Interglycosidic Acetals IV.[1] Preparation and Regioselective Cleavage of Phenyl 2,2′ : 4,6 : 4′,6′-Tri-*O*-benzylidene-1-thio-β-laminaribiosides

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A (+)-10-Camphorsulfonic acid-catalysed acetal exchange reaction of phenyl 1-thio-β-laminaribioside using 3.5 molar equivalents of α,α-dimethoxytoluene gave a tris(benzylidene acetal), which was isolated and characterized as phenyl 3′-*O*-acetyl-2,2′ : 4,6 : 4′,6′-tri-*O*-benzylidene-1-thio-β-laminaribioside, and the corresponding 3′-*O*-benzyl derivative **6**. Upon a treatment with pyridinium *p*-toluenesulfonate, the interglycosidic 2,2′-acetal in **6** underwent selective cleavage to give the 2,2′-diol. Additionally, a reductive ring-opening reaction of **6** with lithium aluminium hydride/anhydrous aluminium chloride, followed by *O*-acetylation, gave the 2,6,6′-*O*-acetyl-4,2′,3′,4′-tetra-*O*-benzyl derivative in 73% yield. A different regioselectivity was observed in the reduction of **6** with borane-trimethylamine adduct/anhydrous aluminium chloride or sodium cyanotrihydroborate/methanesulfonic acid, giving the corresponding 2,4,4′-triol as the major product.

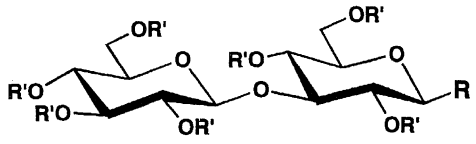
Acid-catalyzed acetalizations with alkenyl ether or 1,1-dialkoxyalkane have been widely used in carbohydrate chemistry to give cyclic acetals bearing five- or six-membered rings.[2] We have recently reported that a 3,2′-eight-membered interglycosidic benzylidene acetal of maltooligosaccharides can be obtained in moderately good yields under carefully controlled conditions.[1,3] Similar products were previously isolated in relatively low yields by the acetonation of disaccharides with methyl isopropenyl ether,[4] or 2,2-dimethoxypropane,[5] and benzylidenation with benzylidene bromide.[6]

In our previous studies on laminaribiose, 3-*O*-(β-D-glucopyranosyl)-D-glucopyranose, which is prepared by the chemical and enzymatic partial degradation of β(1→3)-glucan, such as curdlan[7] or pachyman,[8] we reported a short-cut for synthesizing several biologically important oligosaccharides with a β(1→3) glycosidic linkage.[7,9] However, recognizing the difficulty in discriminating the two D-glucopyranose residues and in converting regioselectively the hydroxyl groups into other functional groups, we sought to overcome the problems by investigating the formation and chemical behaviors of a similar interglycosidic benzylidene derivative of laminaribiose. In this paper, we report on the results of trimolar benzylidenation of laminaribioside as well as on a structure determination of the products and their chemical behavior.

Results and Discussion

Phenyl 2,4,6,2′,3′,4′,6′-hepta-*O*-acetyl-1-thio-β-laminaribioside (**2**) was chosen as the starting material for these studies because thioglycosides are stable under various chemical transformations and can be activated as glycosyl donors in the glycosidation reactions. Compound **2** was synthesized from fully acetylated β-laminaribiose[10] **1** by Lewis acid-catalyzed thioglycosidation using (phenylthio)-trimethylsilane/zinc(II) iodide[11] or benzene thiol/zirconium(IV) chloride[12] in 78 and 64% yields, respectively. Compound **1** was treated with methanolic sodium methoxide to give a quantitative yield of unprotected 1-thioglycoside (**3**), which was used for the next benzylidenation without further purification (Chart 1).

