Design and synthesis of selenonium and sulfonium ions related to the naturally occurring glucosidase inhibitor salacinol[1]

Hui Liu and B. Mario Pinto

Abstract: Four series of analogues of the naturally occurring glucosidase inhibitor salacinol were synthesized for structure–activity studies with different glycosidase enzymes. The target zwitterionic compounds were synthesized by means of nucleophilic attack at the least-hindered carbon atom of the 1,3-cyclic sulfates derived from D-glucose and D-mannose by the isopropylidene-protected 1,4-anhydro-4-thio- and seleno-D-allitols and the 4-thio- and seleno-L-allitols. Deprotection of the coupled products afforded the novel sulfonium and selenonium ions containing polyhydroxylated acyclic chains of four and six carbons, with different stereochemistry at the stereogenic centers and with 1,4-anhydro-4-seleno or 4-thio-D- or L- alditol heterocyclic rings. The compounds showed no significant activity against recombinant human maltase glucoamylase (MGA), a critical intestinal glucosidase involved in the processing of oligosaccharides of glucose into glucose itself.

Key words: glycosidase inhibitors, zwitterionic, selenonium salts, sulfonium salts, cyclic sulfates, L-ascorbic acid, D-gulonic-γ-lactone.

Résumé : Afin de pouvoir faire des études de structure–activité avec divers enzymes glycosides, on a réalisé la synthèse de quatre séries d'analogues du salacinol, un inhibiteur naturel de glucosidase. Les composés zwitterioniques cibles ont été synthétisés par le biais d'une attaque nucléophile au niveau de l'atome de carbone le moins encombré de sulfates 1,3-cycliques obtenus à partir du D-glucose et du D-mannose par des 1,4-anhydro-4-thio- et 1,4-anhydro-4-séléno-D-allitols et des 4-thio- et 4-séléno-L-allitols. La déprotection des produits de couplage fournit des nouveaux ions sulfonium et sélénonium qui contiennent des chaînes acycliques polyhydroxylées de quatre et de six carbones, avec des stéréochimies différentes au niveau des centres stéréogènes et hétérocycles 1,4-anhydro-4-séléno- et 1,4-anhydro-4-thio-D- ou L-alditols. Ces composés ne présentent aucune activité significative contre la maltase glucoamylase humaine recombinante (MGA), une glucosidase intestinale critique dans la transformation des oligosaccharides du glucose en glucose.

Mots clés : inhibiteurs de glycosidase, zwitterion, sels de sélénonium, sels de sulfonium, sulfates cycliques, acide L-ascorbique, γ-lactone de l'acide D-gulonique.

[Traduit par la Rédaction]

Introduction

Glycosidases are responsible for the hydrolysis of poly- and oligo-saccharides into monomers or the cleavage of bonds between sugars and non-carbohydrate aglycons. In recent years, much attention has focused on the synthesis and development of glycosidase inhibitors because of an increasing awareness of the vital role played by sugars in biological processes and because of their therapeutic potential (1, 2). In the case of patients suffering from Type II diabetes, the management of blood glucose levels is crucial since their insulin secretion may be normal, but the entry into cells of glucose (normally mediated by insulin) is compromised (3). Glycosidase inhibitors can be used to inhibit the activity of intestinal glucosidases that break down oligosaccharides to glucose. This enzyme inhibition delays glucose absorption into the blood and results in a lowering or smoothing of the blood glucose levels (4, 5).

There are two generally accepted mechanisms for the enzymatic hydrolysis of a glycosidic bond, proceeding either with the inversion or retention of configuration at the anomeric center (6, 7). In either case, protonation of the exocyclic oxygen leads to cleavage of the glycosidic bond with subsequent formation of an oxacarbenium ion. To generate potent glycosidase inhibitors, an attractive approach is to create compounds that mimic the oxacarbenium ion transition state in the enzyme-catalyzed reaction. Some naturally occurring compounds, such as acarbose (**1**) and voglibose (**2**) (Chart 1), are potent glycosidase inhibitors and presumably mimic the oxacarbenium ion, at least in binding to active site carboxylate residues via the protonated nitrogen atom (8, 9).

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Dedicated, with respect, to Dr. Alfred Bader for his impact on the field of chemistry.

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[1]This article is part of a Special Issue dedicated to Dr. Alfred Bader.

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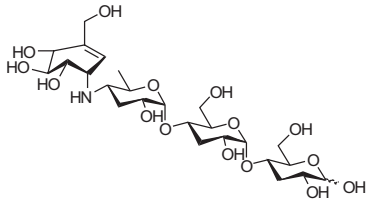
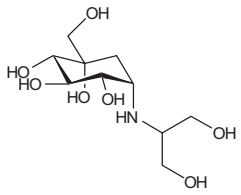
Chart 1.

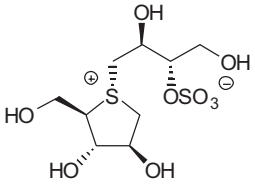


acarbose (**1**)

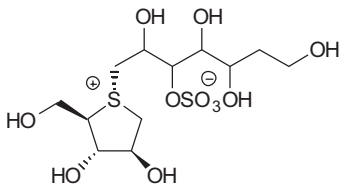


voglibose (**2**)

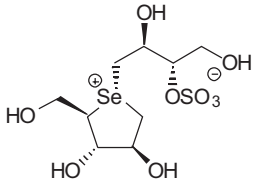
Chart 2.



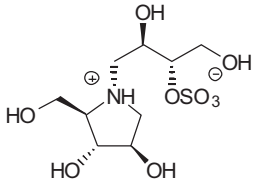
salacinol (**3**)



kotalanol (**4**)



blintol (**5**)

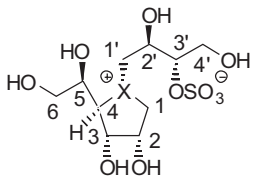


ghavaminol (**6**)

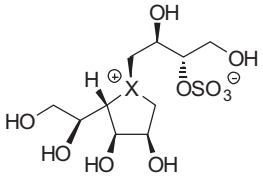
Recently, a new class of glycosidase inhibitors, including salacinol (**3**) and kotalanol (**4**) (Chart 2), with an intriguing inner-salt sulfonium sulfate structure was isolated from the roots and stems of the plant *Salacia reticulata* (10–12). The compounds were shown to be inhibitors of intestinal glucosidase enzymes that attenuate the undesirable spike in blood glucose that is experienced by diabetics after consuming a meal rich in carbohydrates. It is postulated that the inhibition of glucosidases by salacinol and kotalanol is due to their ability to mimic both the shape and charge of the oxocarbenium ion-like transition state involved in the enzymatic reactions.

In our current research program, we have undertaken a limited structure–activity study of salacinol and related compounds. The synthesis of salacinol and its ammonium and selenonium analogues have been reported by us and others (13–17). Analogues containing six-membered heterocyclic rings and some chain-extended analogues of salacinol have also been synthesized (18–21). Some of these analogues exhibited inhibitory activities in the micromolar range for recombinant human maltase glucoamylase, an intestinal glucosidase (20, 21). The studies also showed an interesting variation in the inhibitory power of these compounds against glycosidase enzymes of different origin (14–17, 22). In particular, the stereochemistry at the different stereogenic centers as well as the nature of the heteroatom play significant roles in discrimination between glycosidase enzymes. The molecular basis for this selectivity is being investigated through structural studies of the enzyme-bound inhibitors using molecular modeling in conjunction with conformational analysis by NMR techniques (23) and X-ray crystallography (24).

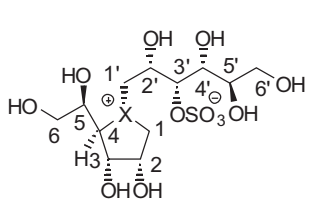
Chart 3.



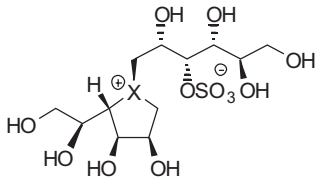
7 X = Se
8 X = S



9 X = Se
10 X = S



11 X = Se
12 X = S



13 X = Se
14 X = S

To further understand the enzyme discrimination of related compounds, we now describe the synthesis of new analogues of salacinol analogues **7**–**14** based on novel seleno- and thio-alditols derived from D-gulonic-γ-lactone and L-ascorbic acid (Chart 3).

Results and discussion

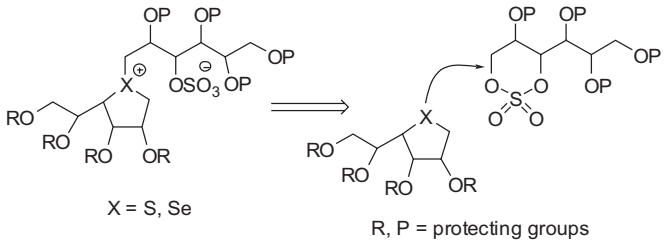
The analogues **7**–**14** can be synthesized by alkylation of a protected anhydroalditol at the ring heteroatom with terminal 1,3-cyclic sulfates. The protected anhydroalditols and the cyclic sulfates can be synthesized from the appropriate carbohydrate starting materials (Scheme 1).

The choice of protecting groups for the thio- and selenoanhydroalditols and the cyclic sulfates, however, merited careful consideration, especially in the case of the selenonium analogues. Hydrogenolysis and strongly basic conditions proved to be problematic deprotection steps for similar selenonium analogues; thus, these conditions needed to be avoided (15–17). Therefore, we chose to use isopropylidene and benzylidene acetals as the protecting groups for the thio- and seleno-anhydroalditols **15**–**18** and the cyclic sulfates **19** and **20** since these acetals are both labile to acidic hydrolysis (Chart 4).

Our previous work also suggested that the release of ring strain in the opening of bicyclic sulfates was beneficial (14–17). Therefore, the benzylidene acetal at the 2,4-positions of the cyclic sulfates **19** and **20** played dual roles as protecting groups and reaction facilitators for the coupling reactions with compounds **15**–**18**. After the coupling reactions, the products could then be readily deprotected by simple treatment with trifluoroacetic acid.

The synthesis of the isopropylidene-protected 1,4-anhydro-4-seleno-D-allitol (**15**) and 1,4-anhydro-4-thio-D-allitol (**16**) started from the commercially available D-gulonic-γ-lactone (**21**, Scheme 2). 2,3,5,6-Di-*O*-isopropylidene-D-gulonic-γ-lactone (**22**) (25) was reduced with sodium borohydride to afford the corresponding diol **23**. Compound

Scheme 1.



Scheme 2.

