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Synthesis of a thio-linked Lewis A (Le^a) epitope [1]

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Abstract

The synthesis of heptyl (α-L-fucopyranosyl)-(1 → 4)-*S*-[(β-D-galactopyranosyl)-(1 → 3)]-1,4-dithio-β-D-glucopyranoside (**2**), as thio-linked Lewis A analogue was based on thexyldimethylsilyl 3-*O*-allyl-2-*O*-benzoyl-6-*O*-(4-methoxybenzyl)-4-thio-β-D-glucopyranoside (**15**) which was readily obtained from D-galactose. Reaction of **15** with *O*-3,4-di-*O*-acetyl-2-*O*-(4-methoxybenzyl)-α-L-fucopyranosyl trichloroacetimidate (**8**) as fucosyl donor afforded the α-(1 → 4)-thio-linked disaccharide. Replacement of the 4-methoxybenzyl groups by acetyl groups and removal of the 3a-*O*-allyl group afforded as 3a-O-unprotected acceptor thexyldimethylsilyl (2,3,4-tri-*O*-acetyl-α-L-fucopyranosyl)-(1 → 4)-*S*-6-*O*-acetyl-2-*O*-benzoyl-4-thio-β-D-glucopyranoside (**19**), which gave with 2,3,4,6-tetra-*O*-acetyl-α-D-galactopyranosyl trichloroacetimidate as galactosyl donor (**20**) the trisaccharide. Transformation into a trichloroacetimidate as glycosyl donor, glycosylation of heptylmercaptan, and then removal of the *O*-acyl protective groups afforded target molecule **2**.

Keywords: S-Glycosylation; Base-promoted; Acid catalyzed; S-Glycosides; Anomeric S-alkylation; Glycosyl trichloroacetimidates; Lewis A analogues; Oligosaccharides, thio; Carbohydrates

1. Introduction

The main antigens of the Lewis blood group system found in erythrocytes are Lewis A (Le^a; Scheme 1, **1**) and Lewis B (Le^b) [2]. Both epitopes were also detected in the plasma and in numerous secretions [3]. In the course of our investigations on sulfur-linked oligosaccharides [4–8] we concentrated also on the synthesis of partially thio-linked Le^a-analogue **2** because thioglycosides are generally more stable to glycosidase action than the corresponding natural oxygen compounds [9]; yet thio-linked analogues may exhibit similar epitope character in biological investigations.

The retrosynthesis of **2** in Scheme 1 shows that thio-linked disaccharide **A** is an essential building block, which should be available from fucosyl donor **C** and 4-thio-glucoside **D**. Thus, D-galactose will not only provide galactosyl donor **B** but also—via a 4-*O*-unprotected derivative—building block **D**.

2. Results and discussion

The lability of totally *O*-benzyl-protected fucopyranosyl residues towards acid-catalyzed hydrolytic

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[1] Glycosylimidates, Part 79. For Part 78, see Ref. [1].

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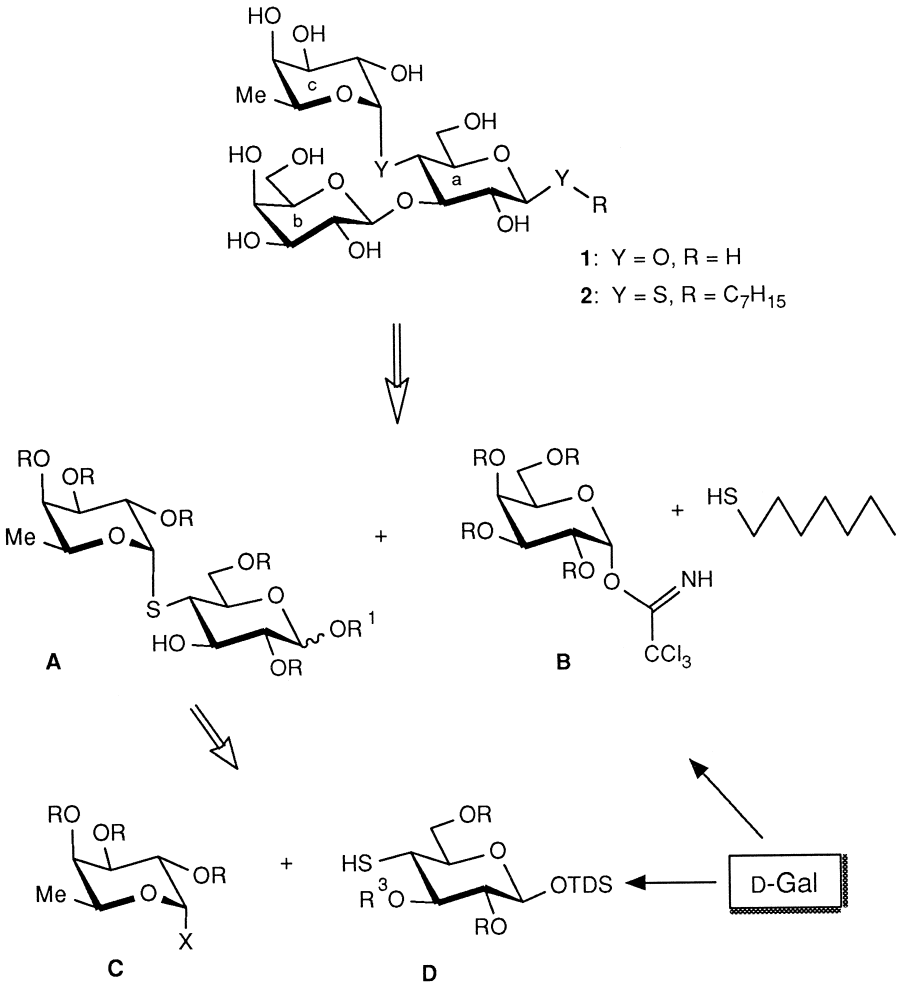


Scheme 1.

cleavage [10] was the reason to introduce a 3,4-*O*-di-*O*-acetyl-2-*O*-benzyl-protected fucose derivative, which could be readily attached to acceptors via the corresponding trichloroacetimidate as glycosyl donor [11]. Because hydrogenolytic cleavage of benzyl groups is generally not compatible with sulfur linkages, we generated the corresponding 2-*O*-(4-methoxyphenylmethyl) (MPM)-protected fucosyl donor **8** as building block **C** (Scheme 2); based on comparative studies, oxidative cleavage of the MPM group in the presence of sulfur linkages seemed to be possible [8]. Compound **8** was readily obtained from allyl 3,4-*O*-isopropylidene-fucopyranoside **3**, which is gained in a one-pot procedure from L-fucose. Treatment of **3** with 4-methoxyphenylmethyl chloride in the presence of sodium hydride in *N*,*N*-dimethylformamide (→ **4**), acid-catalyzed removal of the *O*-isopropylidene group (→ **5**), and then *O*-acetylation with acetic anhydride in pyridine afforded allyl fucoside **6** in very high yield. The allyl group was removed by treatment with Wilkinson's catalyst and then with aqueous acid [12] to furnish 1-O-unprotected derivative **7** as α/β-mixture. Treatment of **7** with trichloro-acetonitrile in the presence of 1,8-diazabicyclo[5.4.0]-undec-7-ene (DBU) as base afforded the desired fucosyl donor **8** in 95% yield.

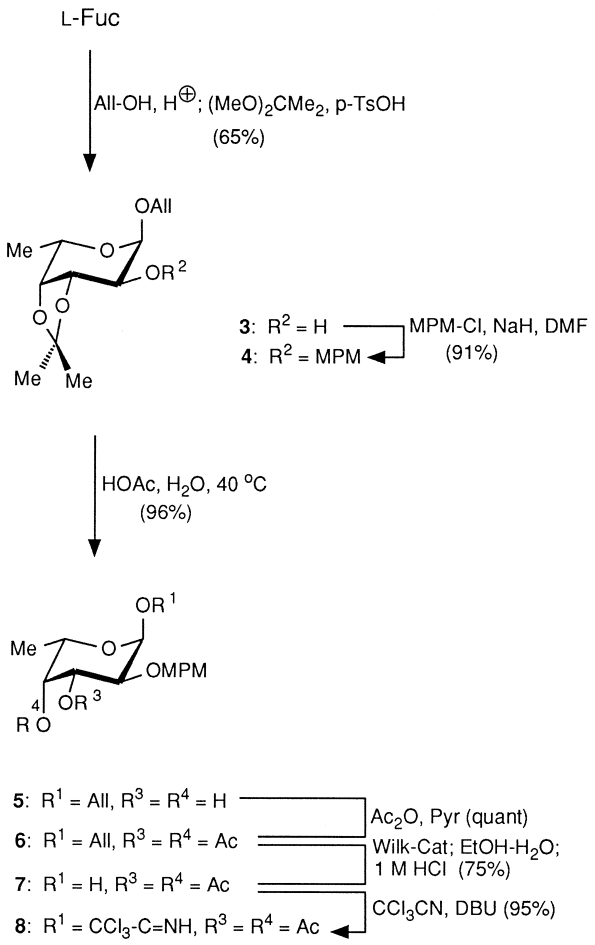
The synthesis of the 4-thio-glucose building block **D** was based on known thexyldimethylsilyl 4,6-*O*-benzylidene-D-galactoside **9** [7,13] (Scheme 3). Regioselective 3-*O*-allylation of **9** by treatment firstly with dibutyltin oxide (Bu_2SnO) [14,15] [2] and then with allyl bromide in the presence of tetrabutylammonium bromide (TBABr) furnished compound **10** in good yield. Benzoylation with benzoyl chloride in pyridine (→ **11**) followed by hydrolytic removal of

[2] 1-*O*-Thexyldimethylsilyl protection was chosen because sulfur-containing substrates interfere with tin compounds; see Ref. [15].

the benzylidene group and then regioselective introduction of the 4-methoxyphenylmethyl group at O-6 by treatment with dibutyltin oxide [14,15] [1] and then with 4-methoxyphenylmethyl chloride in the presence of tetrabutylammonium iodide (TBAI) led to 4-O-unprotected galactose derivative **13** in high yield; **13** is a unique building block because it offers selective access to each of the hydroxy groups. The critical introduction of the thiol group [4,5] was performed via nucleophilic substitution; thus **13** was transformed into the 4-*O*-trifluoromethanesulfonate by treatment with trifluoromethanesulfonic anhydride (Tf_2O) in the presence of pyridine at 0 °C and then with potassium thioacetate in *N*,*N*-dimethylformamide to afford 4-*S*-acetyl-4-thioglucoside **14**; selective removal of the *S*-acetyl group could be readily accomplished with sodium methanolate in methanol to give acceptor **15**.