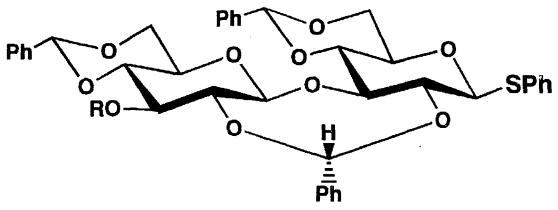
The acetal exchange reaction of **3** was examined under modified Evans' conditions[13] using α,α-dimethoxytoluene as the reagent. The treatment of **3** with 3.5 molar equivalents of the reagent and (+)-10-camphorsulfonic acid in *N*,*N*-dimethylformamide (DMF) showed the presence of one major product upon a TLC analysis of the reaction mixture. Although the product was characterized as tris(benzylidene acetal) **4** by ^{1}H NMR spectroscopy, attempts to purify **4** by chromatography on silica gel failed because of its poor solubility in toluene, hexane, and chlorform. In order to isolate the product, the reaction mixture was directly treated with acetic anhydride/pyridine, and then subjected to column chromatography on silica gel using toluene–ethyl acetate–pyridine as the eluant. The yield of the monoacetylated tri-*O*-benzylidene derivative **5** was 48%. The low yield of the acetate **5** was probably due to decomposition of the acid labile benzylidene group by a trace of acetic acid contaminated during the work-up and chromatographic procedure. On the other hand, a treatment of the reaction mixture containing **4** with sodium hydride/benzyl bromide gave the mono *O*-ben-



1: R = OAc, R' = Ac

2: R = SPh, R' = Ac

3: R = SPh, R' = H

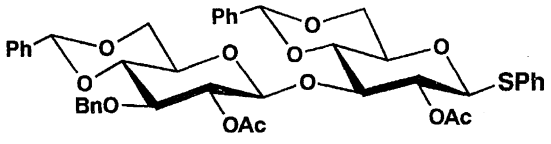


4: R = H

5: R = Ac

6: R = Bn

Chart 1.



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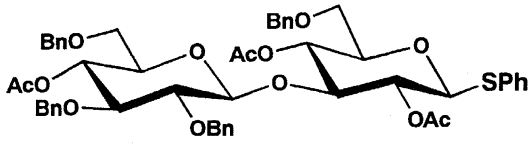

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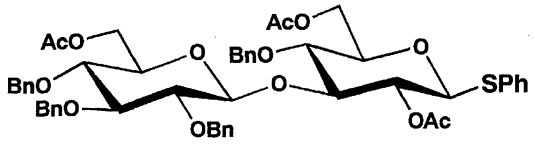

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Chart 2.

zyl derivative **6** in 64% yield. The protection of the hydroxyl group in **4** with alkyl groups seemed to be better than that with acyl groups.

The structure of isolated benzylidene acetals was elucidated mainly on the basis of ^{1}H NMR spectroscopy. In the NMR spectrum of **5**, three one-proton singlets (δ = 5.49, 5.60, and 5.69) and a one-proton triplet (δ = 5.45) were observed. The latter was assigned to H-3′ by COSY experiments, suggesting that an acetyl group was located at this position. Therefore, the structure of **5** was determined to be phenyl 3-*O*-acetyl-2,2′ : 4,6 : 4′,6′-tri-*O*-benzylidene-1-thio-β-laminaribioside (**5**). Further studies on the stereochemistry of the tris(benzylidene acetal) were carried out using the corresponding 3′-*O*-benzyl derivative **6**. A complete assignment of the ring protons of both D-glucopyranose moieties was achieved by a two-dimensional (2D) HOHAHA experiment. The large vicinal coupling constants of the ring protons revealed that both D-glucopyranosyl residues adopt the $^4C_1$ conformation. Moreover, cross-peaks between one of the methine protons (δ = 5.71) and both of the H-2 (δ = 3.60 and 3.72) protons were observed in the NOESY spectrum, suggesting that these three protons were oriented in the same direction as the eight-membered ring, i.e., the configuration of the acetalic methine carbon of the 2,2′-*O*-benzylidene group in **6** was elucidated as R. Furthermore, an n.O.e. cross-peak was also observed between H-3 and H-1′. Thus, the structure of the major product **4** was 2,2′ : 2,2′ : 4′,6′-tri-*O*-benzylidene-1-thio-β-laminaribioside.

