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# A Straightforward and General Strategy Towards 1,5-Dithio-1-enopyranosides

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**Keywords:** Carbohydrates / Thiosugars / Ketene dithioacetal / Cyclization / Olefination

The synthesis of a new class of thiosugar derivatives, 1,5-dithio-1-enopyranosides, has been achieved in a two-step sequence from easily available aldofuranoses. In the first step, a carbohydrate-derived ketene dithioacetal was formed by Peterson olefination of an aldofuranose and a lithiated α-silyl thioacetal. In the second step, intramolecular nucleophilic substitution of an activated hydroxy group by a sulfur atom of the ketene dithioacetal function led to the target compounds in good yields.



## Introduction

Thiosugars are carbohydrate analogues in which the intracyclic oxygen is replaced by a sulfur atom, both in pyranoside and furanoside structures.[1] To date, except for 5-thio-D-mannose, which was isolated in 1987 from marine sponge *Clathria pyramida*,[2] thiosugars have not been found in nature. Since the first synthesis of a 5-thio-D-hexopyranose in 1961,[3] thiosugars have been obtained by the transformation of natural monosaccharides.[4]

Owing to their interesting biological activities, these compounds have recently attracted considerable interest from chemists and biochemists.[5] In particular, 1,5-dithio-D-xylopyranose-derived glycosides like **1** (Figure 1) have proved to be orally active anti-thrombotic agents.[6]

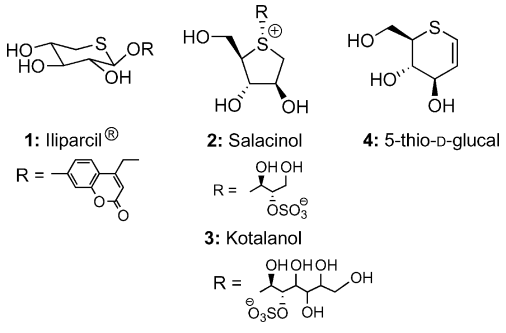


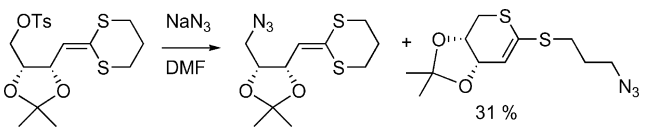

Figure 1. Selected thiosugars and derivatives of biological interest.

A new class of glycosidase inhibitors, namely salacinol **2** and kotalanol **3** with inner-salt sulfonium–sulfate structures (Figure 1), were recently isolated from the plant *Salacia reticulata*, which is widespread in Sri Lanka and South India.[7] These sulfonium derivatives have been found to be potent inhibitors of intestinal α-glucosidase. Many syntheses of salacinol, its stereoisomers, selenium and nitrogen analogues, as well as six-membered derivatives have been reported.[8]

Six-membered analogues of salacinol generally possess weak or no activity against glycosidases, but interestingly, 5-thio-D-glucal (**4**) was found to competitively inhibit α-D-mannosidase and β-D-glucosidase.[9] Therefore, the presence of the double bond could modify the geometry of the heterocycle and mimic the transition state involved in the enzymatic transformation.

Owing to their potential value as therapeutic agents, thiosugars and their derivatives have become important targets and the search for original compounds remains a challenging topic. As a part of our research in the field of sugars of biological interest, we have explored a general strategy towards the synthesis of a new class of six-membered thiosugars: 1,2-unsaturated 1,5-dithiopyranosides.

To the best of our knowledge, only two examples of unsaturated 1,5-dithiopyranosides have been reported in literature. Gallagher and co-workers[10] reported the formation of a 1:1 mixture of the expected product and an azido 1,5-dithiopyranoside during the conversion of a primary tosylate obtained from the ketene dithioacetal derived from 2,3-*O*-isopropylidene-D-erythrose to the corresponding azide (Scheme 1).




Scheme 1.

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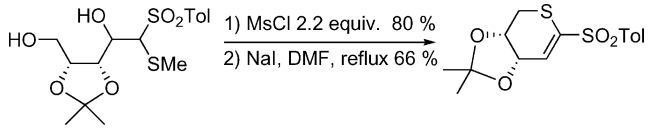
In the second example,[11] 1,5-dithiopyranosides were obtained from the condensation of 2,3-*O*-isopropylidene-D- or -L-erythrose with methylthiomethyl *p*-tolyl sulfone, followed by mesylation of two free hydroxy groups leading to elimination and intramolecular cyclization (Scheme 2). These two examples have proved the participation of one of the sulfur atoms of the ketene dithioacetal function in the cyclization step.




Scheme 2.

In this paper, we report a general strategy towards unsaturated 1,5-dithiopyranosides starting from carbohydrate-derived ketene dithioacetals. The cyclization step was studied, optimized and generalized for several ketene dithioacetals with various protecting groups.

