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Note

# An improved synthesis of 5-thio-D-ribose from D-ribono-1,4-lactone

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**Abstract**

5-Thio-D-ribopyranose was synthesized from D-ribono-1,4-lactone (**1**) by two approaches: (i) 5-bromo-5-deoxy-D-ribono-1,4-lactone (**2**) was successively transformed into 5-bromo-5-deoxy, 5-*S*-acetyl-5-thio or 5-thiocyanato-D-ribofuranose derivatives; appropriate treatment then lead to 5-thio-D-ribopyranose (**7**) in 46–48% overall yield and; (ii) **2** was transformed into the 5-*S*-acetyl-5-thio-D-ribono-1,4-lactone derivative (**11**). Reduction and deprotection of **11** afforded 5-thio-D-ribopyranose (**7**) in 57% overall yield. 

*Keywords:* 5-Bromo-5-deoxy-D-ribono-1,4-lactone; 5-Bromo-5-deoxy-D-ribofuranose; 5-*S*-Acetyl-5-thio-D-ribono-1,4-lactone; 5-Thiocyanato-D-ribono-1,4-lactone; 5-Thio-D-ribopyranose

## 1. Introduction

5-Thioaldopyranoses[1] exhibit remarkable biological activities, such as inhibition of glycosidases. 5-Thio-D-glucose inhibits D-glucose transport across membranes and also the release of insulin.[2] 5-Thio-L-fucose was found to be a potent inhibitor of bovine α-L-fucosidase.[3] Glycosides of 1,5-dithio-D-xylopyranose, in particular, have proved to be orally active antithrombotic agents.[4] Among naturally occurring thiosugars with a sulfur atom in the ring, 5-thio-D-mannose has been isolated from the marine sponge *Clathria pyramida*.[5]

Syntheses of thiosugars have been reported since the 1960s. D-Ribose,[6] D-galactose,[7] L-rhamnose,[8] and 2-acetamido-2-deoxy-D-glucose[9] 5-thio-analogs have been synthesized.[7] These syntheses require usually tedious and long synthetic strategies to lead to substantially low yields. Very often two strategies are employed, which uses two key steps: conversion of the pyranose structure into a furanose followed by conversion of a 5,6-epoxide into the 5,6-episulfide. The second strategy requires a primary-*O*-sulfonate displacement of furanoside by use of reagents containing nucleophilic sulfur: thiocyanate ion, benzylthiolate, ethyl xanthate[10] and thiolacetic acid salt,[5,8,11] which can be used to give sulfur-containing products and thence thiosugars by deprotection. Recently, Hughes et al. have used the latter strategy and obtained 5-thio-D-ribose from 2,3-*O*-isopropylidene-D-ribopyranose in 15% overall yield.[12] We previously described a rapid synthesis of 5-bromo-5-deoxy-D-pentono-1,4-lactones. Based on our previous results of synthesis of D-pentonolactams,[13] we now report on two routes for a convenient and efficient synthesis of 5-thio-D-ribopyranose using D-ribono-1,4-lactone as starting material: either via 5-bromo-5-deoxy-D-ribose derivative (Pathway A, Scheme 1) or via the 5-*S*-acetyl-5-thio-D-ribono-1,4-lactone derivative (Pathway B, Scheme 1).

## 2. Results and discussion

In pathway A, selective bromination of the primary hydroxyl group in D-ribono-1,4-lactone (**1**) by thionyl bromide in *N*,*N*-dimethylformamide gave the 5-bromo-5-deoxy-D-ribono-1,4-lactone (**2**)[14] (95%), which on iso-

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[1] For a recent review, see Ref. 1.