We next focused our attention on the selective cleavage of the benzylidene acetals in **6**. First, the tris(benzylidene acetal) **6** was treated with pyridinium *p*-toluenesulfonate (PPTS) in chloroform–methanol at room temperature for 10 h. The interglycosidic benzylidene acetal in **6** was found to undergo selective hydrolysis to give the 2,2′-unprotected derivative, which was directly acetylated with acetic anhydride-pyridine. The 2,2′-diacetate (**7**) was isolated by silica-gel column chromatography in 68% overall yield (Chart 2). In the ^{1}H NMR spectrum of **7**, a doublet of doublets (J = 9.1 and 9.9 Hz) and a triplet (J = 7.6 Hz) assignanable to H-2 and H-2′ were observed at a lower magnetic field (δ = 5.33 and 6.22), suggesting that the acetyl groups are present at the O-2 and O-2′ positions. The high reactivity of the interglycosidic acetal, as compared to those found in six-membered ring, was probably due to a transannular interaction of the eight-membered ring.[14] Moreover, the reductive cleavage of the benzylidene acetals in **6** was investigated using three reagent systems. The treatment of **6** with lithium aluminium hydride/anhydrous aluminium chloride[15] in diethyl ether–dichloromethane under reflux for 3 h resulted in a complete reduction of the benzylidene groups. The crude product thus obtained was directly acetylated with acetic anhydride/pyridine, and then purified and characterized as the 2,6,6′-tri-*O*-acetyl-2′,3′,4,4′-tetra-*O*-benzyl derivative (**8**). An alternative direction in reductive opening of the benzylidene groups was observed in reactions with borane trimethylamine adduct/anhydrous aluminium chloride[16] or sodium cyanotrihydroborate/methanesulfonic acid in oxolane. Although the reaction mixtures were slightly complex compared to the reaction with lithium aluminium hydride, the major product isolated after acetylation was identified as phenyl 2,4,4′-tri-

O-acetyl-2′,3′,6,6′-tetra-*O*-benzyl-1-thio-β-laminaribioside (**9**). The regioselectivities observed in the reductive cleavages of the six-membered acetals were the same as those previously reported for the monosaccharide system. By contrast, the eight-membered benzylidene acetal gave the ethers predominantly at O-2′, which might be explained by a steric hindrance around the O-2′ position or the coordination of a Lewis acid on the sulfur atom at the C-1 position.

In conclusion, the formation of the interglycosidic benzylidene acetal and its subsequent regioselective cleavage afforded partially protected laminaribioside derivatives. These derivatives might prove to be versatile building blocks for synthetic glycotecnology.

Experimental

General Procedures. The melting points were determined in a capillary with a Yamato melting-point apparatus (Model MP-21) and are uncorrected. The optical rotations were determined with a JASCO DIP-140 Digital polarimeter at 20 °C. ^{1}H NMR spectra were recorded at 300.13 MHz or 400.13 MHz with Bruker ASX-300 or JEOL JNM-EX 400 spectrometers, using tetramethylsilane as the internal standard. The reactions were monitored by TLC on a precoated plate of silica-gel 60 F_{254} (layer thickness, 0.25 mm; E. Merck, Darmstadt, Germany). The spots were visualized under a UV lamp at 254 nm or by spraying 10% aqueous sulfuric acid followed by heating on a hot plate for a few minutes. Column chromatography was performed on silica-gel 60 (230—400 mesh; E. Merck, Darmstadt, Germany). Molecular sieves 4A were activated at 180—200 °C under reduced pressure prior to use.

Preparation of Phenyl 2,4,6,2′,3′,4′,6′-Hepta-*O*-acetyl-1-thio-β-laminaribioside (2). Method A: with Trimethyl(phenylthio)silane/zinc(II) Iodide: After a solution of 1,2,2′,3′,4,4′,6,6′-octa-*O*-acetyl-β-laminaribiose **1** (5.4 g, 8.0 mmol) in 1,2-dichloroethane (50 cm^3) and zinc(II) iodide (5.1 g, 15.2 mmol) was stirred at room temperature for 30 min, and then trimethyl(phenylthio)silane (3.0 cm^3, 15.2 mmol) was added to the mixture. The suspension was stirred at room temperature for 1 d, and then partitioned between 10% hydrochloric acid and toluene. The organic layer was successively washed with 10% hydrochloric acid, aqueous sodium hydrogencarbonate and brine, dried over anhydrous sodium sulfate, and concentrated under reduced pressure. Column chromatography with toluene/ethyl acetate (5 : 2 v/v) as the eluant gave 4.5 g (78%) of the 1-thioglycoside **2**.