Acid-catalyzed glycosylation of **15** with glycosyl donor **8** in the presence of trimethylsilyl triflate as catalyst gave the desired α-linked thiodisaccharide **16** in high yield (Scheme 4). For the cleavage of the two 4-methoxyphenylmethyl groups, which had fulfilled their task, a mild oxidizing agent was required. Dichlorodicyanobenzoquinone (DDQ) in water containing dichloromethane [16] proved to be ideal; it furnished 6a,2b-O-unprotected thiodisaccharide **17** in high yield. Acetylation with acetic anhydride in pyridine (→ **18**) and then removal of the 3a-*O*-allyl group by subsequent treatment with zinc chloride, tetrakis(triphenylphosphine)palladium and then with triethylsilane [17] afforded 3a-O-unprotected acceptor **19**, representing building block **A**, in high yield.

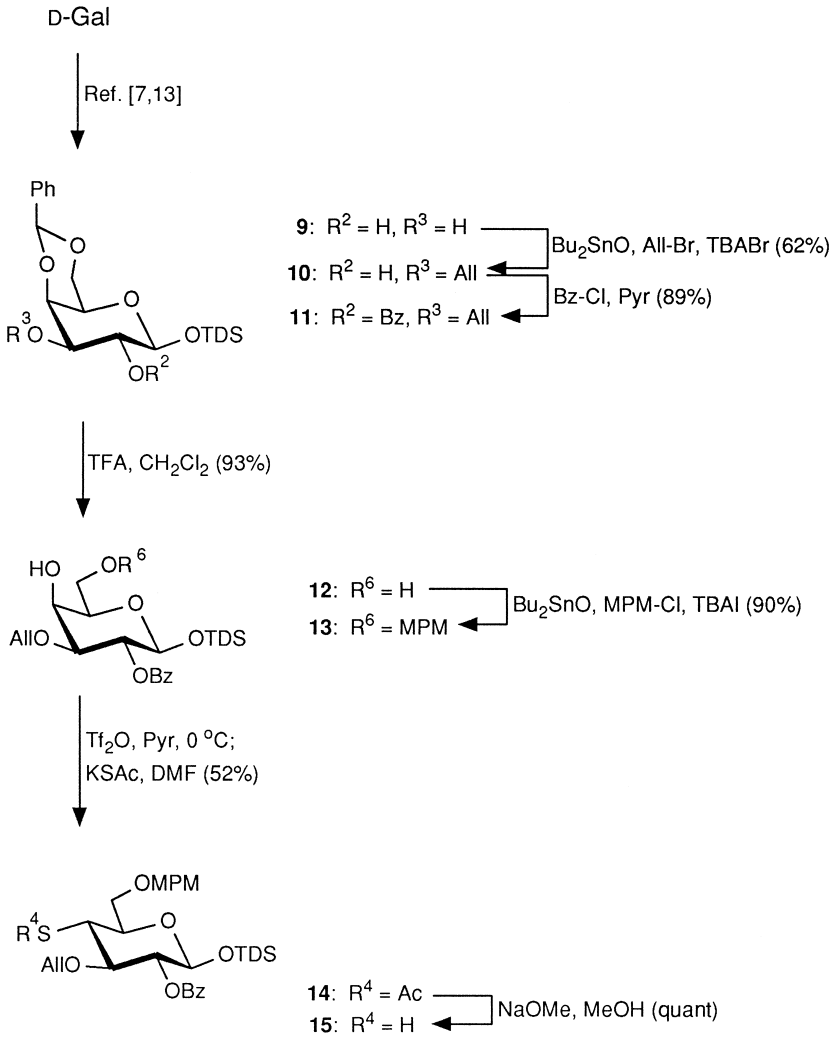
Glycosylation of acceptor **19** with known galactosyl donor **20** [4] as building block **B** afforded with 0.02 equiv. of trimethylsilyl triflate as catalyst practically exclusively ortho-ester derivative **22**, as indicated by the ^{1}H NMR data (δ 1.70; s, 3 H, O_3CCH_3); however, when this reaction was carried out with 0.04 equiv. of trimethylsilyl triflate the desired Le^a-building block **21** was obtained in 70% yield. Removal of the thexyldimethylsilyl (TDS) group by treatment with tetrabutylammonium fluoride (TBAF) in the presence of acetic acid furnished 1-O-unprotected trisaccharide **23**, which gave with trichloroacetonitrile in the presence of 1,8-diazabicyclo[5.4.0]undec-7-ene as base the desired glycosyl donor **24**. Acid catalyzed S-glycosylation of heptylmercaptan in the presence of trimethylsilyl triflate as catalyst led to thioglycoside **25** in practically quantitative yield. Treatment of **25** with sodium methanolate in methanol (Zemplén conditions [18]) provided target molecule **2**. The anomeric configurations could be readily derived from the ^{1}H NMR data: **25**: δ 4.39 (d, $J_{1a,2a}$ 10.1 Hz, H-1a), 4.65 (d, $J_{1b,2b}$ 8.1 Hz, H-1b), 5.60 (d, $J_{1c,2c}$ 4.3 Hz, H-1c); **2**: δ 4.35 (d, $J_{1a,2a}$ 10 Hz, H-1a), 4.77 (d, $J_{1b,2b}$ 7.4 Hz, H-1b), 5.49 (d, $J_{1c,2c}$ 4.8 Hz, H-1c).



Scheme 2.

3. Experimental

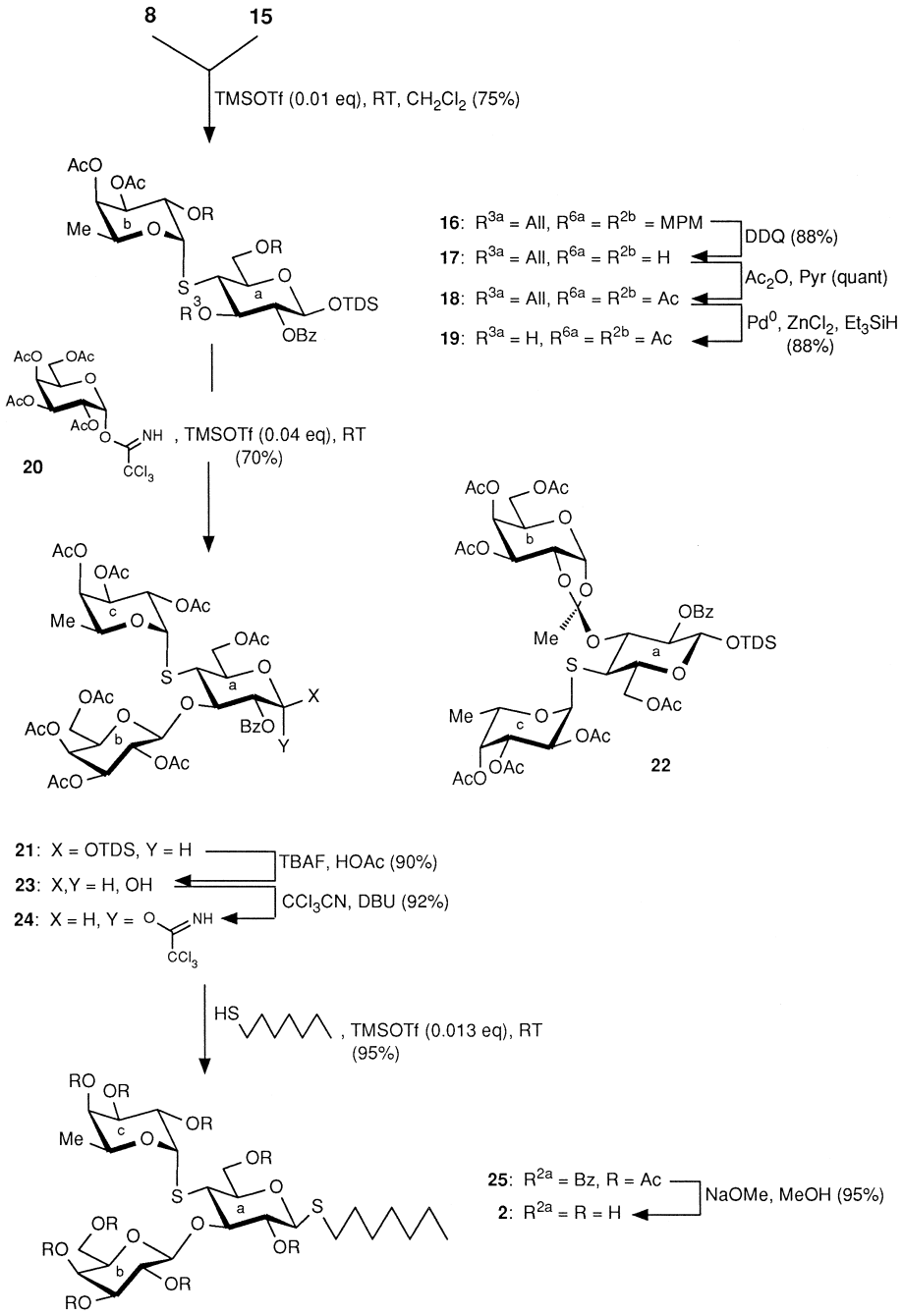
General.—Melting points are uncorrected values. ^{1}H NMR spectra were recorded on Bruker AC 250 Cryospec and Bruker DRX 600 instruments. Optical rotations were performed with Perkin–Elmer polarimeter 241 MC (1-dm cell). TLC was carried out with plastic sheets, Silica Gel $60F_{254}$ (Merck), and detection was done by UV light (254 nm) or by spraying with 5% ammonium molybdate and 0.1% cerium sulfate in 10% H_2SO_4 and heating to 120 °C. Flash chromatography was carried out with Silica Gel 60 (Baker, particle size 40 μm).



