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New synthesis of 2,6-anhydro-β-D-fructofuranoses, pivotal [2.2.1] bicyclic acetals for the conversion of D-fructose into 2,2,5-trisubstituted tetrahydrofurans

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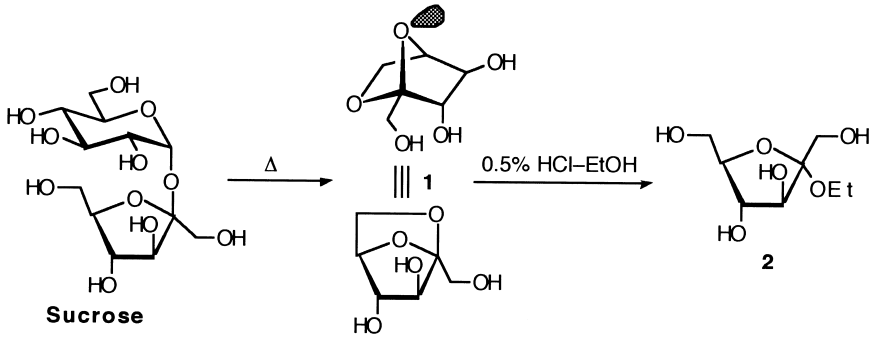
Abstract—2,6-Anhydro-β-D-fructofuranose derivatives were prepared by a novel tin-promoted 2,5-cyclisation of phenyl 2-thio-β-D-fructopyranosides. They were regioselectively opened by allyltrimethylsilane in the presence of catalytic $Sc(OTf)_3$ to give 2,2,5-trisubstituted tetrahydrofurans in high yields and major α-stereoselectivity.

The synthesis of functionalized tetrahydrofuran rings has received considerable attention because of their presence in many biologically active compounds.[1] Polyether antibiotics, such as lonomycin C, ionomycin or monensin, contain 2,5-di and 2,2,5-trisubstituted tetrahydrofuran units[2] which can be obtained by *C*-glycosylation techniques. Nucleophilic substitution at the anomeric centre of a carbohydrate derivative can be to this respect an excellent strategy, provided that the required furanosides are readily attainable. We have recently shown[3] that iodocyclisation of 6-*O*-protected D-galactal, followed by radical reduction, affords [2.2.1] bicyclic acetals which are then regioselectively opened by various nucleophiles in the presence of an acid promoter to give exclusively furanosyl compounds. A 2,5-di-substituted tetrahydrofuran fragment of annonaceous acetogenins was thus prepared from D-galactal in a limited number of steps.[4] Extension of these reactions to ketose derivatives should lead to 2,2,5-trisubstituted tetrahydrofurans which have been only scarcely obtained[5,6] by *C*-glycosylation of furanose precursors.

In 1960 Goldschmid and Perlin[7] reported the isolation of crystalline 2,6-anhydro-β-D-fructofuranose (or 2,5-anhydro-α-D-fructopyranose) **1** in 9% yield among the products obtained by thermolysis of sucrose at 180°C. Acidic ethanolysis of **1** gave rapidly ethyl α-D-fructo*furanoside* **2** which slowly anomerized to the β-isomer (Scheme 1). Later on, **1** could be prepared[8,9] in better yields under modified conditions of sucrose thermolysis; chromatography techniques were however required for its isolation. Vacuum pyrolysis of free ketoses gives the corresponding 2,6-anhydrofuranoses in very low yields.[10]



Scheme 1.

Keywords: allylation; bicyclic heterocyclic compounds; thioglycosides; tin and compounds.
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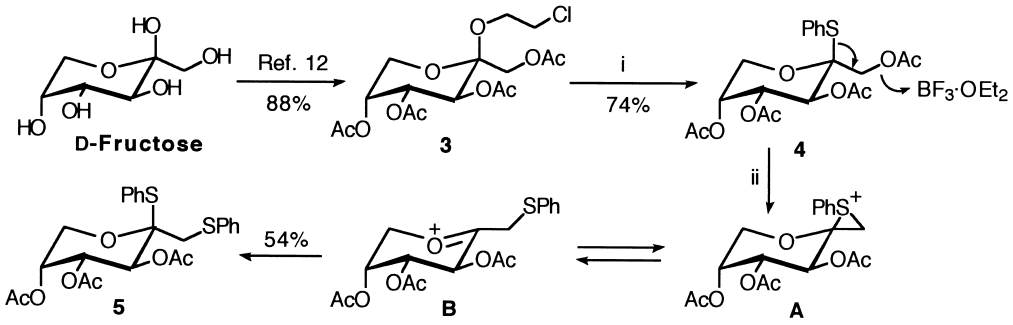
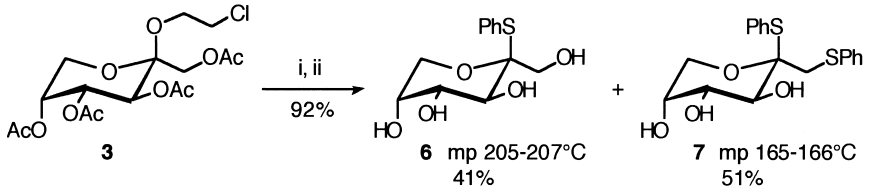


Scheme 2. *Reagents and conditions*: (i) PhSH (1.4 equiv.), $BF_3{\cdot}OEt_2$ (2.9 equiv.), CH_2Cl_2, 0°C→rt, 4 h; (ii) PhSH (1.5 equiv.), $BF_3{\cdot}OEt_2$ (5.4 equiv.), CH_2Cl_2, 0°C→rt, 8 h.



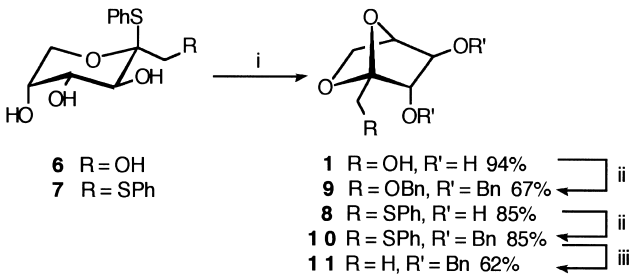
Scheme 3. *Reagents and conditions*: (i) PhSH (3.1 equiv.), $BF_3{\cdot}OEt_2$ (9.1 equiv.), CH_2Cl_2, rt, 14 h; (ii) 5:1:1 MeOH–NEt_3–H_2O, 40°C.

We now report a new access to various [2.2.1] bicyclic acetal derivatives of D-fructose based on the chemistry of 2-thio-β-D-fructopyranosides.

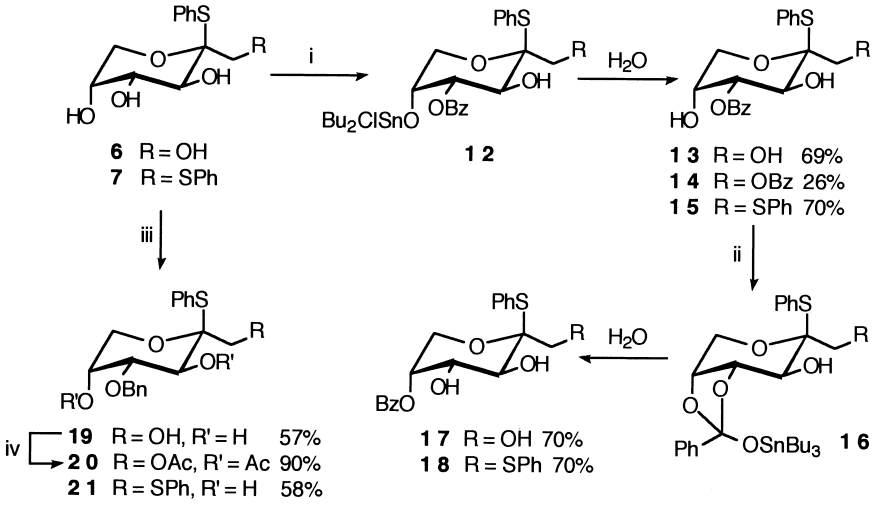
Benzyl 2-thio-β-D-fructopyranoside is the only reported[11] 2-thio-D-fructopyranoside; it was isolated in 10% yield among a mixture of thermodynamically equilibrated glycosides obtained by addition of α-toluenethiol to D-fructose in DMSO at 60°C. We envisaged that crystalline 2′-chloroethyl β-D-fructopyranoside, readily prepared[12,13] from D-fructose in high yield, could be a convenient precursor of 2-thio-D-fructopyranosides, since glycosides of ketoses exhibit a high acid lability due to the easy formation of a tertiary oxycarbenium ion.[12] The standard Ferrier conditions[14] (thiophenol, $BF_3{\cdot}OEt_2$ as a promoter in CH_2Cl_2 at room temperature) allowed indeed the conversion of the acetylated derivative **3** of 2′-chloroethyl β-D-fructopyranoside into the 2-thio-β-D-fructopyranoside **4** in 74% yield. But further treatment of **4** with $BF_3{\cdot}OEt_2$ and thiophenol gave the 1,2-dithio compound **5** in 54% yield together with unreacted **4** (Scheme 2). Migrations of anomeric sulfur atoms have been often reported[15] among 1-thio-aldoglycosides, but only once for an heptulopyranose derivative.[16] In the case of **4**, the addition of a second molecule of thiol occurs exclusively from the β-face delivering compound **5** stabilized by the anomeric effect of the sulfur atom, which implies that a 1,2-episulfonium intermediate A must be in equilibrium with an oxycarbenium ion B.[17]

