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Conformational evaluation of some 4-deoxyhex-4-enopyranose derivatives and their use in the preparation of a previously undescribed class of 3-thio-L-sorbopyranosides and their 6-*C*-methoxy analogues

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Abstract

A new series of thio-substituted sugars were synthesised relying on the totally regio- and stereoselective cycloaddition of 4-deoxyhex-4-enopyranose derivatives to 'in situ' generated oxothiones. Conformational studies of the above unsaturated sugars showed a marked prevalence of the all-axial conformer. © 2002 Elsevier Science Ltd. All rights reserved.

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1. Introduction

Monosaccharide glycals constitute one of the most useful classes of synthetic sugar intermediates, largely employed in several types of transformations.[1] The versatile reactivity of the glycal's C-1–C-2 double bond allows for the introduction of several functional groups at both carbon atoms. Glycals have, for example, been successfully used to introduce oxygen,[2] nitrogen,[3] sulfur[4,5] or selenium[6] at C-2 of the sugar skeleton. Another attractive use of glycals as building blocks regards the stereoselective synthesis of 2-deoxyglycosides, a widespread class of compounds, whose preparation requires 'tailored' transformations.[7] While aldopyranose glycals are widely used intermediates, their ketopyranose analogues were scarcely employed, owing to the difficulties encountered in their synthesis.[8,9] A satisfactory preparation of D-fructal derivatives, based on a reductive elimination from ketopyranosyl bromides was devised by Ness and Fletcher[8] and subsequently improved by Lichtenthaler and co-workers.[9] A synthesis of 1,5-anhydro-L-*threo*-4-deoxyhex-4-enitol derivatives of preparative value was based on a conceptually different method, exploiting the facile base promoted acetone elimination from 1,5-anhydro-3,4-*O*-isopropylidene-D-galactitol derivatives.[10] Application of the same reaction to alkyl 3,4-*O*-isopropylidene-D-galactopyranoside lead to α-L-*threo*-4-deoxyhex-4-enopyranosides such as **2** (Scheme 1).[11,12]

We report here the conformational investigation of unsaturated sugars **1**–**6** and their evaluation as electron rich dienophiles in etherocycloadditions to α,α′-dioxothiones and *ortho*-thioquinones to give a new class of enantiomerically pure thiosugars.

2. Results and discussion

The preparation of **1** has been achieved in overall 72% yield from 1,5-anhydro-D-galactitol through a previ-

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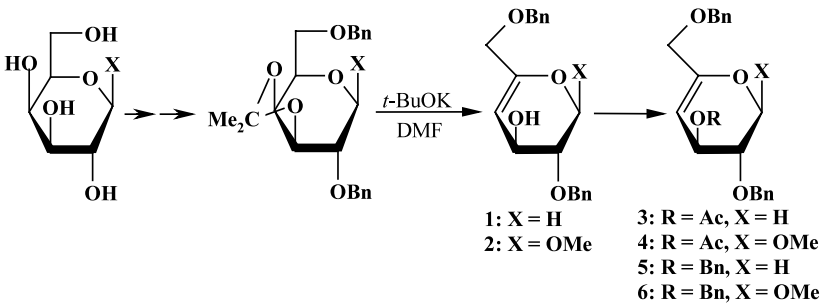
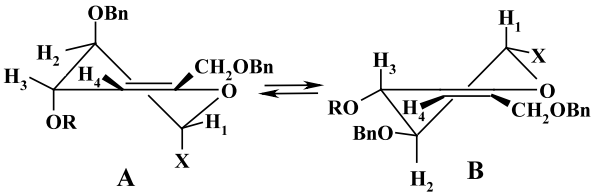


Scheme 1.

ously described sequence of acetonation, benzylation and acetone elimination reactions;[10] the 4-deoxyhex-4-eno derivative **2** was obtained (Scheme 1) by the same reaction sequence starting from methyl β-D-galactopyranoside.[11,12] Because the protection of the free hydroxyl group of **1** and **2** may alter the reactivity of the enolic double bond, benzyl ethers **5** and **6** and acetates **3** and **4** were also prepared. Compounds **3**[10] and **6**[13] were previously described, whereas **4** and **5** were routinely prepared in high yield by reaction of **2** with acetic anhydride in pyridine and of **1** with benzyl bromide, KOH and 18-crown-6, respectively.

2.1. Conformational analysis of unsaturated sugars

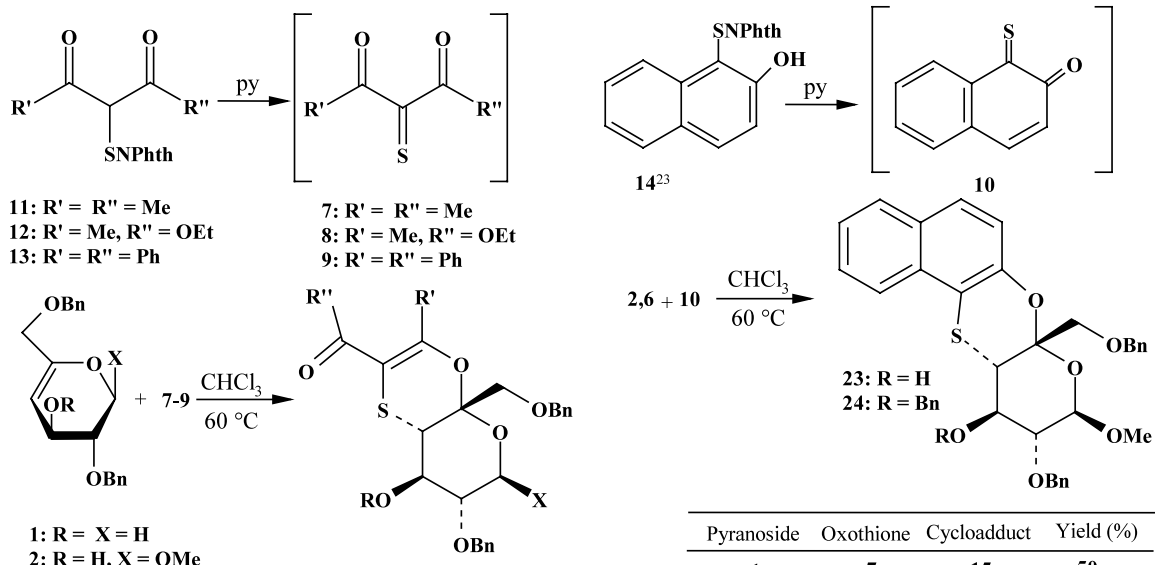
Previous studies on the conformation of compound **3**[10] and the structurally related hex-4-enopyranosyl uronates,[14,15] suggest that: i) compounds **1**–**6** exist as an equilibrium between the two half-chair conformations $^{2}H_{1}$(L) (**A**) and $^{1}H_{2}$(L) (**B**); ii) a conformer with all-axial sustituents, could substantially contribute to the equilibrium, because of the so called 'allylic effect' introduced by Ferrier in 1966[16] to explain the pseudo-axial preference for allylic oxygenated substituents. Although this effect was occasionally invoked to explain the conformational properties of various



unsaturated pyranose derivatives,[17,18] an evaluation of the dependence of the axial preference on substituents has, to the best of our knowledge, not yet been attempted. The conformational analysis of compounds **1**–**6** could give, thus, some interesting informations about this point. An estimate of the population of the **A** and **B** conformers was made by comparing the experimental vicinal coupling constants of the three non-vinylic protons H-3, H-2 and H-1 with the corresponding calculated values for the two limit conformations, applying the Karplus equation modified by Altona[19] to the dihedral angles obtained by molecular mechanics calculations performed with the PC MODEL program. The calculated and experimental values of the coupling constants for compounds **1**–**6** are reported in Table 1. The conformational equilibrium for all 1,5-anhydro-4-deoxyhex-4-enitols **1**, **3** and **5** showed a marked preference (about 85%) for conformer **A**. For the 4-deoxyhex-4-enopyranoside **2**, a similar population was inferred, despite the presence of