Method B: with Thiophenol/zirconium(IV) Chloride: To a stirring solution of **1** (3.4 g, 5 mmol) at 0 °C in dichloromethane (30 cm^3) were successively added zirconium(IV) chloride (1.17 g, 5 mmol) and thiophenol (0.87 cm^3, 8.5 mmol). The suspension was stirred at room temperature for 4 d and partitioned between 10% hydrochloric acid and chloroform. A work-up as described above, followed by column chromatography with toluene/ethyl acetate (5 : 2 v/v) as the eluant, gave 2.3 g (64%) of the 1-thioglycoside **2**: Mp 168—170 °C; $[\alpha]_D^{20}$ −22.7° (*c* 0.22, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ = 3.69 (2 H, m, H-5, 5′), 3.90 (1 H, t, *J* = 9.29 Hz, H-3), 4.04 (1 H, dd, *J* = 2.26 and 12.44 Hz, H-4), 4.19 (1 H, t, *J* = 6.34 Hz, H-3′), 4.37 (1 H, dd, *J* = 4.41 and 12.46 Hz, H-4′), 4.59 (1 H, d, *J* = 10.15 Hz, H-1), 4.60 (1 H, d, *J* = 8.85 Hz, H-1′), 5.02 (6 H, m, H-2, 6a, 6b, 2′, 6′a, 6′b). Found: C, 52.91; H, 5.46; S, 4.48%. Calcd for $C_{32}H_{40}O_{17}S$: C, 52.74: H, 5.53; S, 4.40%.

Preparation of Phenyl 3′-*O*-Acetyl-2,2′ : 4,6 : 4′,6′-tri-*O*-benzylidene-1-thio-β-laminaribioside (5): To a suspension of **2** (0.5 g, 0.7 mmol) in methanol (8 cm^3) was added 1 mol dm^{-3} methanolic sodium methoxide (0.1 cm^3). The mixture was stirred at room temperature for 1 h, neutralized by Amberlite IR-120B (H^+ form). The resin was filtered and washed with methanol. The filtrate and the washings were combined and concentrated to give the unprotected 1-thioglycoside **3** as an amorphous. To a solution of **3** in DMF (40 cm^3) was added α,α-dimethoxytoluene (0.38 cm^3, 2.5 mmol). The solution was acidified to pH 3 with (+)-10-camphorsulfonic acid. The mixture was stirred at 60 °C for 4 h under reduced pressure (ca. 2 kPa) and allowed to cool to room temperature. TLC analysis showed the presence of one major product. Neutralization with sodium hydrogencarbonate followed by evaporation and silica-gel column chromatography with toluene–ethyl acetate (9 : 1 v/v) gave crude tris(benzylidene acetal) **4**: ^{1}H NMR ($CDCl_3$) δ = 4.32 (1 H, dd, *J* = 5.0 and 10.5 Hz, H-6ax), 4.41 (1 H, dd, *J* = 4.9 and 10.4 Hz, H-6eq), 4.78 (1 H, d, *J* = 7.3 Hz, H-1 or 1′) 4.84 (1 H, d, *J* = 9.7 Hz, H-1 or 1′), 5.54, 5.59, 5.71 (3H, 3×s, 3×PhC*H*). To a DMF solution of the benzylidenation, pyridine (2 cm^3) and acetic anhydride (0.5 cm^3) were added successively. The mixture was stirred at room temperature for 1 d and quenched by methanol. The mixture was extracted with chloroform, washed with 10% hydrochloric acid, aqueous sodium hydrogencarbonate and water, then dried over anhydrous sodium sulfate and concentrated. Column chromatography of the residue with toluene–ethyl acetate (30 : 1 v/v) as the eluant gave 0.52 g (49%) of the 3′-*O*-acetyl derivative **5**: $[\alpha]_D^{20}$ −18.9° (*c* 0.10, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ = 3.56 (2 H, m, H-5, 5′), 3.65 (1 H, t, *J* = 9.45 Hz, H-4′), 3.68 (1 H, t, *J* = 9.45 Hz, H-4), 3.79 (4 H, m, H-2, 6a, 2′, 6′a), 4.12 (1 H, t, *J* = 9.21 Hz, H-3), 4.34 (1 H, dd, *J* = 4.98 and 10.72 Hz, H-6b), 4.41 (1 H, dd, *J* = 5.05 and 10.58 Hz, H-6′b), 4.82 (1 H, d, *J* = 9.60 Hz, H-1), 4.85 (1H, d, *J* = 6.22 Hz, H-1′), 5.45 (1 H, t, *J* = 9.53 Hz, H-3′), 5.49 (1 H, s, C*H*Ph), 5.60 (1 H, s, C*H*Ph), 5.69 (1 H, s, C*H*Ph). Found: C, 66.37; H, 5.63; S, 4.15%. Calcd for $C_{37}H_{40}O_{11}S$: C, 66.47; H, 5.44; S, 4.33%.