$^2C_5$ (D) Chair conformations of thioglycosides **4** and **5** were ascertained by the respective values of coupling constant $J_{3,4}$ 10.2 and 9.7 Hz and their β-configuration by the values of $[\alpha]_D$ −200 and −113. For preparative purposes it was found more advantageous to perform the addition of thiophenol (3.1 equiv.) to compound **3** in the presence of a large excess of $BF_3{\cdot}OEt_2$ (9.1 equiv.) and to let the reaction go until a ~1:1 mixture of **4** and **5** with only traces of **3** became apparent on t.l.c. (~14 h); prolonged treatment usually brought extensive decomposition. Deacetylation of the crude mixture of **4** and **5** gave crystalline thioglycosides **6** and **7** which were readily separated by extraction of **6** (41%) in hot water and crystallization of residual **7** (51%) from ethanol (Scheme 3).

Treatment of polyols with $(Bu_3Sn)_2O$ is known[18] to give an equilibrium of partially *O*-stannylated products, which then reacts regioselectively with an electrophile in an inter- or intramolecular reaction. When thioglycosides **6** and **7** were reacted with $(Bu_3Sn)_2O$ (1 mol equiv.) in boiling propionitrile, smooth 2,5-cyclisation occurred to give the bicyclic acetals **1** (94%) and **8** (85%), respectively (Scheme 4). Remarkably, no electrophilic activation of the anomeric sulfur was found to be necessary. The driving force of these unprecedented cyclisations must be the formation of the thermodynamically stable Sn–S bond[19] (Bu_3SnSPh was indeed isolated from reaction mixtures); but the 2,5-*trans* diaxial configuration of reacting oxygen and sulfur atoms and the higher lability of anomeric groups in ketosides are also crucial. A 6-*O*-protected phenyl 1-thio-α-D-galactopyranoside[20] did not undergo cyclisation under the above conditions.



Scheme 4. *Reagents and conditions*: (i) $(Bu_3Sn)_2O$ (1 mol equiv.), EtCN, 4 Å mol. sieves, reflux; (ii) BnBr, NaH, DMF, rt; (iii) Raney Ni, THF, rt.



Scheme 5. *Reagents and conditions*: (i) Bu_2SnO (1.2 equiv.), CH_3CN, 4 Å mol. sieves, reflux, then BzCl (1.5 equiv.), rt; (ii) $(Bu_3Sn)_2O$ (1 mol equiv.), EtCN, 4 Å mol. sieves, reflux; (iii) Bu_2SnO (1.3 equiv.), MeOH, reflux, then concentration, BnBr (1.5 equiv.), CsF (1.3 equiv.), DMF, rt; (iv) Ac_2O, pyridine, rt.

Acetals **1** and **8** were *O*-benzylated to give **9** (67%) and **10** (85%) respectively. Desulfurization of **10** with Raney nickel in THF gave acetal **11** with an angular methyl group in 62% yield (Scheme 4).

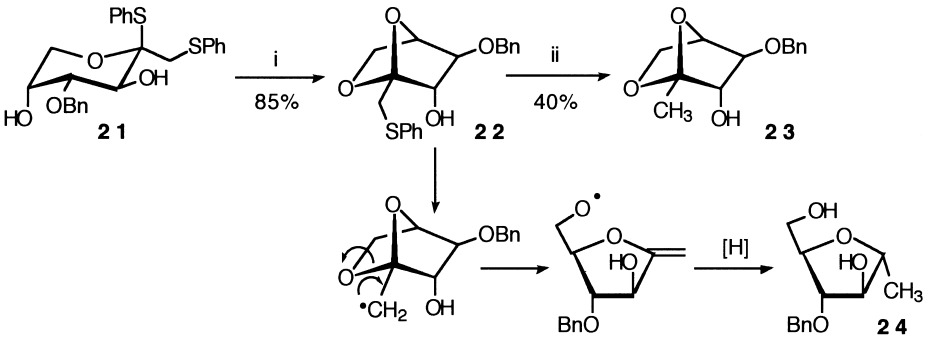
Treatment of thioglycosides **6** and **7** with Bu_2SnO induced no cyclisation; mixtures of dibutylstannanediyl acetals ('stannylene') thus obtained[18] reacted rather with benzoyl chloride preferentially at equatorial O-4 to give respectively **13** (69%) and crystalline **15** (70%), where signals of H-4 at δ 5.24 and 5.42 were largely deshielded by the benzoyl group (Scheme 5). In the case of **6**, a 1,4-di-*O*-benzoyl derivative **14** (26%) was also isolated. The postulated tin derivative **12** obtained by opening of the 4,5-stannylene ring did not undergo cyclisation even after prolonged heating, most probably because the electron-attracting influence of the chlorine atom reduced too much the nucleophilicity of O-5.

Treatment of the 4-*O*-benzoyl compounds **13** and **15** with $(Bu_3Sn)_2O$ induced no cyclisation either, but gave orthoester intermediates **16** which were hydrolyzed regioselectively[21] during work-up to give the 5-*O*-benzoyl isomers **17** (70%) and **18** (70%) respectively, where signals of H-5 at δ 5.31 and 5.49 confirmed the 4⟶5 migration of the benzoyl group (Scheme 5). The absence of migration (and cyclisation as well) in intermediates such as **12** has already been observed[22] in carbohydrates, but does not apply to more flexible systems (phenylethylene glycol).[23]

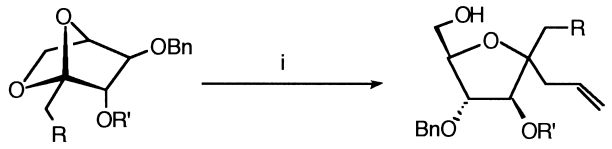
4-*O*-Benzyl derivatives **19** (57%) and **21** (42%) were also obtained by reaction of the stannylene derivatives of **6** and **7** with benzyl bromide in refluxing acetonitrile (Scheme 5); the moderate yields can be attributed to side reactions of the anomeric thiophenyl group leading to sulfonium salts. The yield of **21** could be slightly improved (58%) by performing benzylation of **7** in DMF at room temperature under CsF activation.[24] Conversion of triol **19** into the acetylated derivative **20** allowed to ascertain the location of benzyl group at O-4 (H-4 at δ 3.94), H-3 and H-5 being respectively deshielded at δ 5.66 and 5.41 by acetyl groups.

Thioglycoside **21** underwent cyclisation by treatment with $(Bu_3Sn)_2O$ to give the bicyclic acetal **22** in 85% yield. Raney nickel desulfurization of **22** gave the deoxy compound **23** in modest yield (40%); a side radical elimination led to a tetrahydrofuran intermediate with an *exo* methylene group, which was reduced into 2,5-anhydro-1-deoxy-D-mannitol **24** (Scheme 6).

Its methyl group appeared as a doublet (J=6.6 Hz) at δ 1.30 in ^{1}H NMR spectrum and gave a ^{13}C signal at δ 18.63. A minor product, C-2 epimer of 24 (α–β~9:1), gave corresponding signals at δ_H 1.29 (J=6.4 Hz) and δ_C 13.34. The



Scheme 6. *Reagents and conditions*: (i) $(Bu_3Sn)_2O$ (1 equiv.), EtCN, 4 Å mol. sieves, reflux; (ii) Raney Ni, THF, rt.



9 R = OBn, R' = Bn
11 R = H, R' = Bn
23 R = R' = H

25 R = OBn, R' = Bn 83%, α: β 82:18
26 R = H, R' = Bn 79%, α: β 67:33
27 R = R' = H 85%, α: β 70:30

Scheme 7. *Reagents and conditions*: (i) $Me_3SiCH_2CH{=}CH_2$ (5 equiv.), $Sc(OTf)_3$ (0.1 equiv.), CH_2Cl_2, −30→0°C, then MeOH–AcOH.