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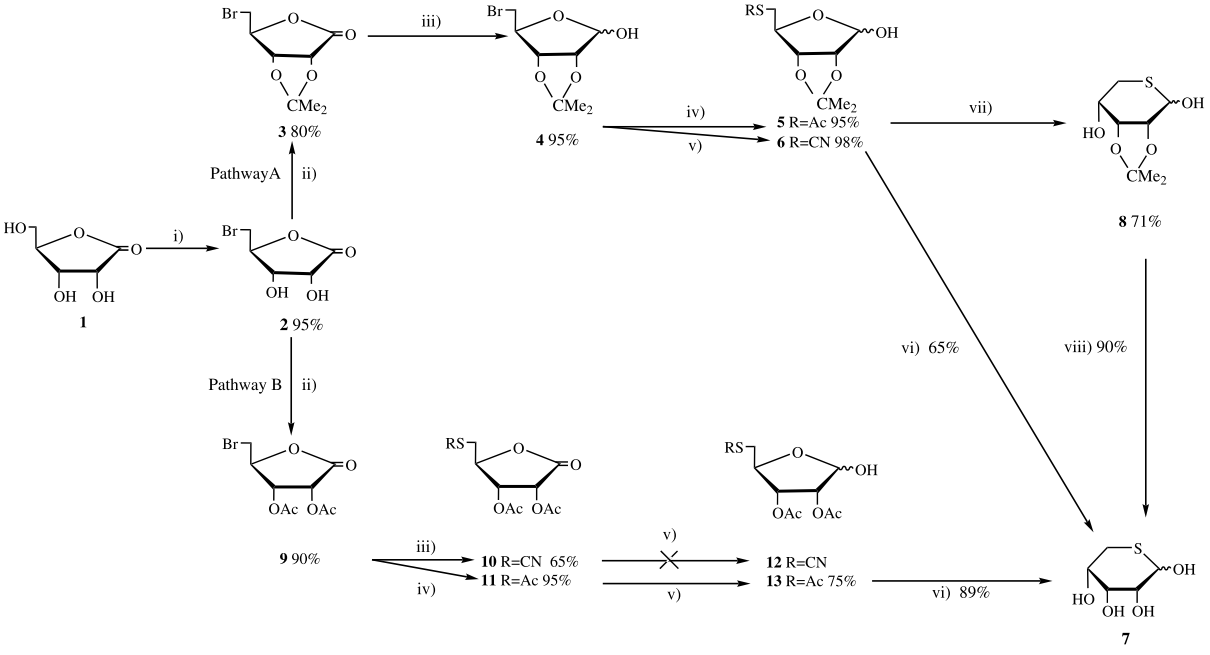
propylidenation gave **3** (80%). More conveniently and more efficiently, **3** could be obtained by a one pot sequential bromination-protection of **1** (80%). TLC of the reduction product of **3** by disiamylborane showed the presence of a mixture of products. NMR analysis of the crude mixture shows in particular formation of the 5-deoxy-D-ribono-1,4-lactone derivative due to cleavage of the C–Br bond. On the other hand, when **3** was treated with diisobutylaluminium hydride (DIBAL-H) in THF, TLC of the crude product (Table 2) showed the presence of a single spot. $^{13}C$ NMR analysis showed disappearance of the carbonyl group (173.6 ppm) and the presence of two new signals at 97.7 and 103.5 ppm characteristic of two anomeric carbons in **4** (95%). Displacement of the bromide group in **4** with potassium thioacetate in *N*,*N*-dimethylformamide gave 5-*S*-acetyl-2,3-*O*-isopropylidene-5-thio-D-ribofuranose (**5**) in 95% yield. Methanolysis of **5** with sodium methoxide in MeOH afforded 2,3-*O*-isopropylidene-5-thio-D-ribopyranose (**8**) ($\alpha/\beta = 1:1$) in 71% yield. Acid hydrolysis of **8** gave 5-thio-D-ribopyranose (**7**) ($\alpha/\beta = 1:1$) in 90% yield. The $^{13}C$ NMR spectra showed the presence of α- and β-forms. In comparison, reaction of 5-bromo-5-deoxy-2,3-*O*-isopropylidene-D-ribofuranose (**4**) with potassium thiocyanate gave **6** in 98% yield. Treatment of **6** with commercially available zinc in acetic acid[10b] did not afford the desired product **7** but required activated zinc.[15] The overall yields of the **1**→**3**→**4**→**5**→**8**→**7** reaction sequence and **1**→**3**→**4**→**6**→**7** were 46 and 48%, respectively.