Preparation of Phenyl 3′-*O*-Benzyl-2,2′ : 4,6 : 4′,6′-tri-*O*-benzylidene-1-thio-β-laminaribioside (6): A DMF solution of the tris(benzylidene acetal) **4** was prepared in the same way as described above from the per-acetate **2** (0.3 g, 0.4 mmol). To the mixture with stirring at 0 °C was added sodium hydride (0.3 g, 8.3 mmol); the mixture was stirred for 1 h. Benzyl bromide (0.5 cm^3, 4.1 mmol) was added to the mixture, which was stirred at room temperature for 1 d and then quenched by successive addition of methanol and concentrated aqueous ammonia. The organic layer was extracted with chloroform, washed with 10% hydrochloric acid, aqueous sodium hydrogencarbonate and water, dried (Na_2SO_4) and concentrated. Column chromatography of the residual syrup with toluene/ethyl acetate (30 : 1 v/v) as eluant gave 0.21 g (64%) of the 3′-*O*-benzyl derivative **5**: Mp 228—230 °C (EtOH); $[\alpha]_D^{20}$ −21.1° (*c* 0.52, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ = 3.53 (2 H, m, H-5, 5′), 3.66 (1 H, t, *J* = 9.77 Hz, H-4), 3.71 (1 H, dd, *J* = 7.81 and 9.77 Hz, H-2), 3.80 (5 H, m, H-2, 6a, 3′, 4′, 6′a), 4.09 (1 H, t, *J* = 8.62 Hz, H-3), 4.33 (1 H, dd, *J* = 4.92 and 10.54 Hz, H-6′b), 4.41 (1 H, dd, *J* = 4.81 and 10.49 Hz, H-6b), 4.69 (1 H, d, *J* = 10.89 Hz, 1/2×CH_2Ph), 4.78 (1 H, d, *J* = 6.61 Hz, H-1), 4.83 (1 H, d, *J* = 9.68 Hz, H-1′), 4.91 (1 H, d, *J* = 10.80 Hz, 1/2×CH_2Ph), 5.59 (2 H, s, 2×C*H*Ph), 5.70 (1 H, s, C*H*Ph). Found: C, 69.92; H, 5.46; S, 4.18%. Calcd for $C_{46}H_{44}O_{10}S$: C, 70.03: H, 5.62; S, 4.06%.

Preparation of Phenyl 2,2′-Di-*O*-acetyl-3′-*O*-benzyl-4,6 : 4′,6′-di-*O*-benzylidene-1-thio-β-laminaribioside (7): The tris(benzylidene acetal) **6** (120 mg, 0.15 mmol) was suspended in chloroform/methanol (1 : 1 v/v, 38 cm^3) containing 1% w/v of pyridinium *p*-toluenesulfonate. The mixture was stirred at room temperature, giving a clear solution after several hours. Stirring was continued