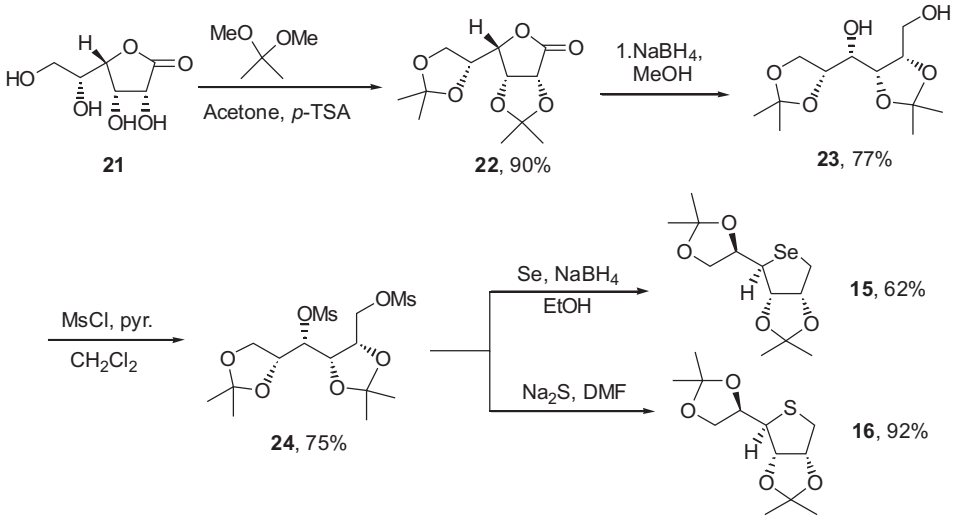
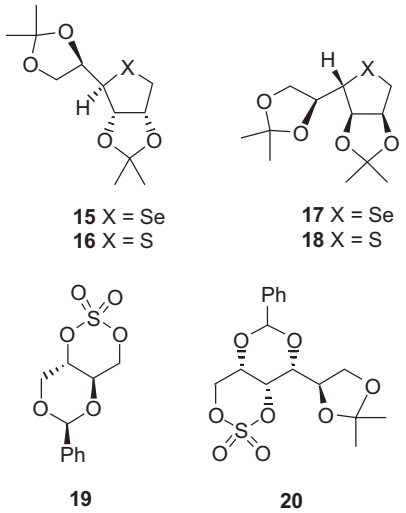


Chart 4.

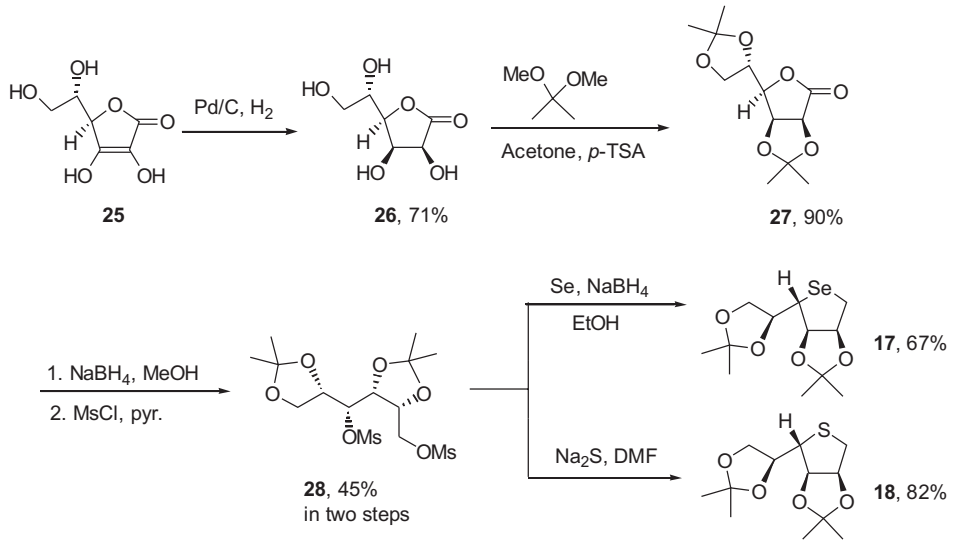


23 was then converted to the dimesylate **24** by treatment with methanesulfonyl chloride and pyridine in 80% yield (26). When the dimesylate **24** was reacted with selenium metal and sodium borohydride in EtOH at 60–65 °C, the isopropylidene-protected 1,4-anhydro-4-seleno-D-allitol **15** was obtained in 62% yield. The isopropylidene-protected 1,4-anhydro-4-thio-D-allitol **16** was prepared in 92% yield by treatment of the dimesylate **24** with sodium sulfide in DMF (Scheme 2).

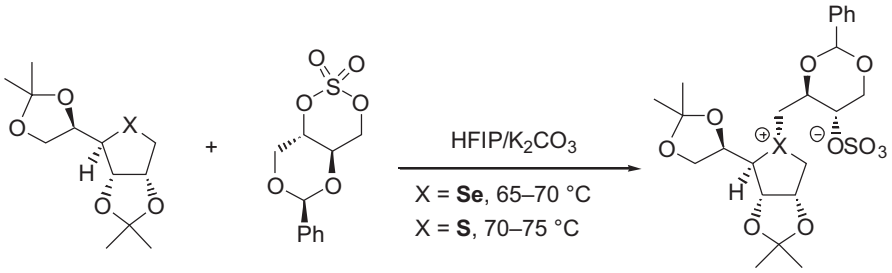
Although the enantiomeric isopropylidene-protected 1,4-anhydro-4-seleno-L-allitol (**17**) and 1,4-anhydro-4-thio-L-allitol (**18**) could, in principle, be prepared from L-gulonic-γ-lactone, the high cost of this starting material made these syntheses unrealistic. Thus, inexpensive and commercially available L-ascorbic acid (**25**) was used as the starting material to give the L-gulonic-γ-lactone (**26**) in 71% yield (27) (Scheme 3). Compound **26** was then treated with 2,2-dimethoxypropane in dry acetone containing *p*-toluenesulfonic acid as a catalyst to give 2,3,5,6-di-*O*-isopropylidene-L-gulonic-γ-lactone (**27**) (25). The lactone **27** was subsequently reduced with sodium borohydride to afford the corresponding diol that was, in turn, converted to the dimesylate **28** by treatment with methanesulfonyl chloride and pyridine. When the dimesylate **28** was reacted with selenium metal and sodium borohydride in EtOH at 60–65 °C, the isopropylidene-protected 1,4-anhydro-4-seleno-L-allitol **17** was obtained in 67% yield. The isopropylidene-protected 1,4-anhydro-4-thio-L-allitol **18** was prepared in 82% yield by treatment of the dimesylate **28** with sodium sulfide in DMF.

Since salacinol **3** and its selenonium analogue, blintol (**5**) (Chart 2), are the most active, so far, of this class of glycosidase inhibitors against human maltase glucoamylase, we first concentrated on the coupling reactions of **15** and **16** with the cyclic sulfate **19**, which would yield the identical side chain present in salacinol and blintol (Scheme 4). The solvent chosen for the coupling reactions was the unusual solvent 1,1,1,3,3,3-hexafluoroisopropanol (HFIP), which offers significant advantage in these types of coupling reactions compared with other solvents (15–17). The cyclic sulfates **19**, prepared as described previously (16), were reacted with **15** and **16**, to give the corresponding protected

Scheme 3.



Scheme 4.



selenonium and sulfonium sulfates **29** and **30**, respectively (Scheme 4).

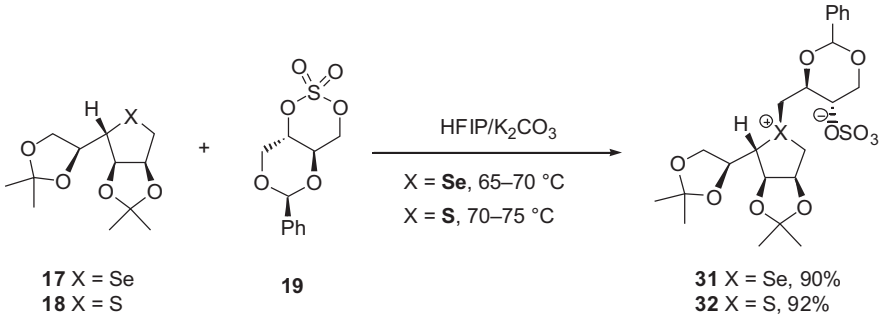
The coupling reactions of enantiomeric **17** and **18** with the cyclic sulfate **19** were carried out analogously, to give the corresponding protected selenonium and sulfonium sulfates **31** and **32**, respectively (Scheme 5).

We next turned our attention to the possibility of attaching longer side chains to the anhydroalditols **15**–**18**. Our interest in longer side chains stemmed from the fact that kotalanol **4**, which has a seven-carbon side chain instead of four-carbon side chain of the salacinol, exhibits stronger inhibitory activities toward certain glycosidase enzymes. Since the exact stereochemistry of kotalanol **4** is not yet known, it is necessary and important to study the structure–activity relationships of these types of compounds systematically by attaching side chains with different chain lengths and different stereochemistry at the stereogenic centers to the heterocyclic rings of the anhydroheteroalditols. The cyclic sulfate **20**, which consisted of a protected polyhydroxylated six-carbon chain (19), was chosen for this purpose. The cyclic sulfate **20** reacted with **15** and **16** and their enantiomers **17** and **18** in HFIP to give the corresponding protected selenonium and sulfonium compounds **33**–**36**, respectively (Scheme 6).

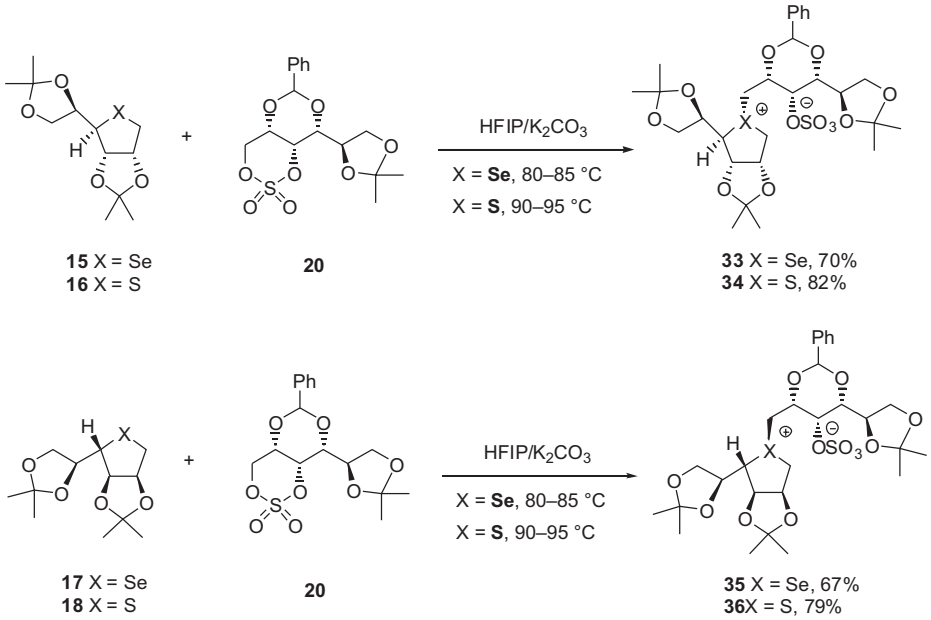
The reactivity of **15**–**18** with cyclic sulfates **19** and **20** varied slightly. With the same anhydroalditols, the cyclic sulfate **19** was more reactive than the cyclic sulfate **20**, also resulting in higher yields of the coupling reactions. Thus, the coupling reactions with the cyclic sulfate **19** usually proceeded in yields of 90%–95%, while the cyclic sulfate **20** typically gave yields of 70%–80%, with the remainder consisting of starting materials and a small amount of decomposition products. With the same cyclic sulfate, the selenoalditols were slightly more reactive than their sulfur counterparts, as demonstrated by the different reaction temperatures required in the coupling reactions. The reactivities of the enantiomeric pairs, compounds **15**–**17** and **16**–**18** with the cyclic sulfates **19** and **20** were virtually the same. Selectivity for attack at the primary center of the cyclic sulfates **19** and **20** over possible alternative attack at the secondary center by compounds **15**–**18** was invariably excellent, and in no case were isolable quantities of the regioisomers detected. In the case of the coupling reaction of **15** and L-allitol **17** with the cyclic sulfates **19** and **20**, there was a small amount (5%–10%) of the stereoisomer formed through electrophilic attack on the β face of the seleno-D-allitol **15** and the α face of the seleno-L-allitol **17** to give products that were diastereomeric at the selenonium center, but could not be isolated in pure form. However, this type of minor product was not detected in the reactions of the corresponding thioallitols.