D-*manno* configuration (α-methyl) of major **24** could be deduced by the higher value of the ^{13}C signal of its methyl group ($\Delta\delta$ +5.29 ppm), since the ^{13}C chemical shift of the carbon atom attached to the 'anomeric position' of *C*-glycosides and *C*-nucleosides is at higher field when this atom has a *cis*-relationship with the OR-group attached at C-3.[5,25,26]

The reaction of [2.2.1] bicyclic acetals **9**, **11** and **23** with allyltrimethylsilane in the presence of a Lewis acid revealed a total regioselectivity leading exclusively to 2,2,5-trisubstituted tetrahydrofuran derivatives **25**, **26** and **27** respectively (Scheme 7).

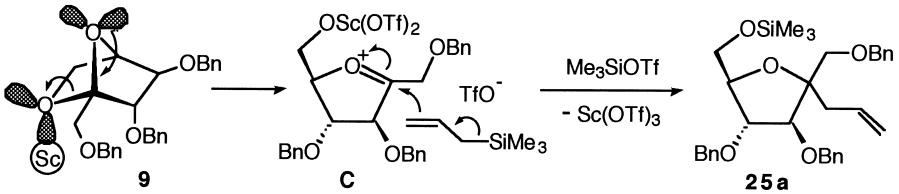
When conducted with TMS triflate as a promoter, allylation of **9** in acetonitrile or CH_2Cl_2 gave **25** in 63% yield (α–β 73:27). Configuration at the 'anomeric center' was ascertained as above for compound **24**; ^{13}C NMR signal of allylic CH_2 appeared at lower field (δ 39.76) in the major α-*C*-allyl glycoside than in the β-isomer (δ 37.61). Yield and stereoselectivity were both increased when catalytic $Sc(OTf)_3$ was used (83%, α–β 82:18). Lanthanide triflates are known to catalyze allylation reactions of carbonyl compounds[27,28] and aldehyde acetals, but not ketone dimethyl acetals.[29] Coordination of the small Sc(III) cation at the more nucleophilic O-6 atom induces formation of the five-membered cyclic oxycarbenium ion C which is preferentially attacked by the nucleophile on its less hindered α-face with concomitant formation of TMS triflate. The Sc alkoxide then reacts with TMS triflate to regenerate $Sc(OTf)_3$ and deliver the 6-*O*-trimethylsilyl derivative **25a** which can be visualized by tlc and is converted to **25** by acid treatment (Scheme 8).

Yamamoto[30] has reported stereoselective reductions of bicyclic acetals by DIBAH or $Et_3SiH–TiCl_4$ in CH_2Cl_2; the total lack of regioselectivity in the case of a [2.2.1] bicyclic acetal is striking and can be probably attributed to the bigger size of Al and Ti Lewis acids when compared to Sc cation. The absence of oxygen substituents precludes any chelation at the opposite of carbohydrate bicyclic acetals; coordination of O-1 and O-3 to Sc in intermediate **C** might contribute to the increase of diastereoisomeric excess when going from TMS triflate to $Sc(OTf)_3$ (de 46 vs 64%).

Acetal **11** reacted with allyltrimethylsilane in the presence of catalytic $Sc(OTf)_3$ to give the tetrahydrofuran compound **26** (79%, α–β 67:33). Diastereoisomers **26**α and **26**β were separated by chromatography and showed optical rotation values $[\alpha]_D$ +49 and +36 respectively. Their five-membered ring structure was ascertained as follows: addition of trichloroacetyl isocyanate ($Cl_3CCONCO$) to ^1H NMR samples induced $\Delta\delta$ +0.7 and +0.5–0.6 ppm shifts of H-6a and H-6b signals due to the formation of a carbamate function at O-6; H-5 underwent only a 0.1 ppm shift, whereas the presence of a carbamate group at O-5 of a six-membered ring isomer would have shifted it more than 1 ppm. ^{13}C NMR signals of the methyl group at δ 21.27 and 23.31 and allylic CH_2 at δ 43.19 and 41.22 in α- and β-products respectively confirmed the attribution of configuration.

Finally, acetal **23** with a free OH-3 group gave under $Sc(OTf)_3$-promoted allylation a 70:30 mixture of α- and β-*C*-allyl furanosides **27** in 85% yield.

In conclusion, the opening reaction of now easily accessible 2,6-anhydro-β-D-fructofuranoses by allyltrimethylsilane in the presence of catalytic $Sc(OTf)_3$ occurs with a total regioselectivity and an acceptable α-stereoselectivity, leading to 2,2,5-trisubstituted tetrahydrofurans in high yield. Other *C*-nucleophiles, such as 2-(trimethylsilyloxy)furan and various silyl enolates, might lead to highly functionalized fragments of natural products. The 2→1 migration of anomeric phenylthio group in D-fructopyranosides can probably be extended to other thiols and PhSeH, offering better opportunities for radical reduction and coupling reactions at C-1.



Scheme 8.

1. Experimental

1.1. General methods

Melting points were determined using a Kofler hot stage apparatus under a Reichert microscope and are uncorrected. Optical rotations were measured at room temperature on a Perkin–Elmer 341 automatic polarimeter (concentration in g/100 mL). NMR spectra were recorded on a Bruker ARX-400 instrument. ^{1}H NMR were obtained at 400.13 MHz (s= singlet, d=doublet, t=triplet, m=multiplet, bd=broad). Assignments were confirmed by homonuclear 2D COSY correlated experiments. ^{13}C NMR were obtained at 100.62 MHz in the proton-decoupled mode. Heteronuclear 2D correlated spectra were recorded in order to assist in carbon resonance assignments. Chemical shifts are given in ppm relative to internal TMS (δ scale) and coupling constants (J) in Hz. Thin layer chromatography (TLC) was performed on Merck DC-Alufolien Kieselgel 60 F_{254} Art. 5554 with detection by UV light and charring with 1:10 H_2SO_4–EtOH. Flash chromatography was performed on Merck Kieselgel 60 (40–63 μm). All solvents were dried and distilled according to standard laboratory procedures. Elemental analyses were performed by the Service de Microanalyse du Centre National de la Recherche Scientifique (Gif-sur-Yvette, France). High resolution mass spectra (HRMS) were obtained by electrospray ionization (ESI) in a positive mode on a MS/MS ZABSpec TOF spectrometer (Micromass) at the Centre Régional de Mesures Physiques de l'Ouest.

1.1.1. Phenyl 1,3,4,5-tetra-*O*-acetyl-2-thio-β-D-fructopyranoside (4). Boron trifluoride etherate (1.78 mL, 14.2 mmol) was added dropwise under stirring to a solution of 2′-chloroethyl 1,3,4,5-tetra-*O*-acetyl-β-D-fructopyranoside **3** (Ref. 12, 2 g, 4.9 mmol) and thiophenol (0.73 mL, 7.1 mmol) in dry CH_2Cl_2 (11 mL) at 0°C under nitrogen. The mixture was stirred at room temperature for 4 h, then diluted with CH_2Cl_2 (20 mL) and washed with saturated aqueous $NaHCO_3$ (25 mL) until neutral. The aqueous phase was extracted with CH_2Cl_2 (30 mL) and the combined organic extracts were dried ($MgSO_4$), then concentrated. The residue was crystallized from ethanol to give **4** (1.09 g, 51%); R_f 0.69 (CH_2Cl_2-Et_2O, 9:1); mp 130–131°C; $[\alpha]_D$ −200 (c 1, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 7.46–7.30 (m, 5H, Ph), 5.77 (d, 1H, $J_{3,4}$=10.2 Hz, H-3), 5.43 (m, 1H, H-5), 5.41 (dd, 1H, $J_{4,5}$=3.3 Hz, H-4), 4.58 (dd, 1H, $J_{5,6a}$=1 Hz, $J_{6a,6b}$=13 Hz, H-6a), 4.35 (d, 1H, $J_{1a,1b}$=12.2 Hz, H-1a), 3.96 (dd, 1H, $J_{5,6b}$=1.8 Hz, H-6b), 3.89 (d, 1H, H-1b), 2.16, 2.10, 2.07 and 2.01 (4 s, 12H, 4 OAc); ^{13}C NMR ($CDCl_3$): δ 170.40, 170.27, 170.07 and 169.48 (4C=O), 135.82 (C quat. arom.), 129.32, 129.18 and 128.07 (5C arom.), 91.31 (C-2), 69.03, 68.89, 66.44, 65.40 and 63.22 (C-1,3,4,5,6), 20.99, 20.81, 20.75 and 20.73 (4 CH_3CO). Anal. Calcd for $C_{20}H_{24}O_9S$: C, 54.54; H, 5.49. Found: C, 54.55; H, 5.48.

The mother liquors were chromatographed on silica gel (CH_2Cl_2–Et_2O, 95:5) to give a further amount of **4** (0.49 g, 23%).