for 10 h; TLC showed the presence of two products and a small amount of unchanged **6**. The mixture was diluted with chloroform and washed successively with 1 mol dm^{-3} hydrochloric acid, aqueous sodium hydrogencarbonate, and brine, dried over anhydrous sodium sulfate, and concentrated. The residue was dissolved in pyridine (10 cm^3) and acetic anhydride (5 cm^3). The solution was stirred at room temperature overnight, poured into ice-water, and extracted with chloroform. The extract was washed successively with 1 mol dm^{-3} hydrochloric acid, aqueous sodium hydrogencarbonate, and brine, dried over anhydrous sodium sulfate, and concentrated. Chromatographic separation of the residue on silica gel using toluene/ethyl acetate (20 : 1 v/v) as the eluant gave 80mg (68%) of the 2,2′-diacetate **7**: $[\alpha]_D^{20}$ −19.0° (*c* 0.23, $CHCl_3$); ^{1}H NMR (C_6D_6) δ = 1.96 (3 H, s, OAc), 2.02 (3 H, s, OAc), 3.10 (1 H, dd, *J* = 4.3 and 9.7 Hz, H-5), 3.19 (1 H, t, *J* = 9.4 Hz, H-6ax), 3.34 (2 H, m, H-5′, 6′ax), 3.85 (1 H, t, *J* = 9.1 Hz, H-3), 4.03 (1 H, dd, *J* = 4.8 and 10.3 Hz, H-6′eq), 4.27 (1 H, dd, *J* = 4.9 and 10.1 Hz, H-6eq), 4.33 (1 H, t, *J* = 9.5 Hz, H-3′), 4.52 (1 H, d, *J* = 10.1 Hz, H-1), 4.66 (1 H, d, *J* = 12.1 Hz, 1/2 Hz, 1/2×C*H*$_2$Ph), 4.72 (1 H, d, *J* = 7.5 Hz, H-1′), 4.87 (1H, d, *J* = 11.9 Hz, 1/2×C*H*$_2$Ph), 5.33 (1 H, dd, *J* = 9.1 and 9.9 Hz, H-2), 6.22 (1 H, t, *J* = 7.6 Hz, H-2′). Found; C, 65.56; H, 5.46; S, 4.37%. Calcd for $C_{43}H_{44}O_{12}S$: C, 65.80: H, 5.65; S, 4.09%.

Preparation of Phenyl 2,6,6′-Tri-*O*-acetyl-2′,3′,4,4′-tetra-*O*-benzyl-1-thio-β-laminaribioside (8): To a solution of **6** (0.79 g, 1 mmol) in diethyl ether/dichloromethane (2 : 1 v/v, 40 cm^3), lithium aluminium hydride (0.15 g, 4 mmol) was added by portions at 0 °C over the course of 30 min. A solution of anhydrous aluminium chloride (0.44 g, 3.3 mmol) in diethyl ether (5 cm^3) was added dropwise to the suspension. The mixture was stirred under reflux for 3 h and quenched by the successive addition of ethyl acetate and water, and extracted with chloroform. The organic layer was washed successively with aqueous sodium potassium tartrate and brine, and dried over anhydrous sodium sulfate and concentrated. The residual syrup was dissolved in pyridine (7 cm^3) and acetic anhydride (3 cm^3), stirred at room temperature for 1 d, poured into crushed ice, and extracted with chloroform. The extract was washed successively with 1 mol dm^{-3} hydrochloric acid, aqueous sodium hydrogencarbonate, and water, dried anhydrous sodium sulfate and concentrated. Column chromatography of the residue on silica gel using toluene/ethyl acetate (40 : 1 v/v) as the eluant gave 0.67 g (73%) of the 2,6,6′-triacetate **8**: Mp 122—123 °C (EtOH); $[\alpha]_D^{20}$ −21.2° (*c* 0.48, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ = 3.52 (4 H, m, H-5, 2′, 3′, 5′), 4.09 (1 H, t, *J* = 8.83 Hz, H-3), 4.28 (2 H, m, H-4, 4′), 4.52 (2 H, m, H-6a, 6′a), 4.64 (1H, d, *J* = 10.14 Hz, H-1), 4.65 (1 H, d, *J* = 8.12 Hz, H-1′), 4.85 (10 H, m, H-6b, 6′b, 4×C*H*$_2$Ph), 5.12 (1 H, t, *J* = 9.70 Hz, H-2). Found: C, 67.80; H, 6.22; S, 3.58%. Calcd for $C_{52}H_{56}O_{13}S$: C, 67.81: H, 6.13; S, 3.48%.

