogenated over 10% Pd–C under H_2 atmosphere to give the desired compound **2**, whose physical and spectral data were identical with those previously reported.[3,5] This was further transformed to the methyl ester **3** according to the procedures previously described.[5,6] Similarly compound **16** was efficiently converted, *via* tetraacetates **19**, into the thioanalogue **4** according to the method described for the synthesis of L-fucose **1** from substrate **12**. Attempts to obtain sulfide **4** through acidic hydrolysis of a thiol **17** derived from compound **16** were unsuccessful.

The imino ester **3** inhibited *Charonia Lampas* α-L-fucosidase to 50% (18 μM), whereas 1.4 mM of compound **4** was required to inhibit this enzyme to the same extent.

In conclusion, we have developed a new method for the simple preparation of either an L-*galacto*- or a D-*altro*-deoxyfuranoside derivative (**10** or **11**) by reaction of the key pentodialdofuranoside intermediate **9** with MeMgI–$ZnCl_2$ or Me_3Al, respectively. This enabled us to synthesize the biologically important compounds **1**–**4** from D-arabinose.

Experimental

Mps were determined in a capillary with an Ishii melting-point apparatus and are uncorrected. Optical rotations were determined with a JASCO DIP-370 polarimeter, and $[\alpha]_D$-values are given in 10^{-1} deg cm^2 g^{-1}. IR spectra were recorded with a Shimadzu-FTIR-8100M spectrophotometer. ^{1}H NMR spectra were recorded at 400 MHz or 500 MHz with JEOL JNM-α 400 or GX 500 spectrometers. Tetramethylsilane (TMS), δ_H 0.0, and DHO, δ_C 4.8, were used as internal references for the $CDCl_3$ and D_2O solutions, respectively. ^{13}C NMR spectra were recorded at 100 MHz with a JEOL JNM-α 400 spectrometer, using 1,4-dioxane, δ_C 67.4, as an external reference for D_2O solutions. Column chromatography was performed on silica gel 60 (230–400 mesh; E. Merck, Darmstadt, Germany). Merck precoated silica gel 60 F_{254} plates, 0.25 mm thickness, was used for analytical TLC. Organic solutions obtained after extractive work-up were dried over $MgSO_4$, filtered through a pad of Celite, and evaporated under reduced pressure. L-Fucose **1** was purchased from Fluka Co.

Methyl 2,3-di-*O*-(*tert*-butyldimethylsilyl)-5-*O*-pivaloyl-α-D-arabinofuranoside 6

To a stirred solution of the tribenzoate **5** (2.38 g, 5.0 mmol) in THF–methanol (1 : 1; 15 cm^3) was added sodium methoxide (90 mg, 1.67 mmol) and then the mixture was stirred at room temperature for18 h, and made neutral with Dowex 50W X-8 (H^+) resin. The mixture was filtered, and the filtrate was evaporated, co-evaporated with toluene and pyridine to give a triol (2.20 g), which was dissolved in dichloromethane–pyridine (1 : 1; 10 cm^3). To this stirred solution was added dropwise a solution of pivaloyl chloride (0.68 cm^3, 5.5 mmol) in dichloromethane (3 cm^3) at −20 °C. The mixture was stirred at −20 ⟶ 0 °C for 7.5 h. Then *tert*-butylchlorodimethylsilane (4.52 g, 30.0 mmol) and imidazole (2.78 g, 40.8 mmol) were added and stirring was continued for an additional 17.5 h. After addition of ice–water, the resulting mixture was stirred for 4 h and extracted with toluene. The extract was washed successively with water, aq. copper sulfate, aq. sodium hydrogen carbonate, water and brine, dried, and evaporated to dryness. Chromatography on silica gel with hexane–ethyl acetate (50 : 1) as the eluent yielded the *pivaloyl ester* **6** (1.64 g, 69%) (Found: C, 58.1; H, 10.2. $C_{23}H_{48}O_6Si_2$ requires C, 57.9; H, 10.2%); $[\alpha]_D^{26}$ +42.8 (*c* 0.77 in $CHCl_3$); ν_{max}(film)/cm^{-1} 1730 (PivO); δ_H(500 MHz; $CDCl_3$) 0.06, 0.08, 0.09 and 0.10 (each 3 H, 4 s, 4 × MeSi), 0.88 and 0.89 (each 9 H, 2 s, 2 × Bu^{t}Si), 1.23 (9 H, s, Bu^{t}CO), 3.36 (3 H, s, OMe), 3.96 (1 H, dd, $J_{2,3}$ 3.4, $J_{3,4}$ 7.0, 3-H), 4.00 (1 H, dd, $J_{1,2}$ 1.5, $J_{2,3}$ 3.4, 2-H), 4.01 (1 H, ddd, $J_{3,4}$ 7.0, $J_{4,5}$ 2.9 and 5.0, 4-H), 4.09 (1 H, dd, $J_{4,5}$ 5.0, J_{gem} 12, 5-H^a), 4.37 (1 H, dd, $J_{4,5}$ 2.9, J_{gem} 12, 5-H^b) and 4.67 (1 H, d, $J_{1,2}$ 1.5, 1-H).