To avoid the necessary generation of the thiol group from the thioacetate or thiocyanate functionality, we have attempted the treatment of **4** with sodium sulfide nonahydrate. However, a mixture of the 1,4-anhydro compound **14**,[12] as major product, traces of **8** and bis-(2,3-*O*-isopropylidene-D-ribofuranose) 5,5′-sulfide (**15**) (Scheme 2) was identified by NMR and mass spectroscopy. Basic conditions were presumably responsible of the intramolecular displacement of the bromide atom by the C-1 oxyanion and formation of **14**. In less alcaline conditions, by using sodium sulfide, the anhydride **14** was undetected but compounds **8** and **15** were obtained in equal amount.

To prevent any cleavage of the C–Br bond during the reduction step, and to improve the synthesis of 5-thio-D-ribopyranose (**7**), we have investigated a second route involving reduction of the lactone after displacement of the bromide group (pathway B, Scheme 1).

In pathway B, **2** was acetylated to give **9** (90%). A one pot sequential bromination–acetylation of **1** afforded **9** in 90% yield. Displacement of the bromide group with potassium thiocyanate gave the thiocyanate **10** in 65% yield and treatment of **9** with potassium thioacetate gave the thioacetate derivative **11** in 95% isolated yield. When **10** was treated with diisobutylaluminium hydride or disiamylborane in THF, TLC showed the presence of a complex mixture of products. NMR analysis of the crude material showed that partial deacetylation and reduction of the thiocyanate group occurred and any trace of expected compound 2,3-*O*-isopropylidene-5-thiocyanato-D-ribofuranose




Scheme 1. Pathway A: (i) $SOBr_2$/DMF; (ii) acetone/$I_2$; (iii) DIBAL-H/THF; (iv) KSAc/DMF; (v) KSCN/DMF; (vi) activated zinc/AcOH; (vii) MeONa/MeOH; (viii) TFA/$H_2O$. Pathway B: (i) $SOBr_2$/DMF; (ii) $AC_2O$; (iii) KSCN/DMF; (iv) KSAc/DMF; (v) disiamylborane/THF; (vi) MeONa/MeOH.