The deprotection of the coupled products **29**–**36** was carried out by treatment with trifluoroacetic acid (Scheme 7). After rinsing away the cleaved protecting groups with dichloromethane, the resulting residues were purified by flash

Scheme 5.



Scheme 6.



chromatography to yield compounds **7**–**10** as amorphous, hygroscopic solids. In the cases of compounds **33**–**36**, however, some of the benzylidene acetal protecting group (up to 30% by NMR measurements) remained even after prolonged (up to 48 h) treatment with TFA. The remaining benzylidene acetal was eventually cleaved by hydrogenolysis in 80% acetic acid to give the corresponding deprotected products **11**–**14** as amorphous, hygroscopic solids. The yields of compounds **11**–**14** were low, partly because of the adsorption of the products on the Pd–C catalyst. Compounds **7**–**14** were characterized by spectroscopic methods. The MALDI-TOF mass spectra of compounds **7**–**14** showed major fragmentation peaks ($M + Na^+ - SO_3$) together with the molecular ion peaks ($M + Na^+$) of much lower intensities.

The absolute stereochemistry at the heteroatom center of compounds **7**–**14** was established by 1D-NOE NMR spectroscopy. For example, in the 1D-NOE spectrum of compound **8** (Fig. 1), the H-4 to H-1′b correlation was clearly exhibited, implying that these two hydrogens are syn-facial. Therefore, C-1′ of the side chain must be anti to C-5 of the sulfonium salt ring.

As a final point of interest, compounds **7**–**14** were screened against recombinant human maltase glucoamylase (MGA), a critical intestinal glucosidase involved in the processing of oligosaccharides of glucose into glucose itself. The compounds showed no significant activity.[3]

Conclusions

Four series of analogues of the naturally occurring glucosidase inhibitor salacinol were synthesized. These analogues contained the acyclic chains of salacinol and extended acyclic chains of six carbons, as well as ring heteroatom substitution (Se, S). In addition, the heterocyclic ring bore the D- or L-allitol configuration. These syntheses utilized the 1,3-cyclic sulfates derived from commercially available D-glucose and D-mannose. The isopropylidene and benzylidene acetal protecting groups on the coupled products ensured facile deprotection with TFA to yield the final compounds **7**–**14**. The compounds showed no inhibitory activity against human maltase glucoamylase.

Experimental section

General

Optical rotations were measured at 23 °C. ^1H and ^{13}C

[3] L. Sim and D.R. Rose. Unpublished data.

Scheme 7.

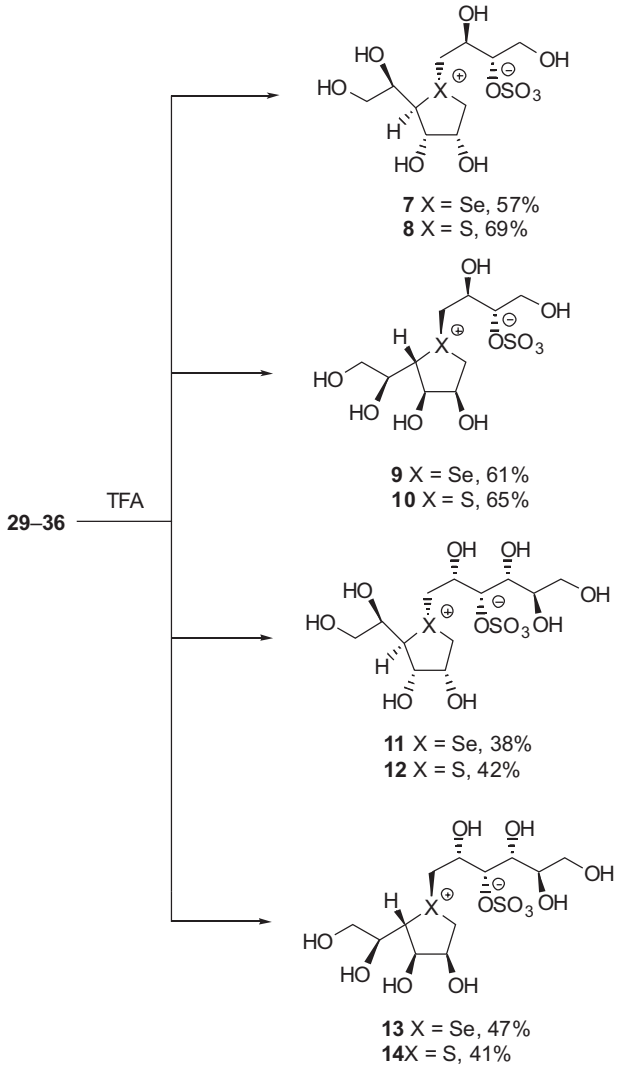
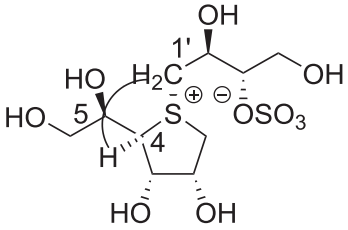


Fig. 1. NOE correlation observed in the 1D-NOE spectrum of compound **8**.



NMR spectra were recorded at 500 and 125 MHz, respectively. All assignments were confirmed with the aid of two-dimensional ^{1}H and ^{1}H (COSYDFTP) or ^{1}H and ^{13}C (INVBTP) experiments using standard Bruker pulse programs. Column chromatography was performed with Merck silica gel 60 (230–400 mesh). MALDI mass spectra were obtained on a PerSeptive Biosystems Voyager DE time-of-flight spectrometer for samples dispersed in a 2,5-dihydroxybenzoic acid matrix. High-resolution mass spectra were obtained by the electrospray ionization (ESI) technique, using a ZabSpec oaTOF mass spectrometer at 10 000 RP.

2,3,5,6-Di-*O*-isopropylidene-1,4-di-*O*-methanesulfonyl-D-gulitol (24)

2,3,5,6-Di-*O*-isopropylidene-1,4-di-*O*-methanesulfonyl-D-gulitol (**24**) was prepared by the literature method (26) with slight variations. To a solution of commercially available D-gulonic-γ-lactone **21** (10.0 g, 56.1 mmol) in dry acetone (200 mL), 2,2-dimethoxypropane (40 mL, 0.32 mmol) was added at RT. To this solution, *p*-toluenesulfonic acid (200 mg) was added as a catalyst. The progress of the reaction was followed by TLC analysis of the aliquots (hexane–EtOAc, 1:1). When the starting material **21** had been essentially consumed, the reaction was stopped by addition of triethylamine (1 mL) to the reaction mixture. The solvent was then evaporated under reduced pressure and the residue was purified by column chromatography (hexane–EtOAc, 1:1) to give compound **22** as a white solid (13.1 g, 90%). The NMR spectrum of compound **22** matched that of the published data (25). The lactone **22** (5.0 g, 19.3 mmol) was dissolved in THF (20 mL) and MeOH (50 mL) was then added. To this solution, $NaBH_4$ was added portionwise at 0 °C. The progress of the reaction was followed by TLC analysis of the aliquots (hexane–EtOAc, 1:1). When the starting material **22** had been consumed, the solvent was evaporated under reduced pressure. The residue was redissolved in EtOAc (50 mL), washed with aqueous tartaric acid solution (2 × 10 mL) and brine (50 mL), and dried over Na_2SO_4. Purification by column chromatography (hexane–EtOAc, 2:1) yielded compound **23** as a colourless syrup (3.9 g, 77%). The NMR spectrum of compound **23** matched that of the published data (26). The diol **23** (5.0 g, 19.1 mmol) was dissolved in CH_2Cl_2 (50 mL) and the solution was added dropwise to a mixture of pyridine (100 mL) and methanesulfonyl chloride (6 mL, 77.5 mmol) and cooled to 0 °C. The reaction mixture was stirred at 0 °C for 30 min and then allowed to warm to RT for 6 h. When TLC analysis of the aliquots (hexane–EtOAc, 1:1) showed total consumption of the starting material, the reaction mixture was poured into ice water, extracted with CH_2Cl_2 (3 × 100 mL), washed with brine (50 mL), and dried over Na_2SO_4. Purification by column chromatography (hexane–EtOAc, 2:1) yielded compound **24** as a colourless syrup (5.9 g, 75%). $[\alpha]^{22}_{D}$ –46° (*c* 1, CH_2Cl_2). ^{1}H NMR ($(CD_3)_2O$) δ: 4.87 (dd, 1H, $J_{3,4}$ = 5.8 Hz, $J_{4,5}$ = 4.7 Hz, H-4), 4.56 (ddd, 1H, $J_{1b,2}$ = 6.0 Hz, $J_{1a,1b}$ = 12.0 Hz, H-1b), 4.56–4.48 (m, 2H, H-2, H-3, H-1a), 4.48 (dd, 1H, H-1a), 4.46 (ddd, 1H, H-5), 4.14 (dd, 1H, $J_{5,6b}$ = 6.8 Hz, $J_{6a,6b}$ = 8.7 Hz, H-6b), 4.02 (dd, 1H, $J_{5,6a}$ = 6.7 Hz, H-6a), 3.23, 3.14 (2 s, 6H, 2 × OSO_2CH_3), 1.51, 1.41, 1.38, 1.34 (4 s, 12H, 4 × CH_3). ^{13}C NMR ($(CD_3)_2O$) δ: 110.1, 109.6 ($(CH_3)_2C(OR)_2$), 79.1 (C-4), 75.6 (C-3), 75.0 (C-2), 74.9 (C-1), 68.7 (C-5), 65.4 (C-6), 38.8, 36.7 (2 × OSO_2CH_3), 26.9, 25.6, 25.1, 25.0 (4 × CH_3). Anal. calcd. for $C_{14}H_{26}O_{10}S_2$: C 40.18, H 6.26; found: C 40.35, H 6.14.