Table 1
Conformational equilibrium for unsaturated derivatives **1**–**6** calculated from NMR data in CD_3CN

Compound	$J_{3,4}$	$J_{2,3}$	$J_{1,2}$	$J_{1,3}$	%**A** (from $J_{2,3}$)	%**A** (from $J_{1,2}$)
1	4.70	n.d.	3.97	1.51	n.d.	80
3	4.96	2.87	3.39	1.69	88	88
5	4.69	3.0	3.72	1.57	86	83
*Calcd for **A***	*4.99*	*2.09*	*2.45*	–		
*Calcd for **B***	*2.69*	*8.49*	*10.67*	–		
2	4.81	3.03	3.52	1.08	82	84
4	4.05	3.52	4.15	0.85	75	72
6	3.46	4.39	5.37	0.62	62	50
*Calcd for **A***	*4.63*	*1.77*	*2.63*	–		
*Calcd for **B***	*2.75*	*8.65*	*8.04*	–		



Pyranoside	Oxothione	Cycloadduct	Yield (%)
1	7	15	50
2	7	16	51
5	7	17	60
6	7	18	86
2	8	19	48
6	8	20	42
2	9	21	47
6	9	22	48
2	10	23	48
6	10	24	66

Scheme 2.

an additional axial substituent at the anomeric position. Instead, when the allylic substituent was an acetoxy (compound **4**) or a benzyloxy (compound **6**), the population of conformer **A** decreased to about 75 and 55%, respectively.

These results indicate that allylic hydroxy, acetoxy or benzyloxy groups (see **1**, **3** and **5**) determine an analogous prevalence of the **A** conformer. The 1,3-diaxial steric effect between the allylic and the anomeric substituents in the 4-deoxyhex-4-enopyranoside series was, in the case of alcohol **2**, completely counterbalanced by a combination of the anomeric and the allylic effects and, likely, by the presence of a stabilising intramolecular H-bond between the OH and the OMe groups. In the absence of this latter interaction, (*i.e.* compounds **4** and **6**), a larger amount of the **B** conformer is observed, raising to about 50% for the more sterically demanding benzyloxy group.

2.2. Synthesis of the cycloadducts

Cycloaddition of **1**, **2**, **5** and **6** to the α,α′-dioxothiones **7**–**9** and *ortho*-thioquinone **10** which, in turn, were generated in situ by the base treatment of the parent phthalimide derivatives **11**–**14**,[20,21] gave compounds **15**–**24**, as depicted in Scheme 2.

These cycloadditions are inverse electron-demand Diels-Alder reactions which typically involve the HOMO of the dienophile and the LUMO of the α,α′-dioxotiones.[22]

Reactions were generally performed by adding to a solution of enol ether in chloroform, the phthalimido derivative and a weak base such as pyridine and heating the solution to 60 °C. Cycloadditions were all quite slow; the required refluxing time ranged from four days (cycloadduct **18**, see Section 3) to ten days (cycloadducts **15**, **23** and **24**). Compounds **3** and **4** (see Scheme 1) could not be used as dienophiles because the electron withdrawing acetyl group made the reaction very sluggish.[23]

The described cycloadditions showed outstanding selectivities: all reactions occurred with a complete chemo-,[20] regio-[20] and stereoselectivity, giving isomerically pure products. Moreover, the stereochemical outcome appeared to be independent of the nature of the substituents R and X on dienophiles (see Scheme 2). The regio- and stereochemistry of cycloadducts **15**–**24** were unambiguously determined by ^{1}H NMR analysis: indeed, δ H-3 (**15** and **17**) or H-4 (**16**, **18**–**24**) clearly indicate the presence of a geminal sulfur atom, and $J_{3,4}$, are typical diaxial ^3J coupling constants. In the case of oxothione **8**, the complete chemoselectivity,[20] due to the exclusive participation of the ketone carbonyl, was confirmed by the presence of the ester signal in the ^{13}C NMR spectrum.

The formation of cycloadducts **15**–**24** as single stereoisomers can be ascribed to a fast interconversion between **A** and **B** with respect to the reaction times (see Section 3), and assuming that the attack of the oxothiones occurs from the bottom-face (anti to the allylic substituents) of the presumably more reactive **B**, in agreement with the general rule[24] predicting that in all-equatorial glycal series a bottom-site attack is preferred.[25]

Although conformer **A** is more abundant, no correlation between the stereoselectivity of the reaction of thiones with glycals and their conformational preferences can be likely expected.[25,26] As a matter of fact, the product distribution is not determined by the distribution of the ground state conformers (see Curtin-Hammett principle) but by the relative transition states energy.

2.3. Reactivity of cycloadducts

Compounds **15**–**24** represent a new class of thiosubstituted sugars, efficiently and selectively obtained by cycloaddition of 4-deoxyhex-4-eno derivatives to oxothiones, which are promising building blocks for the synthesis of carbohydrate derivatives. With this in mind we carried out a preliminary investigation on the reactivity which, to our knowledge, has not been reported up to date.

Although analogies with previously reported cycloadducts of related oxathiines was observed, unexpected differences raised the interest in these new class of thiosugars. Treatment of **16** and **18** with Raney nickel in wet THF at room temperature afforded derivatives **25** and **26**, respectively with a small amount of compounds **2** (8%, from **16**) and **6** (9%, from **18**). Under reducing desulfurisation conditions compounds **16** and **18** underwent the expected desulfurisation but also the unpredictable[21,23] reduction of the conjugated double bond. Different reaction conditions (EtOH as solvent, at r.t. or 60 °C) increased the amount of **2** and **6**. No reaction was observed instead with cycloadducts **17** and **24**.

As already reported for related 1,4-oxathiines,[5] reduction of **18** with $LiAlH_4$ in THF at room temperature afforded the corresponding allylic alcohol **27** (Scheme 3). Under oxidation conditions (*m*-CPBA, CH_2Cl_2, r.t.), **23** gave the corresponding sulfoxide **28** with complete diasteroselectivity.[27]

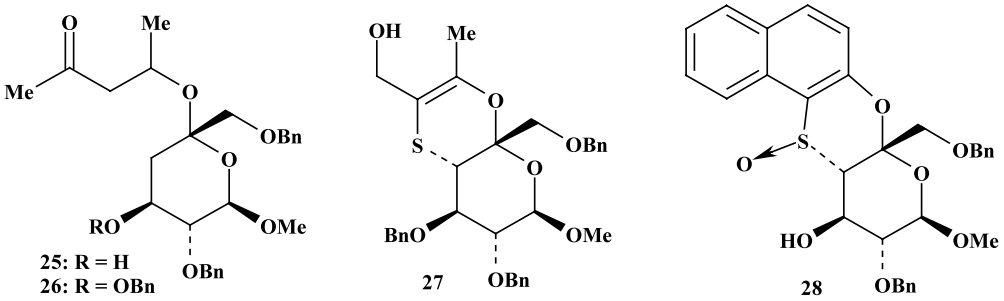
In conclusion, in this paper we reported conformational studies of 4-deoxyhex-4-eno derivatives **1**–**6**. An equilibrium between two half-chair forms **A** and **B** was inferred with prevalence for the all-axial (**A**), conformer. The prevalence of **A** was explained taking into account the steric and anomeric effects as well as the less familiar allylic effect. An evaluation of the dependence of the latter on different types of substituents was also estimated. Compounds **1**,**2**,**5**,**6** were successfully cycloadded with oxothiones **7**–**10**, to give a new class of enantiomerically pure thiosubstituted sugars. A preliminary investigation of the chemical behaviour of this class of thiosugars highlighted their potentials as precursors of non-natural thio-substituted- or deoxy-carbohydrates.

Further investigations on these interesting building-blocks are currently in progress in our laboratories.