## Results and Discussion

In our study, the title thiosugar analogues were readily synthesized from carbohydrate-derived ketene dithioacetals, which are easily available from protected aldofuranoses.[12] Condensation of the lithium derivative of bis(methylsulfanyl)trimethylsilylmethane with the protected aldofuranoses 2,3-*O*-isopropylidene-L-erythrofuranose (**5**),[13] 2,3-di-*O*-benzyl-D-threofuranose (**6**), the commercially available 2,3,5-tri-*O*-benzyl-D-arabinofuranose (**7**) and 2,3-*O*-isopropylidene-5-*O*-trityl-D-ribofuranose (**8**)[13] afforded the intermediate sugar-derived ketene dithioacetals **9**–**12** in good yields (Table 1). Compound **6** was prepared from methyl 2,3-di-*O*-benzyl-5-*O*-trityl-D-arabinofuranoside[14] according to the sequence depicted in Scheme 3.

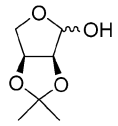
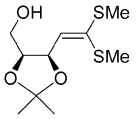
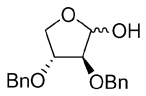
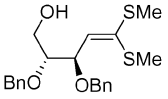
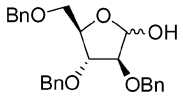
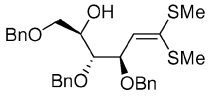
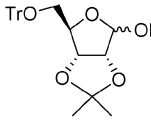
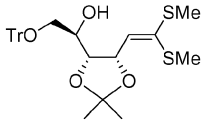
Ketene dithioacetals **9**–**12** were used immediately after purification as they underwent spontaneous *O*-cyclization, as described previously in the literature.[12b] Owing to its instability, compound **10** was used without purification.

The next step of the reaction required the activation of the free hydroxy group of the ketene dithioacetals **9**–**12** to induce ring closure by intramolecular nucleophilic attack of one of the sulfur atoms of the ketene dithioacetal function.

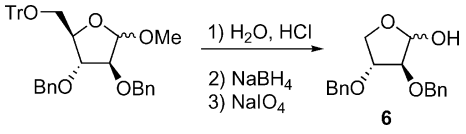
The first attempts were carried out with compound **11**. Under the experimental conditions described in the literature for a similar cyclization of dithioacetals ($PPh_3$, $I_2$, imidazole[15] or mesylation of the free hydroxy group[16]), the starting material decomposed. Only traces of the target compound **15** were obtained.

The use of a triflate as a more efficient leaving group was then envisioned. Compound **11** was treated with trifluoromethanesulfonic anhydride (2 equiv.) in the presence of an excess of pyridine (6 equiv.) at –20 °C. The corresponding triflate was not isolated and, at room temperature, cyclization occurred to afford the unsaturated 1,5-dithiopyranoside **15** in 50% yield. The spontaneous transformation of

Table 1. Synthesis of ketene dithioacetals **9**–**12**.

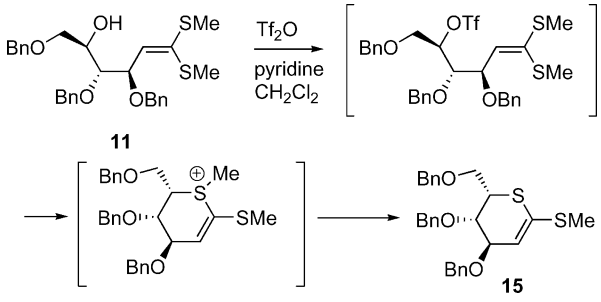
| | Aldofuranose | Compound | Yield |
|---|---|---|---|
| 1 |  **5** |  **9** | 87 % |
| 2 |  **6** |  **10** | not isolated[a] |
| 3 |  **7** |  **11** | 81 % |
| 4 |  **8** |  **12** | 56% |

[a] Compound **10** was unstable to silica gel chromatography and was used without purification in the next step.




Scheme 3. Synthesis of the aldofuranose **6**.

the intermediate sulfonium into **15** was assumed to be due to the presence of an excess of pyridine as a nucleophile is essential to remove the methyl group at the sulfur atom (Scheme 4).



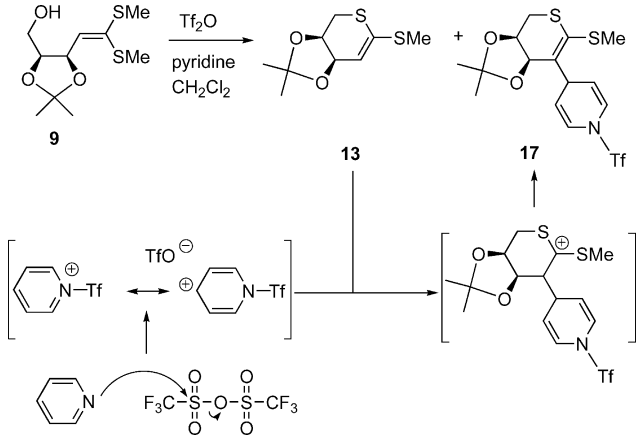

Scheme 4. Mechanism for the formation of the unsaturated 1,5-dithiopyranoside **15**.