1.1.2. Phenyl 3,4,5-tri-*O*-acetyl-1-deoxy-1-phenylthio-2-thio-β-D-fructopyranoside (5). Boron trifluoride etherate (0.86 mL, 6.8 mmol) was added dropwise under stirring to a solution of **4** (1 g, 2.3 mmol) and thiophenol (0.36 mL, 3.5 mmol) in dry CH_2Cl_2 (10 mL) at 0°C under nitrogen. The mixture was stirred at room temperature for 8 h, further additions of boron trifluoride etherate (2×0.35 mL, 2×2.8 mmol) being made after 2 and 5 h. The solution was worked up as described for the preparation of **4**. The residue was purified by chromatography (CH_2Cl_2–Et_2O, 97:3) to give **5** (0.6 g, 54%) as an amorphous solid; R_f 0.52 (CH_2Cl_2–Et_2O, 95:5); $[\alpha]_D$ −113 (c 1, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 7.40–7.06 (m, 10H, 2Ph), 6.01 (d, 1H, $J_{3,4}$=9.7 Hz, H-3), 5.35–5.32 (m, 2H, H-4,5), 4.42 (d, 1H, $J_{6a,6b}$=13 Hz, H-6a), 3.79 (dd, 1H, $J_{5,6b}$=1.5 Hz, H-6b), 3.32 (d, 1H, $J_{1a,1b}$=13.7 Hz, H-1a), 3.07 (d, 1H, H-1b), 2.10, 2.03 and 1.95 (3 s, 9H, 3 OAc); ^{13}C NMR ($CDCl_3$): δ 170.52, 170.15 and 169.45 (3C=O), 136.78 and 135.98 (2C quat. arom.), 130.15, 129.12, 129.09, 129.05, 129.01, 128.62, 128.26, 126.27 and 125.34 (10C arom.), 93.54 (C-2), 69.48, 68.85 and 68.29 (C-3,4,5), 63.02 (C-6), 42.77 (C-1), 21.07, 20.91 and 20.75 (3 CH_3CO). Anal. Calcd for $C_{24}H_{26}O_7S_2$: C, 58.76; H, 5.34. Found: C, 58.68; H, 5.35.

1.1.3. Phenyl 2-thio-β-D-fructopyranoside (6) and phenyl 1-deoxy-1-phenylthio-2-thio-β-D-fructopyranoside (7). Boron trifluoride etherate (5.6 mL, 44.6 mmol) was added dropwise under stirring to a solution of **3** (2 g, 4.9 mmol) and thiophenol (1.55 mL, 15.2 mmol) in dry CH_2Cl_2 (20 mL). The mixture was stirred for 14 h at room temperature, then worked up as described for the preparation of **4**. A solution of the residue in MeOH–NEt_3–H_2O (5:1:1, 35 mL) was heated for 16 h at 40°C, then concentrated. The resulting solid was extracted several times with hot water, then crystallized from ethanol to give **7** (0.9 g, 51%); R_f 0.50 (CH_2Cl_2-MeOH, 9:1); mp 165–166°C; $[\alpha]_D$ −122 (c 1, MeOH); ^{1}H NMR (CD_3OD): δ 7.51–7.08 (m, 10H, 2Ph), 4.48 (d, 1H, $J_{3,4}$=9.9 Hz, H-3), 4.42 (dd, 1H, $J_{5,6a}$=1.3 Hz, $J_{6a,6b}$=12.5 Hz, H-6a), 3.98 (m, 1H, H-5), 3.88 (dd, 1H, $J_{4,5}$=3.3 Hz, H-4), 3.78 (dd, 1H, $J_{5,6b}$=1.8 Hz, H-6b), 3.58 (d, 1H, $J_{1a,1b}$=13.5 Hz, H-1a), 3.24 (d, 1H, H-1b); ^{13}C NMR (CD_3OD): δ 137.26 (2C quat. arom.), 131.88, 130.31, 129.87, 129.65, 129.60 and 126.71 (10C arom.), 97.34 (C-2), 72.06 (C-4), 70.87 (C-5), 70.45 (C-3), 66.91 (C-6), 42.96 (C-1). Anal. Calcd for $C_{18}H_{20}O_4S_2$: C, 59.32; H, 5.53. Found: C, 59.23; H, 5.54.

The cooled aqueous filtrate was extracted with EtOAc, then concentrated. The residue was crystallized from ethanol to give **6** (0.54 g, 41%); R_f 0.22 (CH_2Cl_2–MeOH, 9:1); mp 205–207°C; $[\alpha]_D$ −277 (c 1, MeOH); ^{1}H NMR (CD_3OD): δ 7.49–7.30 (m, 5H, Ph), 4.47 (dd, 1H, $J_{5,6a}$=1.4 Hz, $J_{6a,6b}$=12.4 Hz, H-6a), 4.28 (d, 1H, $J_{3,4}$=10 Hz, H-3), 3.95 (m, 1H, H-5), 3.88 (dd, 1H, $J_{4,5}$=3.5 Hz, H-4), 3.86 (d, 1H, $J_{1a,1b}$=11.7 Hz, H-1a), 3.80 (dd, 1H, $J_{5,6b}$=1.9 Hz, H-6b), 3.43 (d, 1H, H-1b); ^{13}C NMR (CD_3OD): δ 137.01 (C quat. arom.), 131.67, 129.68 and 129.39 (5C arom.), 96.25 (C-2), 72.02 (C-4), 71.04 (C-5), 69.23 (C-3), 66.60 (C-6), 66.03 (C-1). Anal. Calcd for $C_{12}H_{16}O_5S$: C, 52.93; H, 5.92. Found: C, 52.86; H, 5.94.

1.1.4. 2,6-Anhydro-β-D-fructofuranose (1). A mixture of thioglycoside **6** (0.5 g, 1.8 mmol), $(Bu_3Sn)_2O$ (0.94 mL, 1.8 mmol) and activated 4 Å powdered molecular sieves (2 g) in dry propionitrile (25 mL) was heated at reflux for

20 h under vigorous stirring. The suspension was cooled, then filtered. The filtrate was concentrated and the residue was vigorously stirred for 1 h at room temperature in petroleum ether–H_2O (1:1, 30 mL). The aqueous phase was evaporated under reduced pressure to give **1** (0.28 g, 94%) as an oil; R_f 0.38 (CH_2Cl_2–MeOH, 4:1); $[\alpha]_D$ −110 (*c* 0.5, MeOH); lit.[7] mp 118–119°C, $[\alpha]_D$ −107 (*c* 1, H_2O); ^1H NMR (CD_3OD): δ 4.50 (dd, 1H, $J_{3,5}$=1.6 Hz, $J_{5,6exo}$=3.9 Hz, H-5), 3.84 (dd, 1H, $J_{3,4}$=1.3 Hz, H-3), 3.82 (s, 2H, H-1a,1b), 3.69 (d, 1H, H-4), 3.67 (d, 1H, $J_{6endo,6exo}$=7.1 Hz, H-6*endo*), 3.61 (dd, 1H, H-6*exo*); ^{13}C NMR (CD_3OD): δ 109.23 (C-2), 84.38 (C-3), 82.96 (C-5), 80.11 (C-4), 67.50 (C-6), 59.19 (C-1). Anal. Calcd for $C_6H_{10}O_5$: C, 44.55; H, 6.22. Found: C, 44.20; H, 6.25.

1.1.5. 2,6-Anhydro-1,3,4-tri-*O*-benzyl-β-D-fructofuranose (9). Sodium hydride (60% suspension in oil, 266 mg, 6.65 mmol) was added portionwise to a solution of triol **1** (300 mg, 1.85 mmol) and benzyl bromide (0.8 mL, 6.74 mmol) in dry DMF (3 mL) at 0°C. The mixture was stirred at room temperature for 5 h, then quenched at 0°C with MeOH (2 mL), diluted with ether (35 mL), washed with saturated aqueous NaCl, dried ($MgSO_4$) and concentrated. The residue was purified by chromatography (CH_2Cl_2) to give **9** (534 mg, 67%) as a yellow oil; R_f 0.62 (CH_2Cl_2–Et_2O, 95:5); $[\alpha]_D$ −28 (*c* 1.14, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 7.33–7.22 (m, 15H, 3Ph), 4.67 (dd, 1H, $J_{3,5}$=1.6 Hz, $J_{5,6exo}$=4.2 Hz, H-5), 4.64 and 4.53 (2d, 2H, *J*=12.1 Hz, CH_2Ph), 4.54 and 4.49 (2d, 2H, *J*=12.1 Hz, CH_2Ph), 4.43 and 4.36 (2d, 2H, *J*=12 Hz, CH_2Ph), 3.98 (dd, 1H, $J_{3,4}$=1.3 Hz, H-3), 3.83 (d, 1H, $J_{1a,1b}$=11.7 Hz, H-1a), 3.79 (d, 1H, H-1b), 3.66 (dd, 1H, $J_{6endo,\ 6exo}$=7.1 Hz, H-6*exo*), 3.59 (d, 1H, H-6*endo*), 3.57 (d, 1H, H-4); ^{13}C NMR ($CDCl_3$): δ 137.84, 137.83 and 137.68 (3C quat. arom.), 128.63, 128.55, 128.53, 128.31, 128.10, 128.05, 127.98 and 127.88 (15C arom.), 107.35 (C-2), 86.54, 83.97 and 80.36 (C-3,4,5), 73.79, 72.91 and 71.15 (3 *C*H_2Ph), 66.42 and 66.23 (C-1,6). HRMS *m/z* 473.1932 [$C_{27}H_{28}O_5{\cdot}H_2O$ Na ($M+H_2O+Na^+$) requires 473.19401].

