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Note

# β-D-Galactopyranosyl-thiohydroximates and D-galactopyranosylidene-spiro-oxathiazoles: synthesis and enzymatic evaluation against *E. coli* D-galactosidase

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Dedicated to Professor András Lipták on the occasion of his 70th birthday in appreciation of his outstanding contributions to carbohydrate chemistry

**Abstract**—By reaction with arylhydroximoyl chlorides, 2,3,4,6-tetra-*O*-acetyl-1-thio-β-D-galactopyranose was converted to the corresponding β-D-galactopyranosyl-thiohydroximates, which gave predominantly (1*S*)-D-galactopyranosylidene-spiro-oxathiazoles on illumination in the presence of NBS. Conventional *O*-deacetylation of both thiohydroximates and oxathiazoles gave weak inhibitors of *E. coli* D-galactosidase ($K_i$ 1.1–11.1 mM).


*Keywords:* Spiro sugars; Galactosyl-thiohydroximates; Galactosylidene-spiro-oxathiazoles; Galactosidase inhibitors

Spiroanomeric sugar derivatives,[1–3] produced by microorganisms or more frequently obtained by chemical synthesis, constitute a growing class of carbohydrates. Interest toward spirosugars increased notably after the isolation of several structures in which one monosaccharide unit with a spiroanomeric carbon was linked to another sugar by a spiroorthoester linkage. Such compounds known as orthosomycins[4] attracted much interest because of their particular structure and antibiotic properties. Later on, (+)-hydantocidin, also produced by microorganisms,[5] appeared to be a ribofuranosylidene-spirohydantoin,[6] with herbicidal activity. Much efforts were made to prepare isomers and analogs of (+)-hydantocidin,[7,8] in order to investigate their bioactivities. Other studies showed that a glucopyranosylidene-spirohydantoin and its thiohydantoin analog inhibited glycogen phosphorylase (GP),[9] the enzyme which releases D-glucose-1-phosphate from glycogen. As another class of anomeric spiro derivatives, D-glucopyranosylidene-spiro-oxathiazoles were shown to be weak inhibitors of β-D-glucosidase from sweet almond,[10] ($K_i$ 4.5–5.9 mM) and also of GP ($K_i$ 26–140 μM).[11] These findings confirmed that sugar-derived structures with a spiro moiety may often have interesting bioactivities. So, we decided to test the activity of D-galactopyranosylidene-spiro-oxathiazoles against β-D-galactosidase from *Escherichia coli*.

Our previous results[10] demonstrated that D-*gluco*-configurated sugar thiohydroximates undergo oxidative cyclization when illuminated in $CCl_4$ in the presence of *N*-bromosuccinimide (NBS) to afford the corresponding spiro-oxathiazoles (~60%), with, predominantly, a 1(*S*) configuration (*S*/*R* ratio: ~5:1). A D-*galacto*-configurated precursor subjected to these conditions underwent spirocyclization with comparable yield and stereoselectivity. For extending this approach to the D-*galacto* series, 2,3,4,6-tetra-*O*-acetyl-1-thio-β-D-galactopyranose[12] (**1**) was reacted with hydroximoyl chlorides, which were obtained from selected aldehydes by converting them into oximes followed by chlorination with NCS.[13] Addition of a mixture of **1** and $Et_3N$ to the hydroximoyl

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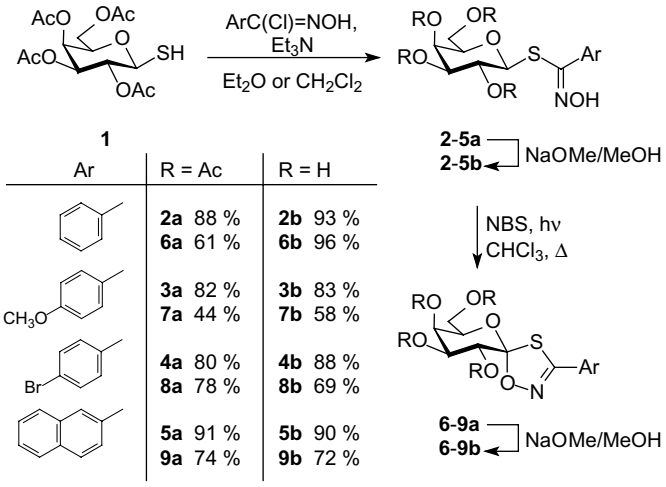