The overall transformation was easily monitored by TLC, which showed the formation of the apolar triflate at –20 °C, its transformation into the polar sulfonium deriva-

tive at 0 °C and finally the formation of the expected unsaturated thiosugar at room temperature.

Under the same experimental conditions, ketene dithioacetal **9** led to a mixture of the expected thiosugar **13** and a by-product in a 1:1 ratio (Scheme 5). After careful separation by flash chromatography over silica gel and spectroscopic studies, the structure of the thiosugar **17** was assigned to this by-product. The formation of compound **17** results from electrophilic substitution of the ethylenic proton of 1,5-dithiopyranoside **13** by the species generated from the interaction of pyridine with trifluoromethanesulfonic anhydride.[17]



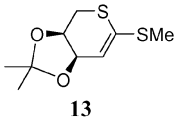
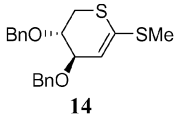
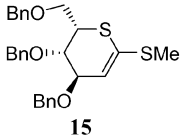
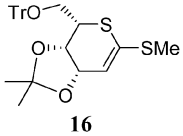

Scheme 5. Formation of the by-product **17** from the carbohydrate-derived ketene dithioacetal **9**.

This transformation was confirmed by the reaction of 1,5-dithiopyranoside **13** with a solution of the electrophilic species, obtained by reaction of trifluoromethanesulfonic anhydride and pyridine at 0 °C. Under these conditions, compound **17** was quantitatively obtained. In order to avoid this electrophilic substitution, pyridine substituted at the 4-position was used instead of pyridine. Thus, in the presence of 2 equiv. of trifluoromethanesulfonic anhydride and 6 equiv. of 4-picoline (4-methylpyridine), the target 1,2-unsaturated 1,5-dithiopyranosides **13**–**16** were obtained in good yields (Table 2). The $S_N2$ mechanism involved in the cyclization step led to an inversion of configuration at C–5, as confirmed by a NOE experiment on compound **16** (9.5% between H-4 and H-5).

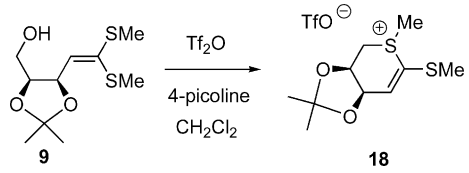
Finally, in order to prove the mechanistic pathway of the overall transformation, we attempted to isolate the intermediate sulfonium formed during the formation of **13** from **9** (Scheme 6).

By using 1.6 equiv. of 4-picoline and 1.2 equiv. of trifluoromethanesulfonic anhydride at 0 °C, the reaction effectively stopped, according to TLC, at the sulfonium step. However, purification of the sulfonium **18** by silica gel chromatography proved to be tedious due to the presence of the 4-methylpyridinium salt. Nevertheless, a small amount of pure sulfonium **18**, with trifluoromethanesulfonate as the counter-ion, was isolated as a single diastereomer and then fully characterized.

Table 2. Synthesis of unsaturated 1,5-dithiopyranosides **13**–**16**.

| | Ketene dithioacetal | Unsaturated 1,5-dithiopyranoside | Yield |
|---|---|---|---|
| 1 | **9** |  **13** | 95 % |
| 2 | **10** |  **14** | 46 %[a] |
| 3 | **11** |  **15** | 86 % |
| 4 | **12** |  **16** | 87% |

[a] Overall yield from the protected aldofuranose.




Scheme 6. Synthesis of sulfonium **18**.

## Conclusions

In this study we have developed a general and efficient method for the synthesis of original 1,5-dithio-1-enopyranosides from easily available protected aldofuranoses in a two-step sequence in good yields. These compounds possess a ketene dithioacetal function that allows the introduction of various substituents at the 2-position of the heterocycle by well-known electrophilic or radical reactions.[18] These new thiosugars have potential as precursors of modified 5-thiopyranosides as well as precursors of glycosidase inhibitors and demand further investigation.

## Experimental Section

**General:** All reactions were performed under argon. The solvents were dried and distilled prior to use. THF was distilled from sodium benzophenone ketyl and dichloromethane from calcium hydride. *n*-Butyllithium (2.5 M) was purchased from Acros Organics and titrated in THF against menthol in the presence of *ortho*-phenanthroline. Merck silica gel F254 (0.2 mm) was used to prepare TLC plates. Flash column chromatography was performed over silica gel (Merck 9385 Kieselgel 60, 40–63 μm). NMR spectra were recorded with Bruker spectrometers (250 or 500 MHz for $^1$H, 63

or 125 MHz for $^{13}C$, as indicated). Chemical shifts are expressed in parts per million (ppm) using TMS as the internal standard, coupling constants are in Hz and splitting pattern abbreviations are as follows: br broad, s singlet, d doublet, t triplet, q quartet, m multiplet. Optical rotations were determined at 20 °C with a Perkin–Elmer Model 241 polarimeter. High-resolution mass spectra (HRMS) were performed with Q-TOF Micro micromass positive ESI (CV = 30 V) spectrometer.