1.1.6. 2,6-Anhydro-1-deoxy-1-phenylthio-β-D-fructofuranose (8). A mixture of thioglycoside **7** (0.21 g, 0.58 mmol), $(Bu_3Sn)_2O$ (0.29 mL, 0.58 mmol) and activated 4 Å powdered molecular sieves (0.5 g) in dry propionitrile (10 mL) was heated at reflux for 5 h under vigorous stirring. The mixture was worked up as described for the preparation of **1** to give **8** (0.124 g, 85%) as an oil; R_f 0.46 (Et_2O–acetone, 4:1); $[\alpha]_D$ −58 (*c* 0.83, MeOH); ^1H NMR (CD_3OD): δ 7.46–7.15 (m, 5H, Ph), 4.50 (dd, 1H, $J_{3,5}$=1.5 Hz, $J_{5,6exo}$=4.1 Hz, H-5), 3.91 (dd, 1H, $J_{3,4}$= 1.3 Hz, H-3), 3.72 (d, 1H, H-4), 3.69 (d, 1H, $J_{6endo,6exo}$= 7.1 Hz, H-6*endo*), 3.64 (dd, 1H, H-6*exo*), 3.45 (d, 1H, $J_{1a,1b}$=14.4 Hz, H-1a), 3.38 (d, 1H, H-1b); ^{13}C NMR (CD_3OD): δ 138.39 (C quat. arom.), 130.17, 129.87 and 127.06 (5C arom.), 108.99 (C-2), 84.97 (C-3), 84.42 (C-5), 80.18 (C-4), 67.92 (C-6), 34.09 (C-1). Anal. Calcd for $C_{12}H_{14}O_4S{\cdot}0.25H_2O$: C, 55.69; H, 5.65. Found: C, 55.69; H, 5.72.

1.1.7. 2,6-Anhydro-3,4-di-*O*-benzyl-1-deoxy-1-phenylthio-β-D-fructofuranose (10). Sodium hydride (60% suspension in oil, 200 mg, 5 mmol) was added portionwise to a solution of diol **8** (575 mg, 2.26 mmol) and benzyl bromide (0.65 mL, 5.43 mmol) in dry DMF (3 mL) at 0°C. The mixture was stirred at room temperature for 1 h, then worked up as described for the preparation of **9**. The residue was purified by chromatography (CH_2Cl_2–Et_2O, 95:5) to give **10** (837 mg, 85%) as an oil; R_f 0.72 (petroleum ether–EtOAc, 1:1); $[\alpha]_D$ −43 (*c* 0.99, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 7.43–7.15 (m, 15H, 3Ph), 4.69 (dd, 1H, $J_{3,5}$=1.6 Hz, $J_{5,6exo}$=4.2 Hz, H-5), 4.51 and 4.42 (2d, 2H, *J*=12 Hz, CH_2Ph), 4.49 and 4.45 (2d, 2H, *J*=12.8 Hz, CH_2Ph), 3.96 (dd, 1H, $J_{3,4}$=1.2 Hz, H-3), 3.75 (dd, 1H, $J_{6endo,6exo}$=7.1 Hz, H-6*exo*), 3.65 (d, 1H, H-6*endo*), 3.61 (d, 1H, H-4), 3.48 (d, 1H, $J_{1a,1b}$=14.4 Hz, H-1a), 3.38 (d, 1H, H-1b); ^{13}C NMR ($CDCl_3$): δ 137.53 and 136.63 (3C quat. arom.), 129.49, 128.94, 128.59, 128.53, 128.12, 128.05, 127.90 and 126.28 (15C arom.), 107.23 (C-2), 88.31 (C-3), 83.89 (C-5), 79.97 (C-4), 72.92 and 71.31 (2 *C*H_2Ph), 66.96 (C-6), 33.82 (C-1). Anal. Calcd for $C_{26}H_{26}O_4S$: C, 71.86; H, 6.03. Found: C, 71.91; H, 6.12.

1.1.8. 2,6-Anhydro-3,4-di-*O*-benzyl-1-deoxy-β-D-fructofuranose (11). Raney nickel (Acros, washed with water, then THF, 550 mg) was added portionwise within 3 h at room temperature to a solution of thioether **10** (150 mg, 0.35 mmol) in dry THF (5 mL). The mixture was filtered and the solid was washed with THF (3×10 mL). The combined filtrates were concentrated and the residue was purified by chromatography (CH_2Cl_2–Et_2O, 95:5) to give **11** (67 mg, 62%) as an oil; R_f 0.54 (petroleum ether–EtOAc, 3:2); $[\alpha]_D$ −35 (*c* 0.94, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 7.39–7.29 (m, 10H, 2Ph), 4.63 (dd, 1H, $J_{3,5}$=1.5 Hz, $J_{5,6exo}$=4.3 Hz, H-5), 4.62 and 4.58 (2d, 2H, *J*=12.2 Hz, CH_2Ph), 4.53 and 4.45 (2d, 2H, *J*=12 Hz, CH_2Ph), 3.70 (dd, 1H, $J_{6endo,6exo}$=7.1 Hz, H-6*exo*), 3.66 (dd, 1H, $J_{3,4}$=1.1 Hz, H-3), 3.59 (d, 1H, H-4), 3.58 (d, 1H, H-6*endo*), 1.59 (s, 3H, CH_3); ^{13}C NMR ($CDCl_3$): δ 137.58 (2C quat. arom.), 128.61, 128.55, 128.14, 128.05 and 127.92 (10C arom.), 106.56 (C-2), 90.01, 84.16 and 79.67 (C-3,4,5), 72.85 and 71.33 (2 *C*H_2Ph), 66.50 (C-6), 16.47 (C-1). Anal. Calcd for $C_{20}H_{22}O_4$: C, 73.60; H, 6.79. Found: C, 73.57; H, 6.79.

1.1.9. Phenyl 4-*O*-benzoyl-2-thio-β-D-fructopyranoside (13) and phenyl 1,4-di-*O*-benzoyl-2-thio-β-D-fructopyranoside (14). A mixture of thioglycoside **6** (200 mg, 0.73 mmol), Bu_2SnO (220 mg, 0.88 mmol) and activated 4 Å powdered molecular sieves (500 mg) in dry acetonitrile (10 mL) was heated at reflux for 5 h under vigorous stirring, then cooled to room temperature under a stream of nitrogen. Benzoyl chloride (128 μL, 1.1 mmol) was added and the mixture was stirred for 2.5 h at room temperature. The solution was filtered, then concentrated and the residue was purified by chromatography (petroleum ether–EtOAc, 1:1) to give first dibenzoate **14** (90 mg, 26%) which crystallized from ethanol; R_f 0.85 (CH_2Cl_2-MeOH, 4:1); mp 180°C; $[\alpha]_D$ −128 (*c* 1.07, $CHCl_3$); ^1H NMR (CD_3OD): δ 8.06 and 7.97 (2d, 4H, *J*=7.2 Hz, C_6H_3H–*o*H–*o*′CO), 7.51–7.28 (m, 11H, Ph), 5.35 (dd, 1H, $J_{3,4}$=10.5 Hz, $J_{4,5}$=3.1 Hz, H-4), 4.73 (d, 1H, H-3), 4.59 (d, 1H, $J_{1a,1b}$=11.6 Hz, H-1a), 4.50 (dd, 1H, $J_{5,6a}$=1 Hz, $J_{6a,6b}$=12.5 Hz, H-6a), 4.31 (d, 1H, H-1b), 4.24 (m, 1H, H-5), 3.78 (dd, 1H, $J_{5,6b}$=1.9 Hz, H-6b); ^{13}C NMR ($CDCl_3$): δ 166.86 and 166.47 (2C=O), 135.93, 133.61 and 133.44 (3C quat. arom.), 129.97, 129.95, 129.54, 129.44,

129.23, 129.17, 128.58, 128.56 and 128.52 (15C arom.), 94.09 (C-2), 73.97, 68.23, 67.33, 66.30 and 65.28 (C-1,3,4,5,6). Anal. Calcd for $C_{26}H_{24}O_7S\cdot0.5H_2O$: C, 63.79; H, 5.15. Found: C, 63.97; H, 5.01.