2,3,5,6-Di-*O*-isopropylidene-1,4-di-*O*-methanesulfonyl-L-gulitol (28)

To a solution of commercially available L-ascorbic acid **25** (30.0 g, 0.17 mmol) in distilled water (200 mL), palladium

on activated carbon (10%, 1.0 g) was added as a catalyst at RT. The reaction mixture was placed in a steel reaction vessel and underwent hydrogenation (100 psi, 1 psi = 6.894 757 kPa) at 60 °C for 48 h. The progress of the reaction was followed by TLC analysis of the aliquots (EtOAc–MeOH–H_2O, 10:3:1). When the starting material **25** had been essentially consumed, the reaction was stopped and the reaction mixture was filtered under vacuum and washed with water (2 × 50 mL). The filtrate and the wash were combined and the water was then evaporated under reduced pressure. The residue was recrystallized from methanol – ethyl acetate to give compound **26** as a white solid (21.5 g, 71%). The NMR spectrum of compound **26** matched that of the published literature (26). To a suspension of the lactone **26** (10.0 g, 56.1 mmol) in dry acetone (200 mL), 2,2-dimethoxypropane (40 mL, 0.32 mmol) was added at RT. To this mixture, *p*-toluenesulfonic acid (200 mg) was added as a catalyst. The progress of the reaction was followed by TLC analysis of the aliquots (hexane–EtOAc, 1:1). When the starting material **26** had been essentially consumed, the reaction was stopped by addition of triethylamine (1 mL). The solvent was then evaporated under reduced pressure and the residue was purified by column chromatography (hexane–EtOAc, 1:1) to give compound **27** as a white solid. The NMR spectrum of compound **26** matched that of the published data (25). Lactone **27** (5.0 g, 19.3 mmol) was dissolved in THF (20 mL) and MeOH (50 mL) was then added. To this solution, $NaBH_4$ was added portionwise at 0 °C. The progress of the reaction was followed by TLC analysis of the aliquots (hexane–EtOAc, 1:1). When the starting material **27** had been consumed, the solvent was evaporated under reduced pressure. The residue was redissolved in EtOAc (50 mL), washed with aqueous tartaric acid solution (2 × 10 mL) and brine (50 mL), and dried over Na_2SO_4. After evaporating the solvent, the crude diol was used directly in the next step. The crude diol was dissolved in CH_2Cl_2 (50 mL). The solution was added dropwise to a mixture of pyridine (100 mL) and methanesulfonyl chloride (6 mL, 77.5 mmol) and cooled to 0 °C. The reaction mixture was stirred at 0 °C for 30 min, then allowed to warm to RT for 6 h. When TLC analysis of the aliquots (hexane–EtOAc, 1:1) showed total consumption of the starting material, the reaction mixture was poured into ice water, extracted with CH_2Cl_2 (3 × 100 mL), washed with brine (50 mL), and dried over Na_2SO_4. Purification by column chromatography (hexane–EtOAc, 2:1) yielded compound **28** as a colourless syrup (3.6 g, 45% for two steps). $[\alpha]^{22}_D$ +54° (*c* 4, CH_2Cl_2). ^{1}H NMR (($CD_3)_2O$) δ: 4.87 (dd, 1H, $J_{3,4}$ = 6.1 Hz, $J_{4,5}$ = 4.8 Hz, H-4), 4.57 (ddd, 1H, $J_{1b,2}$ = 6.0 Hz, $J_{1a,1b}$ = 12.0 Hz, H-1b), 4.56–4.48 (m, 3H, H-2, H-3, H-1a), 4.45 (ddd, 1H, H-5), 4.13 (dd, 1H, $J_{5,6b}$ = 6.7 Hz, $J_{6a,6b}$ = 8.6 Hz, H-6b), 4.03 (dd, 1H, $J_{5,6a}$ = 6.6 Hz, H-6a), 3.24, 3.15 (2 s, 6H, 2 × OSO_2CH_3), 1.52, 1.41, 1.38, 1.34 (4 s, 12H, 4 × CH_3). ^{13}C NMR (($CD_3)_2O$) δ: 114.3, 113.8 (($CH_3)_2C(OR)_2$), 83.3 (C-4), 79.7 (C-3), 79.0 (C-2), 78.9 (C-1), 72.9 (C-5), 69.6 (C-6), 43.0, 40.9 (2 × OSO_2CH_3), 31.3, 29.9, 29.3, 29.2 (4 × CH_3). Anal. calcd. for $C_{14}H_{26}O_{10}S_2$: C 40.18, H 6.26; found: C 39.89, H 6.02.

1,4-Anhydro-2,3,5,6-di-*O*-isopropylidene-4-seleno-D-allitol (15)

To a suspension of grey selenium metal (1.6 g, 20.2 mmol) and 95% EtOH (100 mL), $NaBH_4$ was added portionwise until the black Se color disappeared. To this mixture, a solution of the dimesylate **24** (7.0 g, 16.8 mmol) in THF (10 mL) was added and the reaction mixture was heated at 70 °C for 12 h. The solvent was evaporated under reduced pressure, the residue was redissolved in EtOAc, washed with water (20 mL) and brine (20 mL), and dried over Na_2SO_4. After evaporating the solvent, the crude product was purified by column chromatography (hexane–EtOAc, 3:1) to give **15** as a colourless oil (3.2 g, 62%). $[\alpha]^{22}_D$ +152° (*c* 1, CH_2Cl_2). ^{1}H NMR (($CD_3)_2O$) δ: 4.98 (ddd, 1H, $J_{1b,2}$ = 4.5 Hz, H-2), 4.91 (dd, 1H, $J_{2,3}$ = 5.6 Hz, H-3), 4.12 (dd, 1H, $J_{6a,6b}$ = 8.4 Hz, $J_{5,6b}$ = 6.4 Hz, H-6b), 4.04 (ddd, 1H, $J_{5,6a}$ = 5.9 Hz, $J_{4,5}$ = 5.8 Hz, H-5), 3.71 (dd, 1H, H-6a), 3.18 (m, 1H, H-4), 3.16 (dd, 1H, $J_{1a,1b}$ = 12.8 Hz, H-1b), 2.78 (dd, 1H, H-1a), 1.42, 1.38, 1.29, 1.28 (4 s, 12H, 4 × CH_3). ^{13}C NMR (($CD_3)_2O$) δ: 110.3, 109.8 (($CH_3)_2C(OR)_2$), 85.6 (C-3), 83.9 (C-2), 76.4 (C-5), 69.0 (C-6), 57.7 (C-4), 37.4 (C-1), 26.5, 26.0, 25.1, 24.1 (4 × CH_3). Anal. calcd. for $C_{12}H_{20}O_4Se$: C 46.91, H 6.56; found: C 46.67, H 6.37.

1,4-Anhydro-2,3,5,6-di-*O*-isopropylidene-4-thio-D-allitol (16)

To a solution of the dimesylate **24** (5.0 g, 11.9 mmol) in DMF (80 mL), $Na_2S{\cdot}9H_2O$ (4.0 g, 16.7 mmol) was added and the reaction mixture was heated at 90 °C for 12 h. The reaction mixture was poured into water (100 mL), extracted with Et_2O (4 × 50 mL), washed with water (10 × 20 mL), and dried over Na_2SO_4. After evaporating the solvent, the crude product was purified by column chromatography (hexane–EtOAc, 3:1) to give **16** as a colourless oil (2.9 g, 92%). $[\alpha]^{22}_D$ +127° (*c* 1, CH_2Cl_2). ^{1}H NMR (($CD_3)_2O$) δ: 5.04 (ddd, 1H, $J_{1b,2}$ = 4.7 Hz, H-2), 4.91 (dd, 1H, $J_{2,3}$ = 5.6 Hz, H-3), 4.15–4.12 (m, 1H, H-4), 4.13 (dd, 1H, H-6b), 3.68 (ddd, 1H, $J_{5,6a}$ = 6.7 Hz, $J_{4,5}$ = 9.2 Hz, $J_{5,6b}$ = 8.2 Hz, H-5), 3.45 (dd, 1H, $J_{6a,6b}$ = 8.5 Hz, H-6a), 3.29 (dd, 1H, $J_{1a,1b}$ = 11.2 Hz, H-1b), 2.92 (dd, 1H, H-1a), 1.42, 1.38, 1.29, 1.27 (4 s, 12H, 4 × CH_3). ^{13}C NMR (($CD_3)_2O$) δ: 109.9, 109.8 (($CH_3)_2C(OR)_2$), 87.1 (C-3), 85.3 (C-2), 77.1 (C-5), 69.6 (C-6), 52.6 (C-4), 29.7 (C-1), 26.6, 26.2, 25.2, 24.1 (4 × CH_3). Anal. calcd. for $C_{12}H_{20}O_4S$: C 55.36, H 7.74; found: C 55.64, H 7.72.

1,4-Anhydro-2,3,5,6-di-*O*-isopropylidene-4-seleno-L-allitol (17)

To a suspension of grey selenium metal (1.4 g, 18.7 mmol) and EtOH (100 mL, 95%), $NaBH_4$ was added portionwise until the black Se color disappeared. To this mixture, a solution of the dimesylate **28** (6.0 g, 14.3 mmol) in THF (10 mL) was added and the reaction mixture was heated at 65–70 °C for 12 h. The solvent was evaporated under reduced pressure and the residue was redissolved in EtOAc, washed with water (20 mL) and brine (20 mL), and dried over Na_2SO_4. After evaporating the solvent, the crude product was purified by column chromatography (hexane–EtOAc, 3:1) to give **17** as a colourless oil (2.9 g, 67%). $[\alpha]^{22}_D$ −143° (*c* 1, CH_2Cl_2). ^{1}H NMR (($CD_3)_2O$) δ: 5.03 (ddd, 1H, H-2), 4.91 (dd, 1H, $J_{2,3}$ = 5.6 Hz, H-3), 4.15–4.10 (m, 2H, H-5, H-6b), 3.68 (dd, 1H, $J_{5,6a}$ = 8.9 Hz, $J_{6a,6b}$ = 11.4 Hz, H-6a), 3.45 (dd, 1H, H-4), 3.27 (dd, 1H, $J_{1b,2}$ = 4.7 Hz, $J_{1a,1b}$ = 12.0 Hz, H-1b), 2.92 (dd, 1H, $J_{1b,2}$ = 0.7 Hz,

H-1a), 1.42, 1.37, 1.29, 1.27 (4 s, 12H, 4 × CH_3). ^{13}C NMR ($(CD_3)_2O$) δ: 110.0, 109.8 ($(CH_3)_2C(OR)_2$), 87.1 (C-3), 85.3 (C-2), 77.1 (C-5), 69.6 (C-6), 52.6 (C-4), 29.8 (C-1), 26.6, 26.2, 25.3, 24.1 (4 × CH_3). Anal. calcd. for $C_{12}H_{20}O_4Se$: C 46.91, H 6.56; found: C 46.76, H 6.66.

1,4-Anhydro-2,3,5,6-di-*O*-isopropylidene-4-thio-L-allitol (18)

To a solution of the dimesylate **28** (5.0 g, 11.9 mmol) in DMF (80 mL), $Na_2S·9H_2O$ (4.0 g, 16.7 mmol) was added and the reaction mixture was heated at 90 °C for 12 h. The reaction mixture was poured into water (100 mL), extracted with Et_2O (4 × 50 mL), washed with water (10 × 20 mL), and dried over Na_2SO_4. After evaporating the solvent, the crude product was purified by column chromatography (hexane–EtOAc, 3:1) to give **18** as a colourless oil (2.5 g, 82%). $[\alpha]^{22}_D$ –139° (*c* 1, CH_2Cl_2). ^{1}H NMR ($(CD_3)_2O$) δ: 4.99 (ddd, 1H, H-2), 4.92 (dd, 1H, $J_{2,3}$ = 5.6 Hz, H-3), 4.12 (dd, 1H, $J_{6a,6b}$ = 8.2 Hz, $J_{5,6b}$ = 6.4 Hz, H-6b), 4.04 (ddd, 1H, H-5), 3.71 (dd, 1H, $J_{5,6a}$ = 5.9 Hz, H-6a), 3.19–3.15 (m, 1H, H-4), 3.17 (dd, 1H, H-1b), 2.80 (dd, 1H, $J_{1a,1b}$ = 12.9 Hz, H-1a), 1.42, 1.38, 1.29, 1.28 (4 s, 12H, 4 × CH_3). ^{13}C NMR ($(CD_3)_2O$) δ: 110.3, 109.8 ($(CH_3)_2C(OR)_2$), 85.6 (C-3), 83.9 (C-2), 76.3 (C-5), 69.0 (C-6), 57.7 (C-4), 37.4 (C-1), 26.5, 26.0, 25.1, 24.1 (4 × CH_3). Anal. calcd. for $C_{12}H_{20}O_4S$: C 55.36, H 7.74; found: C 55.16, H 7.58.