Methyl 2,3-di-*O*-(*tert*-butyldimethylsilyl)-5-*O*-(4,4′-dimethoxytriphenylmethyl)-α-D-arabinofuranoside 7

As described above, the tribenzoate **5** (2.38 g, 5.0 mmol) was converted into a triol (2.20 g), which was dissolved in pyridine (40 ml). To this stirred mixture was added 4,4′-dimethoxytriphenylmethyl chloride (1.86 g, 5.5 cm^3) at −20 °C and then

the mixture was stirred at −20 ⟶ 0 °C for 9 h. Then *tert*-butylchlorodimethylsilane (4.52 g, 30.0 mmol) and imidazole (2.78 g, 40.8 mmol) were added to the resulting mixture and stirring was continued for an additional 17.5 h. After addition of ice–water, the resulting mixture was stirred for 8 h and extracted with toluene. The extract was washed successively with water, aq. copper(II) sulfate, aq. sodium hydrogen carbonate, water and brine, dried, and evaporated to dryness. Chromatography on silica gel with hexane–ethyl acetate–triethylamine (500:10:1) as the eluent yielded the *trityl ether* **7** (2.89 g, 83%) (Found: C, 67.1; H, 8.4. $C_{39}H_{58}O_7Si_2$ requires C, 67.4; H, 8.4%); $[\alpha]_D^{24}$ +19.6 (*c* 0.15 in $CHCl_3$); δ_H(500 MHz; $CDCl_3$) −0.19, −0.02, 0.06 and 0.07 (each 3 H, 4 s, 4 × MeSi), 0.76 and 0.87 (each 9 H, 2 s, 2 × Bu^{t}Si), 3.10 (1 H, dd, $J_{4,5}$ 6.1, J_{gem} 10, 5-H^a), 3.25 (1 H, dd, $J_{4,5}$ 3.2, J_{gem} 10, 5-H^b), 3.42 (3 H, s, OMe), 3.76 (6 H, s, OMe), 3.93 (1 H, dd, $J_{2,3}$ 3.7, $J_{3,4}$ 6.7, 3-H), 3.99 (1 H, dd, $J_{1,2}$ 1.8, $J_{2,3}$ 3.7, 2-H), 4.06 (1 H, ddd, $J_{3,4}$ 6.7, $J_{4,5}$ 3.2 and 6.1, 4-H), 4.74 (1 H, d, $J_{1,2}$ 1.8, 1-H), 6.81 (4 H, d, *J* 8.9, ArH), 7.19–7.26 (3 H, m, ArH), 7.36 (4 H, dd, *J* 1.1 and 8.9, ArH) and 7.49 (2 H, dd, *J* 1.2 and 8.6, ArH).

Methyl 2,3-di-*O*-(*tert*-butyldimethylsilyl)-α-D-arabinofuranoside 8

From the pivaloyl ester 6. To a stirred solution of the pivaloyl ester **6** (150 mg, 0.31 mmol) in diethyl ether (3 cm^3) was added lithium aluminium hydride (12 mg, 0.32 mmol) at 0 °C and then the mixture was stirred for 2.5 h at 0 °C. The reaction was quenched by addition of aq. ammonium chloride, and then $MgSO_4$ was added. The resulting mixture was filtered through a pad of Celite, evaporated, and then co-evaporated with toluene to dryness. Chromatography on silica gel with hexane–ethyl acetate (10:1) as the eluent yielded the disilyl ether **8** (113 mg, 91%).

From the trityl ether 7. A solution of the trityl ether **7** (142 mg, 0.20 mmol) in acetic acid–THF–water (7:7:2; 3.2 cm^3) was stirred at room temperature for 10 h, then made neutral with aq. sodium hydroxide. The resulting mixture was extracted with diethyl ether. The extract was washed successively with aq. sodium hydrogen carbonate, water and brine, dried, and evaporated to dryness. Chromatography on silica gel with hexane–ethyl acetate (10:1) as the eluent yielded the *bissilyl ether* **8** (63 mg, 79%) (Found: C, 54.9; H, 10.2. $C_{18}H_{40}O_5Si_2$ requies C, 55.1; H, 10.3%); $[\alpha]_D^{22}$ +46 (*c* 1.0, $CHCl_3$); ν_{max}(film)/cm^{-1} 3484 (OH); δ_H(500 MHz; $CDCl_3$) 0.07, 0.08, 0.09 and 0.10 (each 3 H, 4 s, 4 × MeSi), 0.88 and 0.90 (each 9 H, 2 s, 2 × Bu^{t}Si), 1.97 (1 H, dd, $J_{5,OH}$ 4.6 and 7.6, OH), 3.36 (3 H, s, OMe), 3.65 (1 H, ddd, $J_{4,5}$ 4.0, J_{gem} 12, $J_{5,OH}$ 7.6, 5-H^a), 3.83 (1 H, ddd, $J_{4,5}$ 2.4, J_{gem} 12, $J_{5,OH}$ 4.6, 5-H^b), 3.96 (1 H, ddd, $J_{3,4}$ 6.1, $J_{4.5}$ 2.4 and 4.0, 4-H), 4.00 (1 H, dd, $J_{2,3}$ 3.4, $J_{3.4}$ 6.1, 3-H), 4.02 (1 H, dd, $J_{1,2}$ 1.5, $J_{2,3}$ 3.4, 2-H) and 4.70 (1 H, d, $J_{1,2}$ 1.5, 1-H).