Table 1
$^1$H NMR data

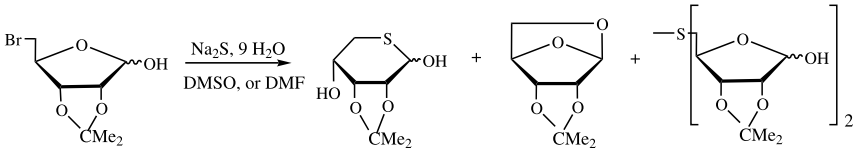
| Compound | Chemical shifts (ppm) | | | | | | Other signals | Coupling constants (Hz) | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | H-1 | H-2 | H-3 | H-4 | H-5a | H-5b | | $J_{1,2}$ | $J_{2,3}$ | $J_{3,4}$ | $J_{4,5a}$ | $J_{4,5b}$ | $J_{5a,5b}$ |
| **3** [a] | | 4.60 (d) | 4.81 (d) | 4.77 (t) | 3.56–3.57 (m) | | 1.24; 1.32 ($CMe_2$) | | 5.93 | 0 | 3.37 | 3.37 | |
| **4α** [a] | 5.51 (d) | 4.71 (m) | 4.66 (m) | 4.45 (m) | 3.50 (m) | | 1.56; 1.39 ($CMe_2$) | | | | | | |
| **4β** [a] | 5.51 (s) | 4.66 (d) | 4.82 (dd) | 4.42 (ddd) | 3.46 (m) | | 1.51; 1.34($CMe_2$) | 0 | 5.92 | 1.03 | 6.16 | 9.24 | 10.2 |
| **5α** [a] | 5.30 (d) | 4.62 (m) | 4.45 (dd) | 4.16 (m) | 3.05 (m) | | 1.51; 1.33 ($CMe_2$) 2.30 ($SCOCH_3$) | 4.04 | 2.39 | 6.62 | | | |
| **5β** [a] | 5.41 (s) | 4.62 (m) | | 4.16 (m) | 3.16 (dd) | 3.07 (dd) | 1.41; 1.24 ($CMe_2$) 2.30 ($SCOCH_3$) | 0 | | 0.72 | 7.73 | 7.73 | 13.89 |
| **6α** [a] | 5.40 (d) | 4.64–4.67 (m) | | 4.39 (m) | 3.22 (dd) | 3.13 (dd) | 1.60; 1.42 ($CMe_2$) | 4.12 | | | 5.4 | 6.2 | 13.6 |
| **6β** [a] | 5.52 (s) | 4.64–4.67 (m) | | 4.42 (m) | 3.34 (dd) | 3.12 (dd) | 1.49; 1.34 ($CMe_2$) | 0 | | 0.83 | 8.92 | 6.34 | 13.33 |
| **7α** [b,c] | 4.73 (d) | 3.81 (t) | 3.96 (m) | 3.93 (m) | 2.79 (dd) | 2.61 (dd) | | 3.12 | 3.10 | 2.52 | 9.02 | 3.45 | 13.56 |
| **7β** [b,c] | 4.82 (d) | 3.70 (dd) | 3.88 (t) | 3.85 (m) | 2.88 (dd) | 2.37 (dd) | | 7.62 | 2.64 | 2.45 | 10.96 | 4.03 | 13.21 |
| **8α** [a,c] | 4.70 (d) | 3.65–3.76 (m) | | | 2.99 (dd) | 2.66 (dd) | 1.49; 1.36 ($CMe_2$) | 4.1 | | | 8.1 | 3.36 | 13.1 |
| **8β** [a,c] | 4.78 (d) | 4.18 (m) | 4.37 (m) | 4.21 (m) | 2.88 (dd) | 2.61 (dd) | 1.49; 1.36 ($CMe_2$) | 6.9 | | | 10.65 | 4.3 | 12.13 |
| **9** [a] | | 5.67 (d) | 5.37 (dd) | 4.75 (m) | 3.61 (d) | | 2.09; 2,07 ($OCOCH_3$) | | 6.62 | 1.19 | 4.78 | | |
| **10** [a] | | 5.65 (d) | 5.44 (dd) | 4.76 (m) | 3.40 (dd) | 3.31 (dd) | 2.12; 2.11 ($OCOCH_3$) | | 6.27 | 1.45 | 5.60 | 7.73 | 14.35 |
| **11** [a] | | 5.56 (d) | 5.16 (dd) | 4.38 (m) | 3.09 (d) | | 1.89; 1.87 ($OCOCH_3$) 2.17 ($SCOCH_3$) | | 5.91 | 0.69 | 7.0 | | |
| **13α** [a] | 5.48 (d) | 5.04 (m) | 5.17 (m) | 4.34 (m) | 3.23–3.15 (m) | | 2.06; 2.05 ($OCOCH_3$) 2.32 ($SCOCH_3$) | 4.0 | | | 5.45 | 9.39 | |
| **13β** [a] | 5.27 (s) | 5.04 (m) | 5.22 (m) | 4.14 (m) | 3.23 (dd) | 3.15 (dd) | 2.05; 2.03 ($OCOCH_3$) 2.33 ($SCOCH_3$) | | | | 4.94 | 5.23 | 14.24 |

[a] In $CDCl_3$.
[b] In $D_2O$.
[c] Ref. 12.