Scheme 3.

Allyl 3,4-O-*isopropylidene*-α-L-*fucopyranoside* (**3**).—L-Fucose (40 g, 243.7 mmol) was suspended in dry allyl alcohol (1 L) and then boiled under reflux in the presence of Amberlite IR 120 (H^+ form). After 4 h, the ion-exchange resin was separated by filtration and the solution concentrated in vacuo. The residue was suspended in dry acetone (1.3 L) and then *p*-toluenesulfonic acid (700 mg, 3.64 mmol) added. After stirring for 2 h the reaction mixture was neutralized with triethylamine and then concentrated in vacuo. Flash chromatography (5:2 light petroleum–EtOAc) afforded **3** (38.64 g, 65%) as colourless oil; TLC (1:1 light petroleum–EtOAc): R_f 0.38; $[\alpha]_D$ −128° (*c* 1, $CHCl_3$); ^{1}H NMR (250 MHz, $CDCl_3$): δ 5.97–5.86 (m, 1 H, CH_2–C*H*=CH_2), 5.33–5.19 (m, 2 H, CH_2–CH=CH_2), 4.87 (d, 1 H, $J_{1,2}$ 3.9 Hz, H-1), 4.29–4.01 (m, 5 H, H-3,4,5 and CH_2–CH=CH_2), 3.84–3.76 (ddd, 1 H, $J_{1,2}$ 3.9, $J_{2,3}$ 6.9, $J_{2,OH}$ 6.9 Hz, H-2), 2.31–2.28 (d, 1 H, $J_{2,OH}$ 6.9 Hz, OH), 1.52 (s, 3 H, CH_3), 1.35 (s, 3 H, CH_3), 1.33–1.30 (d, 3 H, $J_{5,6}$ 6.3 Hz, CH_3). Anal. Calcd for $C_{12}H_{20}O_5$ (244.28): C, 59.00; H, 8.25. Found: C, 58.86; H, 8.17.

Allyl 3,4-O-*isopropylidene-2*-O-p-*methoxybenzyl*-α-L-*fucopyranoside* (**4**).—To a solution of compound **3** (38.6 g, 158.7 mmol) in dry Me_2NCHO (350 mL) were added *p*-methoxybenzyl bromide (25 mL, 184.4 mmol) and NaH (4.55 g, 189.9 mmol) at 0 °C. After stirring for 30 min at room temperature, MeOH (10 mL) was added to destroy excess base. The reaction mixture was diluted with water (350 mL) and extracted with Et_2O (3 × 150 mL). The organic extract was washed with water (3 × 200 mL), dried ($MgSO_4$), and evaporated in vacuo. Flash chromatography (6:1 → 5:1 light petroleum–EtOAc) yielded compound **4** (52.5 g, 91%) as a colourless oil; TLC (2:1 light petroleum–EtOAc): R_f 0.60; $[\alpha]_D$ −96.2° (*c* 1.0, $CHCl_3$); ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.31–7.24



Scheme 4.

(m, 2 H, Ph), 6.87–6.81 (m, 2 H, Ph), 5.95–5.81 (m, 1 H, CH_2–C*H*=CH_2), 5.34–5.15 (m, 2 H, CH_2–CH=C*H*$_2$), 4.72 (d, 1 H, $J_{1,2}$ 3.6 Hz, H-1), 4.65 and 4.56 (2 d, each 1 H, J_{gem} 12.3 Hz, C*H*$_2$Ph), 4.29 (dd, 1 H, $J_{2,3}$ 7.9, $J_{3,4}$ 5.5 Hz, H-3), 4.17–3.91 (m, 4 H, C*H*$_2$–CH=CH_2 and H-4,5), 3.77 (s, 3 H, OCH_3), 3.47 (dd, 1 H, $J_{1,2}$ 3.6, $J_{2,3}$ 8 Hz, H-2), 1.39 and 1.32 (2 s, each 3 H, 2 CH_3), 1.29 (d, 3 H, $J_{5,6}$ 6.7 Hz, 3 H-6). Anal. Calcd for $C_{20}H_{28}O_6$ (364.44): C, 65.91; H, 7.74. Found: C, 65.87; H, 7.67.

Allyl 2-O-p-*methoxybenzyl*-α-L-*fucopyranoside* (**5**). —A solution of **4** (50 g, 137.2 mmol) in aqueous 70% HOAc (250 mL) is heated at 40 °C for 6 h. The mixture was then concentrated in vacuo and purified by flash chromatography (1:1 → 1:3 light petroleum–EtOAc) to give **5** (42.7 g, 96%) as an amorphous, colourless mass; TLC (1:2 light petroleum–EtOAc): R_f 0.29; $[\alpha]_D$ −115.3° (*c* 1.0, $CHC1_3$); ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.27–7.22 (m, 2 H, Ph), 6.88–6.82 (m, 2 H, Ph), 5.97–5.81 (m,

1 H, CH_2–C*H*=CH_2), 5.34–5.16 (m, 2 H, CH_2–CH=C*H*$_2$), 4.81 (d, 1 H, $J_{1,2}$ 3.5 Hz, H-1), 4.58 and 4.51 (2 d, each 1 H, J_{gem} 11.6 Hz, C*H*$_2$Ph), 4.16–3.88 (m, 4 H, H-3,5 and C*H*$_2$–CH=CH_2), 3.79–3.78 (m, 4 H, H-4 and OCH_3), 3.66 (dd, 1 H, $J_{1,2}$ 3.5, $J_{2,3}$ 9.9 Hz, H-2), 2.50 (s, 1 H, OH), 2.35 (s, 1 H, OH), 1.25 (d, 3 H, $J_{5,6}$ 6.6 Hz, 3 H-6). Anal. Calcd for $C_{17}H_{24}O_6$ (324.37): C, 62.95; H, 7.46. Found: C, 62.65; H, 7.40.

Allyl 3,4-di-O-*acetyl-2*-O-*(4-methoxybenzyl)-α*-L-*fucopyranoside* (**6**).—Compound **5** (42 g, 129.5 mmol) was stirred in 1:1 pyridine–Ac_2O (200 mL) at room temperature for 18 h. Concentration of the mixture in vacuo and purification of the residue by flash chromatography (7:2 → 5:2 light petroleum–EtOAc) yielded **6** (52.8 g, quantitative) as a colourless oil; TLC (4:1 light petroleum–EtOAc): R_f 0.16; $[\alpha]_D$ −61.4° (*c* 1.0, $CHCl_3$); ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.24–7.20 (m, 2 H, Ph), 6.87–6.81 (m, 2 H, Ph), 5.96–5.81 (m, 1 H, CH_2–C*H*=CH_2), 5.33–5.16 (m, 4 H, H-3,4 and CH_2CH=C*H*$_2$), 4.79 (d, 1 H, $J_{1,2}$ 3.6 Hz, H-1), 4.61 and 4.49 (2 d, each 1 H, J_{gem} 11.9 Hz, C*H*$_2$Ph), 4.17–3.92 (m, 3 H, H-5 and C*H*$_2$–CH=CH_2), 3.79 (dd, 1 H, $J_{1,2}$ 3.6, $J_{2,3}$ 10.3 Hz, H-2), 3.78 (s, 3 H, OCH_3), 2.11 and 1.97 (2 s, each 3 H, 2 Ac), 1.07 (d, 3 H, $J_{5,6}$ 6.6 Hz, 3 H-6). Anal. Calcd for $C_{21}H_{28}O_8$ (408.45): C, 61.75; H, 6.91. Found: C, 61.73; H, 6.99.