**2,3-Di-*O*-benzyl-D-threofuranose (6):** Water (1 mL) and 37% hydrochloric acid (1 mL) were added to a solution of methyl 2,3-di-*O*-benzyl-5-*O*-trityl-D-arabinofuranoside (0.96 g, 1.64 mmol) in dioxane (8.1 mL). The temperature was raised to 80 °C and the reaction was stirred overnight. A saturated aqueous $NaHCO_3$ solution was then added and the aqueous phase was extracted with dichloromethane (3 × 20 mL). The combined organic layers were dried with $Na_2SO_4$ and concentrated in vacuo. The crude product was purified by flash chromatography over silica gel (petroleum ether/EtOAc, 4:6) to give the pure 2,3-di-*O*-benzyl-D-arabinofuranose in 58% yield (314.8 mg, 0.95 mmol).

$NaBH_4$ (322 mg, 8.51 mmol) was added portionwise over 1 h to a solution of 2,3-di-*O*-benzyl-D-arabinofuranose (1.12 g, 3.41 mmol) in methanol (6.4 mL) at 0 °C. The mixture was stirred for 1 h at 0 °C and then the temperature was allowed to rise to room temp. and stirred for 2 h. The solvent was evaporated in vacuo and the crude product was used in the next step without further purification.

$NaIO_4$ (2.92 g, 13.64 mmol) was added portionwise to a solution of the previous product in *tert*-butyl alcohol/water (3:2, 5.6 mL/3.8 mL). The resulting mixture was stirred for 24 h. Saturated aqueous $NaHCO_3$ was then added, the solution was filtered and the solid washed with dichloromethane. The aqueous phase was extracted with dichloromethane (3 × 20 mL). The combined organic layers were dried with $Na_2SO_4$ and concentrated in vacuo. The crude product was purified by flash chromatography over silica gel (petroleum ether/EtOAc, 8:2) to give 2,3-di-*O*-benzyl-D-threofuranose (**6**) in 65% yield over two steps (682 mg, 2.27 mmol).

Oil, yield 65% (over two steps). $^1H$ NMR (250 MHz, $CDCl_3$): $\delta$ = 7.33–7.25 (m, 12 H, Ar), 5.43 (dd, $J$ = 8.4, $J$ = 4.1 Hz, 0.4 H, 1β-H), 5.32 (d, $J$ = 9.6 Hz, 0.6 H, 1α-H), 4.64–4.48 (m, 4 H, C$H_2$Ph), 4.20–4.06 (m, 2.6 H, 3-H, 2 × 4α-H, 4β-H), 3.99–3.94 (m, 1 H, 2-H), 3.85–3.79 (m, 0.4 H, 4β-H) ppm. $^{13}C$ NMR (63 MHz, $CDCl_3$): $\delta$ = 137.7, 137.5, 137.2 and 137.0 (Ar), 128.8–127.9 (10 $C_{Ar}$), 101.2 (C-1α), 96.7 (C-1β), 85.3 (C-2β), 82.3 (C-2α), 81.4 (C-3β), 81.2 (C-3α), 73.1, 72.1, 71.8 (C$H_2$Ph), 71.7 (C$H_2$Ph and C-4α), 69.3 (C-4β) ppm. MS (ESI): $m/z$ = 523.1 $[M + Na]^+$. HRMS (ESI): calcd. for $C_{18}H_{20}O_4Na$ $[M + Na]^+$ 323.1266; found 323.1259.

**General Procedure for the Preparation of Ketene Dithioacetals 9–12:** A solution of *n*BuLi in hexane (2.1 equiv.) was added dropwise to a solution of bis(methylsulfanyl)trimethylsilylmethane (2 equiv.) in anhydrous THF (2 mL per mmol) at –30 °C. The resulting mixture was stirred for 2 h at –30 °C and was then cooled to –78 °C. Simultaneously, a solution of the protected sugar (1 equiv.) in anhydrous THF (1.2 mL mmol$^{-1}$) was added dropwise to a suspension of 60% NaH (1.2 equiv.) in anhydrous THF (2 mL mmol$^{-1}$) at 0 °C. After 2 h, the silyl reagent solution was slowly added to the sugar solution and the mixture was stirred overnight, the temperature being allowed to rise to room temp. Saturated aqueous $NH_4Cl$ was then added and the aqueous phase was extracted with $Et_2O$ (2 × 15 mL). The combined organic layers were dried with $MgSO_4$ and concentrated in vacuo. The crude product was purified by flash chromatography over silica gel (petroleum ether/EtOAc, 75:25) to afford the pure ketene dithioacetals.