Preparation of Phenyl 2,4,4′-Tri-*O*-acetyl-2′,3′,6,6′-tetra-*O*-benzyl-1-thio-β-laminaribioside (9). Method A: Borane-trimethylamine Adduct/Aluminium Chloride: To a suspension of **6** (0.79 g, 1 mmol), powdered molecular sieves 4A (2 g) and borane-trimethylamine adduct (1.45 g, 20 mmol) in oxolane (50 cm^3), anhydrous aluminium chloride (2.7 g, 20 mmol) was added by portions. The mixture was stirred at room temperature for 4 d, filtered through a Celite pad and washed with chloroform. The filtrate and the washings were combined and washed with aqueous sodium hydrogencarbonate and water, then dried and concentrated. To the residual syrup, pyridine (20 cm^3) and acetic anhydride (10 cm^3) were added, and the mixture was stirred at room temperature for 1 d, quenched with water, and extracted with chloroform. The organic layer was washed with 10% hydrochloric acid, aqueous sodium hydrogencarbonate and water, dried, and concentrated. Column chromatography with toluene/ethyl acetate (40 : 1 v/v) as the eluant gave 0.44 g, (48%) of the 2,4,4′-triacetate **9**. Further elution of the column with toluene/ethyl acetate (20 : 1 v/v) gave 0.12 g (13%) of a mixture of tetra acetates: ^{1}H NMR ($CDCl_3$) δ = 1.90, 1.91, 2.00, 2.03 (12 H, 4×s, 4×Ac).

Method B: Sodium Cyanotrihydroborate/Methanesulfonic Acid. To a suspension of **6** (0.40 g, 0.5 mmol), powdered molecular sieves 4A (2.5 g) and sodium cyanotrihydroborate (0.5 g, 8.9 mmol) in oxolane (40 cm^3), methanesulfonic acid was added by portions until hydrogen chloride gas was no longer generated. The mixture was stirred at room temperature for 30 min, filtered through Celite pad and washed with chloroform. The filtrate and the washings were combined and washed with aqueous sodium hydrogencarbonate and water, then dried and concentrated. To the residual syrup, pyridine (20 cm^3) and acetic anhydride (10 cm^3) were added successively, and the mixture was stirred at room temperature for 1 d, quenched with water, and extracted with chloroform. The organic layer was washed with 10% hydrochloric acid, aqueous sodium hydrogencarbonate, and water, then dried (Na_2SO_4) and concentrated. Column chromatography with toluene–ethyl acetate (40 : 1 v/v) as the eluant gave 0.04 g (9%) of phenyl 4′,2′-di-*O*-acetyl-4,6-*O*-benzylidene-2,3′,6′-tri-*O*-benzyl-1-thio-β-laminaribioside: $[\alpha]_D^{20}$ −18.7° (*c* 0.12, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ = 1.97, 2.01 (6 H, 2×s, 2×Ac), 3.40—3.46 (2 H, m, H-5,5′), 3.49 (1 H, t, *J* = 9.65 Hz, H-2′), 3.58—3.40 (5 H, m, H-3, 4,6ax, 6eq, 6′ax), 3.93 (1 H, t, *J* = 9.30 Hz, H-3′), 4.32 (1 H, dd, *J* = 4.5 and 10.1 Hz, H-6′eq), 4.51 (2 H, s, C*H*$_2$Ph), 4.64 (1 H, d, *J* = 9.8 Hz, H-1′), 4.67 (1 H, d, *J* = 12.14 Hz, 1/2×C*H*$_2$Ph), 4.91—4.99 (5 H, m, H-1, 4′, 3/2×C*H*$_2$Ph), 5.26 (1 H, t, *J* = 9.22 Hz, H-2), 5.47 (1 H, s, C*H*Ph). Found: C, 67.93; H, 6.22; S, 3.56%. Calcd for $C_{50}H_{52}O_{12}S$: C, 68.48; H, 5.98; S, 3.66%. Further elution of the column with the same solvent gave 0.20 g (44%) of the 2,4,4′-triacetate **9**: Mp 132—134 °C (EtOH); $[\alpha]_D^{20}$ −12.7° (*c* 0.42, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ = 3.43 (1 H, t, *J* = 7.81 Hz, H-2′), 3.54 (3 H, m, H-5, 3′, 5′), 3.91 (1 H, t, *J* = 9.67 Hz, H-3), 4.32 (8 H, m, 4×C*H*$_2$Ph), 4.47 (4 H, m, H-6a, 6b, 6′a, 6′b), 4.73 (1 H, d, *J* = 11.72 Hz, H-1), 4.88 (1 H, d, *J* = 11.38 Hz, H-1′), 5.18 (1 H, t, *J* = 12.40 Hz, H-4′), 5.21 (1 H, t, *J* = 11.16 Hz, H-4), 5.36 (1 H, t, *J* = 10.91 Hz, H-2). Found: C, 67.93; H, 6.22; S, 3.56%. Calcd for $C_{52}H_{56}O_{13}S$: C, 67.81: H, 6.13; S, 3.48%.

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