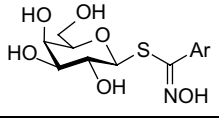
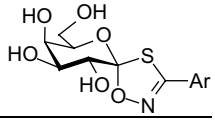
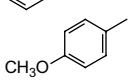
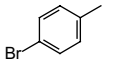
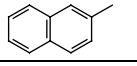

**Scheme 1.**

chlorides resulted in the addition of the thiosugar to the in situ formed nitrile oxides,[14] affording the β-D-*galacto*-configurated thiohydroximates **2**–**5a** in high yields (Scheme 1). Upon their treatment with NBS in 2-fold excess, in a $CHCl_3$ solution illuminated with an incandescent lamp, oxidative spirocyclization took place to produce the spiro-oxathiazoles **6**–**9a** in 44–78% yield, shown to be ~7:1 *S*/*R* mixtures by NMR. The 1(*S*) configuration of the major products was established by comparison of their optical rotations ($[\alpha]_D$ +83–87) with those previously measured (*S*-**6a**: $[\alpha]_D$ +83; *R*-**6a**: $[\alpha]_D$ +221).[10] While $CHCl_3$ has been shown to be advantageous for free-radical bromination,[15] as compared to $CCl_4$, investigations are still needed to better understand the spirocyclization mechanism and selectivity, questions that are being addressed during ongoing work.

The acetylated thiohydroximates and spiro-(*S*)-oxathiazoles were deacetylated under Zemplén conditions to give **2**–**5b** and **6**–**9b**, respectively.

Enzymatic measurements (Table 1) showed that the prepared compounds inhibited β-D-galactosidase from *E. coli* with $K_i$ in the millimolar range, except for the methoxy derivatives **3b** and **7b** showing no inhibition. Lineweaver–Burk plots showed they were competitive inhibitors. The D-*gluco* counterparts of **6b** and **8b**, and two other *p*-halogenated analogs, were shown to be weak inhibitors of β-D-glucosidase, with no inhibition found for a (*R*)-epimer.[10] The D-*gluco* counterpart of **6b**, and its *p*-fluoro analog, also inhibited rabbit muscle glycogene phosphorylase *b* with $K_i$ in the millimolar range.[11] Therefore, the hypothesis that glycosyl-spiro-oxathiazoles could be inhibitors of sugar-processing enzymes because of a modified environment near the anomeric center, as compared to *O*-glycosides, appeared well grounded.

**Table 1.** Inhibition constants ($K_i$ [mM]) obtained with *E. coli* β-D-galactosidase

| Ar |  | |  | |
|---|---|---|---|---|
|  | **2b** | 2.3 | **6b** | 5.6 |
|  | **3b** No inhibition | | **7b** No inhibition | |
|  | **4b** | 1.1 | **8b** Insoluble | |
|  | **5b** | 11.1 | **9b** | 4.4 |

## 1. Experimental

### 1.1. General methods

Melting points were measured in open capillary tubes or on a Kofler hot-stage and are uncorrected. Optical rotations were determined on a Perkin–Elmer 241 polarimeter at room temperature. IR spectra were measured with a Perkin–Elmer 16 PC FT-IR spectrometer. NMR spectra were recorded with Bruker WP 360 SY (360/90 MHz for $^1H/^{13}C$) and Varian UNITYINOVA 400 WB (400/100 MHz for $^1H/^{13}C$) spectrometers. Chemical shifts are referenced to $Me_4Si$ as the internal reference ($^1H$) or the residual solvent signal ($^{13}C$). TLC was performed on DC Alurolle Kieselgel 60 $F_{254}$ (E. Merck), the plates were visualized by gentle heating. For column chromatography, Kieselgel 60 (E. Merck, particle size 0.063–0.200 mm) was used. Distilled solvents ($CH_2Cl_2$, $CHCl_3$, 1,4-dioxane, $Me_2SO$) were dried by storage over 4 Å molecular sieves. Organic solns were dried over anhyd $MgSO_4$ and concentrated under diminished pressure at 40–50 °C (water bath).