Methyl 2,3-di-*O*-(*tert*-butyldimethylsilyl)-α-D-*arabino*-pentodialdo-1,4-furanoside 9

To a stirred solution of oxalyl dichloride (4.37 g, 34 mmol) in dichloromethane (75 cm^3) was added dropwise a solution of DMSO (4.95 g, 68 mmol) in dichloromethane (15 cm^3) at −78 °C under Ar and the mixture was stirred for 20 min at −78 °C. At −70 °C a solution of the alcohol **8** (4.50 g, 12 mmol) in dichloromethane (10 cm^3) was added dropwise and the mixture was stirred at the same temperature for 30 min. Triethylamine (19.2 cm^3, 138 mmol) was added and the resulting stirred mixture was gradually warmed to room temperature and poured into ice–water. The mixture was extracted with diethyl ether and the extract was washed successively with aq. ammonium chloride, water and brine, dried, and evaporated and co-evaporated with toluene to dryness to give the unstable aldehyde **9** (4.46 g), which was employed in the next step without purification, ν_{max}(film)/cm^{-1} 1730 (C=O); δ_H(400 MHz; $CDCl_3$) 0.06 and 0.08 (each 3 H, 2 s, 2 × MeSi), 0.09 (6 H, s, 2 × MeSi), 0.85 and 0.89 (each 9 H, 2 s, 2 × Bu^{t}Si), 3.40 (3 H, s, OMe), 3.99 (1 H, br d, $J_{2,3}$ 2.0, 2-H), 4.07 (1 H, dd, $J_{2,3}$ 2.0, $J_{3,4}$ 2.4, 3-H), 4.31 (1 H, dd, $J_{3,4}$ 2.4, $J_{4,5}$ 1.5, 4-H), 4.90 (1 H, br s, 1-H) and 9.58 (1 H, d, $J_{1,2}$ 1.5, 5-H); δ_C(100 MHz; $CDCl_3$) −5.0, −4.9, −4.7, 25.5, 25.6, 55.3, 80.9, 81.0, 90.3, 111.1 and 201.5.

Methyl 2,3-di-*O*-(*tert*-butyldimethylsilyl)-6-deoxy-β-L-galactofuranoside 10 and methyl 2,3-di-*O*-(*tert*-butyldimethylsilyl)-6-deoxy-α-D-altrofuranoside 11

Reaction of the aldehyde 9 with MeMgI–$ZnCl_2$. A mixture of the aldehyde **9** (100 mg, 0.256 mmol) and zinc chloride (140 mg, 1.03 mmol) was stirred in dichloromethane (5 cm^3) at −78 °C for 1 h under Ar, and then to the stirred mixture was added dropwise a solution of methylmagnesium iodide in diethyl ether (2.0 M solution; 0.50 cm^3) and the mixture was stirred at the same temperature for 1.5 h. Aq. ammonium chloride was added and the resulting mixture was extracted with benzene. The extract was washed successively with water and brine, dried, and evaporated to dryness. Chromatography on silica gel with benzene–ethyl acetate (50:1) as the eluent yielded the alcohols **10** and **11** (71 mg, 68%; L-*galacto*:D-*altro* = 97:3 by ^{1}H NMR analyses).

Reaction of the aldehyde 9 with Me_3Al. To a stirred solution of trimethylaluminium in hexane (0.20 M solution; 250 cm^3) was added dropwise a solution of the aldehyde **9** (5.00 g, 13 mmol) in hexane (10 cm^3) at −78 °C under Ar and the mixture was stirred at the same temperature for 4 h. Aq. ammonium chloride was added and the resulting mixture was vigorously stirred for 30 min and then poured into ice–water. The precipitate was filtered off on a pad of Celite and the filtrate was extracted with benzene. The extract was washed successively with water and brine, dried, and evaporated to dryness. Chromatography on silica gel with benzene–ethyl acetate (50:1) as the eluent yielded the alcohols **10** and **11** (3.70 g, 70%; L-*galacto*:D-*altro* = 4:96 by ^{1}H NMR analyses).

These alcohols (**10** and **11**) were separated into each isomer by chromatography on silica gel with hexane–ethyl acetate (10:1) as the eluent.