**2-Deoxy-3,4-*O*-isopropylidene-L-*erythro*-pent-1-enose Dimethyl Dithioacetal (9):** Following the general procedure, *n*BuLi (11.3 mL, 13.94 mmol), bis(methylsulfanyl)trimethylsilylmethane (2.41 g, 12.69 mmol), 60% NaH (305 mg, 7.62 mmol) and **5** (1.02 g, 6.35 mmol) yielded **9** as a yellow oil (1.38 g, 87%). $[\alpha]_D^{20}$ = –149.0 ($c$ = 2.3, $CHCl_3$). $^1H$ NMR (250 MHz, $CDCl_3$): $\delta$ = 5.72 (d, $J$ = 8.1 Hz, 1 H, 2-H), 5.35 (dd, $J$ = 6.8, $J$ = 8.1 Hz, 1 H, 3-H), 4.28 (dt, $J$ = 4.4, $J$ = 6.8 Hz, 1 H, 4-H), 3.52 (m, 2 H, 5-H), 2.34 (s, 3 H, $SCH_3$), 2.30 (s, 3 H, $SCH_3$), 1.50 [s, 3 H, $C(CH_3)$], 1.40 [s, 3 H, $C(CH_3)$] ppm. $^{13}C$ NMR (63 MHz, [$D_6$]acetone): $\delta$ = 139.0 (C-1), 128.6 (C-2), 109.6 [$C(CH_3)_2$], 80.5 (C-4), 76.7 (C-3), 62.9 (C-5), 28.9 and 26.3 [2 C, $C(CH_3)_2$], 18.1 and 17.3 ($SCH_3$) ppm. MS (ESI): $m/z$ = 273.0 $[M + Na]^+$, 523.1 $[2M + Na]^+$. HRMS (ESI): calcd. for $C_{10}H_{18}O_3NaS_2$ $[M + Na]^+$ 273.0595; found 273.0600.

**3,4,6-Tri-*O*-benzyl-2-deoxy-D-*arabino*-hex-1-enose Dimethyl Dithioacetal (11):** Following the general procedure, *n*BuLi (2.97 mL, 5.34 mmol), bis(methylsulfanyl)trimethylsilylmethane (918 mg, 5.09 mmol), 60% NaH (122 mg, 3.05 mmol) and **7** (1.07 g, 2.55 mmol) yielded **11** as a yellow oil (1.05 g, 81%). $[\alpha]_D^{20}$ = –49.6 ($c$ = 1.0, $CHCl_3$). $^1H$ NMR (250 MHz, $CDCl_3$): $\delta$ = 7.31–7.25 (m, 15 H, 3 × Ar), 5.83 (d, $J$ = 8.8 Hz, 1 H, 2-H), 4.95 (dd, $J$ = 3.6, $J$ = 8.8 Hz, 1 H, 3-H), 4.65–4.36 (m, 7 H, 5-H, 3 × C$H_2$Ph), 4.06–3.97 (m, 1 H, 5-H), 3.63–3.58 (m, 3 H, 4-H, 6-H), 2.93 (d, $J$ = 5.6 Hz, 1 H, OH), 2.27 (s, 3 H, $SCH_3$), 2.24 (s, 3 H, $SCH_3$) ppm. $^{13}C$ NMR (63 MHz, $CDCl_3$): $\delta$ = 138.3 (C-1), 138.0 ($C_{ipso}$, Ar), 128.4–127.6 (15 $C_{Ar}$, C-2), 80.7 (C-4), 76.4 (C-3), 73.9, 73.4 and 71.2 (C$H_2$Ph), 70.8 (C-6), 70.5 (C-5), 17.0 and 16.4 ($SCH_3$) ppm. MS (ESI): $m/z$ = 517.1 $[M + Li]^+$, 533.1 $[M + Na]^+$, 549.1 $[M + K]^+$. HRMS (ESI): calcd. for $C_{29}H_{34}O_4NaS_2$ $[M + Na]^+$ 533.1796; found 533.1784.