Per-*O*-acetylated 1-thio-β-D-galactopyranose[12] and the arylhydroximoyl chlorides,[13] were prepared following published methods.

### 1.2. General method I for the preparation of 2,3,4,6-tetra-*O*-acetyl-1-*S*-(*Z*)-arylhydroximoyl-1-thio-β-D-galactopyranoses 2–5a (adapted from Ref. 14)

Per-*O*-acetylated 1-thio-β-D-galactopyranose (**1**, 0.363 g, 1 mmol) dissolved in $CH_2Cl_2$ (5 mL) and $Et_3N$ (0.42 mL, 3 mmol) were added under an Ar atmosphere with continuous stirring to a soln of a hydroximoyl chloride (1.2 mmol) in $Et_2O$ or $CH_2Cl_2$ (5 mL). After immediate precipitation of $Et_3N{\cdot}HCl$, the mixture was stirred further at rt. When TLC (see eluent with the individual compounds) indicated completion of the transformation, 0.5 M $H_2SO_4$ (20 mL) was added, and the organic phase was separated, washed by water (2 × 20 mL), and dried. After removal of the solvent under diminished pressure, the residue was purified by crystallization or column chromatography. For NMR data see Tables 2 and 3.

### 1.3. General method II for the preparation of 'acetylated oxathiazoles' 6–9a (adapted from Ref. 10)

*N*-Bromosuccinimide (2 equiv) was added to a soln of a thiohydroximate (**2–5a**) in $CHCl_3$ (20 mL/mmol). The mixture was boiled and illuminated by a 250 W heat lamp. After disappearance of the starting material (TLC, 1:1 EtOAc–hexane) the soln was washed with 5% aq $Na_2SO_3$ (2 × 10 mL), satd aq $NaHCO_3$

**Table 2.** $^1$H NMR data for per-*O*-acetylated compounds **2a–9a** (for $CDCl_3$ solutions, 360 MHz, $\delta$ [ppm], $J$ [Hz])

| Compound | H-1 ($J_{1,2}$) | H-2 ($J_{2,3}$) | H-3 ($J_{3,4}$) | H-4 ($J_{4,5}$) | H-5 ($J_{5,6}$) | H-6 ($J_{6,6'}$) | H-6′ ($J_{5,6'}$) | OAc | Aromatics ($J$) | N–O*H* | $OCH_3$ |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **2a** | 4.43, d (10.2) | 5.27, t (10) | 4.84, dd (3.4) | 5.26, m (1.2) | 3.34, dt (6.5) | 4.01–3.99 (m) | | 2.13, 2.06, 2.05, 2.04 | 7.55–7.43 (m) | 8.80 | — |
| **3a** | 4.45, d (10.1) | 5.25, t (9.8) | 4.83, dd (3.4) | 5.26, m (<1) | 3.43, t (6.4) | 4.05, dd (11.3) | 4.01, dd (4.5) | 2.14, 2.06, 2.05, 1.95 | 7.45 (d, 8.8) 6.92 (d, 8.8) | 9.40 | 3.84 |
| **4a** | 4.51, d (10.1) | 5.27, t (9.8) | 4.89, dd (3.4) | 5.31, m (1.1) | 3.49, dt (6.4) | 4.04, dd (8.3) | 4.01, dd (5.3) | 2.14, 2.07, 2.06, 1.96 | 7.58 (d, 8.7) 7.47 (d, 8.7) | 8.39 | — |
| **5a** | 4.55, d (10.3) | 5.29, t (9.6) | 4.79, dd (3.7) | 5.22, d (<1) | 3.32, t (6.6) | 4.05–3.95 (m) | | 2.07 (2×), 2.00, 1.93 | 8.10–7.52 (m) | 9.84 | — |
| **6a**[*] | — | 5.86, d (11.0) | 5.51, dd (2.9) | 5.58, br d (1.5) | 4.66, dt (5.9) | 4.19, dd (11.0) | 4.08, dd (6.6) | 2.19, 2.09, 2.01 (2×) | 7.70–7.43 (m) | — | — |
| **7a**[*] | — | 5.84, d (11.0) | 5.49, dd (2.9) | 5.59, br d (<1) | 4.64, br t (7.4) | 4.18, dd (11.0) | 4.08, dd (5.9) | 2.19, 2.09, 2.02, 2.01 | 7.61 (d, 8.8) 6.94 (d, 8.8) | | 3.85 |
| **8a**[*] | — | 5.84, d (11.2) | 5.49, dd (3.3) | 5.57, br d (1) | 4.64, dt (6.6) | 4.18, dd (11.2) | 4.08, dd (6.6) | 2.19, 2.09, 2.02, 2.01 | 7.58 (d, 8.8) 7.54 (d, 8.8) | — | — |
| **9a**[*] | — | 5.90, d (10.3) | 5.54, dd (2.9) | 5.61, br s (<1) | 4.69, t (6.6) | 4.20, dd (11.0) | 4.09, dd (5.9) | 2.21, 2.10, 2.03, 2.01 | 8.10–7.50 (m) | — | — |