3,4-Di-O-*acetyl-2*-O-*(4-methoxybenzyl)-α / β*-L-*fucopyranose* (**7**).—To a solution of **6** (52.5 g, 128.53 mmol) in 9:1 EtOH–water (1200 mL) were added tris(triphenylphosphine)rhodium(I) chloride (600 mg, 649 μmol) and 1,8-diazabicyclo[5.4.0]undec-7-ene (2.4 mL, 16 mmol). The reaction mixture was heated to reflux temperature (bath temperature 90 °C) for 1 h, filtered, and evaporated in vacuo. The oily residue was redissolved in 2:1 acetone–1 M HCl (1200 mL) and stirred for 32 h at room temperature. The reaction mixture was extracted with EtOAc (3 × 300 mL), washed with saturated aqueous $NaHCO_3$ (3 × 150 mL) and dried ($MgSO_4$). Purification of the residue by flash chromatography (3:2 → 4:3 light petroleum–EtOAc) yielded **7** (35.5 g, 75%) in the ratio α:β = 1:1 as an inseparable mixture; TLC (3:2 light petroleum–EtOAc): R_f 0.21; $[\alpha]_D$ −37.6° (*c* 1.0, $CHCl_3$); ^{1}H NMR (250 MHz, $CDCl_3$): **7**α: δ 7.27–7.19 (m, 2 H, Ph), 6.88–6.81 (m, 2 H, Ph), 5.28–5.17 (m, 2 H, H-3,4), 4.75 (dd, 1 H, $J_{1,OH}$ 5.4, $J_{1,2}$ 3.6 Hz, H-1), 4.64–4.55 (m, 2 H, C*H*$_2$Ph), 3.80–3.73 (m, 5 H, H-2,5 and OCH_3), 3.46 (d, 1 H, $J_{1,OH}$ 5.4 Hz, OH), 2.13 and 2.12 (2 s, each 3 H, 2 Ac), 1.17 (d, 3 H, $J_{5,6}$ 6.4 Hz, 3 H-6). 7β: δ 7.27–7.19 (m, 2 H, Ph), 6.88–6.81 (m, 2 H, Ph), 5.28 (dd, 1 H, $J_{3,4}$ 3.5, $J_{4,5}$ < 1 Hz, H-4), 4.93 (dd, 1 H, $J_{2,3}$ 10.2, $J_{3,4}$ 3.5 Hz, H-3), 4.72 (dd, 1 H, $J_{1,OH}$ 1.9, $J_{1,2}$ 7.7 Hz, H-1), 4.64–4.55 (m, 2 H, C*H*$_2$Ph), 4.33 (dq, 1 H, $J_{4,5}$ < 1, $J_{5,6}$ 6.5 Hz, H-5), 3.77 (s, 3 H, OCH_3), 3.54 (dd, 1 H, $J_{1,2}$ 7.7, $J_{2,3}$ 10.2 Hz, H-2), 3.07 (d, 1 H, $J_{1,OH}$ 1.9 Hz, OH), 1.99 and 1.96 (2 s, each 3 H, 2 Ac), 1.09 (d, 3 H, $J_{5,6}$ 6.5 Hz, 3 H-6). Anal. Calcd for $C_{18}H_{24}O_8$ (368.38): C, 58.69; H, 6.57. Found: C, 58.63; H, 6.86.

3,4-Di-O-*acetyl-2*-O-*(4-methoxybenzyl)-α*-L-*fucopyranosyl trichloroacetimidate* (**8**).—To a solution of **7** (32.4 g, 87.9 mmol) in CH_2Cl_2 (350 mL) were added trichloroacetonitrile (90 mL, 880 mmol) and 1,8-diazabicyclo[5.4.0]undec-7-ene (330 μL, 2.2 mmol). After 30 min, the mixture was concentrated in vacuo. Flash chromatography of the residue (3:2 light petroleum–EtOAc) yielded **8** (42.84 g, 95%) in the ratio α:β = 6:1 as a colorless foam. Repeated treatment of the anomeric mixture with trichloroacetonitrile and 1,8-diazabicyclo[5.4.0]undec-7-ene converted the β-trichloroacetimidate into pure α-anomer. Compound **8** could be crystallized from Et_2O. TLC (3:2 light petroleum–EtOAc): R_f 0.52; mp 133–134 °C; $[\alpha]_D$ −69.9° (*c* 1.0, $CHCl_3$); ^{1}H NMR (250 MHz, $CDCl_3$): δ 8.57 (s, 1 H, NH), 7.21–7.17 (m, 2 H, Ph), 6.86–6.80 (m, 2 H, Ph), 6.45 (d, 1 H, $J_{1,2}$ 3.6 Hz, H-1), 5.34–5.29 (m, 2 H, H-3,4), 4.57 (2 d, each 1 H, J_{gem} 11.6 Hz, C*H*$_2$Ph), 4.31 (dq, 1 H, $J_{4,5}$ < 1, $J_{5,6}$ 6.6 Hz, H-5), 3.97 (dd, 1 H, $J_{1,2}$ 3.6, $J_{2,3}$ 9.8 Hz, H-2), 3.77 (s, 3 H, OCH_3), 2.13 and 1.98 (2 s, each 3 H, 2 Ac), 1.12 (d, $J_{5,6}$ 6.6 Hz, 3 H, 3 H-6). Anal. Calcd for $C_{20}H_{24}Cl_3NO_8$ (512.77): C, 46.85; H, 4.72; N, 2.73. Found: C, 46.91; H, 4.72; N, 2.69.

Thexyldimethylsilyl 3-O-*allyl-4,6*-O-*benzylidene-β*-D-*galactopyranoside* (**10**).—A mixture of compound **9** [7,13] (2.1 g, 5.11 mmol) and dibutyltin oxide (1.4 g, 5.6 mmol) in dry toluene (100 mL) was heated at reflux for 18 h in an apparatus for the continuous removal of water. The solution was then concentrated to two-thirds of its original volume by continued evaporation, cooled to 60 °C and allyl bromide (4.4 mL, 51.1 mmol) and Bu_4NBr (1.82 g, 5.6 mmol) were added. After 18 h at 60 °C, the reaction mixture was concentrated in vacuo. Flash chromatography (4:1 light petroleum–EtOAc) of the residue yielded **10** (1.4 g, 62%) as a colourless oil; TLC (4:1 light petroleum–EtOAc): R_f 0.2; $[\alpha]_D$ +28.9° (*c* 0.3, $CHCl_3$); ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.51–7.29 (m, 5 H, Ph), 6.00–5.86 (m, 1 H, C*H*=CH_2), 5.50 (s, 1 H, C*H*Ph), 5.34–5.15 (m, 2 H, CH=C*H*$_2$), 4.55 (d, 1 H, $J_{1,2}$ 7.4 Hz, H-1), 4.24 (dd, 1 H, $J_{5,6}$

1.5, $J_{6,6'}$ 12.3 Hz, H-6), 4.21–4.17 (m, 3 H, H-4 and CH_2–CH=CH_2), 4.03 (dd, 1 H, $J_{5,6'}$ 1.9, $J_{6,6'}$ 12.3 Hz, H-6′), 3.83 (dd, 1 H, $J_{1,2}$ 7.4, $J_{2,3}$ 9.8 Hz, H-2), 3.42 (dd, 1 H, $J_{2,3}$ 9.8, $J_{3,4}$ 3.6 Hz, H-3), 3.37–3.36 (m, 1 H, H-5), 1.70–1.59 (m, 1 H, CH), 0.89, 0.88, 0.87 and 0.86 (4 s, each 3 H, 4 CH_3), 0.20 and 0.17 (2 s, each 3 H, $SiMe_2$). Anal. Calcd for $C_{24}H_{38}O_6Si$ (450.65): C, 63.97; H, 8.50. Found: C, 63.95; H, 8.63.

*Thexyldimethylsilyl 3-*O*-allyl-2-*O*-benzoyl-4,6-*O*-benzylidene-β-*D*-galactopyranoside* (**11**).—A solution of compound **10** (1 g, 2.21 mmol) in dry pyridine (20 mL) was treated with benzoyl chloride (386 μL, 3.33 mmol) at room temperature. After stirring for 18 h, the reaction mixture was poured into ice water (30 mL) and extracted with EtOAc (2 × 30 mL). The organic layer was washed with water (2 × 20 mL) and with saturated NaCl (2 × 20 mL), dried ($MgSO_4$), and concentrated in vacuo. Flash chromatography (35:1 toluene–acetone) of the residue yielded **11** (109 g, 89%) as a colourless syrup; TLC (35:1 toluene–acetone): R_f 0.25; $[\alpha]_D$ +35.4° (*c* 1.0, $CHCl_3$); ^{1}H NMR (250 MHz, $CDCl_3$): δ 8.05–8.01 (m, 2 H, Ph), 7.57–7.31 (m, 8 H, Ph), 5.84–5.69 (m, 1 H, CH_2–C*H*=CH_2), 5.55 (s, 1 H, C*H*Ph), 5.52 (dd, 1 H, $J_{1,2}$ 7.6, $J_{2,3}$ 10.2 Hz, H-2), 5.23–5.04 (m, 2 H, CH_2–CH=CH_2), 4.84 (d, 1 H, $J_{1,2}$ 7.6 Hz, H-1), 4.31–4.27 (m, 2 H, H-4,6), 4.16–4.00 (m, 3 H, CH_2–CH=CH_2 and H-3,6′), 3.69 (dd, 1 H, $J_{2,3}$ 10.2, $J_{3,4}$ 3.6 Hz, H-3), 3.44–3.43 (m, 1 H, H-5), 1.55–1.44 (m, 1 H, CH), 0.71, 0.70, 0.69, and 0.68 (4 s, each 3 H, 4 CH_3), 0.16 and 0.07 (2 s, each 3 H, $SiMe_2$). Anal. Calcd for $C_{31}H_{42}O_7Si$ (554.76): C, 67.12; H, 7.63. Found: C, 67.23; H, 7.61.