Table 2
$^{13}C$ NMR data

| Compound | Chemical shifts (ppm) | | | | | Other signals |
|---|---|---|---|---|---|---|
| | C-1 | C-2 | C-3 | C-4 | C-5 | |
| **3** [a] | 173.3 | 77.7 | 75.1 | 80.6 | 33.0 | 113.5($C$Me$_2$)<br>26.4; 25.2 (C$Me_2$) |
| **4α** [a] | 97.7 | 79.8 | 83.3 | 80.5 | 33.6 | 115.0 ($C$Me$_2$)<br>26.5; 25.3 (C$Me_2$) |
| **4β** [a] | 103.5 | 86.1 | 83.3 | 87.1 | 33.6 | 113.2($C$Me$_2$)<br>26.8; 25.3 (C$Me_2$) |
| **5α** [a] | 96.9 | 79.9–79.7 | | 83.1 | 31.1 | 115.0 ($C$Me$_2$)<br>26.5; 25.3 (C$Me_2$)<br>S$C$OCH$_3$: 195.9; SCO$C$H$_3$: 30.9 |
| **5β** [a] | 103.5 | 83.9 | 86.4 | 86.4 | 33.7 | 112.9 ($C$Me$_2$)<br>26.5; 25.3 (C$Me_2$)<br>S$C$OCH$_3$: 195.9; SCO$C$H$_3$: 30.9 |
| **6α** [a] | 96.4 | 82.8–80.0–79.69 | | | 35.9 | 112.3 (S$C$N, $C$Me$_2$)<br>26.3; 24.9 (C$Me_2$) |
| **6β** [a] | 103.2 | 86.0–86.0–83.6 | | | 37.6 | 111.4 (S$C$N, $C$Me$_2$)<br>26.3; 24.9 (C$Me_2$) |
| **7α** [b,c] | 73.9 | 74.1 | 71.6 | 70.6 | 28.5 | |
| **7β** [b,c] | 73.0 | 74.5 | 71.3 | 70.2 | 22.7 | |
| **8α** [a,d] | 75.1 | 72.1 | 69.5 | 66.0 | 26.8 | 112.4 ($C$Me$_2$)<br>25.6; 25.2 (C$Me_2$) |
| **8β** [a,d] | 79.6 | 76.2 | 73.1 | 67.2 | 27.5 | 109.3 ($C$Me$_2$)<br>26.6; 25.2 (C$Me_2$) |
| **9** [a] | 170.5 | 66.6 | 70.4 | 81.8 | 30.8 | 20.7; 20.4 (CO$C$H$_3$)<br>170.1; 169.6 ($C$OCH$_3$) |
| **10** [a] | 170.1 | 66.5 | 70.1 | 81.1 | 34.8 | 111.4 (S$C$N); 20.8; 20.5 (CO$C$H$_3$)<br>170.9; 169.7 ($C$OCH$_3$) |
| **11** [a] | 170.8 | 66.2 | 70.3 | 81.0 | 29.7 | 194.5 (S$C$OCH$_3$); 30.2 (SCO$C$H$_3$)<br>168.9; 169.9 (O$C$OCH$_3$); 20.4; 20.1 (OCO$C$H$_3$) |
| **13α** [a] | 95.6 | 79.6 | 72.4 | 71.3 | 31.5 | 195.3 (S$C$OCH$_3$); 30.9 (SCO$C$H$_3$)<br>170.3; 170.3 (O$C$OCH$_3$); 20.9; 20.9 (OCO$C$H$_3$) |
| **13β** [a] | 100.4 | 79.5 | 76.1 | 73.8 | 33.2 | 195.9 (S$C$OCH$_3$); 309 (SCO$C$H$_3$)<br>170.3; 170.3 (O$C$OCH$_3$); 20.9; 20.9 (OCO$C$H$_3$) |

[a] In $CDCl_3$.
[b] In $D_2O$.
[c] Refs. 6,12.
[d] Ref. 12.




**4** **8** **14** **15**

Scheme 2.

(**12**) was formed. On another hand, reduction of **11** with disiamylborane in THF gave **13** in 75% yield. Methanolysis of **13** gave 5-thio-D-ribopyranose **7** (α/β = 1:1) in 89% yield. The overall yield of the **1** → **9** → **11** → **13** → **7** reaction sequence was 57%.