Then was eluted monobenzoate **13** (192 mg, 69%) as an oil; R_f 0.74 (CH_2Cl_2–MeOH, 4:1); ^{1}H NMR (CD_3OD): δ 8.02 (d, 2H, J=7.2 Hz, C_6H_3H–oH–o'CO), 7.51–7.18 (m, 8H, Ph), 5.24 (dd, 1H, $J_{3,4}$=10.6 Hz, $J_{4,5}$=3.2 Hz, H-4), 4.60 (d, 1H, H-3), 4.47 (dd, 1H, $J_{5,6a}$=1 Hz, $J_{6a,6b}$=12.4 Hz, H-6a), 4.16 (m, 1H, H-5), 3.81 (d, 1H, $J_{1a,1b}$=11.8 Hz, H-1a), 3.72 (dd, 1H, $J_{5,6b}$=1.9 Hz, H-6b), 3.38 (d, 1H, H-1b). HRMS m/z 399.0879 [$C_{19}H_{20}O_6NaS$ ($M+Na^+$) requires 399.08783].

1.1.10. Phenyl 4-*O*-benzoyl-1-deoxy-1-phenylthio-2-thio-β-D-fructopyranoside (15). A mixture of thioglycoside **7** (500 mg, 1.37 mmol), Bu_2SnO (376 mg, 1.51 mmol) and activated 4 Å powdered molecular sieves (2 g) in dry acetonitrile (25 mL) was heated at reflux for 5 h under vigorous stirring, then cooled in an ice-bath under a stream of nitrogen. Benzoyl chloride (160 μL, 1.37 mmol) was added and the mixture was stirred for 16 h at room temperature under nitrogen. The solution was filtered, then concentrated and the residue was purified by chromatography (petroleum ether–EtOAc, 7:3) to give **15** (450 mg, 70%) which crystallized from ethanol; R_f 0.80 (EtOAc–petroleum ether, 3:2); mp 170.5°C; $[\alpha]_D$ −87 (c 0.82, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 8.10 (d, 2H, J=7.1 Hz, C_6H_3H–oH–o'CO), 7.61–7.12 (m, 13H, Ph), 5.42 (dd, 1H, $J_{3,4}$=10.4 Hz, $J_{4,5}$=3.1 Hz, H-4), 4.90 (dd, 1H, $J_{3,OH}$=5 Hz, H-3), 4.59 (dd, 1H, $J_{5,6a}$=1 Hz, $J_{6a,6b}$=12.4 Hz, H-6a), 4.31 (m, 1H, H-5), 3.94 (dd, 1H, $J_{5,6b}$=2.1 Hz, H-6b), 3.60 (d, 1H, $J_{1a,1b}$=13.9 Hz, H-1a), 3.37 (d, 1H, H-1b), 2.57 (d, 1H, OH-3), 2.34 (bd, 1H, OH-5); ^{13}C NMR ($CDCl_3$): δ 166.70 (C=O), 136.79, 136.13 and 133.64 (3C quat. arom.), 130.00, 129.49, 129.42, 129.15, 129.10, 128.96, 128.91, 128.59 and 126.25 (15C arom.), 95.91 (C-2), 74.70, 68.28, 68.27 and 65.36 (C-3,4,5,6), 42.25 (C-1). Anal. Calcd for $C_{25}H_{24}O_5S_2\cdot0.25H_2O$: C, 63.47; H, 5.22. Found: C, 63.51; H, 5.21.

1.1.11. Phenyl 5-*O*-benzoyl-2-thio-β-D-fructopyranoside (17). A mixture of the 4-*O*-benzoyl compound **13** (50 mg, 0.13 mmol), $(Bu_3Sn)_2O$ (71 μL, 0.13 mmol) and activated 4 Å powdered molecular sieves (200 mg) in dry propionitrile (4 mL) was heated at reflux for 2.5 h under vigorous stirring, then cooled, filtered and concentrated. The residue was purified by chromatography (EtOAc–petroleum ether, 7:3) to give **17** (35 mg, 70%) as an oil; R_f 0.48 (EtOAc–petroleum ether, 7:3); ^{1}H NMR (CD_3OD): δ 7.97 (d, 2H, J=7.2 Hz, C_6H_3H–oH–o'CO), 7.48–7.15 (m, 8H, Ph), 5.31 (m, 1H, H-5), 4.44 (dd, 1H, $J_{5,6a}$=1 Hz, $J_{6a,6b}$=12.5 Hz, H-6a), 4.42 (d, 1H, $J_{3,4}$=10.1 Hz, H-3), 4.05 (dd, 1H, $J_{4,5}$=3.4 Hz, H-4), 3.83 (dd, 1H, $J_{5,6b}$=1.9 Hz, H-6b), 3.80 (d, 1H, $J_{1a,1b}$=11.9 Hz, H-1a), 3.35 (d, 1H, H-1b); ^{13}C NMR (CD_3OD): δ 167.65 (C=O), 137.14 and 134.23 (2C quat. arom.), 131.62, 131.53, 130.89, 130.69, 129.72, 129.46, 129.43 and 129.36 (10C arom.), 96.33 (C-2), 74.15, 70.52, 69.37, 65.57 and 64.24 (C-1,3,4,5,6). HRMS m/z 399.0877 [$C_{19}H_{20}O_6NaS$ ($M+Na^+$) requires 399.08783].

1.1.12. Phenyl 5-*O*-benzoyl-1-deoxy-1-phenylthio-2-thio-β-D-fructopyranoside (18). A mixture of the 4-*O*-benzoyl compound **15** (50 mg, 0.11 mmol), $(Bu_3Sn)_2O$ (54 μL, 0.11 mmol) and activated 4 Å powdered molecular sieves (200 mg) in dry propionitrile (5 mL) was heated at reflux for 35 min under vigorous stirring, then cooled, filtered and concentrated. The residue was purified by chromatography (petroleum ether–EtOAc, 3:2) to give **18** (35 mg, 70%) as an oil; R_f 0.34 (petroleum ether–EtOAc, 3:2); ^{1}H NMR ($CDCl_3$): δ 8.15 (d, 2H, J=7.2 Hz, C_6H_3H–oH–o'CO), 7.58–7.04 (m, 13H, Ph), 5.49 (m, 1H, H-5), 4.73 (d, 1H, $J_{3,4}$=9.9 Hz, H-3), 4.52 (d, 1H, $J_{6a,6b}$=12.9 Hz, H-6a), 4.22 (dd, 1H, $J_{4,5}$=2.9 Hz, H-4), 4.02 (dd, 1H, $J_{5,6b}$=1 Hz, H-6b), 3.62 (d, 1H, $J_{1a,1b}$=13.9 Hz, H-1a), 3.34 (d, 1H, H-1b), 3.00 (m, 2H, 2 OH); ^{13}C NMR ($CDCl_3$): δ 166.53 (C=O), 136.86, 135.95 and 133.47 (3C quat. arom.), 130.08, 129.71, 129.36, 129.27, 129.08, 128.95, 128.87, 128.52 and 126.16 (15C arom.), 95.12 (C-2), 71.85, 70.48, 70.19 and 63.41 (C-3,4,5,6), 42.00 (C-1).

1.1.13. Phenyl 1,3,5-tri-*O*-acetyl-4-*O*-benzyl-2-thio-β-D-fructopyranoside (20). A mixture of thioglycoside **6** (200 mg, 0.73 mmol), Bu_2SnO (220 mg, 0.88 mmol) and activated 4 Å powdered molecular sieves (500 mg) in dry acetonitrile (10 mL) was heated at reflux for 5 h under vigorous stirring, then cooled to room temperature under a stream of nitrogen. Benzyl bromide (105 μL, 0.88 mmol) and tetrabutylammonium iodide (271 mg, 0.73 mmol) were added and the mixture was again heated at reflux for 17 h under stirring, then cooled, filtered and concentrated. The residue was purified by chromatography (petroleum ether, then EtOAc–petroleum ether, 3:2) to give **19** (153 mg, 57%) as an oil; R_f 0.54 (EtOAc).