*Thexyldimethylsilyl 3-*O*-allyl-2-*O*-benzoyl-β-*D*-galactopyranoside* (**12**).—Compound **11** (1 g, 1.8 mmol) was dissolved in CH_2Cl_2 (35 mL) and aqueous 50% CF_3CO_2H (7 mL). After being stirred for 3 h at room temperature, the mixture was diluted with CH_2Cl_2 (25 mL), washed with saturated aqueous $NaHCO_3$ (2 × 20 mL), dried ($MgSO_4$), and evaporated in vacuo. The residue was purified by flash chromatography (4:1 toluene–acetone) to give **12** (781 mg, 93%) as an amorphous mass; TLC (1:1 light petroleum–EtOAc): R_f 0.27; $[\alpha]_D$ −60.2° (*c* 0.5, $CHCl_3$); ^{1}H NMR (250 MHz, $CDCl_3$): δ 8.04–8.00 (m, 2 H, Ph), 7.58–7.39 (m, 3 H, Ph), 5.78–5.64 (m, 1 H, CH_2–C*H*=CH_2),5.36 (dd, 1 H, $J_{1,2}$ 7.7, $J_{2,3}$ 9.8 Hz, H-2), 5.21–5.06 (m, 2 H, CH_2–CH=CH_2), 4.76 (d, 1 H, $J_{1,2}$ 7.7 Hz, H-1), 4.14–3.95 (m, 4 H, H-4,6 and CH_2–CH=CH_2), 3.81 (dd, 1 H, $J_{5,6'}$ 4.6, $J_{6,6'}$ 11.6 Hz, H-6′), 3.63–3.55 (m, 2 H, H-3,5), 2.08 (bs, 2 H, OH), 1.52–1.41 (m, 1 H, CH), 0.69, 0.68, 0.67, and 0.66 (4 s, each 3 H, 4 CH_3), 0.12 and 0.03 (2 s, each 3 H, $SiMe_2$). Anal. Calcd for $C_{24}H_{38}O_7Si$ (466.65): C, 61.77; H, 8.21. Found: C, 61.62; H, 8.32.

*Thexyldimethylsilyl 3-*O*-allyl-2-*O*-benzoyl-6-*O*-(4-methoxybenzyl)-β-*D*-galactopyranoside* (**13**).—A mixture of compound **12** (16.6 g, 35.47 mmol) and Bu_2SnO (9.71 g, 39 mmol) in dry toluene (500 mL) was heated at reflux for 4 h in an apparatus for the continuous removal of water. The solution was then concentrated to two-thirds of its original volume by continued evaporation, cooled to 90 °C and *p*-methoxybenzyl chloride (15.5 mL, 113.5 mmol) and Bu_4NI (14.41 g, 39 mmol) were added. After 22 h at 100 °C, the reaction mixture was concentrated in vacuo. The oily residue was redissolved in EtOAc (400 mL), washed with aqueous 5% $Na_2S_2O_3$ (2 × 150 mL), dried ($MgSO_4$), and concentrated in vacuo. Flash chromatography (7:2 light petroleum–EtOAc) of the residue yielded **13** (18.73 g, 90%) as colourless oil; TLC (7:2 light petroleum–EtOAc): R_f 0.20; $[\alpha]_D$ −5.0° (*c* 0.3, $CHCl_3$); ^{1}H NMR (250 MHz, $CDCl_3$): δ 8.03–7.99 (m, 2 H, Ph), 7.56–7.22 (m, 5 H, Ph), 6.88–6.83 (m, 2 H, Ph), 5.77–5.62 (m, 1 H, CH_2–C*H*=CH_2), 5.34 (dd, 1 H, $J_{1,2}$ 7.7, $J_{2,3}$ 9.8 Hz, H-2), 5.19–5.04 (m, 2 H, CH_2–CH=CH_2), 4.71 (d, 1 H, $J_{1,2}$ 7.7 Hz, H-1), 4.51 (s, 2 H, CH_2Ph), 4.13–3.60 (m, 9 H, H-4,5,6,6′, OCH_3, and CH_2–CH=CH_2), 3.54 (dd, 1 H, $J_{2,3}$ 9.8, $J_{3,4}$ 3.4 Hz, H-3), 2.54 (bs, 1 H, OH), 1.51–1.39 (m, 1 H, CH), 0.67, 0.66, 0.65 and 0.64 (4 s, each 3 H, 4 CH_3), 0.11 and 0.02 (2 s, each 3 H, $SiMe_2$). Anal. Calcd for $C_{32}H_{46}O_8Si$ (586.80): C, 65.50; H, 7.90. Found: C, 66.11; H, 8.18.

*Thexyldimethylsilyl 4-*S*-acetyl-3-*O*-allyl-2-*O*-benzoyl-6-*O*-(4-methoxybenzyl)-4-thio-β-*D*-glucopyranoside* (**14**).—A solution of compound **13** (18.7 g, 31.92 mmol) in CH_2Cl_2 (300 mL) and pyridine (10.5 mL) was treated at 0 °C with trifluoromethanesulfonic anhydride (8.4 mL, 51.1 mmol), stirred for 1 h at 0 °C and for 30 min at room temperature. The reaction mixture was diluted with CH_2Cl_2 (200 mL) and washed with saturated aqueous $NaHCO_3$ (2 × 150 mL). The organic layer was dried ($MgSO_4$), filtered, and evaporated in vacuo. The residue was redissolved in dry Me_2NCHO (200 mL) and treated for 1 h with potassium thioacetate (7.5 g, 65.7 mmol) at room temperature. The reaction mixture was concentrated in vacuo, redissolved in EtOAc (300 mL), washed with water (3 × 100 mL), dried ($MgSO_4$), and evaporated in vacuo. Flash chro-

matography (50:1 toluene–EtOAc) of the residue yielded **14** (10.6 g, 52%) as a colourless syrup; TLC (50:1 toluene–EtOAc): R_f 0.15; $[\alpha]_D$ +2.0° (*c* 0.3, $CHCl_3$); ^{1}H NMR (250 MHz, $CDCl_3$): δ 8.03–7.99 (m, 2 H, Ph), 7.57–7.14 (m, 5 H, Ph), 6.87–6.82 (m, 2 H, Ph), 5.75–5.61 (m, 1 H, CH_2–C*H*=CH_2), 5.17 (dd, 1 H, $J_{1,2}$ 7.7, $J_{2,3}$ 9.1 Hz, H-2), 5.09–4.93 (m, 2 H, CH_2–CH=C*H*$_2$), 4.75 (d, 1 H, $J_{1,2}$ 7.7 Hz, H-1), 4.48 (s, 2 H, C*H*$_2$Ph), 4.10–3.60 (m, 9 H, H-3,5,6,6′, OCH_3, and C*H*$_2$–CH=CH_2), 3.51 (dd, 1 H, $J_{3,4}$ = $J_{4,5}$ = 10.8 Hz, H-4), 2.30 (s, 3 H, Ac), 1.52–1.41 (m, 1 H, CH), 0.69, 0.68, 0.67, and 0.66 (4 s, each 3 H, 4 CH_3), 0.13 and 0.03 (2 s, each 3 H, $SiMe_2$). Anal. Calcd for $C_{34}H_{48}O_8SSi$ (644.90): C, 63.32; H, 7.50. Found: C, 62.70; H, 7.53.

*Thexyldimethylsilyl 3-*O*-allyl-2-*O*-benzoyl-6-*O*-(4-methoxybenzyl)-4-thio-β-*D*-glucopyranoside* (**15**).—To a solution of compound **14** (10.4 g, 16.13 mmol) in dry MeOH (200 mL) was added 1 M NaOMe in MeOH (17 mL, 17 mmol). The resulting mixture was stirred for 20 min at room temperature and then neutralized with Amberlite IR 120 (H^+) resin. The solvent was evaporated to give compound **15** (9.72 g, quantitative) as a colourless oil. The crude product was used for the next step without further purification. TLC (20:1 toluene–EtOAc): R_f 0.39; ^{1}H NMR (250 MHz, $CDCl_3$): δ 8.02–7.99 (m, 2 H, Ph), 7.56–7.23 (m, 5 H, Ph), 6.88–6.82 (m, 2 H, Ph), 5.83–5.68 (m, 1 H, CH_2–C*H*=CH_2), 5.16–4.97 (m, 3 H, H-2 and CH_2–CH=C*H*$_2$), 4.72 (d, 1 H, $J_{1,2}$ 7.7 Hz, H-1), 4.56 (d, 1 H, *J* 11.7 Hz, C*H*$_2$Ph), 4.48 (d, 1 H, *J* 11.7 Hz, C*H*$_2$Ph), 4.20–3.40 (m, 9 H, H-3,5,6,6′, OCH_3, and C*H*$_2$–CH=CH_2), 3.09 (dd, 1 H, $J_{3,4}$ = $J_{4,5}$ = 10.4 Hz, H-4), 1.80 (s, 1 H, SH), 1.50–1.39 (m, 1 H, CH), 0.68, 0.67, 0.66 and 0.65 (4 s, each 3 H, 4 CH_3), 0.11 and 0.01 (2 s, each 3 H, $SiMe_2$).