General procedure for the preparation of sulfonium and selenonium sulfates 29–36

A mixture of **15**, **16**, **17**, or 1**8**, and the cyclic sulfate **19** or **20** in HFIP (1,1,1,3,3,3-hexafluoroisopropanol) was placed in a reaction vessel and K_2CO_3 (20 mg) was added. The stirred reaction mixture was heated in a sealed tube at the indicated temperature for the indicated time, as given later. The progress of the reaction was followed by TLC analysis of the aliquots (EtOAc–MeOH, 10:1). When the limiting reagent had been essentially consumed, the mixture was cooled, diluted with CH_2Cl_2, and evaporated to give a syrupy residue. Purification by column chromatography (EtOAc to EtOAc–MeOH, 10:1) gave the purified sulfonium salts and selenonium salts **29**–**36**.

1,4-Anhydro-2,3,5,6-di-*O*-isopropylidene-1-[(S)-[(2′S,3′S)-2′,4 -benzylidenedioxy-3′-(sulfooxy)butyl]selenonio]-D-allitol inner salt (29)

The reaction of compound **15** (500 mg, 1.63 mmol) with the cyclic sulfate **19** (530 mg, 1.94 mmol) in HFIP (2.0 mL) for 12 h at 80–85 °C gave compound **29** as a colourless, amorphous solid (850 mg, 90% based on **15**). $[\alpha]^{22}_D$ +12° (*c* 0.5, CH_2Cl_2). ^{1}H NMR ($(CD_3)_2O$) δ: 7.56–7.38 (m, 5H, H-Arom.), 5.74 (s, 1H, C*H*Ph), 5.52 (ddd, 1H, $J_{1b,2}$ = 5.2 Hz, $J_{2,3}$ = 5.7, H-2), 5.27 (dd, 1H, H-3), 4.78 (ddd, 1H, ddd, 1H, $J_{5,6b}$ = 7.3 Hz, $J_{5,6a}$ = 5.2 Hz, $J_{4,5}$ = 3.8 Hz, H-5), 4.62 (dd, 1H, H-4), 4.46–4.37 (m, 4H, H-1′b, H-2′, H-3′, H-4′b), 4.28 (dd, 1H, $J_{1'a,1'b}$ = 13.4 Hz, $J_{1'a,2'}$ = 3.8 Hz, H-1′a), 4.25 (dd, 1H, $J_{6a,6b}$ = 9.5 Hz, $J_{5,6b}$ = 7.3 Hz, H-6b), 4.10 (dd, 1H, $J_{1b,2}$ = 5.2 Hz, $J_{1a,1b}$ = 15.4 Hz, H-1b), 3.97 (dd, 1H, H-1a), 3.96 (dd, 1H, $J_{5,6a}$ = 5.2 Hz, H-6a), 3.78 (m, 1H, H-4′a), 1.64, 1.42, 1.38, 1.32 (4 s, 18H, 4 × CH_3). ^{13}C NMR ($(CD_3)_2O$) δ: 142.3, 133.9, 133.0, 131.1 (C-Ar), 116.9, 115.7 (2 $(CH_3)_2C(OR)_2$), 106.1 (*C*HPh), 89.9 (C-3), 89.8 (C-2), 81.3 (C-2′), 79.0 (C-5), 73.9 (C-4), 73.5 (C-4′), 71.8 (C-6), 71.5 (C-3), 52.8 (C-1), 50.4 (C-1′), 30.3, 30.1, 28.2, 27.1 (4 × *C*H_3). HRMS calcd. for $C_{23}H_{33}O_{10}SSe$: 581.0594 (M + H^+); found: 581.0597.

1,4-Anhydro-2,3,5,6-di-*O*-isopropylidene-1-[(S)-[(2′S,3′S)-2′,4′-benzylidenedioxy-3′-(sulfooxy)butyl]sulfonio]-D-allitol inner salt (30)

The reaction of compound **16** (500 mg, 1.92 mmol) with the cyclic sulfate **19** (630 mg, 2.31 mmol) in HFIP (2.0 mL) for 12 h at 70–75 °C gave compound **30** as a colourless, amorphous solid (960 mg, 94% based on **16**). $[\alpha]^{22}_D$ +1.2° (*c* 0.1, CH_2Cl_2). ^{1}H NMR ($(CD_3)_2O$) δ: 7.56–7.38 (m, 5H, H-Arom.), 5.74 (s, 1H, C*H*Ph), 5.52 (ddd, 1H, $J_{1b,2}$ = 5.2 Hz, $J_{2,3}$ = 5.7 Hz, H-2), 5.26 (dd, 1H, H-3), 4.79 (ddd, 1H, ddd, 1H, $J_{5,6b}$ = 7.4 Hz, $J_{5,6a}$ = 5.1 Hz, $J_{4,5}$ = 3.9 Hz, H-5), 4.63 (dd, 1H, H-4), 4.49–4.36 (m, 4H, H-1′b, H-2′, H-3′, H-4′b), 4.28 (dd, 1H, $J_{1'a,1'b}$ = 13.4 Hz, $J_{1'a,2'}$ = 3.7 Hz, H-1′a), 4.25 (dd, 1H, $J_{6a,6b}$ = 9.4 Hz, H-6b), 4.10 (dd, 1H, $J_{1b,2}$ = 5.2 Hz, $J_{1a,1b}$ = 14.4 Hz, H-1b), 3.97 (dd, 1H, H-1a), 3.97 (dd, 1H, $J_{5,6a}$ = 5.1 Hz, H-6a), 3.78 (m, 1H, H-4′a), 1.64, 1.42, 1.38, 1.32 (4s, 18H, 4 × CH_3). ^{13}C NMR ($(CD_3)_2O$) δ: 138.5, 129.3, 128.4, 126.5 (C-Ar), 112.3, 111.1 (2 $(CH_3)_2C(OR)_2$), 101.4 (*C*HPh), 85.3 (C-3), 85.2 (C-2), 76.7 (C-2′), 74.4 (C-5), 69.2 (C-4′), 68.8 (C-4), 67.1 (C-6), 67.0 (C-3′), 48.2 (C-1), 45.8 (C-1′), 25.7, 25.5, 23.6, 22.5 (4 × *C*H_3). Anal. calcd. for $C_{23}H_{32}O_{10}S_2$: C 51.86, H 6.06; found: C 52.06, H 5.87. HRMS calcd. for $C_{23}H_{33}O_{10}S_2$: 533.1510 (M + H^+); found: 533.1512.

1,4-Anhydro-2,3,5,6-di-*O*-isopropylidene-1-[(S)-[(2′S,3′S)-2′,4 -benzylidenedioxy-3′-(sulfooxy)butyl]selenonio]-L-allitol inner salt (31)

The reaction of compound **17** (500 mg, 1.63 mmol) with the cyclic sulfate **19** (530 mg, 1.94 mmol) in HFIP (2.0 mL) for 12 h at 65–70 °C gave compound **31** as a colourless, amorphous solid (850 mg, 90% based on **17**). $[\alpha]^{22}_D$ +18° (*c* 1.0, CH_2Cl_2). ^{1}H NMR (CD_2Cl_2) δ: 7.48–7.38 (m, 5H, H-Arom.), 5.61 (s, 1H, C*H*Ph), 5.41 (ddd, 1H, H-2), 5.15 (dd, 1H, $J_{2,3}$ = 5.3 Hz, H-3), 4.81 (ddd, 1H, $J_{4,5}$ = 2.0 Hz, $J_{5,6a}$ = 4.6 Hz, $J_{5,6b}$ = 7.8 Hz, H-5), 4.60 (m, 1H, H-4), 4.55 (ddd, 1H, H-3′), 4.52 (dd, 1H, H-4′b), 4.42 (d, 2H, H-1′b, H-1′a), 4.38–4.32 (m, 1H, H-2′), 4.20 (dd, 1H, $J_{5,6b}$ = 7.8 Hz, $J_{6a,6b}$ = 9.6 Hz, H-6b), 3.95 (dd, 1H, $J_{5,6a}$ = 4.6 Hz, H-6a), 3.85 (dd, 1H, $J_{4'a,4'b}$ = 10.0 Hz, H-4′a), 3.63 (dd, 1H, H-1b), 3.60 (dd, 1H, $J_{1a,2}$ = 5.1 Hz, $J_{1a,1b}$ = 13.9 Hz, H-1a), 1.60, 1.44, 1.36, 1.32 (4 s, 12H, 4 × CH_3). ^{13}C NMR (CD_2Cl_2) δ: 137.0, 129.5, 128.6, 126.3 (C-Ar), 112.1, 111.2 (2 $(CH_3)_2C(OR)_2$), 101.8 (*C*HPh), 87.8 (C-2), 85.7 (C-3), 76.9 (C-3′), 74.7 (C-5), 70.5 (C-4), 69.3 (C-4′), 67.7 (C-2′), 67.2 (C-6), 44.5 (C-1′), 43.2 (C-1), 26.2, 26.0, 23.3, 22.9 (4 × *C*H_3). Anal. calcd. for $C_{23}H_{32}O_{10}SSe$: C 47.67, H 5.57; found: C 47.89, H 5.67.

1,4-Anhydro-2,3,5,6-di-*O*-isopropylidene-1-[(S)-[(2′S,3′S)-2′,4′-benzylidenedioxy-3′-(sulfooxy)butyl]sulfonio]-L-allitol inner salt (32)

The reaction of compound **18** (500 mg, 1.92 mmol) with the cyclic sulfate **19** (630 mg, 2.31 mmol) in HFIP (2.0 mL) for 12 h at 80–85 °C gave compound **32** as a colourless, amorphous solid (940 mg, 92% based on **18**). $[\alpha]^{22}_D$ +10° (*c* 0.5, CH_2Cl_2). ^{1}H NMR ($(CD_3)_2O$) δ: 7.48–7.39 (m, 5H, H-

Arom.), 5.59 (s, 1H, C*H*Ph), 5.26 (ddd, 1H, H-2), 5.10 (dd, 1H, $J_{2,3}$ = 5.8 Hz, H-3), 4.88 (ddd, 1H, $J_{4,5}$ = 7.6 Hz, H-5), 4.68 (ddd, 1H, H-3′), 4.54 (m, 1H, H-4), 4.50 (dd, 1H, $J_{3',4'}$ = 1.8 Hz, H-4′), 4.40 (d, 2H, H-1′b, H-1′a), 4.34 (m, 1H, H-2′), 4.32 (dd, 1H, $J_{5,6b}$ = 7.9 Hz, $J_{6a,6b}$ = 9.8 Hz, H-6b), 4.01 (dd, 1H, $J_{5,6a}$ = 4.6 Hz, H-6a), 3.82 (dd, 1H, H-4′a), 3.68 (dd, 1H, $J_{1b,2}$ = 5.3 Hz, $J_{1a,1b}$ = 15.0 Hz, H-1b), 3.62 (dd, 1H, H-1a), 1.60, 1.44, 1.36, 1.34 (4 s, 12H, 4 × CH_3). ^{13}C NMR ($(CD_3)_2O$) δ: 136.9, 129.6, 128.6, 126.3 (C-Ar), 112.8, 111.5 (2 $(CH_3)_2C(OR)_2$), 101.9 (*C*HPh), 86.2 (C-2), 84.1 (C-3), 76.9 (C-3′), 74.8 (C-5), 71.4 (C-4), 69.2 (C-2), 67.3 (C-6), 65.7 (C-4′), 47.7 (C-1), 45.9 (C-1′), 26.0, 25.9, 23.3, 22.6 (4 × *C*H_3). HRMS calcd. for $C_{23}H_{33}O_{10}S_2$: 533.1510 ($M + H^+$); found: 533.1515.