Acetic anhydride (1 mL) was added to a solution of compound **19** (153 mg, 0.42 mmol) in dry pyridine (3 mL). The solution was left for 16 h at room temperature, then quenched at 0°C with MeOH (0.5 mL) and concentrated. The residue was purified by chromatography (petroleum ether–EtOAc, 4:1) to give **20** (186 mg, 90%) as an oil; $[\alpha]_D$ −109 (c 1.1, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 7.39–7.19 (m, 10H, 2Ph), 5.66 (d, 1H, $J_{3,4}$=10.3 Hz, H-3), 5.41 (ddd, 1H, H-5), 4.63 and 4.43 (2d, 2H, J=12 Hz, CH_2Ph), 4.42 (dd, 1H, $J_{5,6a}$=1.3 Hz, $J_{6a,6b}$= 13 Hz, H-6a), 4.28 (d, 1H, $J_{1a,1b}$=12.1 Hz, H-1a), 3.94 (dd, 1H, $J_{4,5}$=3.5 Hz, H-4), 3.92 (dd, 1H, $J_{5,6b}$=2.1 Hz, H-6b), 3.77 (d, 1H, H-1b), 2.09, 2.01 and 1.99 (3 s, 9H, 3 OAc); ^{13}C NMR ($CDCl_3$): δ 170.32, 170.30 and 169.29 (3C=O), 137.32 and 135.47 (2C quat. arom.), 128.95, 128.89, 128.27, 128.15, 127.69 and 127.39 (10C arom.), 91.25 (C-2), 74.23 (C-4), 71.47 (CH_2Ph), 67.71 and 67.61 (C-3,5), 65.26 and 63.26 (C-1,6), 20.91, 20.68 and 20.54 (3 CH_3CO). HRMS m/z: 511.1407 [$C_{25}H_{28}O_8NaS$ ($M+Na^+$) requires 511.14026].

1.1.14. Phenyl 4-*O*-benzyl-1-deoxy-1-phenylthio-2-thio-β-D-fructopyranoside (21). A mixture of thioglycoside **7** (4 g, 11 mmol) and Bu_2SnO (3.55 g, 14.3 mmol) in methanol (80 mL) was heated at reflux for 4 h under vigorous stirring, then cooled and concentrated. The residue was dried under good vacuum to eliminate traces of methanol, then dissolved in DMF (30 mL). Benzyl bromide (2 mL, 16.7 mmol) and CsF (2.17 g, 14.3 mmol) were added and the mixture was stirred at room temperature for 17 h, then diluted with CH_2Cl_2 (80 mL). The solution was

washed with 1 M aqueous KF (100 mL), then water (100 mL), dried ($MgSO_4$) and concentrated. The residue was purified by chromatography (CH_2Cl_2-MeOH, 99.5:0.5) to give **21** (2.88 g, 58%) which crystallized from ethanol; R_f 0.80 (EtOAc–petroleum ether, 3:2); mp 172°C; $[\alpha]_D$ −52 (*c* 1.01, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 7.49–7.10 (m, 15H, 3Ph), 4.76 and 4.68 (2d, 2H, J=11.5 Hz, C*H*$_2$ Ph), 4.64 (dd, 1H, $J_{3,4}$=9.8 Hz, $J_{3,OH}$=3.1 Hz, H-3), 4.40 (dd, 1H, $J_{5,6a}$=1.1 Hz, $J_{6a,6b}$=12.6 Hz, H-6a), 4.13 (m, 1H, H-5), 3.97 (dd, 1H, $J_{5,6b}$=1.8 Hz, H-6b), 3.84 (dd, 1H, $J_{4,5}$=3.2 Hz, H-4), 3.58 (d, 1H, $J_{1a,1b}$=13.8 Hz, H-1a), 3.32 (d, 1H, H-1b), 2.58 (d, 1H, OH-3), 2.47 (bd, 1H, OH-5); ^{13}C NMR ($CDCl_3$): δ 137.63, 137.07 and 135.94 (3C quat. arom.), 129.67, 129.60, 129.14, 128.92, 128.90, 128.46, 128.14 and 126.19 (15C arom.), 95.09 (C-2), 78.97 (C-4), 72.10, 69.02, 66.71 and 64.99 (C-3,5,6, *C*H_2Ph), 42.39 (C-1). Anal. Calcd for $C_{25}H_{26}O_4S_2$: C, 66.05; H, 5.76. Found: C, 66.15; H, 5.77.

1.1.15. 2,6-Anhydro-4-*O*-benzyl-1-deoxy-1-phenylthio-β-D-fructofuranose (22). A mixture of thioglycoside **21** (455 mg, 1 mmol), $(Bu_3Sn)_2O$ (0.5 mL, 1 mmol) and activated 4 Å powdered molecular sieves (1 g) in dry propionitrile (20 mL) was heated at reflux for 5 h under vigorous stirring, then cooled, filtered and concentrated. The residue was purified by chromatography (petroleum ether, then petroleum ether–EtOAc, 7:3) to give **22** (293 mg, 85%) as an oil; R_f 0.40 (CH_2Cl_2–Et_2O, 95:5); ^1H NMR ($CDCl_3$): δ 7.44–7.16 (m, 10H, 2Ph), 4.68 (dd, 1H, $J_{3,5}$=1.4 Hz, $J_{5,6exo}$=4 Hz, H-5), 4.63 and 4.52 (2d, 2H, J=12 Hz, C*H*$_2$Ph), 4.06 (ddd, 1H, H-3), 3.72 (dd, 1H, $J_{6endo,6exo}$=7.3 Hz, H-6*exo*), 3.62 (d, 1H, H-6*endo*), 3.52 (d, 1H, $J_{3,4}$=1 Hz, H-4), 3.49 (d, 1H, $J_{1a,1b}$=14.4 Hz, H-1a), 3.42 (d, 1H, H-1b), 2.35 (d, 1H, $J_{3,OH}$=10 Hz, OH-3); ^{13}C NMR ($CDCl_3$): δ 137.40 and 136.27 (2C quat. arom.), 129.85, 129.12, 128.69, 128.12 and 126.67 (10C arom.), 107.70 (C-2), 85.87, 82.04 and 80.90 (C-3,4,5), 70.82 (*C*H_2Ph), 67.36 (C-6), 33.74 (C-1). HRMS *m/z* 367.0981 [$C_{19}H_{20}O_4NaS$ ($M+Na^+$) requires 367.09800].

1.1.16. 1-(1,3,4-Tri-*O*-benzyl-D-fructofuranosyl)-prop-2-ene (25). TMSOTf (135 μL, 0.75 mmol) was added to a solution of acetal 9 (300 mg, 0.69 mmol) and allyltrimethylsilane (0.57 mL, 3.57 mmol) in dry acetonitrile (5 mL) at −30°C under nitrogen. The mixture was allowed to warm to 0°C, then stirred for 1.5 h at 0°C, diluted with CH_2Cl_2 and washed with saturated aqueous $NaHCO_3$ until neutral. The organic phase was dried ($MgSO_4$) and concentrated. The residue was purified by chromatography (petroleum ether–EtOAc, 4:1) to give a non separable 73:27 mixture of **25**α and **25**β (209 mg, 63%) as an oil; R_f 0.42 (CH_2Cl_2–Et_2O, 95:5); ^1H NMR ($CDCl_3$): δ 7.38–7.26 (m, 15H, 3Ph), 5.93 (m, 0.27H, C*H*═), 5.79 (m, 0.73H, C*H*═), 5.14–5.06 (m, 0.54H, CH_2═), 5.10 (dd, 0.73H, ^2J=2.2 Hz, ^3J=10.2 Hz, C*Ha*Hb═), 5.03 (dd, 0.73H, ^3J=17.1 Hz, CHa*Hb*═), 4.70–4.53 (m, 6H, 3CH_2Ph), 4.39 (dd, 0.73H, $J_{3,4}$=5.5 Hz, $J_{4,5}$=6.7 Hz, H-4), 4.19 (d, 0.27H, $J_{3,4}$=4.8 Hz, H-3), 4.12 (dd, 0.27H, $J_{4,5}$=6.6 Hz, H-4), 4.07 (d, 0.73H, H-3), 4.00–3.94 (m, 1H, H-5), 3.86–3.78 (m, 1H, H-6a), 3.65–3.58 (m, 1H, H-6b), 3.57 (d, 0.73H, $J_{1a,1b}$=9.7 Hz, H-1a), 3.48 (d, 0.73H, H-1b), 3.46 (s, 0.54H, H-1a,1b), 2.88 (m, 0.73H, OH-6), 2.57–2.32 (m, 2H, CH_2CH═), 2.05 (m, 0.27H, OH-6); ^{13}C NMR ($CDCl_3$, bold for **25**α): δ **138.27**, 138.11, **138.09**, 138.07 and **137.91** (3C quat. arom.), 134.56 and **133.11** (*C*H═), 128.69–127.76 (15C arom.), **118.98** and 118.46 (*C*H_2═), **86.42** and 86.29 (C-4), 84.62 and **84.29** (C-2), 83.38 and **83.02** (C-5), **81.49** and 80.86 (C-3), **73.71**, 73.62, **72.90**, **72.73**, 72.65, 72.63, 72.54 and **72.13** (C-1, *C*H_2Ph), 65.44 and **62.89** (C-6), **39.76** and 37.61 (*C*H_2CH═). Anal. Calcd for $C_{30}H_{34}O_5 \cdot H_2O$: C, 73.15; H, 7.37. Found: C, 73.25; H, 7.16.