## 3. Experimental

*General methods.*—Melting points were determined on a Buchi 535 apparatus and are uncorrected. Optical rotations were measured with a JASCO DIP-370 digital

polarimeter, using a sodium lamp ($\lambda = 589$ nm) at 20 °C. $^1$H and $^{13}$C NMR spectra (Tables 1 and 2) were recorded in $D_2O$ or $CDCl_3$. $Me_4Si$ was used as an internal standard on a Bruker 300 MHz spectrometer. Thin-layer chromatography (TLC) was performed on E. Merck glass plates silica gel sheets (Silica Gel $F_{254}$) and visualized under UV light and stained with phosphomolybdic acid–aq $H_2SO_4$ solution. Column chromatography was performed on Kiesel gel (E. Merck 230–400 mesh). All solvents were distilled before use.

*5-Bromo-5-deoxy-2,3-*O*-isopropylidene-*D*-ribono-1,4-lactone* (**3**).—D-Ribono-1,4-lactone (**1**) (0.5 g, 3.4 mmol) was stirred in anhyd DMF (5 mL) under an inert atmosphere. Freshly distilled $SOBr_2$ (0.445, 1.7 equiv) was added dropwise at 0 °C. The mixture was stirred for 30 min, then MeOH was added and the solution was kept for 10 min at rt and concentrated. The crude material was diluted with water and washed with $CH_2Cl_2$. The water extracts were, filtered and concentrated. The residue was treated with anhyd acetone (20 mL) and $I_2$ (150 mg, 0.59 mmol). The reaction mixture was stirred overnight at rt under an inert atmosphere. Saturated aq sodium thiosulfate was added to the mixture. The solution was concentrated under diminished pressure to yield a crude product which was partitioned between $CH_2Cl_2$ and water. The $CH_2Cl_2$ extracts were dried, filtered and concentrated under reduced pressure. The residue was chromatographed on silica gel. Elution with (4:1 then 3:2) hexanes–EtOAc gave **3** (0.68 g, 80%) as white solid: $R_f$ 0.89 (1:1 hexanes–EtOAc); mp 82–84 °C; $[\alpha]_D$ −45° (*c* 0.59, $CHCl_3$). Anal. Calcd for $C_8H_{11}BrO_4$: C, 38.27; H, 4.42; Br, 31.82. Found C, 38.07; H, 4.12; Br 31.94.

*5-Bromo-5-deoxy-2,3-*O*-isopropylidene-*D*-ribofuranose* (**4**).—To a solution of **3** (1 g, 3.4 mmol) in dry toluene or freshly distilled THF (10 mL), under an inert atmosphere, at −80 °C was added DIBAL-H (3.4 mL, 1.1 equiv). The mixture was stirred for 30 min at −80 °C, then MeOH was added and the solution was kept for 30 min at rt and concentrated under reduced pressure. The crude material was partitioned between $CH_2Cl_2$ and water. The $CH_2Cl_2$ extracts were dried filtered and concentrated. The residue was chromatographed on silica gel. Elution with 7:3 hexanes–EtOAc gave **4** (0.96 g, 95%) as a white solid: $R_f$ 0.89 (1:1 hexanes–EtOAc); mp 73.5–74.5 °C; $[\alpha]_D$ −39° ($\alpha/\beta = 1:9$) (*c* 1.04, $CH_2Cl_2$). Anal. Calcd for $C_8H_{13}BrO_4$: C, 37.96; H, 5.18; Br, 31.57. Found: C, 37.93; H, 5.22; Br, 31.61.

*5-*S*-Acetyl-2,3-*O*-isopropylidene-5-thio-*D*-ribofuranose* (**5**).—To a solution of 5-bromo-5-deoxy-2,3-*O*-isopropylidene-D-ribofuranose (**4**) (0.5 g, 2 mmol) in anhyd DMF (5 mL) was added potassium thioacetate (0.27 g, 2.4 mmol). The mixture was kept for 10 min, under an inert atmosphere, at rt. The suspension was filtered, and the filtrate was concentrated under reduced pressure. The crude material was partitioned between $CH_2Cl_2$ and water. The $CH_2Cl_2$ extracts were dried filtered and concentrated. The residue was chromatographed on silica gel. Elution with 4:1 hexanes–EtOAc gave **5** (0.47 g, 95%) as a colorless syrup: $R_f$ 0.51 (7:3 hexanes–EtOAc); $[\alpha]_D$ −7° ($\alpha/\beta = 3:7$) (*c* 1.04, $CH_2Cl_2$). Anal. Calcd for $C_{10}H_{16}O_5S$: C, 48.37; H, 6.50. Found: C, 48.03; H, 6.69.