The *alcohol* **10** (Found: C, 56.1; H, 10.3. $C_{19}H_{42}O_5Si_2$ requires C, 56.1; H, 10.4%); $[\alpha]_D^{22}$ +46.8 (*c* 1.0, $CHCl_3$); ν_{max}(film)/cm^{-1} 3500 (OH); δ_H(500 MHz; $CDCl_3$) 0.08 (3 H, s, MeSi), 0.09 (6 H, s, MeSi), 0.10 (3 H, s, MeSi), 0.88 and 0.90 (each 9 H, 2 s, 2 × Bu^{t}Si), 1.27 (3 H, d, *J* 6.7, 5-Me), 2.29 (1 H, d, $J_{5,OH}$ 6.7, OH), 3.35 (3 H, s, OMe), 3.74 (1 H, dd, $J_{3,4}$ 4.6, $J_{4,5}$ 3.4, 4-H), 3.83 (1 H, m, $J_{4,5}$ 3.4, $J_{5,Me}$ 6.7, $J_{5,OH}$ 6.7, 5-H), 3.97 (1 H, dd, $J_{2,3}$ 2.8, $J_{3,4}$ 4.6, 3-H), 3.99 (1 H, br d, $J_{2,3}$ 2.8, 2-H) and 4.71 (1 H, br s, 1-H).

The *alcohol* **11** (Found: C, 55.8; H, 10.4%); $[\alpha]_D^{22}$ +28.5 (*c* 1.0, $CHCl_3$); ν_{max}(film)/cm^{-1} 3490 (OH); δ_H(500 MHz; $CDCl_3$) 0.09, 0.10, 0.11 and 0.12 (each 3 H, 4 s, 4 × MeSi), 0.88 and 0.89 (each 9 H, 2 s, 2 × Bu^{t}Si), 1.21 (3 H, d, *J* 6.7, 5-Me), 2.39 (1 H, br s, OH), 3.35 (3 H, s, OMe), 3.90 (1 H, dd, $J_{3,4}$ 4.0, $J_{4,5}$ 2.8, 4-H), 3.97 (1 H, br d, $J_{2,3}$ 1.2, 2-H), 3.99 (1 H, dq, $J_{4,5}$ 2.8, $J_{5,Me}$ 6.7, 5-H), 4.06 (1 H, dd, $J_{2,3}$ 1.2, $J_{3,4}$ 4.0, 3-H) and 4.73 (1 H, br s, 1-H).

1,2,3,5-Tetra-*O*-acetyl-6-deoxy-L-galactofuranose 12

The alcohol **10** (37 mg, 0.09 mmol) was dissolved in AcOH–Ac_2O–H_2SO_4 [15:15:1 (v/v/v); 1 cm^3] at 0 °C and the mixture was stirred at 0 °C ⟶ room temperature for 15 h under Ar. After ice–powdered NaOAc had been added to the vigorously stirred mixture the reaction mixture was poured into ice–water, and then extracted with dichloromethane. The extract was washed successively with water, aq. sodium hydrogen carbonate, water and brine, dried, and evaporated to dryness. Chromatography on silica gel with hexane–ethyl acetate (4:1) as the eluent yielded the *tetraacetates* **12** (27 mg, 90%) as an inseparable mixture (anomeric mixture; α:β = 4:1) (Found: C, 50.5; H, 6.1. $C_{14}H_{20}O_9$ requires C, 50.6; H, 6.1%); ν_{max}(film)/cm^{-1} 1750 (AcO); δ_H(500 MHz; $CDCl_3$) 1.22 [0.6 H, d, *J* 6.4, 5-Me(β)], 1.30 [2.4 H, d, *J* 6.4, 5-Me(α)], 2.06, 2.08, 2.09 and 2.13 [each

0.6 H, 4 s, 4 × Ac(β)], 2.07, 2.10, 2.11 and 2.12 [each 2.4 H, 4 s, 4 × Ac(α)], 3.91 [0.2 H, dd, $J_{3,4}$ 6.4, $J_{4,5}$ 6.7, 4-H(β)], 4.21 [0.8 H, dd, $J_{3,4}$ 4.0, $J_{4,5}$ 4.6, 4-H(α)], 5.08 [0.8 H, dd, $J_{2,3}$ 2.0, $J_{3,4}$ 4.0, 3-H(α)], 5.13 [0.2 H, m, 5-H(β)], 5.15 [0.8 H, m, 5-H(α)], 5.17 [0.8 H, br d, $J_{2,3}$ 2.0, 2-H(α)], 5.31 [0.2 H, dd, $J_{1,2}$ 4.6, $J_{2,3}$ 7.3, 2-H(β)], 5.51 [0.2 H, dd, $J_{2,3}$ 7.3, $J_{3,4}$ 6.4, 3-H(β)], 6.18 [0.8 H, br s, 1-H(α)] and 6.31 [0.2 H, d, $J_{1,2}$ 4.6, 1-H(β)].