3. Experimental

3.1. General methods

Solvents were purified and dried according to standard procedures. All reactions were performed under nitrogen in dry solvents unless otherwise stated. TLC was performed on glass-backed Silica Gel (Macherey-Nagel, Durasil-25-UV_{254}). Detection was effected by treatment with a solution of vanillin (3 g) and H_2SO_4 (4 mL) in EtOH (250 mL). Flash chromatography was carried out on silica gel (Macherey-Nagel, 60M). $CHCl_3$ was washed with water and dried with $CaCl_2$ before use. Optical rotations were determined at 25 °C with a Jasco DIP-370 polarimeter (1 dm cell). NMR spectra were recorded with a Varian Gemini 2000 (200 MHz) and a Bruker AM 500 (500 MHz) instruments, using $CDCl_3$ as solvent for ^1H NMR and ^{13}C NMR ($\delta_H = 7.26$ and



Scheme 3.

$\delta_C = 77.0$, respectively, as reference). Melting point are uncorrected and were recorded with a Büchi 510 apparatus. Elemental analyses were performed with a Perkin–Elmer Elementary Analyser 2400 Series II.

Compounds **1** and **3** were prepared according to Ref. 10 and compounds **2** and **6** according to Refs. 12 and 13, respectively. In the preparation of **1**, the overall yield from 1,5-anhydro-galactitol was improved to 72% operating without purification of the intermediates. NMR data for **2**, previously reported in C_6D_6,[12] were now determined in CD_3CN solution and are as follow: ^{1}H NMR (200 MHz, CD_3CN): δ 3.44 (3 H, s, CH_3O), 3.63 (ddd, 1 H, $J_{2,3}$ 3.0 Hz, $J_{2,4}$ 1.1 Hz, H-2), 3.93 (m, 1 H, $J_{3,6'}$ 0.8 Hz, H-6′), 3.94 (m, 1 H, $J_{3,4}$ 4.8 Hz, H-3), 3.95 (m, 1 H, $J_{3,6}$ 0.9 Hz, H-6), 4.67 (s, 2 H, CH_2–Bn), 4.70 (s, 2 H, CH_2–Bn), 5.07 (dd, 1 H, $J_{1,2}$ 3.5 Hz, $J_{1,3}$ 1.1 Hz, H-1), 5.11 (m, 1 H, $J_{4,6}$ 0.7 Hz, $J_{4,6'}$ 0.6 Hz, H-4), 7.29–7.38 (m, 10 H, CH–Ar); ^{13}C NMR (50 MHz, CD_3CN): δ 56.6 (CH_3O), 64.5 (C-3), 70.2 (C-6), 70.2, 72.5 (2 CH_2–Bn), 77.7 (C-2), 100.4 (C-1), 103.5 (C-4), 127.8–130.2 (10 C–Ar); 139.4 (2 Cq); 148.5 (C-5).

3.2. 1,5-Anhydro-2,3,6-tri-*O*-benzyl-4-deoxy-L-*threo*-hex-4-enitol (5)

To a solution of **1** (953 mg, 2.92 mmol) in THF containing 0.5% of water (7.0 mL), 18-crown-6 (35 mg, 0.13 mmol) and powdered KOH (650 mg) were added; the mixture was stirred 20 min at room temperature then treated with benzyl bromide (0.6 mL, 5.04 mmol). The reaction mixture was stirred at room temperature until TLC analysis (1:1 hexane–EtOAc) revealed the complete disappearance of **1** (4 h). Excess benzyl bromide was destroyed by addition of MeOH (15 mL) and stirring at room temperature for 10 min, the solvents were concentrated under diminished pressure, the residue taken up in CH_2Cl_2 (50 mL), washed with H_2O (3 × 25 mL) and the dried organic phase was concentrated under diminished pressure. The crude residue (1.60 g) was submitted to flash column chromatography on silica gel (9:1 hexane–EtOAc + 0.1% Et_3N), to give pure **5** (1.11 g, 91%) as a syrup; $[\alpha]_D = +101.54°$ (*c* 1.30, $CHCl_3$); ^{1}H NMR (200 MHz, CD_3CN) δ: 3.70 (m, 1 H, $J_{2,3}$ 3.0 Hz, $J_{2,4}$ 1.4 Hz, H-2), 3.87 (m, 1 H, $J_{1,3}$ 1.6 Hz, H-3), 3.92 (m, 1 H, $J_{4,6}$ 0.7 Hz, H-6), 3.92 (m, 1 H, $J_{4,6'}$ 0.7 Hz, H-6′), 3.93 (m, 1 H, $J_{1',2}$ 1.9 Hz, H-1′), 4.21 (ddd, 1 H, $J_{1,1'}$ 11.7 Hz, $J_{1,2}$ 3.7 Hz, H-1), 4.49 (s, 2 H, CH_2–Bn), 4.56, and 4.60 (AB system, 2 H, J_{AB} 11.9 Hz, CH_2–Bn), 4.58, and 4.63 (AB system, 2 H, J_{AB} 11.8 Hz, CH_2–Bn), 5.07 (m, 1 H, $J_{3,4}$ 4.7 Hz, H-4), 7.28–7.37 (m, 15 H, CH–Ar.); ^{13}C NMR (50 MHz, CD_3CN) δ: 65.1 (C-6), 70.5 (C-1), 70.6 (C-3), 70.6, 71.7, and 72.7 (3 CH_2–Bn), 73.7 (C-2), 98.3 (C-4), 127.9–129.3 (15 CH–Ar), 139.5, 139.5, and 140.0 (3 C_q), 154.6 (C-5); Anal. Calcd for $C_{27}H_{28}O_4$: C, 77.86; H, 6.78. Found: C, 77.98; H, 6.82.

3.3. Methyl 3-*O*-acetyl-2,6-di-*O*-benzyl-4-deoxy-α-L-*threo*-hex-4-enopyranoside (4)

A solution of **2** (600 mg, 1.68 mmol) in pyridine (8 mL) and acetic anhydride (4 mL) was left 5 h at room temperature, then co-evaporated three times with toluene (3 × 10 mL). The residue was purified by flash column chromatography on silica gel (4:1 hexane–EtOAc + 0.1% Et_3N) to give pure **4** (621 mg, 93%) as a syrup; $[\alpha]_D$ +13.20° (*c* 1.30, $CHCl_3$), ^{1}H NMR (200 MHz, CD_3CN) δ: 1.97 (s, 3 H, CH_3CO), 3.45 (s, 3 H, OCH_3), 3.67 (ddd, 1 H, $J_{2,3}$ 3.5 Hz, $J_{2,4}$ 1.0 Hz, H-2), 3.94 (m, 1 H, $J_{3,6}$ 0.9 Hz, $J_{4,6}$ 0.8 Hz, H-6), 3.94 (m, 1 H, $J_{4,6'}$ 0.8 Hz, $J_{3,6'}$ 0.9 Hz, H-6′), 4.52 (s, 2 H, CH_2–Bn), 4.72 (s, 2 H, CH_2–Bn), 4.98 (dd, 1 H, $J_{1,2}$ 4.2 Hz, $J_{1,3}$ 0.8 Hz, H-1), 5.00 (ddd, 1 H, $J_{3,4}$ 4.0 Hz, H-4), 5.21 (m, 1 H, H-3); ^{13}C NMR (50 MHz, CD_3CN) δ: 21.3 (CH_3CO), 56.9 (OCH_3), 67.6 (C-3), 69.9 (C-6), 70.9, and 73.2 (2 CH_2–Bn), 76.1 (C-2), 99.0 (C-4), 101.0 (C-1), 128.5–129.3 (10 CH–Ar), 139.2, and 139.3 (2 C_q), 148.1 (C-5), 169.6 (C=O); Anal. Calcd for $C_{23}H_{26}O_6$: C, 69.33; H, 6.58. Found: C, 69.57; H, 7.00.