[*] Parent carbohydrate numbering.

**Table 3.** $^{13}$C NMR data for per-*O*-acetylated compounds **2a–9a** (for $CDCl_3$ solutions, 90 MHz, $\delta$ [ppm])

| Compound | C-1 | C-2 to C-5 | C-6 | C=N | CO | $CH_3$ | Aromatics | $OCH_3$ |
|---|---|---|---|---|---|---|---|---|
| **2a** | 81.9 | 74.3, 71.7, 71.5, 67.0 | 61.2 | 152.7 | 170.3, 170.2, 170.0, 169.4 | 20.7, 20.6, 20.5, 20.4 | 132.3, 130.1, 128.8 (2C), 128.3 (2C) | — |
| **3a** | 82.0 | 74.3, 71.7, 67.1, 67.0 | 61.2 | 152.3 | 170.3, 170.2, 170.0, 169.4 | 20.7, 20.6, 20.5, 20.4 | 160.8, 130.3 (2C), 124.6, 113.8 (2C) | 55.3 |
| **4a** | 82.0 | 74.5, 71.6, 67.2, 67.0 | 61.4 | 151.2 | 170.3, 170.2, 170.0, 169.4 | 20.7, 20.6, 20.5, 20.4 | 131.7 (2C), 130.4 (2C), 124.6 | — |
| **5a** | 82.1 | 74.3, 71.6, 67.2, 66.9 | 61.1 | 151.9 | 170.3, 170.2, 170.0, 169.4 | 20.7, 20.6, 20.5, 20.4 | 133.7, 132.7, 130.0 (3C), 128.9, 128.3, 128.0, 127.7, 127.3, 126.7, 125.6 (7CH) | — |
| **6a**[*] | 123.0 | 69.9, 68.8, 67.3, 65.5 | 60.7 | 156.1 | 170.2, 170.0, 169.6, 169.5 | 20.6, 20.5 (2C), 20.4 | 131.5, 128.9 (2C), 127.8 (2C), 127.0 | — |
| **7a**[*] | 122.9 | 69.8, 69.0, 67.4, 65.5 | 60.8 | 155.7 | 170.3, 170.1, 169.8, 169.6 | 20.7, 20.6 (2C), 20.5 | 162.2, 129.6 (2C), 119.6, 114.0 (2C) | 55.5 |
| **8a**[*] | 123.5 | 70.0, 68.8, 67.3, 65.5 | 60.8 | 155.2 | 170.2, 170.0, 169.7, 169.6 | 20.7, 20.6 (2C), 20.5 | 132.2 (2C), 129.2 (2C), 126.1 | — |
| **9a**[*] | 123.0 | 70.0, 68.9, 67.4, 65.6 | 60.9 | 156.3 | 170.2, 170.0, 169.7, 169.6 | 20.7, 20.6 (2C), 20.5 | 134.5, 132.6, 124.6 (3C), 129.7, 129.6, 128.9, 127.9, 127.4, 127.2, 126.9 (7C) | — |

[*] Parent carbohydrate numbering.