**2-Deoxy-3,4-*O*-isopropylidene-6-*O*-trityl-D-*ribo*-hex-1-enose Dimethyl Dithioacetal (12):** Following the general procedure, *n*BuLi (1.92 mL, 3.54 mmol), bis(methylsulfanyl)trimethylsilylmethane (660 mg, 3.66 mmol), 60% NaH (88 mg, 2.20 mmol) and **8** (791 mg, 1.83 mmol) yielded **12** as a white foam (517 mg, 56%). $[\alpha]_D^{20}$ = +51.9 ($c$ = 0.9, $CHCl_3$). $^1H$ NMR (250 MHz, $CDCl_3$): $\delta$ = 7.50–7.34 (m, 5 H, Ar), 7.26 (m, 10 H, 2 × Ar), 5.76 (d, $J$ = 8.8 Hz, 1 H, 2-H), 5.42 (dd, $J$ = 6.2, $J$ = 8.8 Hz, 1 H, 3-H), 4.18 (dd, $J$ = 6.2, $J$ = 8.2 Hz, 1 H, 4-H), 4.68–3.77 (m, 1 H, 5-H), 3.32 (d, $J$ = 4.7 Hz, 2 H, 6-H), 2.34 (s, 3 H, $SCH_3$), 2.29 (s, 3 H, $SCH_3$), 1.36 [s, 6 H, 2 × $C(CH_3)$] ppm. $^{13}C$ NMR (63 MHz, $CDCl_3$): $\delta$ = 144.0 ($C_{ipso}$, Ar), 139.1 (C-1), 128.8–127.1 (15 $C_{Ar}$), 126.0 (C-2), 108.8 [$C(CH_3)_2$], 87.0 [$C(Ar)_3$], 78.2 (C-4), 75.8 (C-3), 69.8 (C-5), 65.2 (C-6), 28.0 and 25.7 [$C(CH_3)_2$], 17.4 and 16.7 ($SCH_3$) ppm. HRMS (ESI): calcd. for $C_{30}H_{34}O_4NaS_2$ $[M + Na]^+$ 545.1796; found 545.1799.

**General Procedure for the Synthesis of 1,2-Unsaturated-1,5-Dithiopyranosides 13–16:** 4-Picoline (3.6 equiv. for **9** and **10**, 6 equiv. for **11** and **12**) was added to a solution of ketene dithioacetal **9**–**12** (1 equiv.) in dichloromethane (10 mL mmol$^{-1}$). The mixture was cooled to –20 °C and trifluoromethanesulfonic anhydride was added dropwise (1.2 equiv. for **9** and **10**, 2 equiv. for **11** and **12**). The resulting mixture was stirred for 15 min at –20 °C and then warmed up to 0 °C and stirred for 1 h. The mixture was stirred overnight and the temperature was allowed to rise to room temp. Dichloromethane was evaporated in vacuo. The crude product was purified by flash chromatography over silica gel (petroleum ether/EtOAc, 8:2) to give the pure cyclized thiosugars.

**Methyl 2-Deoxy-3,4-*O*-isopropylidene-1,5-dithio-L-*erythro*-pent-1-enopyranoside (13):** Following the general procedure, **9** (490 mg, 1.96 mmol), 4-picoline (690 μL, 7.06 mmol) and trifluoromethanesulfonic anhydride (390 μL, 2.35 mmol) yielded **13** as a white solid

(413 mg, 95%). M.p. 62 °C, $[\alpha]_D^{20}$ = –249.0 (*c* = 0.9, $CHCl_3$). $^1H$ NMR (250 MHz, $CDCl_3$): $\delta$ = 5.98 (d, *J* = 4.2 Hz, 1 H, 2-H), 4.49 (dd, *J* = 4.2, *J* = 5.7 Hz, 1 H, 3-H), 4.27 (ddd, *J* = 4.7, *J* = 5.7, *J* = 10.8 Hz, 1 H, 4-H), 2.79 (dd, *J* = 4.7, *J* = 12.4 Hz, 1 H, 5-H), 2.70 (dd, *J* = 10.8, *J* = 12.4 Hz, 1 H, 5′-H), 2.37 (s, 3 H, $SCH_3$), 1.47 [s, 3 H, $C(CH_3)$], 1.38 [s, 3 H, $C(CH_3)$] ppm. $^{13}C$ NMR (63 MHz, $CDCl_3$): $\delta$ = 138.1 (C-1), 116.8 (C-2), 107.4 [$C(CH_3)_2$], 73.3 (C-4), 71.1 (C-3), 31.1 (C-5), 28.3 and 25.5 [2 C, $C(CH_3)_2$], 16.5 ($SCH_3$) ppm. MS (ESI): *m*/*z* = 219.0 $[M + H]^+$, 241.0 $[M + Na]^+$, 257.0 $[M + K]^+$. HRMS (ESI): calcd. for $C_9H_{14}O_2S_2K$ $[M + K]^+$ 257.0072; found 257.0063.