3.4. 1{(4*S*,5*S*)-1,5-Anhydro-2,3-di-*O*-benzyl-4-deoxy-L-*threo*-hexitol[3,2-*b*]-2-methyl-1,4-oxathiin-3-yl}ethanone (15)

To a solution of compound **1** (80 mg, 0.24 mmol) in $CHCl_3$ (3 mL), 82 mg (0.29 mmol) of phthalimide derivative **11** and 21 μL (0.29 mmol) of pyridine were added at room temperature. The reaction mixture was heated to 60 °C and kept at this temperature for 10 days. After this time it was cooled to room temperature, diluted with CH_2Cl_2 (5 mL), washed with a saturated NH_4Cl solution (2 ×) and H_2O (1 ×) and the organic layer dried over Na_2SO_4. Evaporation of the solvent afforded a crude product (223 mg) which was purified by flash column chromatography on silica gel (6:1 hexane–EtOAc) to give **15** (56 mg, 50%) as glassy solid. ^{1}H NMR (200 MHz, $CDCl_3$) δ: 2.27 (s, 3 H, CH_3–C=C), 2.31 (s, 3 H, CH_3–CO), 2.81 (bs, 1 H, OH), 3.32–3.37 (m, 1 H, H-2), 3.46 (B part of an AB system, 1 H, J_{AB} 10.2 Hz, H-6), 3.58–3.64 (m, 3 H, H-1*ax*, H-1*eq*, and H-3), 3.86 (A part of an AB system, 1 H, J_{AB} 10.2 Hz, H-6′), 3.88–3.93 (m, 1 H, H-4), 4.52, and 4.69 (AB system, 2 H, J_{AB} 12.0 Hz, CH_2–Bn), 4.69, and 4.80 (AB system, 2 H, J_{AB} 11.8 Hz, CH_2–Bn), 7.26–7.36 (m, 10 H, 10 CH–Ar); ^{13}C NMR (50 MHz, $CDCl_3$) δ: 21.7 (*C*H$_3$–CO), 30.2 (*C*H$_3$–C=C), 41.6 (C-1), 62.1, 70.0, 71.5, 73.4, 74.1 (C-3, C-4, C-2, 2 CH_2–Bn), 100.4 (C-5), 101.6 (S*C*=C), 127.8, 128.0, 128.3, 128.5 (10 CH–Ar), 137.3, 137.8 (2 C_q), 159.0 (SC=*C*), 195.4 (C=O). Acetylation of **15** under standard conditions afforded the corresponding acetyl derivative quantitatively; $[\alpha]_D = -71.57°$ (*c* 0.17, $CHCl_3$); ^{1}H NMR (200 MHz, C_6D_6) δ: 1.57 (s, 3 H, CH_3–Ac), 2.01 (s, 3 H,

CH_3–C=C), 2.09 (s, 3 H, CH_3–C=O), 3.18–3.31 (m, 1 H, H-2), 3.30 (B part of an AB system, 1 H, J_{AB} 10.0 Hz, H-6), 3.38 (d, 1 H, $J_{3,4}$ 10.6 Hz, H-4), 3.53–3.62 (m, 2 H, H-1*ax*, and H-1*eq*), 3.78 (A part of an AB system, 1 H, J_{AB} 10.0 Hz, H-6′), 4.04 (as, 2 H, CH_2–Bn), 4.14, and 4.27 (AB system, 2 H, J_{AB} 12.2 Hz, CH_2–Bn), 5.28 (dd, 1 H, $J_{2,3}$ 10.4 Hz, $J_{3,4}$ 10.6 Hz, H-3), 7.24–7.35 (m, 10 H, 10 CH–Ar); ^{13}C NMR (50 MHz, $CDCl_3$) δ: 20.9 (CH_3–Ac), 21.5 (*C*H_3–CO), 30.3 (*C*H_3–C=C), 38.8 (C-1), 62.1, 69.6, 71.6, 73.0, 74.2, and 75.3 (C-2, C-3, C-4, C-6, and 2 CH_2–Bn), 100.6, 102.0, 127.6, 127.8, 127.87, 127.9, 128.4, and 128.4 (10 CH–Ar), 137.2, and 137.6 (2 C_q), 158.2 (SC=*C*), 169.7 (CO–Ac), 195.9 (C=O); Anal. Calcd for $C_{27}H_{30}O_7S$: C, 65.04; H, 6.06. Found: C, 65.29; H, 6.00.

3.5. 1-{Methyl (4*S*,5*R*)-2,6-di-*O*-benzyl-4-deoxy-α-L-*threo*-hexopyranosid[4,5-*b*]-2-methyl-1,4-oxathiin-3-yl}-ethanone (16)

To a solution of **2** (200 mg, 0.56 mmol) in 3 mL of $CHCl_3$, 248.9 mg (0.9 mmol) of phthalimide derivative **11** and 35.4 μl (0.45 mmol) of pyridine were added. The reaction mixture was heated at 60 °C for 7 days, after this time the heating was stopped and the mixture diluted with CH_2Cl_2 (3 mL), washed with saturated NH_4Cl solution (2 ×) and water (1 ×) and dried over Na_2SO_4. The organic layer was concentrated and the crude product (630 mg) was purified by flash column chromatography on silica gel (4:1 hexane–EtOAc) to give **16** (140 mg, 51%) and unreacted glycal **2** (30 mg, 60%) as a yellow oil; $[\alpha]_D$ −16.99° (*c* 1.12, $CHCl_3$); ν_{max} (thin film) 3031 (m), 2923 (s), 1673 (s, C=O), 1563 (s, C=C) cm^{-1}; ^{1}H NMR (200 MHz, C_6D_6) δ: 2.14 (s, 3 H, CH_3), 2.27 (s, 3 H, CH_3C=O), 3.34 (s, 3 H, CH_3O), 3.39–3.67 (m, 4 H, H-2, H-3, and CH_2-6), 3.90 (d, 1 H, $J_{3,4}$ 10.2 Hz, H-4), 4.46 (AB system, 2 H, J_{AB} 12.0 Hz, CH_2–Bn), 4.73 (B part of an AB system, 1 H, J_{AB} 11.4 Hz, CH_B–Bn), 4.82 (d, 1 H, $J_{1,2}$ 8.0 Hz, H-1), 4.96 (A part of an AB system, 1 H, J_{AB} 11.8 Hz CH_A–Bn), 7.11–7.42 (m, 10 H, 10CH–Ar); ^{13}C NMR (50 MHz, $CDCl_3$) δ: 21.7 (*C*H_3C=O), 30.1 (*C*H_3–C=), 40.0 (C-6), 57.3 (CH_3O), 68.3, 71.2, 74.0, 74.7, and 81.4 (C-2, C-3, C-4, and 2 CH_2–Bn), 99.8, and 100.6 (C-1, and C-5), 101.8 (S*C*=C); 127.9, 128.0, 128.1, 128.4, and 128.6 (10 CH–Bn), 137.4, and 138.1 (2 Cq), 158.3 (SC=*C*); 195.6 (C=O); Anal. Calcd for $C_{26}H_{30}O_7S$: C, 64.18; H, 6.21. Found: C, 63.69; H, 6.14.