L-Fucopyranose 1

To a stirred solution of the tetraacetate **12** (27 mg, 0.08 mmol) in MeOH (2 cm^3) was added sodium methoxide (2 mg, 0.04 mmol) at 0 °C and then the mixture was stirred for 5 h, and made neutral with Dowex 50W X-8 (H^+) resin. The mixture was filtered, and the filtrate was evaporated to give fucopyranose **1** (10 mg, 75%), which was crystallized from ethanol, mp 137–139 °C (from EtOH); $[\alpha]_D^{22}$ −73.0 (*c* 1.1, water, equilibrium); δ_H(400 MHz; D_2O) 1.22 [0.93 H, d, *J* 6.3, 5-Me(α)], 1.26 [2.07 H, d, *J* 6.3, 5-Me(β)], 3.46 [0.69 H, dd, $J_{1,2}$ 7.8, $J_{2,3}$ 9.8, 2-H(β)], 3.65 [0.69 H, dd, $J_{2,3}$ 9.8, $J_{3,4}$ 3.4, 3-H(β)], 3.76 [0.69 H, dd, $J_{3,4}$ 3.4, $J_{4,5}$ 1.0, 4-H(β)], 3.78 [0.31 H, dd, $J_{1,2}$ 3.9, $J_{2,3}$ 10, 2-H(α)], 3.82 [0.31 H, dd, $J_{3,4}$ 3.4, $J_{4,5}$ 1.0, 4-H(α)], 3.83 [0.69 H, br q, *J* 6.8, 5-H(β)], 3.88 [0.31 H, dd, $J_{2,3}$ 10, $J_{3,4}$ 3.4, 3-H(α)], 4.22 [0.31 H, br q, *J* 6.8, 5-H(α)], 4.57 [0.69 H, d, $J_{1,2}$ 7.8, 1-H(β)] and 5.22 [0.31 H, d, $J_{1,2}$ 3.9, 3-H(α)]; δ_C(100 MHz; D_2O) 18.3, 69.1, 70.8, 72.0, 73.6, 74.2, 74.4, 74.6, 75.7, 95.0 and 99.0.

Methyl 2,3-di-*O*-(*tert*-butyldimethylsilyl)-6-deoxy-5-*O*-(*p*-tolylsulfonyl)-α-D-altrofuranoside 13

A mixture of the alcohol **11** (268 mg, 0.66 mmol) and toluene-*p*-sulfonyl chloride (250 mg, 1.30 mmol) in pyridine (5 cm^3) was stirred at room temperature for 8 days. After ice–water had been added, the mixture was vigorously stirred for 4 h, and then extracted with diethyl ether. The extract was washed successively with water, aq. potassium carbonate, water and brine, dried, and evaporated to dryness to give the tosyl ester **13** (370 mg, quantitative yield), which was employed in the next step without further purification. An *analytical sample* was obtained by chromatography on silica gel with hexane–ethyl acetate (10:1) as the eluent (Found: C, 55.7; H, 8.6; S, 5.5. $C_{26}H_{48}O_7SSi_2$ requires C, 55.7; H, 8.6; S, 5.7%); $[\alpha]_D^{23}$ +40.5 (*c* 1.4, $CHCl_3$); ν_{max}(film)/cm^{-1} 1365 and 1178 (SO_3); δ_H(500 MHz; $CDCl_3$) 0.02, 0.05, 0.06 and 0.09 (each 3 H, 4 s, 4 × MeSi), 0.84 and 0.89 (each 9 H, 2 s, 2 × Bu^{t}Si), 1.29 (3 H, d, *J* 7.4, 5-Me), 2.43 (3 H, s, C_6H_4*Me*), 3.29 (3 H, s, OMe), 3.86 (1 H, dd, $J_{3,4}$ 5.3, $J_{4,5}$ 3.9, 4-H), 3.87 (1 H, dd, $J_{2,3}$ 2.0, $J_{3,4}$ 5.3, 3-H), 3.92 (1 H, br d, $J_{2,3}$ 2.0, 2-H), 4.62 (1 H, br s, 1-H), 4.70 (1 H, dq, $J_{4,5}$ 3.9, $J_{5,Me}$ 7.4, 5-H), 7.31 (2 H, d, *J* 7.8, ArH) and 7.79 (2 H, d, *J* 8.3, ArH).

Methyl 2,3-di-*O*-(*tert*-butyldimethylsilyl)-6-deoxy-5-*O*-methylsulfonyl-α-D-altrofuranoside 14