*2,3-*O*-Isopropylidene-5-thiocyanato-*D*-ribonofuranose* (**6**).—To a solution of the lactone (**4**) (0.5 g, 2 mmol) in anhyd DMF (5 mL), under an inert atmosphere, was added potassium thiocyanate (0.38 g, 2 equiv). The mixture was kept overnight under an inert atmosphere at 70 °C. The solution was concentrated and the crude material was partitioned between $CH_2Cl_2$ and water. The $CH_2Cl_2$ extracts were dried filtered and concentrated. The residue was chromatographed on silica gel. Elution with 7:3 hexanes–EtOAc gave **6** (0.45 g, 98%) as a white solid: $R_f$ 0.57 (3:2 hexanes–EtOAc); mp 67.8–68.8 °C, $[\alpha]_D$ −8° ($\alpha/\beta = 1:4$). Anal. Calcd for $C_9H_{13}NO_4S$: C, 46.74; H, 5.67; N, 6.06. Found: C, 46.78; H, 5.41; N, 5.93.

*2,3-*O*-Isopropylidene-5-thio-*D*-ribopyranose* (**8**).—To a solution of the *S*-acetyl derivative **5** (0.5 g, 1.4 mmol) in MeOH (5 mL) was added NaOMe (0.21 g, 4 mmol). The mixture was stirred for 30 min at rt. The solution was passed through ion exchange resin (Dowex 50 × 8-100 ion) filtered and concentrated. The residue was chromatographed on silica gel. Elution with 1:1 hexanes–EtOAc gave **8** (0.29 g, 71%) as a colorless syrup: $R_f$ 0.42 (1:1 hexanes–EtOAc), lit.: for the β form: mp 136–138 °C, $[\alpha]_D$ −37° (−30° final) (*c* 1.44, MeOH).[12] Anal. Calcd for $C_8H_{14}O_4S$: C, 46.58; H, 6.84; Found: C, 46.63; H, 6.92.

*2,3-Di-*O*-acetyl-5-bromo-5-deoxy-*D*-ribono-1,4-lactone* (**9**).—D-Ribono-1,4-lactone (**1**) (0.5 g, 3.4 mmol) was stirred in anhyd DMF (5 mL) under an inert atmosphere. Freshly distilled $SOBr_2$ (0.445 mL, 1.7 equiv) was added dropwise at 0 °C. The mixture was stirred at rt for 30 min, then MeOH was added and the solution was kept for 10 min at rt and concentrated. The crude material was treated with $Ac_2O$ (10 mL). After 15 min at 60 °C under an inert atmosphere, the solution was concentrated and the residue was added to water and extracted with $CH_2Cl_2$; the extracts were dried, filtered and concentrated under reduced pressure. The residue was chromatographed on silica gel. Elution with 4:1, then 3:2 hexanes–EtOAc gave **9** (0.90 g, 90%) as a colorless syrup: $R_f$ 0.60 (3:2 hexanes–EtOAc); $[\alpha]_D$ +3° (*c* 3.62, $CH_2Cl_2$). Anal. Calcd for $C_9H_{11}BrO_6$: C, 36.63; H, 3.76; Br, 27.08. Found: C, 37.02; H, 4.13; Br, 27.82.

*2,3-Di-*O*-acetyl-5-thiocyanato-*D*-ribono-1,4-lactone* (**10**).—To a solution of **3** (0.5 g, 1.7 mmol) in anhyd DMF (5 mL) was added potassium thiocyanate (0.23 g, 3.4 mmol). The mixture was stirred under an inert

atmosphere at 70 °C for 10 min. The mixture was concentrated under reduced pressure and the residue was added to water and extracted with $CH_2Cl_2$. The $CH_2Cl_2$ extracts were dried, filtered and concentrated. The residue was chromatographed on silica gel. Elution with 4:1 hexanes–EtOAc gave **10** (0.65 g, 65%) as yellow syrup: $R_f$ 0.54 (3:2 hexanes–EtOAc); $[\alpha]_D$ −15° (*c* 1.24, $CH_2Cl_2$). Anal. Calcd for $C_{10}H_{11}NO_6S$: C, 43.95; H, 4.06; N, 5.13. Found: C, 43.99; H, 4.05; N, 4.87.