3.6. 1{(4*S*,5*S*)-1,5-Anhydro-2,3,6-tri-*O*-benzyl-4-deoxy-L-*threo*-hexitol[3,2-*b*]-2-methyl-1,4-oxathiin-3-yl}-ethanone (17)

A solution of **5** (20 mg, 0.05 mmol) in 1.5 mL of $CHCl_3$ was treated with 24 mg (0.09 mmol) of phthalimide derivative **11** and pyridine (3.03 μl). The reaction mixture was heated to 60 °C for 10 days, then cooled to room temperature, diluted with CH_2Cl_2 (3 mL), washed with a saturated NH_4Cl solution (2 ×) and water (1 ×) and dried over Na_2SO_4. After concentration, the crude product (62 mg) was purified by flash column chromatography on silica gel ($CHCl_3$) to give **17** (15.7 mg, 60%) as colourless oil; $[\alpha]_D$ −8.89° (*c* 0.10, $CHCl_3$); ^{1}H NMR (200 MHz, $CDCl_3$) δ: 2.30 (s, 3 H, CH_3), 2.50 (s, 3 H, CH_3–CO), 3.41–3.71 (m, 5H, H-1*ax*, H-1*eq*, H-2, CH_2-6), 3.86–3.94 (m, 1 H, H-3), 3.89 (d, 1 H, $J_{3,4}$ 10.2 Hz, H-4), 4.59 (AB system, 2 H, J_{AB} 11.2 Hz, CH_2–Bn), 4.68 (AB system, 2 H, J_{AB} 11.2 Hz, CH_2–Bn), 4.86 (AB system, 2 H, J_{AB} 10.6 Hz, CH_2–Bn), 7.28–7.42 (m, 15 H, 15CH–Ar); ^{13}C NMR (50 MHz, $CDCl_3$) δ: 21.6 (*C*H_3–CO), 30.1 (*C*H_3–C=C), 40.6 (C-1), 62.2, 71.5, 73.4, 74.1, 76.6, and 78.2 (C-2, C-3, C-4, and 3 CH_2–Bn), 100.8 (C-5), 102.1 (S*C*=C), 127.1, 127.4, 127.7, 127.8, 127.9, 128.0, 128.1, 128.2, 128.4, 128.4, and 128.5 (15 CH–Ar), 137.3, 137.8, and 138.0 (3 Cq), 158.7 (SC=*C*); 195.6 (C=O); Anal. Calcd for $C_{32}H_{34}O_6S$: C, 70.31; H, 6.27. Found: C, 70.42; H, 6.01.

3.7. 1-{Methyl (4*S*,5*R*)-2,3,6-tri-*O*-benzyl-4-deoxy-α-L-*threo*-hexopyranosid[4,5-*b*]-2-methyl-1,4-oxathiin-3-yl}-ethanone (18)

To a solution of **6** (200 mg, 0.45 mmol) in 3 mL of $CHCl_3$, 174.5 mg (0.63 mmol) of phthalimide derivative **11** and 28.4 μl (0.36 mmol) of pyridine were added. The reaction mixture was heated to 60 °C. After 93 h the heating was stopped and the mixture was diluted with CH_2Cl_2 (15 mL), washed with saturated NH_4Cl solution (2 ×) and water (1 ×) and dried over Na_2SO_4. The organic layer was concentrated to give 288 mg of crude product which was purified by flash column chromatography on silica gel (CH_2Cl_2) affording the cycloadduct **18** (224 mg, 86%) as yellow oil; $[\alpha]_D$ −144.81° (*c* 0.14, $CHCl_3$); ν_{max} (thin film) 3031 (m), 2913 (s), 1673 (s, C=O), 1563 (s, C=C) cm^{-1}; ^{1}H NMR (500 MHz, C_6D_6) δ: 1.99 (s, 3 H, CH_3), 2.20 (s, 3 H, CH_3C=O), 3.24 (s, 3 H, CH_3–O), 3.43 (B part of an AB system, 1 H, J_{AB} 10.5 Hz, CH_B–Bn), 3.45–3.54 (m, 2 H, H-2, and H-3), 3.60 (A part of an AB system, 1 H, J_{AB} 10.5 Hz, CH_A–Bn), 3.82 (d, 1 H, $J_{3,4}$ 10.0 Hz, H-4), 4.33 (AB system, 2 H, J_{AB} 12.0 Hz, CH_2–Bn), 4.54 (B part of an AB system, 1 H, J_{AB} 11.2 Hz, CH_B–Bn), 4.68–4.83 (m, 3 H, CH_2–Bn, and H-1), 4.74 (d, 1 H, $J_{1,2}$ 8.0 Hz, H-1), 4.82 (A part of an AB system, 1 H, J_{AB} 11.5 Hz, CH_A–Bn), 6.96–7.28 (m, 15 H, CH–Bn); ^{13}C NMR (50 MHz, C_6D_6) δ: 21.2 (*C*H_3–C=O), 29.6 (CH_3), 41.0 (C-6), 56.6 (CH_3O), 71.59, 73.79, 74.81, 76.29, 76.52, and 82.79 (C-2, C-3, C-4, and 3 CH_2–Bn), 100.05, and 101.21 (C-1, and C-5), 102.34, 127.30, 127.55, 127.77, 128.39; 138.02, 138.75, and 138.86 (3 Cq), 157.49, and 194.08 (C=O); Anal. Calcd for $C_{33}H_{36}O_7S$: C, 68.73; H, 6.29. Found: C, 68.69; H, 6.61.

3.8. Ethyl 1-{methyl (4*S*,5*R*)-2,6-di-*O*-benzyl-4-deoxy-α-L-*threo*-hexopyranosid[4,5-*b*]-2-methyl-1,4-oxatiin-3-yl}formate (19)

To a solution of **2** (50 mg, 0.14 mmol) in 3 mL of $CHCl_3$, 77.36 mg (0.25 mmol) of phthalimide derivative **12** and 11.09 μl (0.14 mmol) of pyridine were added. The mixture was heated to 60 °C for 9 days and after this time the heating was stopped and the reaction diluted with CH_2Cl_2 (10 mL), washed with a saturated NH_4Cl solution (2 ×) and water (1 ×) and dried over Na_2SO_4. After concentration, the crude product (180 mg) was purified by flash column chromatography on silica gel (3:1 hexane–EtOAc) to give **19** (35 mg, 48%); $[\alpha]_D$ +9.13° (*c* 0.15, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ: 1.30 (t, 3 H, *J* 7.2 Hz, CH_3CH_2O), 2.30 (s, 3 H, CH_3–C=C), 3.41 (d, 1 H, $J_{3,4}$ 11.1 Hz, H-4), 3.53–3.57 (m, 4 H, CH_3O, CH-6), 3.81–3.90 (m, 3 H, H-1, H-2, and CH-6′), 4.13–4.26 (m, 3 H, H-3, and CH_3CH_2O), 4.63 (B part of an AB system, 1 H, J_{AB} 11.8 Hz, CH_B–Bn); 4.68 (AB system, 2 H, J_{AB} 11.8 Hz, CH_2–Bn), 4.76 (A part of an AB system, 1 H, J_{AB} 11.8 Hz, CH_A–Bn), 5.07 (s, 1 H, OH), 7.28–7.37 (m, 10 H, 10 CH–Ar); ^{13}C NMR (50 MHz, $CDCl_3$) δ: 14.2 (CH_3CH_2O), 21.4 (CH_3C=C), 34.5 (C-6), 55.8 (CH_3O), 61.0 (CH_3CH_2O), 71.1, 72.2, 74.1, and 75.0 (C-2, C-3, C-4, and 2 CH_2–Bn), 97.4, and 98.9 (C-1, and C-5), 99.7 (SC=C); 127.4, 127.5, 127.9, 128.2, and 128.5 (10 CH–Ar), 137.3, and 137.9 (2 Cq), 157.67 (SC=*C*); 164.92 (OC=O); Anal. Calcd for $C_{27}H_{32}O_8S$: C, 62.77; H, 6.24. Found: C, 62.80; H, 6.13.