**Methyl 3,4-Di-*O*-benzyl-2-deoxy-1,5-dithio-D-*threo*-pent-1-enopyranoside (14):** Following the general procedure, **10** (1.64 mmol), 4-picoline (620 µL, 6.38 mmol) and trifluoromethanesulfonic anhydride (350 µL, 2.13 mmol) yielded **14** as a yellow oil (270 mg, 46% over two steps). $[\alpha]_D^{20}$ = –164.5 (*c* = 0.9, $CHCl_3$). $^1H$ NMR (500 MHz, $CDCl_3$): $\delta$ = 7.28 (m, 10 H, 2 × Ar), 5.82 (d, *J* = 4.4 Hz, 1 H, 2-H), 4.68 (d, *J* = 12.0 Hz, 1 H, C*H*$_2$Ph), 4.60 (s, 2 H, C*H*$_2$Ph), 4.58 (d, *J* = 12.0 Hz, 1 H, C*H*$_2$Ph), 4.01 (ddd, *J* = 0.6, *J* = 4.4, *J* = 5.0 Hz, 1 H, 3-H), 3.95 (ddd, *J* = 2.4, *J* = 5.0, *J* = 7.3 Hz, 1 H, 4-H), 3.07 (dd, *J* = 2.4, *J* = 13.3 Hz, 1 H, 5-H), 3.00 (ddd, *J* = 0.6, *J* = 7.3, *J* = 13.3 Hz, 1 H, 5′-H), 2.34 (s, 3 H, $SCH_3$) ppm. $^{13}C$ NMR (126 MHz, $CDCl_3$): $\delta$ = 138.5 and 138.1 (2 $C_{ipso}$, Ar), 135.1 (C-1), 128.7–128.0 (10 $C_{Ar}$), 118.7 (C-2), 75.0 (C-3), 73.2 (C-4), 71.6 and 71.4 (2 × *C*H$_2$Ph), 29.4 (C-5), 17.1 ($SCH_3$) ppm. MS (ESI): *m*/*z* = 381.1 $[M + Na]^+$, 397.1 $[M + K]^+$. HRMS (ESI): calcd. for $C_{20}H_{22}O_2NaS_2$ $[M + Na]^+$ 381.0959; found 381.0963.

**Methyl 3,4,6-Tri-*O*-benzyl-2-deoxy-1,5-dithio-L-*arabino*-pent-1-enopyranoside (15):** Following the general procedure, **11** (273 mg, 0.54 mmol), 4-picoline (350 µL, 3.56 mmol) and trifluoromethanesulfonic anhydride (200 µL, 2.13 mmol) yielded **15** as a yellow oil (222 mg, 86%). $[\alpha]_D^{20}$ = –143.0 (*c* = 1.0, $CHCl_3$). $^1H$ NMR (250 MHz): $\delta$ = 7.23–7.17 (m, 15 H, 3 × Ar), 5.79 (dd, *J* = 0.7, *J* = 4.4 Hz, 1 H, 2-H), 4.60–4.38 (m, 6 H, 3 × C*H*$_2$Ph), 3.86–3.84 (m, 2 H, 3-H and 4-H), 3.65 (dd, *J* = 5.9, *J* = 8.8 Hz, 1 H, 6′-H), 3.59 (ddd, *J* = 2.0, *J* = 5.9, *J* = 7.3 Hz, 1 H, 5-H), 3.53 (dd, *J* = 7.3, *J* = 8.8 Hz, 1 H, 6-H), 2.28 (s, 3 H, $SCH_3$) ppm. $^{13}C$ NMR (63 MHz, $CDCl_3$): $\delta$ = 138.2, 137.8 and 137.7 (3 $C_{ipso}$, Ar), 134.8 (C-1), 128.3–127.6 (15 $C_{Ar}$), 117.4 (C-2), 73.0 (*C*H$_2$Ph), 72.6 (C-4), 72.0 (C-3), 71.9 and 70.9 (2 × *C*H$_2$Ph), 68.3 (C-6), 43.0 (C-5), 16.8 ($SCH_3$) ppm. MS (ESI): *m*/*z* = 501.4 $[M + Na]^+$. HRMS (ESI): calcd. for $C_{28}H_{30}O_3NaS_2$ $[M + Na]^+$ 501.1534; found 501.1528.

**Methyl 2-Deoxy-3,4-*O*-isopropylidene-6-*O*-trityl-1,5-dithio-L-*ribo*-pent-1-enopyranoside (16):** Following the general procedure, **12** (0.44 g, 0.85 mmol), 4-picoline (0.50 mL, 1.70 mmol) and trifluoromethanesulfonic anhydride (0.28 mL, 5.11 mmol) yielded **16** as an oil (0.36 g, 87%). $[\alpha]_D^{20}$ = –48.4 (*c* = 0.8, $CHCl_3$). $^1H$ NMR (250 MHz, $CDCl_3$): $\delta$ = 7.58–7.50 (m, 5 H, Ar), 7.36–7.27 (m, 10 H, 2 × Ar), 5.83 (d, *J* = 4.0 Hz, 1 H, 2-H), 4.65 (dd, *J* = 4.0, *J* = 6.5 Hz, 1 H, 3-H), 4.54 (dd, *J* = 3.2, *J* = 6.5 Hz, 1 H, 4-H), 3.56–3.49 (m, 1 H, 5-H), 3.31 (m, 2 H, 6-H), 2.42 (s, 3 H, $SCH_3$), 1.38 [s, 3 H, $C(CH_3)$], 1.26 [s, 3 H, $C(CH_3)$] ppm. $^{13}C$ NMR (63 MHz, $CDCl_3$): $\delta$ = 144.0 (Ar), 135.0 (C-1), 129.8–127.2 (15 $C_{Ar}$), 117.7 (C-2), 108.6 [$C(CH_3)_2$], 86.9 [$C(Ar)_3$], 73.3 (C-4), 72.1 (C-3), 61.3 (C-6), 45.8 (C-5), 26.7 and 25.9 [$C(CH_3)_2$], 16.6 ($SCH_3$) ppm. MS (ESI): *m*/*z* = 513.1 $[M + Na]^+$. HRMS (ESI): calcd. for $C_{29}H_{30}O_3NaS_2$ $[M + Na]^+$ 513.1534; found 513.1529.