*2,3-Di*-O-*acetyl-5*-S-*acetyl-5-thio*-D-*ribono-1,4-lactone* (**11**).—To a solution of **9** (0.5 g, 1.7 mmol) in anhyd DMF (5 mL) was added potassium thioacetate (0.23 g, 2 mmol). The mixture was stirred under an inert atmosphere at rt for 10 min. The mixture was filtered and concentrated under reduced pressure to yield a crude product which was partitioned between $CH_2Cl_2$ and water. The $CH_2Cl_2$ extracts were dried, filtered and concentrated. The residue was chromatographed on silica gel. Elution with 4:1 hexanes–EtOAc gave **11** (0.47 g, 95%) as a colorless syrup: $R_f$ 0.54 (3:2 hexanes–EtOAc); $[\alpha]_D$ −20° (*c* 0.66, $CH_2Cl_2$). Anal. Calcd for $C_{11}H_{14}O_7S$: C, 45.51; H, 4.86. Found: C, 45.54; H, 4.96.

*2,3-Di*-O-*acetyl-5*-S-*acetyl-5-thio*-D-*ribofuranose* (**13**).—To 2,3-di-*O*-acetyl-5-*S*-acetyl-D-ribono-1,4-lactone (**11**) (0.5 g,1.72 mmol) at 0 °C was added disiamylborane freshly prepared[16] (8 equiv) in THF. The mixture was stirred, under an inert atmosphere, at rt for 24 h. Then MeOH was added and the solution was kept for 30 min and concentrated. The crude material was diluted with $CH_2Cl_2$ and washed with water. The $CH_2Cl_2$ extracts were dried, filtered and concentrated. The residue was chromatographed on silica gel. Elution with 4:1 hexanes–EtOAc gave **13** (0.292 g, 75%) as a colorless syrup: $R_f$ 0.34 (3:2 hexanes–EtOAc); $[\alpha]_D$ +8° ($\alpha/\beta = 3:7$). Anal. Calcd for $C_{11}H_{16}O_7S$: C, 45.20; H, 5.52. Found: C, 45.44; H, 6.28.

*5-Thio*-D-*ribopyranose* (**7**).—(a) From **6**. To a solution of the thiocyanate (**6**) (0.5 g, 2.16 mmol) in AcOH (10 mL), at 110 °C was added activated zinc[15] (1.7 g, 12 equiv). The mixture was stirred, under an inert atmosphere, for 3 h. The solution was filtered and washed with water, concentrated under reduced pressure to afford a residue. The residue was subjected to flash chromatography on silica gel. Elution with 9:1 then 4:1 $CH_2Cl_2$–MeOH gave **7** (0.21 g, 65%) as a colorless syrup: $R_f$ 0.59 (4:1 $CH_2Cl_2$–MeOH), lit.[12]: mp and mixed mp 143–145 °C.[6,12] Anal. Calcd for $C_5H_{10}O_4S$: C, 36.13; H, 6.06. Found: C, 36.16; H, 5.53.

(b) From **8**. To 9:1 TFA–water (5 mL) was added the thioribose derivative (**8**) (0.2 g, 0.97 mmol). The solution was stirred for 15 min at rt and concentrated under reduced pressure to afford a residue which was chromatographed on silica gel to give **7** (0.145 g, 90%).

(c) From 13. To a solution of the thioacetate (**13**) (0.5 g, 1.71 mmol) in MeOH (5 mL) was added NaOMe (0.092 g, 6 equiv). The mixture was stirred for 3 h at rt. The solution was passed through ion-exchange resin (Dowex 50 × 8-100 ion), filtered and concentrated. The residue was chromatographed on silica gel to give **7** (0.25 g, 89%).

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