To a stirred solution of the alcohol **11** (644 mg, 1.58 mmol) in pyridine (5 cm^3) was added dropwise methanesulfonyl chloride (273 mg, 2.38 mmol) at −10 °C, and the mixture was stirred at −10 °C ⟶ room temperature for 14 h. After ice–water had been added, the mixture was vigorously stirred for 3 h, and then extracted with diethyl ether. The extract was washed successively with water, aq. sodium hydrogen carbonate, water and brine, dried, and evaporated to dryness to give the mesyl ester **14** (762 mg, quantitative yield), which was employed to the next step without further purification. An *analytical sample* was obtained by chromatography on silica gel with hexane–ethyl acetate (10:1) as the eluent (Found: C, 49.6; H, 9.3; S, 6.5. $C_{20}H_{44}O_7SSi_2$ requires C, 49.55; H, 9.15; S, 6.6%); $[\alpha]_D^{23}$ +42.9 (*c* 0.30, $CHCl_3$); ν_{max}(film)/cm^{-1} 1361 and 1180 (SO_3); δ_H(500 MHz; $CDCl_3$) 0.09 and 0.10 (each 3 H, 2 s, 2 × MeSi), 0.11 (6 H, s, 2 × MeSi), 0.88 and 0.90 (each 9 H, 2 s, 2 × Bu^{t}Si), 1.46 (3 H, d, *J* 6.7, 5-Me), 3.02 (3 H, s, Ms), 3.35 (3 H, s, OMe), 3.95 (1 H, dd, $J_{3,4}$ 4.9, $J_{4,5}$ 3.7, 4-H), 3.99 (1 H, br d, $J_{2,3}$ 1.8, 2-H), 4.04 (1 H, dd, $J_{2,3}$ 1.8, $J_{3,4}$ 4.9, 3-H), 4.71 (1 H, br s, 1-H) and 4.92 (1 H, dq, $J_{4,5}$ 3.7, $J_{5,Me}$ 6.7, 5-H).

Methyl 5-azido-2,3-di-*O*-(*tert*-butyldimethylsilyl)-5,6-dideoxy-β-L-galactofuranoside 15

Typical procedure. A mixture of the mesyl ester **14** (762 mg, 1.57 mmol) and sodium azide (308 mg, 4.74 mmol) in DMSO (5 cm^3) was stirred at 80 °C for 5.5 h under Ar. After cooling, the reaction mixture was poured into water, and then was extracted with toluene. The extract was washed with water and brine, dried, and evaporated to dryness. Chromatography on silica gel with hexane–ethyl acetate (100:1) as the eluent yielded the *azide* **15** (583 mg, 85%) (Found: C, 52.8; H, 9.5; N, 9.7. $C_{19}H_{41}N_3O_4Si_2$ requires C, 52.9; H, 9.6; N, 9.7%); $[\alpha]_D^{25}$ +85.1 (*c* 1.0, $CHCl_3$); ν_{max}(film)/cm^{-1} 2114 (N_3); δ_H(500 MHz; $CDCl_3$) 0.08, 0.09, 0.10 and 0.11 (each 3 H, 4 s, 4 × MeSi), 0.88 and 0.91 (each 9 H, 2 s, 2 × Bu^{t}Si), 1.40 (3 H, d, *J* 7.0, 5-Me), 3.36 (3 H, s, OMe), 3.44 (1 H, dq, $J_{4,5}$ 3.7, $J_{5,Me}$ 7.0, 5-H), 3.77 (1 H, dd, $J_{3,4}$ 6.4, $J_{4,5}$ 3.7, 4-H), 3.99 (1 H, br d, $J_{1,2}$ 1.8, $J_{2,3}$ 4.0, 2-H), 4.01 (1 H, dd, $J_{2,3}$ 4.0, $J_{3,4}$ 6.4, 3-H) and 4.64 (1 H, d, $J_{1,2}$ 1.8, 1-H).

Methyl 5-*S*-acetyl-2,3-di-*O*-(*tert*-butyldimethylsilyl)-6-deoxy-5-thio-β-L-galactofuranoside 16

Typical procedure. A mixture of the tosyl ester **13** (253 mg, 0.45 mmol) and potassium thioacetate (206 mg, 1.80 mmol) in HMPA (5 cm^3) was stirred at 80–85 °C for 4 h under Ar. After cooling, the reaction mixture was poured into ice–water, and then extracted with diethyl ether. The extract was washed successively with water and brine, dried, and evaporated to dryness. Chromatography on silica gel with hexane–ethyl acetate (10:1) as the eluent yielded the *thioacetate* **16** (155 mg, 74%) (Found: C, 54.4; H, 9.5; S, 6.8. $C_{21}H_{44}O_5SSi_2$ requires C, 54.3; H, 9.5; S, 6.9%); $[\alpha]_D^{25}$ +27.0 (*c* 1.0, $CHCl_3$); ν_{max}(film)/cm^{-1} 1696 (AcS); δ_H(500 MHz; $CDCl_3$) 0.04, 0.06, 0.07 and 0.08 (each 3 H, 4 s, 4 × MeSi), 0.87 and 0.90 (each 9 H, 2 s, 2 × Bu^{t}Si), 1.42 (3 H, d, *J* 7.0, 5-Me), 2.33 (3 H, s, Ac), 3.34 (3 H, s, OMe), 3.83 (1 H, dq, $J_{4,5}$ 2.4, $J_{5,Me}$ 7.0, 5-H), 3.87 (1 H, dd, $J_{2,3}$ 3.4, $J_{3,4}$ 6.7, 3-H), 3.92 (1 H, dd, $J_{3,4}$ 6.7, $J_{4,5}$ 2.4, 4-H), 3.97 (1 H, br d, $J_{1,2}$ 1.5, $J_{2,3}$ 3.4, 2-H) and 4.64 (1 H, d, $J_{1,2}$ 1.5, 1-H).