(2 × 10 mL), and water (15 mL), then dried. After removal of the solvent, the residue was crystallized or purified by column chromatography. For NMR data see Tables 2 and 3.

### 1.4. General method III for deacetylations

The acetylated compound (**2**–**9a**, 2.7 mmol) was dissolved in dry MeOH (6.5 mL), to which a few drops of a 1 M methanolic NaOMe soln were added. When TLC (7:3 or 1:1 $CHCl_3$–MeOH) indicated completion of the deprotection, sodium ions were removed by Amberlyst 15 ($H^+$ form). After filtration and solvent removal, the residue was used for enzymatic tests. For NMR data see Tables 4 and 5.

### 1.5. 2,3,4,6-Tetra-*O*-acetyl-1-*S*-(*Z*)-benzhydroximoyl-1-thio-β-D-galactopyranose (2a)[16]

According to General method I from **1** (300 mg, 0.82 mmol), reaction time 2.5 h. Yield: 350 mg (88%), colorless syrup ($R_f$ 0.70, 5:2 EtOAc–hexane); $[\alpha]_D$ +29 (*c* 1, $CHCl_3$); lit.:[16] $[\alpha]_D$ +38 (*c* 1, $CHCl_3$). Anal. Calcd for $C_{21}H_{25}NO_{10}S$ (483.49): C, 52.16; H, 5.22; N, 2.90; O, 33.11; S, 6.62. Found: C, 52.31; H, 5.18; N, 2.80; O, 33.26; S, 6.65.

### 1.6. 1-*S*-(*Z*)-Benzhydroximoyl-1-thio-β-D-galactopyranose (2b)

According to General method III from **2a** (152 mg, 0.31 mmol), reaction time 2.5 h. Yield:

**Table 4.** $^1$H NMR data for compounds **2b**–**9b** (for $D_2O$ solutions,[a] 360 MHz, $\delta$ [ppm], *J* [Hz])

| Compound | H-1 ($J_{1,2}$) | H-2 ($J_{2,3}$) | H-3 ($J_{3,4}$) | H-4 ($J_{4,5}$) | H-5 ($J_{5,6}$) | H-6, H-6′ | Aromatics (*J*) | $OCH_3$ |
|---|---|---|---|---|---|---|---|---|
| **2b** | 4.20, d (9.6) | 3.64, t (9.6) | 3.36, dd (3.9) | 3.79, br s (<1) | 2.98, t (5.9) | 3.58–3.50, m | 7.60–7.45 (m) | — |
| **3b** | 4.25, d (10.0) | 3.69, t (9.5) | 3.42, dd (3.2) | 3.86, d (<1) | 3.08, t (5.8) | 3.63–3.59, m | 7.50 (d, 8.8) 7.12 (d, 8.8) | 3.91 |
| **4b** | 4.20 (10.0) | 3.66 (9.5) | 3.39 (3.2) | 3.81 (<1) | 3.03 (5.8) | 3.60–3.56, m | 7.68 (d, 8.7) 7.43 (d, 8.7) | — |
| **5b** | 4.13, d (9.6) | 3.67–3.57 (m) | | | 3.12, d — | 3.52–3.38, m | 8.07–7.18 (m) | — |
| **6b**[*] | — | 4.10 (10.6) | 3.90–3.62 (m) | | | 3.60–3.52, m | 7.88–7.32 (m) | — |
| **7b**[*] | — | 4.31, d (10.3) | 3.99, dd (2.9) | 4.10, d (<1) | 4.25, t (5.9) | 3.76–3.70, m | 7.70 (d, 8.8) 7.11 (d, 8.8) | 3.90 |
| **8b**[*] in $Me_2SO$-$d_6$ | — | 4.08, d (8.1) | 3.67, d (<1) | 3.82, s (<1) | 3.95, br s — | 3.58–3.38, m | 7.72 (d, 7.2) 7.59 (d, 7.2) | — |
| **9b**[*] in $Me_2SO$-$d_6$ + $D_2O$ | — | 4.43, d (10.3) | 4.08, m (~2) | 4.18, s (<1) | 4.33, br s — | 3.90–3.76, m | 8.36–7.74 (m) | — |