1.1.17. 1-(3,4-Di-*O*-benzyl-1-deoxy-α-D-fructofuranosyl)-prop-2-ene (26α) and 1-(3,4-di-*O*-benzyl-1-deoxy-β-D-fructofuranosyl)-prop-2-ene (26β). $Sc(OTf)_3$ (23 mg, 47 μmol) was added to a solution of acetal **11** (175 mg, 0.54 mg) and allyltrimethylsilane (0.44 mL, 2.7 mmol) in dry CH_2Cl_2 (4 mL) at −30°C under nitrogen. The mixture was allowed to warm to 0°C, then stirred for 3 h 40 at 0°C, diluted with CH_2Cl_2, washed with water, dried ($MgSO_4$) and concentrated. The residue was dissolved in 4:1 MeOH–AcOH (5 mL) and the solution was left at room temperature for 4 h, then concentrated. The residue was purified by chromatography (CH_2Cl_2-Et_2O, 95:5) to give a 67:33 mixture of **26**α and **26**β (156 mg, 79%). Further chromatography gave first **26**β (25 mg, 13%) as an oil; R_f 0.69 (CH_2Cl_2–Et_2O, 7:3); $[\alpha]_D$+36 (*c* 1, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 7.39–7.29 (m, 10H, 2Ph), 5.85 (m, 1H, C*H*═), 5.11 and 5.10 (2m, 2H, CH_2═), 4.62 and 4.56 (2d, 2H, J=11.7 Hz, CH_2Ph), 4.61 and 4.48 (2d, 2H, J=11.5 Hz, CH_2Ph), 4.08 (m, 2H, H-4,5), 3.78 (m, 2H, H-3,6a), 3.68 (m, 1H, H-6b), 2.45 (m, 2H, CH_2CH═), 1.98 (bd, 1H, OH-6), 1.33 (s, 3H, CH_3); ^1H NMR ($CDCl_3$+$Cl_3CCONCO$): δ 8.45 (s, 1H, NH), 7.37–7.30 (m, 10H, 2Ph), 5.80 (m, 1H, C*H*═), 5.09 and 5.08 (2m, 2H, ^2J=2.2 Hz, ^3J=9.7 and 17 Hz, CH_2═), 4.61 and 4.55 (2d, 2H, J=11.8 Hz, CH_2Ph), 4.57 and 4.51 (2d, 2H, J=11.6 Hz, CH_2Ph), 4.46 (m, 1H, H-6a), 4.20 (m, 1H, H-5), 4.18 (dd, 1H, $J_{5,6b}$=6.7 Hz, $J_{6a,6b}$=11.4 Hz, H-6b), 3.91 (dd, 1H, $J_{3,4}$=2.7 Hz, $J_{4,5}$=4.5 Hz, H-4), 3.77 (d, 1H, H-3), 2.43 (m, 2H, CH_2CH═), 1.31 (s, 3H, CH_3); ^{13}C NMR ($CDCl_3$): δ 137.88 and 137.73 (2C quat. arom.), 134.60 (*C*H═), 128.59, 128.52, 127.97, 127.90, 127.78, 127.72 and 127.65 (10C arom.), 118.07 (*C*H_2═), 88.14 (C-3), 84.24 (C-2), 83.88 and 81.92 (C-4,5), 72.38 and 71.88 (2 *C*H_2Ph), 63.19 (C-6), 41.22 (*C*H_2CH═), 23.31 (*C*H_3). HRMS *m/z* 391.1891 [$C_{23}H_{28}O_4Na$ ($M+Na^+$) requires 391.18853].

Then were eluted a mixture of **26**α and **26**β (68 mg, 34%) and finally pure **26**α (62 mg, 31%) as an oil; R_f 0.62 (CH_2Cl_2-Et_2O, 7:3); $[\alpha]_D$ +49 (*c* 1.08, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 7.38–7.29 (m, 10H, 2Ph), 5.82 (m, 1H, C*H*═), 5.12 and 5.07 (2m, 2H, ^2J=2, ^3J=10.2 and 17.2 Hz, CH_2═), 4.61–4.51 (m, 4H, 2CH_2Ph), 4.09 (dd, 1H, $J_{3,4}$=3.4 Hz, $J_{4,5}$=5.7 Hz, H-4), 3.99 (ddd, 1H, H-5), 3.85 (d, 1H, H-3), 3.78 (dd, 1H, $J_{5,6a}$=3 Hz, $J_{6a,6b}$= 11.8 Hz, H-6a), 3.61 (dd, 1H, $J_{5,6b}$=4.1 Hz, H-6b), 2.45 and 2.38 (2 dd, 2H, ^2J=13.9, ^3J=6.9 and 7.6 Hz, CH_2CH═), 1.95 (bd, 1H, OH-6), 1.29 (s, 3H, CH_3); ^1H NMR ($CDCl_3$+$Cl_3CCONCO$): δ 8.45 (s, 1H, NH), 7.38–7.28 (m, 10H, 2Ph), 5.79 (m, 1H, C*H*═), 5.11 and 5.05 (2m, 2H, ^2J=2.1, ^3J=10.2 and 17 Hz, CH_2═), 4.60 and 4.53 (2d, 2H, J=11.7 Hz, CH_2Ph), 4.57 and 4.53 (2d, 2H, J=12.2 Hz, CH_2Ph), 4.46 (dd, 1H, $J_{5,6a}$=3.1 Hz, $J_{6a,6b}$=11.3 Hz, H-6a), 4.18 (dd, 1H, $J_{5,6b}$=6.4 Hz, H-6b), 4.11 (ddd, 1H, $J_{4,5}$=5.7 Hz, H-5), 3.94 (dd, 1H, H-4), 3.87 (d, 1H, H-3),

2.40 (m, 2H, CH_2CH═), 1.28 (s, 3H, CH_3); ^{13}C NMR ($CDCl_3$): δ 138.00 and 137.92 (2C quat. arom.), 133.69 (*C*H═), 128.57, 128.50, 127.95, 127.85, 127.72 and 127.66 (10C arom.), 118.54 (*C*H_2═), 86.68 (C-3), 84.32 (C-4), 84.31 (C-2), 81.15 (C-5), 72.51 and 72.02 (2 *C*H_2Ph), 63.02 (C-6), 43.19 (*C*H_2CH═), 21.27 (*C*H_3). HRMS *m/z* 391.1886 [$C_{23}H_{28}O_4Na$ ($M+Na^+$) requires 391.18853].

1.1.18. 1-(4-*O*-Benzyl-1-deoxy-D-fructofuranosyl)-prop-2-ene (27). Raney nickel (4.8 g) was added portionwise within 6 h at room temperature to a solution of thioether **22** (1.65 g, 4.8 mmol) in dry THF (25 mL). The mixture was filtered and the solid washed with THF. The combined filtrates were concentrated and the residue was purified by chromatography (petroleum ether–EtOAc, 1:1) to give **23** (452 mg, 40%) as an oil; R_f 0.64 (EtOAc–petroleum ether, 4:1). Further elution with 7:3 EtOAc–petroleum ether gave **24**β (R_f 0.42) and **24**α (R_f 0.32).

$Sc(OTf)_3$ (31 mg, 63 μmol) was added to a solution of **23** (100 mg, 0.42 mmol) and allyltrimethylsilane (0.35 mL, 2.2 mmol) in dry CH_2Cl_2 (4 mL) at -30°C under nitrogen. The mixture was allowed to warm to 0°C within 2.5 h, then worked up as described for the preparation of **26**. The residue was purified by chromatography (CH_2Cl_2-Et_2O, 4:1) to give a 70:30 mixture (100 mg, 85%) of **27**α (R_f 0.28) and **27**β (R_f 0.40); ^{1}H NMR ($CDCl_3$): δ 7.39–7.28 (m, 5H, Ph), 5.94–5.76 (m, 1H, C*H*═), 5.18–5.06 (m, 2H, CH_2═), 4.75–4.54 (m, 2H, CH_2Ph), 4.09–3.94 (m, 3H, H-3,4,5), 3.84–3.79 (m, 1H, H-6a), 3.63–3.59 (m, 1H, H-6b), 2.70–2.32 (m, 4H, CH_2CH═, 2 OH), 1.32 (s, 2.1H, CH_3), 1.24 (s, 0.9H, CH_3); ^{13}C NMR ($CDCl_3$, bold for **27**α): δ 137.90 (C quat. arom.), 134.55 and **133.85** (*C*H═), 128.59, 128.58, 127.96, 127.94, 127.69 and 127.67 (5C arom.), **118.42** and 118.18 (*C*H_2═), 87.86, **87.31**, 85.68, **85.51**, 82.27, **81.64**, 79.44 and **78.74** (C-2,3,4,5), **72.46** and 72.29 (*C*H_2Ph), **42.43** and 41.24 (*C*H_2CH═), 22.19 and **20.50** (*C*H_3).

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