*Thexyldimethylsilyl [3,4-di-*O*-acetyl-2-*O*-(4-methoxybenzyl)-α-*L*-fucopyranosyl]-(1→4)-*S*-3-*O*-allyl-2-*O*-benzoyl-6-*O*-(4-methoxybenzyl)-4-thio-β-*D*-glucopyranoside* (**16**).—A solution of **15** (200 mg, 331 μmol) and **8** (255 mg, 497 μmol) in dry CH_2Cl_2 (4 mL) was treated at room temperature with 0.02 M Me_3SiOTf in CH_2Cl_2 (250 μL, 5 μmol). After stirring for 10 min, the reaction mixture was neutralized with Et_3N and concentrated in vacuo. The residue was purified by flash chromatography (30:1 toluene–acetone) to give **16** (237 mg, 75%) as a colourless, amorphous mass; TLC (30:1 toluene–acetone): R_f 0.26; $[\alpha]_D$ −91.2° (*c* 0.3, $CHCl_3$); ^{1}H NMR (250 MHz, $CDCl_3$): δ 8.03–8.00 (m, 2 H, Ph), 7.54–7.17 (m, 5 H, Ph), 6.85–6.83 (m, 2 H, Ph), 5.81–5.65 (m, 1 H, CH_2–C*H*=CH_2), 5.59 (d, 1 H, $J_{1b,2b}$ 5.5 Hz, H-1b), 5.18–5.13 (m, 3 H, H-2a,3b,4b), 5.11–5.08 (m, 1 H, CH_2–CH=C*H*$_2$), 4.98–4.96 (m, 1 H, CH_2–CH=C*H*$_2$), 4.69 (d, 1 H, $J_{1a,2a}$ 7.7 Hz, H-1a), 4.59–4.56 (m, 2 H, H-5b and CH_2Ph), 4.51 (d, 1 H, *J* 12 Hz, CH_2Ph), 4.46 (d, 1 H, *J* 11.4 Hz, CH_2Ph), 4.35 (d, 1 H, *J* 11.4 Hz, CH_2Ph), 4.23–4.20 (m, 1 H, C*H*$_2$–CH=CH_2), 4.11–4.08 (m, 1 H, C*H*$_2$–CH=CH_2), 3.99 (dd, 1 H, $J_{1b,2b}$ 5.5, $J_{2b,3b}$ 10.3 Hz, H-2b), 3.86 (dd, 1 H, $J_{5a,6a}$ 4.5, $J_{6a,6'a}$ 11.1 Hz, H-6a), 3.78–3.74 (m, 7 H, H-6′a and 2 OCH_3), 3.55 (m, 1 H, H-5a), 3.42 (dd, 1 H, $J_{2a,3a}$ = $J_{3a,4a}$ = 10.7 Hz H-3a), 3.06 (dd, 1 H, $J_{3a,4a}$ 10.7, $J_{4a,5a}$ 11 Hz, H-4a), 2.11 and 1.95 (2 s, each 3 H, 2 Ac), 1.51–1.42 (m, 1 H, CH), 1.05 (d, 3 H, $J_{5b,6b}$ 6.4 Hz, 3 H-6b), 0.71, 0.70, 0.69, and 0.68 (4 s, each 3 H, 4 CH_3), 0.12 and 0.01 (2 s, each 3 H, $SiMe_2$). Anal. Calcd for $C_{50}H_{68}O_{14}SSi$ (953.23): C, 63.00; H, 7.19. Found: C, 63.02; H, 7.26.

*Thexyldimethylsilyl (3,4-di-*O*-acetyl-α-*L*-fucopyranosyl)-(1→4)-S-3-*O*-allyl-2-*O*-benzoyl-4-thio-β-*D*-glucopyranoside* (**17**).—To a solution of compound **16** (5 g, 5.24 mmol) in CH_2Cl_2 (108 mL) and water (6 mL) was added 2,3-dichloro-5,6-dicyano-*p*-benzoquinone (3.1 g, 13.66 mmol) at room temperature. After stirring overnight, the mixture was diluted with CH_2Cl_2 (50 mL) and washed with saturated aqueous $NaHCO_3$ (2 × 50 mL) and with water (5 × 50 mL). The organic layer was dried ($MgSO_4$), filtered, and evaporated in vacuo. Flash chromatography (6:1 → 4:1 toluene–acetone) yielded **17** (3.3 g, 88%) as a colourless foam; TLC (4:1 toluene–acetone): R_f 0.23; $[\alpha]_D$ −84.0° (*c* 0.3, $CHCl_3$); ^{1}H NMR (250 MHz, $CDCl_3$): δ 8.03–8.00 (m, 2 H, Ph), 7.59–7.40 (m, 3 H, Ph), 5.79–5.65 (m, 1 H, CH_2–C*H*=CH_2), 5.60 (d, 1 H, $J_{1b,2b}$ 5.4 Hz, H-1b), 5.21–4.96 (m, 5 H, H-2a,3b,4b and CH_2CH=C*H*$_2$), 4.77 (d, 1 H, $J_{1a,2a}$ 7.7 Hz, H-1a), 4.46 (dq, 1 H, $J_{4b,5b}$ 1, $J_{5b,6b}$ 6.4 Hz, H-5b), 4.31–3.95 (m, 5 H, H-2b,6a,6′a and C*H*$_2$–CH=CH_2), 3.56–3.47 (m, 2 H, H-3a,5a), 3.12 (dd, 1 H, $J_{3a,4a}$ = $J_{4a,5a}$ = 10.9 Hz, H-4a), 2.30 (d, 1 H, *J* 7.9 Hz, OH), 2.13 and 2.03 (2 s, each 3 H, 2 Ac), 1.51–1.41 (m, 1 H, CH), 1.09 (d, 3 H, *J* 6.4 Hz, 3 H-6b), 0.69, 0.68, 0.67 and 0.66 (4 s, each 3 H, 4 CH_3), 0.09 and 0.01 (2 s, each 3 H, $SiMe_2$). Anal. Calcd for $C_{34}H_{52}O_{12}SSi$ (712.93): C, 57.28; H, 7.35. Found: C, 57.48; H, 7.39.

*Thexyldimethylsilyl (2,3,4-tri-*O*-acetyl-α-*L*-fucopyranosyl)-(1→4)-*S*-6-*O*-acetyl-3-*O*-allyl-2-*O*-benzoyl-4-thio-β-*D*-glucopyranoside* (**18**).—Compound **17** (3 g, 4.21 mmol) was stirred in 1:1 pyridine–Ac_2O (40 mL) at room temperature for 4 h.

Concentration of the mixture in vacuo and purification of the residue by flash chromatography (20:1 toluene–acetone) yielded **18** (3.32 g, quant) as a colourless foam; TLC (20:1 toluene–acetone): R_f 0.20; $[\alpha]_D$ −99.3° (*c* 0.3, $CHCl_3$); ^{1}H NMR (250 MHz, $CDCl_3$): δ 8.02–7.99 (m, 2 H, Ph), 7.58–7.40 (m, 3 H, Ph), 5.78–5.64 (m, 2 H, H-1b and CH_2–C*H*=CH_2), 5.28–4.97 (m, 6 H, H-2a,2b,3b,4b and CH_2–CH=C*H*$_2$), 4.68 (d, 1 H, $J_{1a,2a}$ 7.7 Hz, H-1a), 4.59–4.52 (m, 2 H, H-5b,6a), 4.23–4.05 (m, 3 H, H-6′a and C*H*$_2$–CH=CH_2), 3.64–3.58 (m, 1 H, H-5a), 3.43 (dd, 1 H, $J_{2a,3a}$ 9.4, $J_{3a,4a}$ 11 Hz, H-3a), 2.93 (dd, 1 H, $J_{3a,4a} = J_{4a,5a} = 11$ Hz, H-4a), 2.14, 2.08, 2.05 and 1.97 (4 s, each 3 H, 4 Ac), 1.50–1.39 (m, 1 H, CH), 1.08 (d, 3 H, $J_{5b,6b}$ 6.4 Hz, 3 H-6b), 0.68, 0.67, 0.66 and 0.65 (4 s, each 3 H, 4 CH_3), 0.08 and 0.01 (2 s, each 3 H, $SiMe_2$). Anal. Calcd for $C_{38}H_{56}O_{14}SSi$ (797.01): C, 57.27; H, 7.08. Found: C, 56.99; H, 7.13.

*Thexyldimethylsilyl (2,3,4-tri-*O*-acetyl-α-*L*-fucopyranosyl)-(1 → 4)-*S*-6-*O*-acetyl-2-*O*-benzoyl-4-thio-β-*D*-glucopyranoside* (**19**).—To a solution of compound **18** (3 g, 3.76 mmol) in dry tetrahydrofuran (70 mL) was added dry zinc chloride (1.28 g, 9.41 mmol) at room temperature. After stirring for 15 min, tetrakis(triphenylphosphine)palladium(O) (700 mg, 606 μmol) was added and after another 10 min triethylsilane (2.4 mL, 15.1 mmol). After stirring overnight in the dark, the mixture was diluted with Et_2O (80 mL), washed with water (3 × 50 mL), dried ($MgSO_4$) and concentrated in vacuo. The residue was purified by flash chromatography (5:2 light petroleum–EtOAc) to yield **19** (2.5 g, 88%) as a colourless foam; TLC (5:2 light petroleum–EtOAc): R_f 0.24; $[\alpha]_D$ −109.1° (*c* 0.5, $CHCl_3$); ^{1}H NMR (250 MHz, $CDCl_3$): δ 8.04–8.00 (m, 2 H, Ph), 7.58–7.39 (m, 3 H, Ph), 5.75 (d, 1 H, $J_{1b,2b}$ 5.4 Hz, H-1b), 5.25 (dd, 1 H, $J_{3b,4b}$ 3.1, $J_{4b,5b}$ < 1 Hz, H-4b), 5.19 (dd, 1 H, $J_{1b,2b}$ 5.4, $J_{2b,3b}$ 11.1 Hz, H-2b), 5.11 (dd, 1 H, $J_{2b,3b}$ 11.1, $J_{3b,4b}$ 3.1 Hz, H-3b), 5.02 (dd, 1 H, $J_{1a,2a}$ 7.7, $J_{2a,3a}$ 9.2 Hz, H-2a), 4.75 (d, 1 H, $J_{1a,2a}$ 7.7 Hz, H-1a), 4.55–4.50 (m, 2 H, H-5b,6a), 4.22 (dd, 1 H, $J_{5a,6'a}$ 5.4, $J_{6a,6'a}$ 11.8 Hz, H-6′a), 3.75–3.60 (m, 2 H, H-3a,5a), 2.94 (d, 1 H, $J_{3a,OH}$ 3.6 Hz, OH), 2.87 (dd, $J_{3a,4a} = J_{4a,5a} = 10.7$ Hz, 1 H, H-4a), 2.14, 2.09, 2.05 and 1.97 (4 s, each 3 H, 4 Ac), 1.51–1.41 (m, 1 H, CH), 1.12 (d, $J_{5b,6b}$ 6.4 Hz, 3 H, H-6b), 0.69, 0.68, 0.67 and 0.66 (4 s, each 3 H, 4 CH_3), 0.10 and 0.04 (2 s, each 3 H, $SiMe_2$). $C_{35}H_{52}O_{14}SSi$ (756.94): Anal. Calcd for C, 55.24; H, 6.92. Found: C, 55.31; H, 6.83.