1,2,3-Tri-*O*-acetyl-5-azido-5,6-dideoxy-L-galactofuranose 18

The azide **15** (5,49 g, 12.7 mmol) was dissolved in AcOH–Ac_2O–H_2SO_4 [15:15:1 (v/v/v); 128 cm^3] at 0 °C and the mixture was stirred at 0 °C ⟶ room temperature for 19 h under Ar. Treatment as described for the preparation of compound **12** yielded the *triacetates* **18** (3.90 g, 97%) as an inseparable mixture (anomeric mixture; α:β = 3.4:1) (Found: C, 45.6; H, 5.3; N, 13.3. $C_{12}H_{17}N_3O_7$ requires C, 45.7; H, 5.4; N, 13.3%); ν_{max}(film)/cm^{-1} 2116 (N_3) and 1750 (AcO); δ_H(500 MHz; $CDCl_3$) 1.31 [0.66 H, d, *J* 6.7, 5-Me(β)], 1.40 [2.34 H, d, *J* 6.7, 5-Me(α)], 2.05, 2.08 and 2.13 [each 0.66 H, 3 s, 3 × Ac(β)], 2.11, 2.12 and 2.14 [each 2.34 H, 3 s, 3 × Ac(α)], 3.56 [0.22 H, qd, $J_{4,5}$ 5.2, 5-H(β)], 3.66 [0.78 H, qd, $J_{4,5}$ 4.0, 5-H(α)], 3.91 [0.22 H, dd, $J_{3,4}$ 6.8, $J_{4,5}$ 5.2, 4-H(β)], 4.12 [0.78 H, dd, $J_{3,4}$ 4.9, $J_{4,5}$ 4.0, 4-H(α)], 5.13 [0.78 H, br d, $J_{3,4}$ 6.8, 3-H(α)], 5.18 [0.78 H, br s, 2-H(α)], 5.34 [0.22 H, dd, $J_{1,2}$ 4.6, $J_{2,3}$ 7.3, 2-H(β)], 5.58 [0.22 H, dd, $J_{2,3}$ 7.3, $J_{3,4}$ 6.8, 3-H(β)], 6.23 [0.78 H, br s, 1-H(α)] and 6.39 [0.22 H, d, $J_{1,2}$ 4.6, 1-H(β)].

1,5-Dideoxy-1,5-imino-L-fucitol 2

Treatment of the acetates **18** (315 mg, 1.0 mmol) as described for preparation of compound **1** yielded the corresponding triol (189 mg), which was dissolved in 95% methanol (11 cm^3). To this solution was added 10% Pd–C (20 mg) and the mixture was stirred at room temperature for 7 h under hydrogen. The catalyst was then filtered off and washed with aq. methanol. The filtrate and washings were combined, and concentrated *in vacuo*, and the residual syrup was chromatographed in a column of Dowex 50W X-8 (H^+) resin. The amine fractions, eluted with 1 M NH_4OH, were combined, and concentrated *in vacuo*. The residue was dissolved in water, and lyophilized to give title compound **2** (156 mg, 83%), $[\alpha]_D^{25}$ −48.0 (*c* 0.2, water) {lit.,[3] $[\alpha]_D^{20}$

−48.8 (*c* 0.64, water); lit.,[5] $[\alpha]_D^{20}$ −46.9 (*c* 0.61, water)}; δ_H(500 MHz; D_2O) 1.11 (3 H, d, *J* 6.6, 5-Me), 2.38 (1 H, dd, J_{gem} 13, $J_{1,2}$ 11, 1-H[a]), 2.82 (1 H, br q, *J* 6.6, 5-H), 3.09 (1 H, dd, J_{gem} 13, $J_{1,2}$ 5.4, 1-H[b]), 3.49 (1 H, dd, $J_{2,3}$ 9.7, $J_{3,4}$ 3.2, 3-H), 3.72 (1 H, ddd, $J_{1,2}$ 11 and 5.4, $J_{2,3}$ 9.7, 2-H) and 3.81 (1 H, dd, $J_{3,4}$ 3.2, $J_{4,5}$ 1.2, 4-H); δ_C(100 MHz; D_2O) 16.9, 49.5, 54.0, 68.4, 73.3 and 75.8.