3.9. Ethyl 1-{methyl (4*S*,5*R*)-2,3,6-tri-*O*-benzyl-4-deoxy-α-L-*threo*-hexopyranosid[4,5-*b*]-2-methyl-1,4-oxatiin-3-yl}formate (20)

To a solution of **6** (100 mg, 0.22 mmol) in 3 mL of $CHCl_3$, 82.6 mg (0.26 mmol) of phthalimide derivative **12** and 17.7 μl (0.22 mmol) of pyridine were added and the mixture was heated to 60 °C for 5 days. After this time, the heating was stopped and the reaction mixture was diluted with CH_2Cl_2 (10 mL), washed with saturated NH_4Cl (2 ×) and water (1 ×) and dried over Na_2SO_4. After concentration the crude product (250 mg) was purified by flash column chromatography on silica gel (5:1 hexane–EtOAc) to give **20** (55 mg, 42%) as colourless oil; ^{1}H NMR (200 MHz, $CDCl_3$) δ: 1.30 (t, 3 H, *J* 7.0 Hz, CH_3CH_2O), 2.33 (s, 3 H, CH_3–C=C), 3.37–3.77 (m, 7 H, H-2, H-3, CH_3O, and CH_2-6), 3.90 (d, 1 H, $J_{3,4}$ 10.6 Hz, H-4), 4.21 (q, 2 H, *J* 7.2 Hz, CH_3CH_2O), 4.54–4.87 (m, 7 H, 3 CH_2–Bn, and H-1), 7.25–7.38 (m, 15 H, 15 CH–Ar); ^{13}C NMR (50 MHz, $CDCl_3$) δ: 14.2 (CH_3CH_2O), 21.1 (CH_3–C=C), 41.1 (C-6), 57.3 (CH_3O), 61.0 (CH_3CH_2O), 71.2, 74.0, 75.0, 76.4, 76.5, and 82.4 (C-2, C-3, C-4, and 3 CH_2–Bn), 99.9, and 101.0 (C-1, and C-5), 101.8 (SC=C); 127.6, 127.7, 128.0, 128.2, and 128.3 (15 CH–Bn), 137.7, 138.0, and 138.2 (3 Cq), 158.7 (SC=*C*); 165.1 (OC=O).

3.10. Methyl (4*S*,5*R*)-2,6-di-*O*-benzyl-4-deoxy-α-L-*threo*-hexopyranosid[4,5-*b*]-3-benzoyl-2-phenyl-1,4-oxathiin (21)

A solution of **2** (100 mg, 0.28 mmol) in 3 mL $CHCl_3$ was treated with 202.3 mg (0.50 mmol) of phthalimide derivative **13** and 22.0 μL (0.28 mmol) of pyridine. The reaction mixture was heated to 60 °C for 7 days then cooled to room temperature, diluted with CH_2Cl_2 (15 mL), washed with a saturated NH_4Cl solution (2 ×) and water (1 ×) and dried over Na_2SO_4. The crude product (280 mg) obtained after concentration, was purified by flash column chromatography on silica gel (3:1 hexane–EtOAc) to give **21** (80 mg, 47%) as a pale yellow oil; $[\alpha]_D$ −53.44° (*c* 0.18, $CHCl_3$); ^{1}H NMR (200 MHz, C_6D_6) δ: 3.23 (s, 3 H, CH_3O), 3.48 (dd, 1 H, $J_{1,2}$ 8.0 Hz, $J_{2,3}$ 9.2 Hz, H-2), 3.56 (B part of an AB system, 1 H, J_{AB} 10.6 Hz, CH-6), 3.83–3.93 (m, 1 H, H-3), 3.91 (d, 1H, $J_{3,4}$ 10.4 Hz, H-4), 4.13 (A part of an AB system, 1 H, J_{AB} 10.6 Hz, CH-6′), 4.26 (s, 1 H, OH), 4.54 (s, 2 H, CH_2–Bn), 4.75 (B part of an AB system, 1 H, J_{AB} 11.0 Hz, CH_B–Bn), 4.89 (A part of an AB system, 1 H, J_{AB} 11.0 Hz, CH_A–Bn), 4.93 (d, 1 H, $J_{1,2}$ 8.0 Hz, H-1), 6.72–6.83 (m, 5 H), 7.06–7.36 (m, 13 H), 7.70–7.75 (m, 2 H); ^{13}C NMR (50 MHz, C_6D_6) δ: 44.1 (C-6), 57.0 (CH_3O), 70.3, 71.9, 74.2, 75.0, and 82.4 (C-2, C-3, C-4, and 2 CH_2–Bn), 100.5, and 101.4 (C-1, and C-5), 105.8 (SC=C); 127.0, 127.5, 128.2, 128.5, 128.6, 129.3, 129.5, 129.8, 132.3, and 133.5 (20 CH–Ar.), 135.5, 138.1, 138.3, 139.3, and 153.5 (SC=*C*), 193.82 (C=O); Anal. Calcd for $C_{36}H_{34}O_7S$: C, 70.80; H, 5.61. Found: C, 70.74; H, 5.92.

3.11. Methyl (4*S*,5*R*)-2,3,6-tri-*O*-benzyl-4-deoxy-α-L-*threo*-hexopyranosid[4,5-*b*]-3-benzoyl-2-phenyl-1,4-oxathiin (22)

A solution of **6** (100 mg, 0.22 mmol) in 2 mL $CHCl_3$ was treated with 162.0 mg (0.40 mmol) of phthalimide derivative **13** and 17.7 μL (0.22 mmol) of pyridine. The reaction mixture was heated to 60 °C for 6 days then cooled to room temperature, diluted with CH_2Cl_2 (3 mL), washed with a saturated NH_4Cl solution (2 ×) and water (1 ×) and dried over Na_2SO_4. After concentration, the crude product (300 mg) was purified by flash column chromatography on silica gel (7:1 hexane–EtOAc) to afford cycloadduct **22** (65.0 mg, 48%) as yellowish oil; $[\alpha]_D$ −77.03° (*c* 0.16, $CHCl_3$); ^{1}H NMR (200 MHz, C_6D_6) δ: 3.32 (s, 3 H, CH_3O), 3.69 (at, 1 H, $J_{1,2}$ 7.8 Hz, H-2), 3.81 (d, 1 H, $J_{3,4}$ 10.6 Hz, H-4), 3.99 (B part of an AB syst., 1 H, J_{AB} 10.2 Hz, CH-6), 4.13 (dd, 1 H, $J_{2,3}$ 10.8 Hz, $J_{3,4}$ 10.6 Hz, H-3), 4.26 (A part of an AB syst., 1 H, J_{AB} 10.2 Hz, CH-6′),

4.61 (s, 2 H, CH_2–Bn), 4.75 (B part of an AB syst., 1 H, J_{AB} 11.4 Hz, CH_B–Bn), 4.98 (A part of an AB syst., 1 H, J_{AB} 11.2 Hz, CH_A–Bn), 5.04 (d, 1 H, $J_{1,2}$ 8.0 Hz, H-1), 5.15 (B part of an AB syst., 1 H, J_{AB} 9.8 Hz, CH_B–Bn), 5.30 (A part of an AB syst., 1 H, J_{AB} 9.8 Hz, CH_A–Bn), 6.81–6.92 (m, 5 H), 7.11–7.58 (m, 18 H), 7.80–7.85 (m, 2 H); ^{13}C NMR (50 MHz, $CDCl_3$) δ: 42.4 (C-6), 57.4 (CH_3O), 71.0, 74.1, 75.2, 77.4, 82.7 (C-2, C-3, C-4, 3 CH_2–Bn), 93.2, 100.0 (C-1, C-5), 101.2 (S*C*=C); 127.21, 127.92, 127.97, 128.05, 128.25, 128.45, 128.50, 128.74, 128.85, 129.41, 132.51 (25 CH–Ar.), 135.58, 137.51, 137.69, 138.04, 138.19 (5 Cq), 153.19 (SC=*C*); 185.84 (C=O); *Anal*. Calcd for $C_{43}H_{40}O_7S$: C, 73.69; H, 5.76. Found: C, 73.89; H, 6.25.