*Thexyldimethylsilyl (2,3,4-tri-*O*-acetyl-α-*L*-fucopyranosyl)-(1 → 4)-*S*-[(2,3,4,6-tetra-*O*-acetyl-β-*D*-galactopyranosyl)-(1 → 3)]-6-*O*-acetyl-2-*O*-benzoyl-4-thio-β-*D*-glucopyranoside* (**21**).—A solution of **20** [4] (1.3 g, 2.64 mmol) and **19** (1 g, 1.32 mmol) in dry CH_2Cl_2 (7 mL) was treated at room temperature with 0.1 M Me_3SiOTf in CH_2Cl_2 (1.06 mL, 106 μmol). After stirring for 30 min, the reaction mixture was neutralized with Et_3N and concentrated in vacuo. The residue was purified by flash chromatography (3:2 light petroleum–EtOAc) to give **21** (1 g, 70%) as a colourless foam; TLC (5:4 light petroleum–EtOAc): R_f 0.20; $[\alpha]_D$ −49.1° (*c* 0.5, $CHCl_3$); ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.99–7.96 (m, 2 H, Ph), 7.59–7.43 (m, 3 H, Ph), 5.61 (d, 1 H, $J_{1c,2c}$ 4.1 Hz, H-1c), 5.34–4.98 (m, 6 H, H-2c,3c,4c,2b,4b,2a), 4.64–4.49 (m, 6 H, H-1a,6a,5c,1b,3b,6b), 4.20–4.09 (m, 2 H, H-6′a,6′b), 3.84–3.75 (m, 2 H, H-3a,5b), 3.61–3.56 (m, 1 H, H-5a), 2.90 (dd, 1 H, $J_{3a,4a} = J_{4a,5a} = 11$ Hz, H-4a), 2.15, 2.14, 2.08, 2.07, 2.05, 1.95, 1.92 and 1.85 (8 s, each 3 H, 8 Ac), 1.46–1.36 (m, 1 H, CH), 1.21 (d, 3 H, $J_{5c,6c}$ 6.4 Hz, 3 H-6c), 0.66, 0.65, 0.64 and 0.63 (4 s, each 3 H, 4 CH_3), 0.06 and −0.05 (2 s, each 3 H, $SiMe_2$). Anal. Calcd for $C_{49}H_{70}O_{23}SSi$ (1087.23): C, 54.13; H, 6.49. Found: C, 53.51; H, 6.50.

*Thexyldimethylsilyl (2,3,4-tri-*O*-acetyl-α-*L*-fucopyranosyl)-(1 → 4)-*S*-[(3,4,6,-tri-*O*-acetyl-1,2-orthoacetyl-α-*D*-galactopyranosyloxy)-(1 → 3)]-6-*O*-acetyl-2-*O*-benzoyl-4-thio-β-*D*-glucopyranoside* (**22**). —A solution of **20** [4] (2.1 g, 4.46 mmol) and **19** (1.7 g, 2.23 mmol) in dry CH_2Cl_2 (15 mL) was treated at room temperature with 0.1 M Me_3SiOTf in CH_2Cl_2 (900 μL, 90 μmol). After stirring for 30 min, the reaction mixture was neutralized with Et_3N and concentrated in vacuo. The residue was purified by flash chromatography (3:2 light petroleum–EtOAc) to give **22** (1.95 g, 81%) as a colourless foam; TLC (5:4 light petroleum–EtOAc): R_f 0.31; $[\alpha]_D$ −75.8° (*c* 0.5, $CHCl_3$); ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.97–7.93 (m, 2 H, Ph), 7.54–7.36 (m, 3 H, Ph), 5.71 (d, 1 H, $J_{1b,2b}$ 4.9 Hz, H-1b), 5.63 (d, 1 H, $J_{1c,2c}$ 3.1 Hz, H-1c), 5.28–5.13 (m, 4 H, H-2c,3c,4c,4b), 5.07 (dd, 1 H, $J_{1a,2a}$ 7.7, $J_{2a,3a}$ 8.4 Hz, H-2a), 4.68–4.59 (m, 4 H, H-6a,1a,5c,3b), 4.13–3.97 (m, 5 H, H-6′a,2b,5b,6′b,6b), 3.79 (dd, 1 H, $J_{2a,3a}$ 8.4, $J_{3a,4a}$ 10.7 Hz, H-3a), 3.65–3.59 (m, 1 H, H-5a), 2.91 (dd, 1 H, $J_{3a,4a} = J_{4a,5a} = 10.7$ Hz, H-4a), 2.14, 2.07, 2.05, 2.01, 1.99, 1.96, 1.73 (7 s, each 3 H, 7 Ac), 1.70 (s, 3 H, O_3CMe), 1.49–1.39 (m, 1 H, CH), 1.09 (d, 3 H, $J_{5c,6c}$ 6.4 Hz, 3 H-6c), 0.67, 0.66, 0.65 and 0.64 (4 s, each 3 H, 4 CH_3), 0.06 and −0.04 (2 s, each 3 H, $SiMe_2$).

(2,3,4-Tri-O-*acetyl-α*-L-*fucopyranosyl)-(1 → 4)*-S-*[(2,3,4,6-tetra*-O-*acetyl-β*-D-*galactopyranosyl-(1 → 3)]-6*-O-*acetyl-2*-O-*benzoyl-4-thio-α / β*-D-*glucopyranose* (**23**).—Compound **21** (840 mg, 772 μmol) was dissolved in dry tetrahydrofuran (15 mL). CH_3COOH (45 μL, 795 μmol) and then 1 M Bu_4NF in tetrahydrofuran (911 μL, 911 μmol) were added at 0 °C. The mixture was slowly warmed up to room temperature and stirred for 2 h. After the addition of Et_2O (50 mL), the organic layer was washed with brine (4 × 15 mL), dried ($MgSO_4$), and concentrated in vacuo. Flash chromatography (1:1 light petroleum–EtOAc) yielded **23** (656 mg, 90%) in the ratio $\alpha:\beta$ = 15:1 as a colourless foam; TLC (1:1 light petroleum–EtOAc): R_f 0.15; $[\alpha]_D$ −46.2° (*c* 0.5, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.06–8.03 (m, 2 H, Ph), 7.62–7.47 (m, 3 H, Ph), 5.62 (d, 1 H, $J_{1c,2c}$ 4.3 Hz, H-1c), 5.49 (dd, 1 H, $J_{1a,OH}$ 3.7, $J_{1a,2a}$ 3.6 Hz, H-1a), 5.39–5.34 (m, 2 H, H-4b,4c), 5.28–5.22 (m, 2 H, H-2c,3c), 5.13–5.01 (m, 3 H, H-5c,2b,2a), 4.82 (d, 1 H, $J_{1b,2b}$ 8.2 Hz, H-1b), 4.69 (dd, 1 H, $J_{2b,3b}$ 10.5, $J_{3b,4b}$ 3.4 Hz, H-3b), 4.58 (dd, 1 H, $J_{5b,6b}$ 3.8, $J_{6b,6'b}$ 13.2 Hz, H-6b), 4.52 (dd, 1 H, $J_{5a,6a}$ 6.4, $J_{6a,6'a}$ 11.2 Hz, H-6a), 4.23–4.18 (m, 3 H, H-5a,6′a,6′b), 4.14 (dd, 1 H, $J_{2a,3a}$ 9.6, $J_{3a,4a}$ 10.7 Hz, H-3a), 3.93–3.90 (m, 1 H, H-5b), 2.96 (dd, 1 H, $J_{3a,4a} = J_{4a,5a}$ = 10.7 Hz, H-4a), 2.83 (d, 1 H, $J_{1a,OH}$ 3.7 Hz, OH), 2.15, 2.14, 2.12, 2.08, 2.07, 1.96, 1.85 and 1.67 (8 s, each 3 H, 8 Ac), 1.22 (d, 3 H, $J_{5c,6c}$ 6.4 Hz, 3 H-6c). Anal. Calcd for $C_{41}H_{52}O_{23}S$ (944.92): C, 52.12; H, 5.55. Found: C, 52.27; H, 5.66.

(2,3,4-Tri-O-*acetyl-α*-L-*fucopyranosyl)-(1 → 4)*-S-*[(2,3,4,6-tetra*-O-*acetyl-β*-D-*galactopyranosyl)-(1 → 3)]-6*-O-*acetyl-2*-O-*benzoyl-4-thio-α*-D-*glucopyranosyl trichloroacetimidate* (**24**).—To a solution of **23** (600 mg, 635 μmol) in dry CH_2Cl_2 (18 mL) were added trichloroacetonitrile (640 μL, 6.35 mmol) and 1,8-diazabicyclo[5.4.0]undec-7-ene (2 drops). After 45 min, the mixture was concentrated in vacuo. Flash chromatography (4:1 toluene–acetone) of the residue yielded **24** (636 mg, 92%) as a colourless foam; TLC (5:1 toluene–acetone): R_f 0.23; $[\alpha]_D$ −44.2° (*c* 0.5, $CHCl_3$); ^{1}H NMR (250 MHz, $CDCl_3$): δ 8.53 (s, 1 H, NH), 7.98–7.94 (m, 2 H, Ph), 7.64–7.43 (m, 3 H, Ph), 6.54 (d, 1 H, $J_{1a,2a}$ 3.6 Hz, H-1a), 5.62 (d, 1 H, $J_{1c,2c}$ 4.2 Hz, H-1c), 5.37–5.35 (m, 2 H, H-4b,4c), 5.29–5.18 (m, 3 H, H-2a,2c,3c), 5.10–5.02 (m, 2 H, H-2b,5c), 4.74 (d, 1 H, $J_{1b,2b}$ 8.1 Hz, H-1b), 4.65 (dd, 1 H, $J_{2b,3b}$ 10.4, $J_{3b,4b}$ 3.3 Hz, H-3b), 4.61–4.52 (m, 2 H, H-6a,6b), 4.26–4.12 (m, 3 H, H-5a,6′a,6′b), 4.08 (dd, 1 H, $J_{2a,3a}$ 9.4, $J_{3a,4a}$ 11.1 Hz, H-3a), 3.97–3.91 (m, 1 H, H-5b), 3.08 (dd, 1 H, $J_{3a,4a} = J_{4a,5a}$ = 11.1 Hz, H-4a), 2.16, 2.15, 2.10, 2.08, 2.07, 1.96, 1.85 and 1.73 (8 s, each 3 H, 8 Ac), 1.24 (d, 3 H, $J_{5c,6c}$ 6.4 Hz, 3 H-6c).