1,4-Anhydro-2,3,5,6-di-*O*-isopropylidene-1-[(S)-[(2′R,3′S,4′R,5′R)-2′,4′-benzylidenedioxy-5′,6′-isopropylidenedioxy-3′-(sulfooxy)hexyl]selenonio]-D-allitol inner salt (33)

The reaction of compound **15** (500 mg, 1.63 mmol) with the cyclic sulfate **20** (730 mg, 1.96 mmol) in HFIP (2.0 mL) for 12 h at 80–85 °C gave compound **33** as a colourless, amorphous solid (770 mg, 70% based on **15**). $[\alpha]^{22}_D$ +8° (*c* 0.5, CH_2Cl_2). ^{1}H NMR ($(CD_3)_2O$) δ: 7.58–7.32 (m, 5H, H-Arom.), 5.90 (s, 1H, C*H*Ph), 5.63 (ddd, 1H, $J_{2,3}$ = 5.4 Hz, H-2), 5.26 (dd, 1H, H-3), 4.92 (m, 1H, H-2′), 4.82 (ddd, 1H, $J_{5,6b}$ = 7.7 Hz, $J_{5,6a}$ = 4.9 Hz, $J_{4,5}$ = 3.2 Hz, H-5), 4.62 (dd, 1H, $J_{1'a,1'b}$ = 12.2 Hz, $J_{1'b,2'}$ = 5.9 Hz, H-1′ b), 4.59–4.57 (m, 2H, H-3′, H-4), 4.46 (ddd, 1H, $J_{4',5'}$ = 2.3 Hz, $J_{5',6'a}$ = 8.1 Hz, $J_{5',6'b}$ = 6.8 Hz, H-5′), 4.40 (m, 1H, H-4′), 4.29 (dd, 1H, $J_{6'a,6'b}$ = 8.5 Hz, H-6′b), 4.28 (dd, 1H, H-6b), 4.18 (dd, 1H, H-1′a), 4.16 (dd, 1H, H-6′a), 4.08 (dd, 1H, $J_{6a,6b}$ = 9.5 Hz, H-6a), 3.76 (dd, 1H, $J_{1a,1b}$ = 14.1 Hz, $J_{1b,2}$ = 5.4 Hz, H-1b), 3.60 (dd, 1H, H-1a), 1.59, 1.43, 1.36, 1.33, 1.31, 1.29, 1.28 (6 s, 18H, 6 × CH_3). ^{13}C NMR ($(CD_3)_2O$) δ: 138.2, 129.1, 128.4 and 126.3 (C-Ar), 111.3, 110.6, 107.5 (3 × $(CH_3)_2C(OR)_2$), 100.6 (*C*HPh), 88.1 (C-2), 85.9 (C-3), 78.9 (C-4′), 76.5 (C-5′), 74.8 (C-5), 74.0 (C-2′), 71.1 (C-3′), 69.1 (C-4), 67.1 (C-6), 64.6 (C-6′), 43.9 (C-1′), 43.6 (C-1), 26.0, 25.7, 25.6, 25.5, 23.4, 22.5 (6 × *C*H_3). Anal. calcd. for $C_{28}H_{40}O_{12}SSe$: C 49.48, H 5.93; found: C 49.16, H 6.09.

1,4-Anhydro-2,3,5,6-di-*O*-isopropylidene-1-[(S)-[(2′R,3′S,4′R,5′R)-2′,4′-benzylidenedioxy-5′,6′-isopropylidenedioxy-3′-(sulfooxy)hexyl]sulfonio]-D-allitol inner salt (34)

The reaction of compound **16** (500 mg, 1.92 mmol) with the cyclic sulfate **20** (860 mg, 2.30 mmol) in HFIP (2.0 mL) for 12 h at 90–95 °C gave compound **34** as a colourless, amorphous solid (1.0 g, 82% based on **16**). $[\alpha]^{22}_D$ +5.4° (*c* 0.1, CH_2Cl_2). ^{1}H NMR ($(CD_3)_2O$) δ: 7.60–7.38 (m, 5H, H-Arom.), 5.89 (s, 1H, C*H*Ph), 5.50 (ddd, 1H, H-2), 5.26 (dd, 1H, $J_{2,3}$ = 5.8 Hz, H-3), 4.88 (ddd, 1H, $J_{2',3'}$ = 5.0 Hz, $J_{1'b,2'}$ = 5.0 Hz, $J_{1'a,2'}$ = 2.1 Hz, H-2′), 4.83 (ddd, 1H, $J_{5,6b}$ = 2.8 Hz, $J_{5,6a}$ = 5.1 Hz, $J_{4,5}$ = 7.6 Hz, H-5), 4.59 (dd, 1H, $J_{3,4}$ = 2.4 Hz, H-4), 4.57–4.52 (m, 2H, H-1′b, H-3′), 4.50 (ddd, 1H, $J_{4',5'}$ = 2.1 Hz, $J_{5',6'a}$ = 9.1 Hz, $J_{5',6'b}$ = 7.1 Hz, H-5′), 4.42 (dd, 1H, $J_{3',4'}$ = 1.8 Hz, H-4′), 4.33 (dd, 1H, H-6′b), 4.30 (dd, 1H, $J_{5,6b}$ = 2.8 Hz, H-6b), 4.28 (m, 1H, H-1′a), 4.18 (dd, 1H, $J_{6'a,6'b}$ = 8.4 Hz, H-6′a), 4.11 (dd, 1H, $J_{6a,6b}$ = 9.6 Hz, H-6a), 3.90 (dd, 1H, $J_{1b,2}$ = 5.4 Hz, H-1b), 3.75 (dd, 1H, $J_{1a,1b}$ = 14.3 Hz, H-1a), 1.61, 1.43, 1.37, 1.30, 1.29, 1.28 (6 s, 18H, 6 × CH_3). ^{13}C NMR ($(CD_3)_2O$) δ: 138.2, 129.1, 128.4, 126.3 (C-Ar), 112.1, 110.9, 107.5 (3 × $(CH_3)_2C(OR)_2$), 100.7 (*C*HPh), 86.2 (C-2), 84.5 (C-3), 79.0 (C-4), 76.7 (C-5′), 74.7 (C-5), 74.1 (C-2′), 70.3 (C-3′), 70.0 (C-4′), 67.1 (C-6), 64.6 (C-6′), 47.9 (C-1), 46.1 (C-1′), 23.9, 25.6, 25.5, 25.4, 23.4, 22.4 (6 × *C*H_3). Anal. calcd. for $C_{28}H_{40}O_{12}S_2$: C 53.15, H 6.37; found: C 52.92, H 6.17.

1,4-Anhydro-2,3,5,6-di-*O*-isopropylidene-1-[(S)-[(2′R,3′S,4′R,5′R)-2′,4′-benzylidenedioxy-5′,6′-isopropylidenedioxy-3′-(sulfooxy)hexyl]selenonio]-L-allitol inner salt (35)

The reaction of compound **17** (500 mg, 1.63 mmol) with the cyclic sulfate **20** (730 mg, 1.96 mmol) in HFIP (2.0 mL) for 12 h at 80–85 °C gave compound **35** as a colourless, amorphous solid (740 mg, 67% based on **17**). $[\alpha]^{22}_D$ –12° (*c* 1, CH_2Cl_2). ^{1}H NMR ($(CD_3)_2O$) δ: 7.60–7.38 (m, 5H, H-Arom.), 5.92 (s, 1H, C*H*Ph), 5.55 (ddd, 1H, H-2), 5.21 (dd, 1H, $J_{2,3}$ = 5.4 Hz, $J_{3,4}$ = 1.8 Hz, H-3), 4.96–4.92 (m, 1H, H-2′), 4.60 (dd, 1H, H-3′), 4.53 (dd, 1H, $J_{1'b,2'}$ = 6.4 Hz, $J_{1'b,1'a}$ = 12.2 Hz, H-1′ b), 4.45 (ddd, 1H, $J_{4,5}$ = 2.3 Hz, $J_{5,6'a}$ = 9.2 Hz, $J_{5,6'b}$ = 6.9 Hz, H-5′), 4.41 (dd, 1H, H-4′), 4.40–4.36 (m, 1H, H-5), 4.34 (dd, 1H, $J_{6'a,6'b}$ = 8.6 Hz, H-6′b), 4.24–4.18 (m, 3H, H-4, H-1′a, H-6′a), 3.99 (dd, 1H, 1H, $J_{5,6b}$ = 7.3 Hz, $J_{6a,6b}$ = 9.3 Hz, H-6b), 3.96 (dd, 1H, $J_{1b,2}$ = 5.2 Hz, H-1b), 3.90 (dd, 1H, $J_{1a,1b}$ = 14.2 Hz, H-1a), 3.76 (dd, 1H, $J_{5,6a}$ = 5.2 Hz, H-6a), 1.59, 1.39, 1.35, 1.30, 1.29, 1.25 (6 s, 18H, 6 × C*H*$_3$). ^{13}C NMR ($(CD_3)_2O$) δ: 142.9, 133.9, 133.1, 131.0 (C-Ar), 116.1, 115.3, 112.1 (3 × $(CH_3)_2C(OR)_2$), 105.0 (*C*HPh), 91.5 (C-3), 91.0 (C-2), 83.4 (C-4′), 81.2 (C-5′), 78.7 (C-5), 78.5 (C-2′), 75.5 (C-3′), 72.3 (C-4), 71.6 (C-6), 69.3 (C-6′), 49.3 (C-1), 48.0 (C-1′), 30.7, 30.6, 30.3, 30.2, 28.1, 27.5 (6 × *C*H_3). Anal. calcd. for $C_{28}H_{40}O_{12}SSe$: C 49.48, H 5.93; found: C 49.31, H 5.90.