3.12. Methyl (4*S*,5*R*)-2,6-di-*O*-benzyl-4-deoxy-α-L-*threo*-hexopyranosid[4,5-*b*]naphtho[1,2-*e*]-1,4-oxathiin (23)

A solution of **2** (100 mg, 0.28 mmol) in 2 mL of $CHCl_3$ was treated with 108 mg (0.33 mmol) of phthalimide derivative **14** and 17.75 μL (0.22 mmol) of pyridine. The reaction mixture was heated to 60 °C for 8 days then cooled to room temperature and treated with an additional amount of **14** (89 mg, 0.28 mmol). The heating (60 °C) was maintained for 2 additional days. After this time, the mixture was diluted with CH_2Cl_2 (10 mL), washed with a saturated NH_4Cl solution (2 ×) and water (1 ×) and dried over Na_2SO_4. The organic layer was concentrated and the crude product obtained (268 mg) was purified by flash column chromatography on silica gel (2:1 hexane–EtOAc) to give **23** (72 mg, 48%) as a colourless oil; $[\alpha]_D$ −90.92° (*c* 0.14, $CHCl_3$); ^{1}H NMR (200 MHz, $CDCl_3$) δ: 2.15 (bs, 1 H, OH), 3.41–3.50 (m, 1 H, H-2), 3.64–3.72 (m, 6 H, H-3, CH_2-6, CH_3O), 3.98 (d, 1 H, $J_{3,4}$ 10.6 Hz, H-4), 4.58–4.94 (m, 4 H, 2 CH_2–Bn), 4.95 (d, 1 H, $J_{1,2}$ 8.4 Hz, H-1), 7.03 (d, 1 H, *J* 9.2 Hz, CH–Ar.), 7.24–7.57 (m, 13 H, 3 CH–Ar., 10 CH–Bn), 7.75 (d, 1 H, *J* 7.6 Hz, CH–Ar.), 7.92 (d, 1 H, *J* 8.4 Hz, CH–Ar.); ^{13}C NMR (50 MHz, $CDCl_3$) δ: 41.8 (C-6), 57.4 (CH_3O), 69.5, 71.3, 74.0, 74.6, 81.8 (C-2, C-3, C-4, 2 CH_2–Bn), 98.5 (C-5), 100.6 (C-1), 106.5 (S*C*=C); 119.2, 123.1, 124.6, 126.8, 126.9, 127.8, 127.8, 128.0, 128.4, 128.5 (10 CH–Bn, 6 CH–Ar.), 129.6, 131.2 (2 Cq–Ar.), 137.8, 138.3 (2 Cq–Bn), 148.8 (SC=*C*); *Anal*. Calcd for $C_{31}H_{30}O_6S$: C, 70.17; H, 5.70. Found: C, 70.06; H, 5.78.

3.13. Methyl (4*S*,5*R*)-2,3,6-tri-*O*-benzyl-4-deoxy-α-L-*threo*-hexopyranosid[4,5-*b*]naphtho[1,2-*e*]-1,4-oxathiin (24)

To a solution of **6** (130 mg, 0.29 mmol) in 3 mL of $CHCl_3$, 108 mg (0.29 mmol) of phthalimide derivative **14** and 18.4 μL (0.23 mmol) of pyridine were added. The reaction mixture was heated to 60 °C for 4 days then it was cooled to room temperature and treated with an additional amount of phthalimide derivative **14** (37.4 mg, 0.11 mmol). The heating (60 °C) was maintained for 6 additional days. After this time, the mixture was cooled to room temperature, diluted with CH_2Cl_2 (10 mL), washed with a saturated NH_4Cl solution (2 ×) and water (1 ×) and dried over Na_2SO_4. The crude product (450 mg) was purified by flash column chromatography on silica gel (6:1 hexane–EtOAc) to give **24** (121.4 mg, 66%) as colourless oil; $[\alpha]_D$ −68.22° (*c* 0.14, $CHCl_3$); ^{1}H NMR (200 MHz, $CDCl_3$) δ: 3.51–3.82 (m, 7 H, H-2, H-3, CH_2-6, CH_3O), 4.02 (d, 1 H, $J_{3,4}$ 10.6 Hz, H-4), 4.58–4.76 (m, 6 H, 3 CH_2–Bn), 4.92 (d, 1 H, $J_{1,2}$ 10.6 Hz, H-1), 7.06 (d, 1 H, *J* 9.0 Hz, CH–Ar.), 7.23–7.59 (m, 18 H, 3 CH–Ar., 15 CH–Bn), 7.77 (d, 1 H, *J* 7.7 Hz, CH–Ar.), 7.95 (d, 1 H, *J* 7.6 Hz, CH–Ar.); ^{13}C NMR (50 MHz, $CDCl_3$) δ: 41.4 (C-6), 57.4 (CH_3O), 71.3, 74.0, 75.0, 76.7, 77.3, 82.8 (C-2, C-3, C-4, 3 CH_2–Bn), 98.8 (C-5), 101.0 (C-1), 107.4 (S*C*=C); 119.2, 123.0, 124.6, 126.7, 126.8, 127.7, 127.8, 128.1, 128.2, 128.3, 128.4 (15 CH–Bn, 6 CH–Ar.), 129.6, 131.3 (2Cq–Ar.), 137.9, 138.1, 138.3 (3 Cq–Bn), 148.9 (SC=*C*); *Anal*. Calcd for $C_{38}H_{36}O_6S$: C, 73.53; H, 5.85. Found: C, 73.20; H, 6.22.

3.14. 4-{Methyl (5*S*)-2,6-di-*O*-benzyl-4-deoxy-α-L-*threo*-hexopyranosid-5-*O*-yl}pentan-2-one (25)

To a solution of **16** (60 mg, 0.12 mmol) in 2 mL THF, 0.8 mL of Raney-Ni (W-2) in THF were added; the suspension was vigorously stirred at room temperature for 8 h, after this time a second amount of Raney-Ni (0.2 mL in THF) was added and the stirring kept for additional 12 h. The reaction mixture was then diluted with CH_2Cl_2 (10 mL) and filtered over Celite®. The solvent was evaporated under diminished pressure and the crude obtained (43 mg) was purified by flash column chromatography on silica gel (2:1 eluant hexane–EtOAc) to give **25** (18 mg, 32%) as glassy oil and a recovered amount of glycal **2** (12%); $[\alpha]_D$ +1.2° (*c* 0.28, $CHCl_3$); ^{1}H NMR (200 MHz, $CDCl_3$) δ: 1.24 (d, 3 H, *J* 6.2 Hz, C*H*$_3$–CHO), 1.53 (B part of an ABX syst., 1 H, J_{AB} and J_{BX} 16.2 Hz CH_B-4), 2.06 (s, 3 H, CH_3–CO), 2.36 (B part of an ABX syst., 1 H, J_{AB} 13.2 Hz, J_{BX} 4.8 Hz, CH_B–C=O), 2.50 (A part of an ABX syst., 1 H, J_{AB} 16.0 Hz, J_{BX} 7.8 Hz, CH_A-4), 2.77 (A part of an ABX syst., 1 H, J_{AB} 13.2 Hz, J_{AX} 4.4 Hz, CH_A–C=O), 3.12 (at, 1 H, $J_{1,2}$ 8.0 Hz, H-2), 3.31 (B part of an AB syst., 1 H, J_{AB} 10.2 Hz, CH_B-6), 3.35 (s, 3 H, CH_3–O), 3.68 (A part of an AB syst., 1 H, J_{AB} 10.2 Hz, CH_A-6), 3.89–4.04 (m, 1 H, H-3), 4.38–4.47 (m, 1 H, C*H*–CH_3), 4.52 (s, 2 H, CH_2–Bn), 4.61 (B part of an AB syst., 1 H, J_{AB} 11.2 Hz, CH_B–Bn), 4.68 (d, 1 H, $J_{1,2}$ 7.8 Hz, H-1), 4.93 (A part of an AB syst., 1 H, J_{AB} 11.2 Hz, CH_A–Bn), 7.29–7.36 (m, 10 H, 10 CH–Ar.); ^{13}C NMR (50 MHz, $CDCl_3$) δ: 22.4

(CH_3–CO), 30.4 (CH_3–CHO), 39.7 (C-4), 51.8 (CH_3–O), 56.8 (CH–O), 64.5 (CH_2–CO), 67.2, 71.7, 73.4, 74.4, 83.7, (C-2, C-3, C-6, 2 CH_2–Bn), 99.7, 100.9 (C-1, C-5), 125.4, 127.7, 128.0, 128.4, 128.5, (10 CH–Ar), 137.4, 138.4 (2Cq), 207.2 (C=O); *Anal*. Calcd for $C_{26}H_{34}O_7$: C, 68.10; H, 7.47. Found: C, 67.91; H, 6.68.