**Compound 17:** Oil, $[\alpha]_D^{20}$ = –89.5 (*c* = 1.1, $CHCl_3$). $^1H$ NMR (250 MHz, $CDCl_3$): $\delta$ = 6.52 and 6.42 (2 × d, *J* = 8.4 Hz, 2 × 1 H, 8-H and 9-H), 5.12 and 4.94 (2 × ddd, *J* = 8.4, *J* = 3.6, *J* = 2.3 Hz, 2 H, 7-H and 10-H), 4.73 (br. s, 1 H, 6-H), 4.50 (d, *J* = 5.4 Hz, 1 H, 3-H), 4.21 (dt, *J* = 5.4, *J* = 3.8 Hz, 1 H, 4-H), 2.80–2.68 (m, 2 H, 5-H), 2.38 (s, 3 H, $SCH_3$), 1.42 [s, 3 H, $C(CH_3)$], 1.30 [s, 3 H, $C(CH_3)$] ppm. $^{13}C$ NMR (63 MHz, $CDCl_3$): $\delta$ = 131.8 (C-1), 122.4 and 120.9 (C-8 and C-9), 117.2 (C-2), 112.2 and 111.1 (C-7 and C-10), 107.8 [$C(CH_3)_2$], 73.4 (C-4), 71.8 (C-3), 36.6 (C-6), 31.5 (C-5), 28.5 and 25.4 [$C(CH_3)_2$], 17.1 ($SCH_3$) ppm. MS (ESI): *m*/*z* = 296.1 $[M – SO_2CF_3 + H]^+$. HRMS (ESI): calcd. for $C_{14}H_{18}NO_2S_2$ $[M + H]^+$ 296.0779; found 296.0783.

**Methyl 2-Deoxy-3,4-*O*-isopropylidene-5-[methylepisulfonium]-1-thio-L-*erythro*-pent-1-enopyranoside Trifluoromethanesulfonate Salt (18):** 4-Picoline (150 µL, 1.55 mmol) was added to a solution of ketene dithioacetal **9** (243 mg, 0.97 mmol) in dichloromethane (12.2 mL). The mixture was cooled to –20 °C and trifluoromethanesulfonic anhydride was added dropwise (190 µL, 1.17 mmol). The resulting mixture was stirred for 15 min at –20 °C and then warmed up to 0 °C and stirred for 1 h. The crude product was purified by flash chromatography over silica gel (dichloromethane/methanol, 14:1). As described above, a small amount of pure sulfonium **18** was isolated for characterization. Oil, $[\alpha]_D^{20}$ = +32.5 (*c* = 1.3, MeOH). $^1H$ NMR (250 MHz, $CD_3OD$): $\delta$ = 6.82 (d, *J* = 4.2 Hz, 1 H, 2-H), 4.91–4.81 (m, 2 H, 3-H and 4-H), 4.25 (dd, *J* = 12.9, *J* = 5.3 Hz, 1 H, 5-H), 3.99 (dd, *J* = 12.9, *J* = 2.0 Hz, 1 H, 5′-H), 3.22 (s, 3 H, $S^+CH_3$), 2.57 (s, 3 H, $SCH_3$), 1.42 [s, 6 H, $C(CH_3)_2$] ppm. $^{13}C$ NMR (63 MHz, $CD_3OD$): $\delta$ = 139.3 (C-2), 124.3 (C-1), 111.9 [$C(CH_3)_2$], 71.6 (C-3), 68.8 (C-4), 42.7 (C-5), 27.7 and 26.1 [2 C, $C(CH_3)_2$], 25.6 ($S^+CH_3$), 18.5 ($SCH_3$) ppm. HRMS (ESI): calcd. for $C_{10}H_{17}O_2S_2$ $[M]^+$ 233.0670; found 233.0678.

**Supporting Information** (see also the footnote on the first page of this article): $^1H$ and $^{13}C$ NMR spectra for all new compounds.

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