[*] Parent carbohydrate numbering.
[a] Unless otherwise indicated.

**Table 5.** $^{13}$C NMR data for compounds **2b**–**9b** (for $D_2O$ solutions,[a] 90 MHz, $\delta$ [ppm])

| Compound | C-1 | C-2 to C-5 | C-6 | C=N | Aromatics | $OCH_3$ |
|---|---|---|---|---|---|---|
| **2b** | 84.5 | 79.8, 74.6, 70.0, 69.2 | 61.3 | 157.1 | 132.4, 131.3, 129.7 (2C), 129.5 (2C) | — |
| **3b** in MeOH-$d_4$ | 84.0 | 79.2, 74.1, 69.4, 68.6 | 60.6 | 156.2 | 160.6, 130.8 (2C), 124.5, 114.2 (2C) | 55.6 |
| **4b** | 83.7 | 79.2, 73.9, 69.3, 68.6 | 60.6 | 155.1 | 131.9 (2C), 130.8 (2C), 129.6, 124.2 | — |
| **5b** | 84.2 | 79.4, 74.2, 69.7, 68.8 | 61.0 | 156.6 | 134.0, 132.9, 129.8 (3C), 129.7, 129.3, 129.2, 128.7, 128.2, 127.9, 126.4 (7CH) | — |
| **6b**[*] in $Me_2SO$-$d_6$ | 122.7 | 75.2, 70.9, 68.4, 67.8 | 60.1 | 154.4 | 132.1, 129.2 (2C), 127.7 (2C), 127.1 | — |
| **7b**[*] in $Me_2SO$-$d_6$ | 120.6 | 72.2 (2×), 70.2, 70.1 | 62.0 | 158.8 | 163.3, 131.1 (2C), 127.1, 116.2 (2C) | 57.0 |
| **8b**[*] in $Me_2SO$-$d_6$ | 124.6 | 75.4, 70.8, 68.4, 67.9 | 60.1 | 153.6 | 132.2 (2C), 129.1 (2C) 128.0, 126.7 | — |
| **9b**[*] in $Me_2SO$-$d_6$ | 125.6 | 75.9, 71.7, 69.4, 68.7 | 61.2 | 156.6 | 134.9, 133.3, 127.9 (3C), 129.9, 129.5, 129.2, 128.6, 128.4, 128.1, 123.9 (7CH) | — |

[*] Parent carbohydrate numbering.
[a] Unless otherwise indicated.

92 mg (93%), white crystals from water, mp 188–189 °C ($R_f$ 0.60, 7:3 $CHCl_3$–MeOH); $[\alpha]_D$ +10 (*c* 1, $Me_2SO$). Anal. Calcd for $C_{13}H_{17}NO_6S$ (315.34): C, 49.52; H, 5.43; N, 4.44; O, 30.44; S, 10.17. Found: C, 49.61; H, 5.31; N, 4.58; O, 30.25; S, 10.25.