1,4-Anhydro-2,3,5,6-di-*O*-isopropylidene-1-[(S)-[(2′R,3′S,4′R,5′R)-2′,4′-benzylidenedioxy-5′,6′-isopropylidenedioxy-3′-(sulfooxy)hexyl]sulfonio]-L-allitol inner salt (36)

The reaction of compound **18** (500 mg, 1.92 mmol) with the cyclic sulfate **20** (860 mg, 2.30 mmol) in HFIP (2.0 mL) for 12 h at 90–95 °C gave compound **36** as a colourless, amorphous solid (960 mg, 77% based on **18**). $[\alpha]^{22}_D$ –15° (*c* 0.5, CH_2Cl_2). ^{1}H NMR (CD_2Cl_2) δ: 7.56–7.40 (m, 5H, H-Arom.), 5.76 (s, 1H, C*H*Ph), 5.19 (ddd, 1H, H-2), 4.98 (dd, 1H, $J_{2,3}$ = 5.7 Hz, H-3), 4.68–4.62 (m, 2H, H-2′, H-3′), 4.51 (ddd, 1H, H-5′), 4.42 (dd, 1H, $J_{1'b,2'}$ = 5.7 Hz, $J_{1'b,1'a}$ = 13.5 Hz, H-1′b), 4.28 (dd, 1H, $J_{1'a,2'}$ = 2.3 Hz, H-1′a), 4.28–4.25 (m, 1H, H-5), 4.25–4.18 (m, 3H, H-6′a, H-6′b, H-4′), 4.14 (m, 1H, H-4), 3.90 (dd, 1H, $J_{1a,1b}$ = 15.4 Hz, H-1b), 3.86 (dd, 1H, $J_{1a,2}$ = 4.6 Hz, H-1a), 3.86 (dd, 1H, 1H, $J_{5,6b}$ = 7.8 Hz, H-6b), 3.71 (dd, 1H, $J_{5,6a}$ = 5.1 Hz, $J_{6a,6b}$ = 9.5 Hz, H-6a), 1.62, 1.39, 1.38, 1.37, 1.34, 1.24 (6 s, 18H, 6 × C*H*$_3$). ^{13}C NMR (CD_2Cl_2) δ: 137.4, 129.7, 128.6, 126.3 (C-Ar), 112.7, 111.5, 108.5 (3 × $(CH_3)_2C(OR)_2$), 100.9 (*C*HPh), 85.2 (C-2), 84.8 (C-3), 79.1 (C-4′), 75.5 (C-5′), 74.3 (C-5), 74.0 (C-3′), 70.5 (C-2′), 69.8 (C-4), 67.0 (C-6), 65.0 (C-6′), 47.8 (C-1), 45.9 (C-1′), 26.4, 26.1, 25.9, 25.5, 23.3, 22.8 (6 × *C*H_3). Anal. calcd. for $C_{28}H_{40}O_{12}S_2$: C 53.15, H 6.37; found: C 53.36, H 6.41.

General procedure for the deprotection of the coupled products to yield the final compounds 7–14

The protected coupled products **29**–**36** were dissolved in CH_2Cl_2 (2 mL), TFA (10 mL) was then added, and the mixture was stirred for 6–8 h at RT. The progress of the reaction was followed by TLC analysis of the aliquots (EtOAc–MeOH–H_2O, 7:3:1). When the starting material had been consumed, the TFA and CH_2Cl_2 were removed under reduced pressure. The residue was rinsed with CH_2Cl_2 (4 × 2 mL) and the CH_2Cl_2 was decanted to remove the cleaved protecting groups. The remaining gum was dissolved in water and purified by column chromatography (EtOAc and EtOAc–MeOH, 2:1) to give the purified compounds **7**–**10** as colourless, amorphous, and hygroscopic solids. In the cases of **33**–**36**, the benzylidene groups were not completely cleaved. The residue was then dissolved in 80% AcOH (10 mL) and Pd–C (10%, 200 mg, in two portions) was added and the reaction mixture was subjected to hydrogenolysis for 48 h at RT. After filtering the Pd–C, the filtrate was mixed with water (100 mL) and the solvents were removed under reduced pressure. The remaining gum was dissolved in water and purified by column chromatography (EtOAc and EtOAc–MeOH, 2:1) to give the purified compounds **11**–**14** as colourless, amorphous, and hygroscopic solids.

1,4-Anhydro-1-[(S)-[(2′S,3′S)-2′,4′-dihydroxy-3′-(sufooxy)butyl]selenonio]-D-allitol inner salt (7)

To a solution of **29** (500 mg, 0.86 mmol) in CH_2Cl_2 (2 mL) was added TFA (10 mL) to yield the compound **7** as a colourless, amorphous, and hygroscopic solid (202 mg, 57%). $[\alpha]^{22}_D$ +54° (*c* 2, H_2O). ^{1}H NMR (D_2O) δ: 4.74 (m, 1H, H-2), 4.34 (dd, 1H, $J_{2,3}$ = 9.1 Hz, $J_{3,4}$ = 3.1 Hz, H-3), 4.28 (ddd, 1H, H-3′), 4.25–4.18 (m, 2H, H-2′, H-5), 4.05 (dd, 1H, $J_{4,5}$ = 4.3 Hz, H-4), 3.97 (dd, 1H, $J_{1'b,2'}$ = 3.6 Hz, $J_{1'a,1'b}$ = 12.6 Hz, H-1′b), 3.82 (dd, 1H, $J_{3',4'b}$ = 6.4 Hz, H-4′b), 3.80 (dd, 1H, $J_{1'a,2'}$ = 3.2 Hz, H-1′a), 3.73 (dd, 1H, $J_{3',4'a}$ = 3.3 Hz, 1H, $J_{4'a,4'b}$ = 12.8 Hz, H-4′a), 3.68 (m, 2H, H-6a, H-6b), 3.55 (dd, 1H, $J_{1b,2}$ = 3.7 Hz, H-1b), 3.33 (dd, 1H, $J_{1a,2}$ = 2.1 Hz, $J_{1a,1b}$ = 13.1 Hz, H-1a). ^{13}C NMR (D_2O) δ: 80.8 (C-3′), 76.0 (C-2), 75.9 (C-3), 68.4 (C-5), 66.0 (C-2′), 65.1 (C-4), 63.4 (C-6), 60.1 (C-4′), 48.5 (C-1′), 40.5 (C-1). HRMS calcd. for $C_{10}H_{19}O_{10}SSe$: 410.9859 (M – H); found: 410.9861.

1,4-Anhydro-1-[(S)-[(2′S,3′S)-2′,4′-dihydroxy-3′-(sufooxy)butyl]sulfonio]-D-allitol inner salt (8)

To a solution of **30** (500 mg, 0.94 mmol) in CH_2Cl_2 (2 mL) was added TFA (10 mL) to yield the compound **8** as a colourless, amorphous, and hygroscopic solid (240 mg, 69%). $[\alpha]^{22}_D$ +39° (*c* 2, H_2O). ^{1}H NMR (D_2O) δ: 4.63 (m, 1H, H-2), 4.48 (dd, 1H, $J_{2,3}$ = 8.7 Hz, $J_{3,4}$ = 3.3 Hz, H-3), 4.36–4.30 (m, 2H, H-2′, H-5), 4.27 (ddd, 1H, H-3′), 4.12 (dd, 1H, $J_{1'b,2'}$ = 3.4 Hz, $J_{1'a,1'b}$ = 13.6 Hz, H-1′ b), 4.05 (dd, 1H, $J_{3,4}$ = 3.3 Hz, $J_{4,5}$ = 8.6 Hz, H-4), 3.86 (dd, 1H, $J_{3',4'b}$ = 2.8 Hz, H-4′b), 3.85 (dd, 1H, $J_{1'a,2'}$ = 8.3 Hz, H-1′a), 3.78 (dd, 1H, $J_{3',4'a}$ = 3.2 Hz, 1H, $J_{4'a,4'b}$ = 12.8 Hz, H-4′a), 3.70 (m, 2H, H-6a, H-6b), 3.69 (dd, 1H, $J_{1b,2}$ = 3.3 Hz, H-1b), 3.46 (dd, 1H, $J_{1a,2}$ = 1.6 Hz, $J_{1a,1b}$ = 14.4 Hz, H-1a). ^{13}C NMR (D_2O) δ: 79.8 (C-3′), 74.7 (C-2), 74.4 (C-3), 68.3 (C-2′), 65.6 (C-4), 65.5 (C-5), 63.0 (C-6), 59.9 (C-4′), 51.1 (C-1′), 44.2 (C-1). HRMS calcd. for $C_{10}H_{20}O_{10}S_2Na$: 387.0390 (M + Na); found: 387.0391.

1,4-Anhydro-1-[(S)-[(2′S,3′S)-2′,4′-dihydroxy-3′-(sufooxy)butyl]selenonio]-L-allitol inner salt (9)

To a solution of **31** (500 mg, 0.86 mmol) in CH_2Cl_2 (2 mL) was added TFA (10 mL) to yield the compound **9** as a colourless, amorphous, and hygroscopic solid (216 mg, 61%). $[\alpha]^{22}_D$ –17° (*c* 0.5, H_2O). ^{1}H NMR (D_2O) δ: 4.77 (ddd, 1H, H-2), 4.42 (dd, 1H, $J_{2,3}$ = 8.8 Hz, $J_{3,4}$ = 3.0 Hz, H-3), 4.33–4.25 (m, 2H, H-5, H-2′), 4.25–4.30 (ddd, 1H, H-3′), 4.13 (dd, 1H, $J_{4,5}$ = 8.7 Hz, H-4), 3.97 (dd, 1H, $J_{1'b,2'}$ = 4.0 Hz, $J_{1'a,1'b}$ = 12.4 Hz, H-1′b), 3.94 (dd, 1H, $J_{1'a,2'}$= 8.7 Hz, H-1′a), 3.83 (dd, 1H, $J_{3',4'b}$ = 3.2 Hz, H-4′b), 3.75 (dd, 1H, $J_{3',4'a}$ = 3.2 Hz, 1H, $J_{4'a,4'b}$ = 12.8 Hz, H-4′a), 3.68 (d, 2H, H-6a, H-6b), 3.58 (dd, 1H, $J_{1b,2}$ = 8.5 Hz, H-1b), 3.36 (dd, 1H, $J_{1a,2}$ = 2.2 Hz, $J_{1a,1b}$ = 13.3 Hz, H-1a). ^{13}C NMR (D_2O) δ: 81.0 (C-3), 75.8 (C-2), 75.5 (C-3), 68.7 (C-2), 66.5 (C-5), 65.5 (C-4), 63.4 (C-6), 60.0 (C-4), 48.4 (C-1), 40.4 (C-1). HRMS calcd. for $C_{10}H_{19}O_{10}SSe$: 410.9859 (M – H); found: 410.9857.