Heptyl (2,3,4-tri-O-*acetyl-α*-L-*fucopyranosyl)-(1 → 4)*-S-*[(2, 3, 4, 6-tetra*-O-*acetyl-β*-D-*galactopyranosyl)-(1 → 3)]-6*-O-*acetyl-2*-O-*benzoyl-1, 4-dithio-β*-D-*glucopyranoside* (**25**).—A solution of **24** (190 mg, 174 μmol) and heptyl mercaptan (80 μL, 522 μmol) in dry CH_2Cl_2 (2.5 mL) was treated at room temperature with 0.02 M Me_3SiOTf in CH_2Cl_2 (113 μL, 2.26 μmol). After stirring for 10 min, the reaction mixture was neutralized with Et_3N and concentrated in vacuo. The residue was purified by flash chromatography (7:1 toluene–acetone) to yield **25** (176 mg, 95%) as a colourless foam; TLC (6:1 toluene–acetone): R_f 0.17; $[\alpha]_D$ −112.2° (*c* 0.5, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.01–7.97 (m, 2 H, Ph), 7.64–7.45 (m, 3 H, Ph), 5.60 (d, 1 H, $J_{1c,2c}$ 4.3 Hz, H-1c), 5.34–5.31 (2 H, H-4b,4c), 5.27–5.16 (m, 3 H, H-2c,3c,2a), 5.07–4.99 (m, 2 H, H-2b,5c), 4.65 (m, 1 H, $J_{1b,2b}$ 8.1 Hz, H-1b), 4.61–4.50 (m, 3 H, H-6′a,6′b,3b), 4.39 (d, 1 H, $J_{1a,2a}$ 10.1 Hz, H-1a), 4.21–4.12 (m, 2 H, H-6a,6b), 3.85–3.77 (m, 2 H, H-3a,5b), 3.63–3.57 (m, 1 H, H-5a), 2.98 (dd, 1 H, $J_{3a,4a} = J_{4a,5a}$ = 11 Hz, H-4a), 2.64–2.56 (m, 2 H, SCH_2), 2.15, 2.14, 2.09, 2.06, 2.05, 1.95, 1.94 and 1.85 (8 s, each 3 H, 8 Ac), 1.52–1.41 (m, 2 H, CH_2), 1.24 (d, 3 H, $J_{5c,6c}$ 6.5 Hz, 3 H-6c), 1.23–1.18 (m, 8 H, CH_2), 0.82 (dd, 3 H, *J* 6.4 Hz, CH_3). Anal. Calcd for $C_{48}H_{66}O_{22}S_2$ (1059.17): C, 54.43; H, 6.28. Found: C, 54.75; H, 6.20.

Heptyl (α-L-*Fucopyranosyl)-(1 → 4)*-S-*[(β*-D-*galactopyranosyl)-(1 → 3)]-1,4-dithio-β*-D-*glucopyranoside* (**2**).—To a solution of compound **25** (60 mg, 56 μmol) in dry MeOH (8 mL) was added 2 M NaOMe in MeOH (1.6 mL). The mixture was stirred for 24 h at room temperature, neutralized with Amberlite IR 120 (H^+) resin, filtered, and evaporated in vacuo. Purification of the residue by RP 18 flash chromatography (1:1 EtOH) yielded **2** (33 mg, 95%) as a colourless powder; TLC (5:4:1 $CHCl_3$–MeOH–H_2O): R_f 0.51; RP 18 TLC (1:1 EtOH–H_2O): R_f 0.37; $[\alpha]_D$ − 136.7° (*c* 0.3, MeOH); ^{1}H NMR (600 MHz, D_2O): δ 5.49 (d, 1 H, $J_{1c,2c}$ 4.8 Hz, H-1c), 4.77 (d, 1 H, $J_{1b,2b}$ 7.4 Hz, H-1b), 4.42 (dq, 1 H, $J_{4c,5c} < 1$, $J_{5c,6c}$ 6.5 Hz, H-5c), 4.35 (d, 1 H, $J_{1a,2a}$ 10 Hz, H-1a), 3.94–3.38 (m, 14 H, H2a,3a,5a,6a,6′a,2c,3c,4c,2b,3b,4b,5b,6b,6′b), 2.72 (dd, 1 H, $J_{3a,4a} = J_{4a,5a}$ = 11 Hz, H-4a), 2.62–2.53 (m, 2 H, SCH_2), 1.51–1.44 (m, 2 H, CH_2), 1.29–1.10 (m, 8 H, CH_2), 1.05 (d, $J_{5c,6c}$ 6.5 Hz, 3 H, 3 H-6c),

0.69 (dd, 3 H, *J* 6.6 Hz, CH_3). Anal. Calcd for $C_{25}H_{46}O_{13}S_2 \cdot 0.75H_2O$ (632.27): C, 47.49; H, 7.57. Found: C, 47.48; H, 7.70.

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References

[1] T.G. Mayer and R.R. Schmidt, *Liebigs Ann.*, (1997) 859–863.
[2] A.E. Mourant, *Nature*, 158 (1946) 237–238.
[3] (a) R.R. Race and R. Sanger, *Blood Groups in Man*, Blackwell London, 1962, pp. 239–260; (b) E. Dabelsteen, N. Graem, H. Clausen, and S. Hakomori, *Cancer Res.*, 48 (1988) 181.
[4] R.R. Schmidt and M. Stumpp, *Liebigs Ann. Chem.*, (1983) 1249–1256.
[5] (a) R.R. Schmidt, *Angew. Chem.*, 98 (1986) 213–236; (b) *Angew. Chem., Int. Ed. Engl.*, 25 (1986) 212–235.
[6] T. Eisele, A. Toepfer, G. Kretzschmar, and R.R. Schmidt, *Tetrahedron Lett.*, 37 (1996) 1389–1392.
[7] T. Eisele and R.R. Schmidt, *Liebigs Ann.*, submitted.
[8] T. Eisele, *Dissertation*, Univ. Konstanz, 1996.
[9] P.J. Deschavanne, O.M. Virtelle, and J.M. You, *J. Biol. Chem.*, 253 (1978) 833–836.
[10] (a) R. Bommer, W. Kinzy, and R.R. Schmidt, *Liebigs Ann. Chem.*, (1991) 425–433; (b) R. Bommer, *Dissertation*, Univ. Konstanz, 1990; (c) H. Kunz and C. Unverzagt, *Angew. Chem.*, 100 (1988) 1763–1765; (d) *Angew. Chem. Int. Ed. Engl.*, 27 (1988) 1697–1699.
[11] (a) R. Windmüller and R.R. Schmidt, *Tetrahedron Lett.*, 35 (1994) 7927–7930; (b) R. Windmüller, *Diplomarbeit*, Univ. Konstanz, 1990.
[12] (a) R. Gigg and C.D. Warren, *J. Chem. Soc. C*, (1968) 1903–1911; (b) P.A. Gent and R. Gigg, *J. Chem. Soc., Chem. Commun.*, (1974) 277–278.
[13] (a) M. Mikamo, *Carbohydr. Res.*, 191 (1989) 150–153; (b) J. Peter, *Diplomarbeit*, Univ. Konstanz, 1994.
[14] (a) S. David, A. Thieffry, and A. Veyrieres, *J. Chem. Soc., Perkin Trans 1*, (1981) 1796–1801; (b) M.E. Haque, T. Kikuchi, K. Yoshimoto, and Y. Tsuda, *Chem. Pharm. Bull.*, 33 (1985) 2243–2255; (c) T. Ogawa and S. Nakabayashi, *Carbohydr. Res.*, 97 (1981) 81–86; (d) K.–H. Jung, M. Hoch, and R.R. Schmidt, *Liebigs Ann. Chem.*, (1989) 1099–1106.
[15] H.M. Zuurmond, P.A.M. van der Klein, G.A. van der Marel, and J.H. van Boom, *Tetrahedron*, 49 (1993) 6501–6514.
[16] K. Horita, T. Yoshioka, T. Tanaka, Y. Oikawa, and O. Yonemitsu, *Tetrahedron*, 27 (1986) 3021–3028.
[17] (a) E.J. Corey and J.W. Suggs, *J. Org. Chem.*, 38 (1973) 3224; (b) H. Yin, R.W. Franck, S.-L. Chen, G.J. Quigley, and L.J. Todaro, *J. Org. Chem.*, 57 (1992) 644–651; (c) O. Dangles, F. Guibé, and G. Balavoine, *J. Org. Chem.*, 52 (1987) 4984–4993.
[18] G. Zemplén, *Ber. Dtsch. Chem. Ges.*, 60 (1927) 1555–1564.