### 1.7. 2,3,4,6-Tetra-*O*-acetyl-1-*S*-(*Z*)-4-methoxybenzhydroximoyl-1-thio-β-D-galactopyranose (3a)

According to General method I from **1** (2.51 g, 6.90 mmol), reaction time 1 h. Yield: 2.88 g (82%), foam ($R_f$ 0.17, 1:1 EtOAc–hexane); $[\alpha]_D$ +29 (*c* 1, $CHCl_3$). Anal. Calcd for $C_{22}H_{27}NO_{11}S$ (513.52): C, 51.46; H, 5.30; N, 2.73; O, 34.27; S, 6.24. Found C 51.51; H, 5.21; N, 2.57; O, 34.41; S, 6.30.

### 1.8. 1-*S*-(*Z*)-4-Methoxybenzhydroximoyl-1-thio-β-D-galactopyranose (3b)

According to General method III from **3a** (1.00 g, 1.95 mmol), reaction time 1 day. Yield: 561 mg (83%), brownish crystals from water, mp 99–101 °C ($R_f$ 0.47, 7:3 $CHCl_3$–MeOH); $[\alpha]_D$ +11 (*c* 1, $Me_2SO$). Anal. Calcd for $C_{14}H_{19}NO_7S$ (345.37): C, 48.69; H, 5.55; N, 4.06; O, 32.43; S, 9.28. Found: C, 48.73; H, 5.61; N, 4.12; O, 32.51; S, 9.18.

### 1.9. 2,3,4,6-Tetra-*O*-acetyl-1-*S*-(*Z*)-4-bromobenzhydroximoyl-1-thio-β-D-galactopyranose (4a)

According to General method I from **1** (3.63 g, 10.0 mmol), reaction time 1.5 h. Yield: 4.5 g (80%), foam ($R_f$ 0.30, 1:2 EtOAc–hexane); $[\alpha]_D$ +30 (*c* 1, $CHCl_3$). Anal. Calcd for $C_{21}H_{24}BrNO_{10}S$ (562.39): C, 44.85; H, 4.30, Br 14.21; N, 2.49; O, 28.45; S, 5.70. Found: C, 45.34; H, 4.67, Br 14.28; N, 2.02; O, 29.41; S, 5.72.

### 1.10. 1-*S*-(*Z*)-4-Bromobenzhydroximoyl-1-thio-β-D-galactopyranose (4b)

According to General method III from **4a** (1.00 g, 1.80 mmol), reaction time 2 days. Yield: 624 mg (88%), white crystals from water, mp 151–153 °C ($R_f$ 0.44, 7:3 $CHCl_3$–MeOH); $[\alpha]_D$ +20 (*c* 1, $Me_2SO$). Anal. Calcd for $C_{13}H_{16}BrNO_6S$ (394.24): C, 39.61; H, 4.09, Br 20.27; N, 3.55; O, 24.35; S, 8.13. Found: C, 37.90; H, 4.25, Br 20.88; N, 3.57; O, 25.21; S, 8.25.

### 1.11. 2,3,4,6-Tetra-*O*-acetyl-1-*S*-(*Z*)-(2-naphthhydroximoyl)-1-thio-β-D-galactopyranose (5a)

According to General method I from **1** (1.00 g, 2.75 mmol), reaction time 1 h. Yield: 1.34 g (91%), white crystals from EtOH–hexane, mp 93–95 °C ($R_f$ 0.28, 1:2 EtOAc–hexane 2×); $[\alpha]_D$ +33 (*c* 0.5, $CHCl_3$). Anal. Calcd for $C_{25}H_{27}NO_{10}S$ (533.55): C, 56.28; H, 5.10; N, 2.63; O, 29.99; S, 6.01. Found: C, 56.35; H, 5.16; N, 2.30; O, 30.14; S, 6.05.

### 1.12. 1-*S*-(*Z*)-(2-Naphthhydroximoyl)-1-thio-β-D-galactopyranose (5b)

According to General method III from **5a** (560 mg, 1.05 mmol), reaction time 3 days. Yield: 347 mg (90%), white crystals from water, mp 121–123 °C ($R_f$ 0.63, 7:3 $CHCl_3$–MeOH); $[\alpha]_D$ +23 (*c* 1, $Me_2SO$). Anal. Calcd for $C_{17}H_{19}NO_6S$ (365.40): C, 55.88; H, 5.24; N, 3.83; O, 26.27; S, 8.77. Found: C, 56.05; H, 5.26; N, 3.82; O, 26.21; S, 8.69.