3.15. 4-{Methyl (5*S*)-2,3,6-tri-*O*-benzyl-4-deoxy-α-L-*threo*-hexopyranosid-5-*O*-yl}pentan-2-one (26)

A solution of **18** (70 mg, 0.12 mmol) in 2 mL THF was treated with 0.8 mL of commercially available Raney-nickel;[28] the suspension was vigorously stirred at room temperature for 12 h, after this time a second amount of Raney-Ni (0.2 mL in THF) was added and the stirring kept for additional 12 h. After this time the reaction mixture was diluted with CH_2Cl_2 (10 mL) and filtered over Celite®. After evaporation of the solvent, the crude product (62 mg) was purified by flash column chromatography on silica gel (4:1 hexane–EtOAc) to give **26** (21.5 mg, 32%) and 14 mg (26%) of **6**; $[\alpha]_D^{20}$ + 21.30° (*c* 0.13, $CHCl_3$); ^{1}H NMR (200 MHz, $CDCl_3$) δ: 1.23 (d, 3 H, *J* 5.8 Hz, CH_3–CH), 1.55 (m, 1 H, CH_2-4), 2.04 (s, 3 H, CH_3–CO), 2.41–2.55 (m, 2 H, CH–CO, CH_2-4), 2.77 (A part of an ABX syst., 1 H, J_{AB} 16.0 Hz, J_{BX} 4.4 Hz, CH_A–CO), 3.31 (B part of an AB syst., 1 H, J_{AB} 10.2 Hz, CH_B-6), 3.31 (dd, 1 H, $J_{1,2}$ 9.4, $J_{2,3}$ 7.6 Hz, H-2), 3.53 (s, 3 H, CH_3–O), 3.69 (A part of an AB syst., 1 H, J_{AB} 10.2 Hz, CH_A-6), 3.82–3.95 (m, 1 H, H-3), 4.36–4.45 (m, 1 H, C*H*–CH_3), 4.52 (s, 2 H, CH_2–Bn), 4.67 (AB syst., 2 H, J_{AB} 11.8 Hz, CH_2–Bn), 4.69 (d, 1 H, $J_{1,2}$ 9.4 Hz, H-1), 4.80 (AB syst., 2 H, J_{AB} 11.0 Hz, CH_2–Bn), 7.28–7.36 (m, 15 H, 15 CH–Ar.); ^{13}C NMR (50 MHz, $CDCl_3$) δ: 22.3 (CH_3–CO), 29.7 (CH_3–CHO), 38.5 (C-4), 51.8 (CH_3–O), 57.0 (CH–O), 64.6 (CH_2–CO), 71.6, 72.5, 73.5, 74.9, 75.5, 83.2 (C-2, C-3, C-6, 3 CH_2–Bn), 99.6 (C-1), 101.2 (C-5), 127.5, 127.6, 127.7, 128.0, 128.1, 128.3, 128.4 (15CH–Ar), 137.4, 138.7 (3Cq), 207.4 (C=O); *Anal*. Calcd for $C_{33}H_{40}O_7$: C, 72.24; H, 7.35. Found: C, 72.60; H, 7.50.

3.16. Methyl (4*S*,5*R*)-2,3,6-tri-*O*-benzyl-4-deoxy-α-L-*threo*-hexopyranosid[4,5-*b*]-2-methyl-3-hydroxymethyl-1,4-oxathiin (27)

A solution of **18** (30 mg, 0.05 mmol) in 1 mL of dry THF was cooled to 0 °C and treated with $LiAlH_4$ (2.8 mg, 0.07 mmol). After 15 min, a saturated solution (2 mL) was added at 0 °C and the aqueous phase was extracted with CH_2Cl_2 (2 ×). The combined organic layers were washed with a saturated NH_4Cl solution (1 ×), dried over Na_2SO_4 filtered and concentrated under diminished pressure to give a crude product (48 mg) which was purified by flash column chromatography (5:1 hexane–EtOAc) to give **27** (15 mg, 53%) as colourless oil; $[\alpha]_D$ −184.16° (*c* 0.14, $CHCl_3$); ^{1}H NMR (200 MHz, $CDCl_3$) δ: 1.93 (s, 3 H, C*H*$_3$–C=C), 3.44–3.65 (m, 7 H, H-2, H-3, CH_3–O, CH_2-6), 3.90 (d, 1 H, $J_{3,4}$ 10.6 Hz, H-4), 4.09 (AB syst., 2 H, J_{AB} 12.8 Hz, C*H*$_2$–OH), 4.56–4.93 (m, 7 H, 3 CH_2–Bn, H-1), 5.30 (s, 1 H, OH), 7.26–7.37 (m, 15 H, 15 CH–Ar.); ^{13}C NMR (50 MHz, $CDCl_3$) δ: 17.7 (CH_3–C=), 41.6 (C-6), 57.2 (CH_3–O), 62.0, 70.9, 73.8, 75.0, 76.8, 82.8 (C-2, C-3, C-4, 3 CH_2–Bn), 98.2, 98.5, (C-5, C-1), 100.7 (S*C*=C), 127.5, 127.7, 128.1, 128.2, 128.3 (15CH–Ar.), 137.8, 138.7 (3Cq), 144.8 (SC=*C*); *Anal*. Calcd for $C_{32}H_{36}O_7S$: C, 68.06; H, 6.43. Found: C, 68.33; H, 6.43.

3.17. Methyl (4*S*,5*R*)-2,6-di-*O*-benzyl-4-thio-α-L-*threo*-hexopyranosid[4,5-*b*]naphtho[1,2-*e*]-*S*-*oxo*-1,4-oxathiin (28)

A solution of **23** (50 mg, 0.102 mmol) in 1 mL of CH_2Cl_2 was cooled to −15 °C and treated with a solution of *m*CPBA (23.1 mg, 0.133 mmol) in 1.5 mL CH_2Cl_2. After 45 min, the reaction was complete; it was washed with a 10% $Na_2S_2O_3$ solution (1 ×) and with a saturated $NaHCO_3$ solution (2 ×); the organic layer was dried over Na_2SO_4 and evaporated under diminished pressure. The crude (56 mg) was purified by flash column chromatography on silica gel (5:1 hexane–EtOAc) to give **28** (25 mg, 45%) as glassy solid; $[\alpha]_D$ = + 56.69° (*c* 0.12, $CHCl_3$); ^{1}H NMR (200 MHz, $CDCl_3$) δ: 3.51–3.72 (m, 6 H, H-2, CH_2-6, CH_3–O), 4.12 (d, 1 H, $J_{3,4}$ 10.2 Hz, H-4), 4.45 (A part of an AB syst., 1 H, J_{AB} 11.8 Hz, CH_A–Bn), 4.55 (B part of an AB syst., 1 H, J_{AB} 12.2 Hz, CH_B–Bn), 4.77–4.93 (m, 3 H, H-3, CH_2–Bn), 5.04 (d, 1 H, $J_{1,2}$ 8.0 Hz, H-1), 5.24 (d, 1 H, *J* 1,4 Hz, OH), 7.04 (d, 1 H, *J* 9.0 Hz, CH–Ar.), 7.07–7.81 (m, 13 H, 13 CH–Ar.), 7.88 (d, 1 H, *J* 9.2 Hz, CH–Ar.), 8.39 (d, 1 H, *J* 8.2 Hz, CH–Ar.); ^{13}C NMR (50 MHz, $CDCl_3$) δ: 53.1 (C-6), 57.5 (CH_3–O), 71.6, 72.2, 74.0, 75.3; 81.7 (C-2, C-3, C-4, 2 CH_2–Bn), 100.1 (C-5), 100.4 (C-1), 113.01 (S*C*=C), 118.4, 123.9, 125.2, 127.7, 127.9, 128.1, 128.3, 128.4, 134.4 (16 CH–Bn), 130.2, 131.6 (2 Cq), 136.6, 138.3 (2Cq), 149.0 (SC=*C*); *Anal*. Calcd for $C_{26}H_{34}O_7$: C, 68.12; H, 5.53. Found: C, 68.19; H, 5.90.

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