Methyl 2,3-di-*O*-(*tert*-butyldimethylsilyl)-6-deoxy-5-thio-β-L-galactofuranoside 17

To a stirred solution of the thioacetate **16** (110 mg, 0.24 mmol) in diethyl ether (3 cm^3) was added lithium aluminium hydride (50 mg, 1.32 mmol) at 0 °C under Ar, and the mixture was stirred at the same temperature for 2 h. After being quenched by addition of water, the reaction mixture was filtered through a pad of Celite. The filtrate was concentrated *in vacuo* and was then co-evaporated with toluene. Chromatography on silica gel with hexane–ethyl acetate (40:1) as the eluent yielded the *thiol* **17** (96 mg, 96%) (Found: C, 54.0; H, 9.9; S, 7.3. $C_{19}H_{42}O_4SSi_2$ requires C, 54.0; H, 10.0; S, 7.6%); $[\alpha]_D^{25}$ +60.8 (*c* 1.2, $CHCl_3$); δ_H(400 MHz; $CDCl_3$) 0.08 (3 H, s, MeSi), 0.09 (6 H, s, 2 × MeSi), 0.10 (3 H, s, MeSi), 0.87 and 0.90 (each 9 H, 2 s, 2 × Bu^{t}Si), 1.43 (3 H, d, *J* 7.0, 5-Me), 1.74 (1 H, d, $J_{5,SH}$ 8.3, SH), 3.04 (1 H, dq, $J_{4,5}$ 3.7, $J_{5,Me}$ 7.0, $J_{5,SH}$ 8.3, 5-H), 3.35 (3 H, s, OMe), 3.80 (1 H, dd, $J_{3,4}$ 6.6, $J_{4.5}$ 3.7, 4-H), 4.00 (1 H, dd, $J_{1,2}$ 1.7, $J_{2,3}$ 3.6, 2-H), 4.04 (1 H, dd, $J_{2,3}$ 3.6, $J_{3,4}$ 6.6, 3-H) and 4.68 (1 H, d, $J_{1,2}$ 1.7, 1-H).

1,2,3-Tri-*O*-acetyl-5-*S*-acetyl-6-deoxy-5-thio-L-galactofuranose 19

The thioacetate **16** (80 mg, 0.17 mmol) was dissolved in AcOH–Ac_2O–H_2SO_4 [15:15:1 (v/v/v); 2 cm^3] at 0 °C and the mixture was stirred at 0 °C ⟶ room temperature for 5 h under Ar. Treatment as described for the preparation of compound **12** yielded the *tetraacetates* **19** (58 mg, 90%) as an inseparable mixture (anomeric mixture; α:β = 4.4:1) (Found: C, 47.7; H, 5.8; S, 9.1. $C_{14}H_{20}O_8S·0.3H_2O$ requires C, 47.5; H, 5.9; S, 9.1%); ν_{max}(film)/cm^{-1} 1750 (AcO) and 1696 (AcS); δ_H(500 MHz; $CDCl_3$) 1.36 [0.56 H, d, *J* 7.0, 5-Me(β)], 1.40 [2.44 H, d, *J* 7.3, 5-Me(α)], 2.08, 2.10 and 2.15 [each 0.56 H, 3 s, 3 × Ac(β)], 2.11, 2.12 and 2.13 [each 2.44 H, 3 s, 3 × Ac(α)], 2.34 [2.44 H, s, AcS(α)], 2.35 [0.56 H, s, AcS(β)], 3.86 [0.19 H, m, 5-H(β)], 3.95 [0.81 H, m, 5-H(α)], 4.08 [0.19 H, dd, $J_{3,4}$ 6.7, $J_{4,5}$ 6.1, 4-H(β)], 4.31 [0.81 H, dd, $J_{3,4}$ 6.1, $J_{4,5}$ 3.7, 4-H(α)], 5.07 [0.81 H, dd, $J_{2,3}$ 2.2, $J_{3,4}$ 6.1, 3-H(α)], 5.16 [0.81 H, br d, $J_{2,3}$ 2.2, 2-H(α)], 5.31 [0.19 H, dd, $J_{1,2}$ 4.6, $J_{2,3}$ 7.6, 2-H(β)], 5.56 [0.19 H, dd, $J_{2,3}$ 7.6, $J_{3,4}$ 6.7, 3-H(β)], 6.14 [0.81 H, br s, 1-H(α)] and 6.29 [0.19 H, d, $J_{1,2}$ 4.6, 1-H(β)].

5-Thio-L-fucopyranose 4

Treatment of the acetates **19** (24 mg, 0.07 mmol) as described for preparation of compound **1** yielded the title sulfide **4** (12 mg, 97%) as a semisolid, which was recrystallized from methanol, mp 152–154 °C (from MeOH) (lit.,[8] 159–160 °C); $[\alpha]_D^{22}$ −227 (*c* 1.2, water, equilibrium) {lit.,[8] $[\alpha]_D^{19}$ −233 (*c* 1.2, water, equilibrium)}; δ_H(500 MHz; D_2O) 1.23 (3 H, d, *J* 6.8, 5-Me), 3.52 (1 H, q, $J_{4,5}$ 1.5, 5-H), 3.83 (1 H, dd, $J_{2,3}$ 10, $J_{3,4}$ 2.9, 3-H), 3.95 (1 H, dd, $J_{1,2}$ 2.9, $J_{2,3}$ 10, 2-H), 4.07 (1 H, dd, $J_{3,4}$ 2.9, $J_{4,5}$ 1.5, 4-H) and 4.92 (1 H, d, $J_{1,2}$ 2.9, 1-H); δ_C(100 MHz; D_2O) 16.5, 37.0, 71.1, 71.6, 74.6 and 75.2.

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