1,4-Anhydro-1-[(S)-[(2′S,3′S)-2′,4′-dihydroxy-3′-(sufooxy)butyl]sulfonio]-L-allitol inner salt (10)

To a solution of **32** (500 mg, 0.94 mmol) in CH_2Cl_2 (2 mL) was added TFA (10 mL) to yield the compound **10** as a colourless, amorphous, and hygroscopic solid (223 mg, 65%). $[\alpha]^{22}_D$ +6° (*c* 0.5, H_2O). ^{1}H NMR (D_2O) δ: 4.60 (m, 1H, H-2), 4.47 (dd, 1H, $J_{2,3}$ = 8.3 Hz, $J_{3,4}$ = 3.3 Hz, H-3), 4.32 (ddd, 1H, H-5), 4.28–4.24 (m, 1H, H-2′), 4.22 (ddd, 1H, H-3′), 4.07 (dd, 1H, $J_{4,5}$ = 8.5 Hz, H-4), 3.98 (dd, 1H, $J_{1'b,2'}$ = 3.5 Hz, H-1′b), 3.92 (dd, 1H, $J_{1'a,2'}$ = 8.8 Hz, $J_{1'a,1'b}$ = 13.6 Hz, H-1′a), 3.86 (dd, 1H, $J_{3',4'b}$ = 9.5 Hz, H-4′b), 3.74 (dd, 1H, $J_{3',4'a}$ = 3.2 Hz, 1H, $J_{4'a,4'b}$ = 12.8 Hz, H-4′a), 3.66 (d, 2H, H-6a, H-6b), 3.64–3.61 (m, 1H, H-1b), 3.44 (dd, 1H, $J_{1a,2}$ = 9.7 Hz, $J_{1a,1b}$ = 14.3 Hz, H-1a). ^{13}C NMR (D_2O) δ: 80.5 (C-3′), 74.6 (C-2), 74.5 (C-3), 68.8 (C-5), 66.6 (C-2′), 66.2 (C-4), 63.1 (C-6), 59.9 (C-4′), 50.9 (C-1′), 44.1 (C-1). HRMS calcd. for $C_{10}H_{20}O_{10}S_2Na$: 387.0390 (M + Na); found: 387.0389.

1,4-Anhydro-1-[(S)-[(2′R,3′S,4′R,5′R)-2′,4′,5′,6′-tetrahydroxy-3′-(sufooxy)hexyl]selenonio]-D-allitol inner salt (11)

To a solution of **33** (600 mg, 0.88 mmol) in CH_2Cl_2 (2 mL) was added TFA (10 mL). After removing the cleaved protecting groups, the remaining gum was then dissolved in AcOH (10 mL), Pd–C (10%, 100 mg) was added, and the reaction mixture was subjected to hydrogenolysis to give compound **11** as a colourless, amorphous, and hygroscopic solid (157 mg, 38%). $[\alpha]^{22}_D$ –8° (*c* 0.5, H_2O). ^{1}H NMR (D_2O) δ: 4.80 (m, 1H, H-2), 4.59 (dd, 1H, H-3′), 4.48 (ddd, 1H, H-2′), 4.43 (dd, 1H, $J_{2,3}$ = 8.9 Hz, $J_{3,4}$ = 2.8 Hz, H-3), 4.31 (ddd, 1H, H-5), 4.14 (dd, 1H, $J_{4,5}$ = 8.9 Hz, H-4), 4.08 (dd, 1H, $J_{1'b,2'}$ = 9.9 Hz, $J_{1'a,1'b}$ = 12.2 Hz, H-1′b), 3.95 (dd, 1H, $J_{1'a,2'}$ = 3.5 Hz, H-1′a), 3.84–3.74 (m, 3H, H-4′, H-5′, H-6′b), 3.72 (d, 2H, H-6a, H-6b), 3.62–3.57 (m, 2H, H-6′a, H-1b), 3.38 (dd, 1H, $J_{1a,2}$ = 1.9 Hz, $J_{1a,1b}$ = 13.0 Hz, H-1a). ^{13}C NMR (D_2O) δ: 78.5 (C-3′), 75.8 (C-2), 75.7 (C-3), 70.7 (C-5′), 69.6 (C-4′), 68.8 (C-5), 68.1 (C-2′), 65.5 (C-4), 63.4 (C-

6′), 62.8 (C-6), 47.7 (C-1′), 40.2 (C-1). HRMS calcd. for $C_{12}H_{25}O_9Se$: 393.0658 (M + H – SO_3); found: 393.0656.

1,4-Anhydro-1-[(S)-[(2′R,3′S,4′R,5′R)-2′,4′,5′,6′-tetrahydroxy-3′-(sufooxy)hexyl]sulfonio]-D-allitol inner salt (12)

To a solution of **34** (500 mg, 0.79 mmol) in CH_2Cl_2 (2 mL) was added TFA (10 mL). After removing the cleaved protecting groups, the remaining gum was then dissolved in AcOH (10 mL), Pd–C (10%, 100 mg) was added, and the reaction mixture was subjected to hydrogenolysis to give compound **12** as a colourless, amorphous, and hygroscopic solid (140 mg, 42%). $[\alpha]^{22}_D$ –32° (*c* 2, H_2O). ^{1}H NMR (D_2O) δ: 4.53 (m, 1H, H-2), 4.51 (dd, 1H, $J_{2',3'}$ = 5.1 Hz, $J_{3',4'}$ = 1.1 Hz, H-3′), 4.44 (ddd, 1H, H-2′), 4.26 (dd, 1H, $J_{2,3}$ = 9.6 Hz, $J_{3,4}$ = 3.1 Hz, H-3), 4.12 (ddd, 1H, H-5), 3.95 (dd, 1H, $J_{1b,2}$ = 10.8 Hz, $J_{1'a,1'b}$ = 13.4 Hz, H-1′b), 3.88 (dd, 1H, $J_{1'a,2'}$ = 2.8 Hz, H-1′a), 3.86 (dd, 1H, $J_{4,5}$ = 8.2 Hz, H-4), 3.74 (dd, 1H, $J_{4',5'}$ = 9.2 Hz, H-4′), 3.72 (dd, 1H, $J_{5,6b}$ = 3.1 Hz, $J_{6a,6b}$ = 11.9 Hz, H-6b), 3.67 (dd, 1H, $J_{5',6'b}$ = 2.5 Hz, $J_{6'a,6'b}$ = 11.8 Hz, H-6′b), 3.66–3.63 (m, 1H, H-5′), 3.59 (dd, 1H, $J_{5,6a}$ = 3.9 Hz, H-6a), 3.52–3.46 (m, 3H, H-1a, H-1b, H-6′a). ^{13}C NMR (D_2O) δ: 77.7 (C-3′), 76.1 (C-3), 72.8 (C-2), 70.4 (C-5′), 68.9 (C-4′), 67.8 (C-2′), 67.4 (C-5), 64.6 (C-6), 64.3 (C-4), 62.7 (C-6′), 49.3 (C-1′), 44.4 (C-1). HRMS calcd. for $C_{12}H_{25}O_9S$: 345.1214 (M + H – SO_3); found: 345.1214.

1,4-Anhydro-1-[(S)-[(2′R,3′S,4′R,5′R)-2′,4′,5′,6′-tetrahydroxy-3′-(sufooxy)hexyl]selenonio]-L-allitol inner salt (13)

To a solution of **35** (600 mg, 0.88 mmol) in CH_2Cl_2 (2 mL) was added TFA (10 mL). After removing the cleaved protecting groups, the remaining gum was then dissolved in AcOH (10 mL), Pd–C (10%, 100 mg) was added, and the reaction mixture was subjected to hydrogenolysis to give compound **13** as a colourless, amorphous, and hygroscopic solid (197 mg, 47%). $[\alpha]^{22}_D$ –22° (*c* 1, H_2O). ^{1}H NMR (D_2O) δ: 4.76 (ddd, 1H, H-2), 4.57 (dd, 1H, $J_{2',3'}$ = 5.2 Hz, H-3′), 4.50 (ddd, 1H, H-2′), 4.37 (dd, 1H, $J_{2,3}$ = 9.1 Hz, $J_{3,4}$ = 3.0 Hz, H-3), 4.25 (ddd, 1H, H-5), 4.06 (dd, 1H, $J_{4,5}$ = 7.9 Hz, H-4), 4.00 (dd, 1H, $J_{1'b,2'}$ = 4.0 Hz, $J_{1'a,1'b}$ = 12.4 Hz, H-1′b), 3.89 (dd, 1H, $J_{1'a,2'}$ = 9.0 Hz, H-1′a), 3.84–3.79 (m, 1H, H-5′), 3.72 (d, 2H, H-6a, H-6b), 3.63 (dd, 1H, H-4′), 3.60–3.50 (m, 3H, H-6′b, H-6′a, H-1b), 3.34 (dd, 1H, $J_{1a,2}$ = 2.7 Hz, $J_{1a,1b}$ = 13.0 Hz, H-1a). ^{13}C NMR (D_2O) δ: 78.3 (C-3′), 76.0 (C-3), 75.4 (C-2), 73.1 (C-5′), 69.8 (C-4′), 68.2 (C-5), 67.1 (C-2′), 64.7 (C-4), 62.8 (C-6), 62.6 (C-6′), 47.4 (C-1′), 40.2 (C-1). HRMS calcd. for $C_{12}H_{25}O_9Se$: 393.0658 (M + H – SO_3); found: 393.0656.

1,4-Anhydro-1-[(S)-[(2′R,3′S,4′R,5′R)-2′,4′,5′,6′-tetrahydroxy-3′-(sufooxy)hexyl]sulfonio]-L-allitol inner salt (14)

To a solution of **36** (600 mg, 0.95 mmol) in CH_2Cl_2 (2 mL) was added TFA (10 mL). After removing the cleaved protecting groups, the remaining gum was then dissolved in AcOH (10 mL), Pd–C (10%, 100 mg) was added, and the reaction mixture was subjected to hydrogenolysis to give compound **14** as a colourless, amorphous, and hygroscopic solid (165 mg, 41%). $[\alpha]^{22}_D$ –32° (*c* 1, H_2O). ^{1}H NMR (D_2O) δ: 4.58 (ddd, 1H, H-2), 4.55 (dd, 1H, $J_{2',3'}$ = 4.6 Hz, $J_{3',4'}$ = 0.7 Hz, H-3′), 4.49 (ddd, 1H, H-2′), 4.42 (dd, 1H, $J_{2,3}$ = 8.7 Hz, $J_{3,4}$ = 3.2 Hz, H-3), 4.25 (ddd, 1H, H-5), 4.03 (dd, 1H, $J_{1'b,2'}$ = 3.8 Hz, H-1′b), 4.04–3.99 (m, 1H, H-4), 3.92 (dd, 1H, $J_{1'a,2'}$ = 9.1 Hz, $J_{1'a,1'b}$ = 13.5 Hz, H-1′a), 3.79 (dd, 1H, $J_{4',5'}$ = 8.0 Hz, H-4′), 3.68 (dd, 1H, $J_{5',6'b}$ = 2.4 Hz, H-6′b), 3.68–3.64 (m, 1H, H-5′), 3.67 (d, 2H, H-6a, H-6b), 3.61 (dd, 1H, $J_{1b,2}$ = 3.2 Hz, $J_{1a,1b}$ = 14.2 Hz, H-1b), 3.52 (dd, 1H, $J_{5',6'a}$ = 5.6 Hz, $J_{6'a,6'b}$ = 11.5 Hz, H-6′a), 3.44 (dd, 1H, $J_{1a,2}$ = 8.0 Hz, H-1a). ^{13}C NMR (D_2O) δ: 77.7 (C-3′), 74.8 (C-3), 74.4 (C-2), 70.5 (C-5′), 69.1 (C-4′), 68.3 (C-5), 67.0 (C-2′), 65.0 (C-4), 62.8 (C-6′), 62.7 (C-6), 49.9 (C-1′), 43.9 (C-1). HRMS calcd. for $C_{12}H_{25}O_9S$: 345.1214 (M + H – SO_3); found: 345.1211.

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