### 1.13. (1*S*)-2,3,4,6-Tetra-*O*-acetyl-1,5-anhydro-D-galactitol-spiro[1.5]-3-phenyl-1,4,2-oxathiazole (6a)

According to General method II from **2a** (767 mg, 1.59 mmol), reaction time 60 min. Yield: 61%, syrup ($R_f$ 0.56, 1:1 EtOAc–hexane); other data identical to lit.[10] except for the erroneously reported $\delta$ H-1 value (5.58 ppm) to be changed to 5.86 ppm.

### 1.14. (1*S*)-1,5-Anhydro-D-galactitol-spiro[1.5]-3-phenyl-1,4,2-oxathiazole (6b)

According to General method III from **6a** (300 mg, 0.62 mmol), reaction time 15 min. Yield: 186 mg (96%), brownish crystals from water, mp 115–117 °C ($R_f$ 0.63, 1:1 $CHCl_3$–MeOH); $[\alpha]_D$ −2.7 (*c* 0.19 MeOH). Anal. Calcd for $C_{13}H_{15}NO_6S$ (313.33): C, 49.83; H, 4.83; N, 4.47; O, 30.64; S, 10.23. Found: C, 50.01; H, 4.85; N, 4.44; O, 30.50; S, 10.20.

### 1.15. (1*S*)-2,3,4,6-Tetra-*O*-acetyl-1,5-anhydro-D-galactitol-spiro[1.5]-3-*para*-methoxyphenyl-1,4,2-oxathiazole (7a)

According to General method II from **3a** (800 mg, 1.56 mmol), reaction time 80 min. Yield: 352 mg (44%), foam ($R_f$ 0.47, 1:1 EtOAc–hexane); $[\alpha]_D$ +84 (*c* 1, $CHCl_3$). Anal. Calcd for $C_{22}H_{25}NO_{11}S$ (511.50): C, 51.65; H, 4.93; N, 2.74; O, 34.42; S, 6.26. Found: C, 51.61; H, 5.01; N, 2.67; O, 34.41; S, 6.30.

### 1.16. (1*S*)-1,5-Anhydro-D-galactitol-spiro[1.5]-3-*para*-methoxyphenyl-1,4,2-oxathiazole (7b)

According to General method III from **7a** (152 mg, 0.3 mmol), reaction time 20 min. Yield: 60 mg (58%), brownish crystals from water, mp 188–190 °C ($R_f$ 0.63, 7:3 $CHCl_3$–MeOH); $[\alpha]_D$ +98 (*c* 0.25, $Me_2SO$). Anal. Calcd for $C_{14}H_{17}NO_7S$ (343.35): C, 48.97; H, 4.99; N,

4.08; O, 32.62; S, 9.34. Found: C, 49.05; H, 5.01; N, 4.11; O, 32.75; S, 9.30.

### 1.17. (1*S*)-2,3,4,6-Tetra-*O*-acetyl-1,5-anhydro-D-galactitol-spiro[1.5]-3-*para*-bromophenyl-1,4,2-oxathiazole (8a)

According to General method II from **4a** (1.50 g, 2.67 mmol), reaction time 30 min. Yield: 1.17 g (78%), foam ($R_f$ 0.53, 1:1 EtOAc–hexane); $[\alpha]_D$ +85 (*c* 1, $CHCl_3$). Anal. Calcd for $C_{21}H_{22}BrNO_{10}S$ (560.37): C, 45.01; H, 3.96, Br 14.26; N, 2.50; O, 28.55; S, 5.72. Found: C, 45.98; H, 4.14, Br 14.62; N, 2.13; O, 29.11; S, 5.76.

### 1.18. (1*S*)-1,5-Anhydro-D-galactitol-spiro[1.5]-3-*para*-bromo-phenyl-1,4,2-oxathiazole (8b)

According to General method III from **8a** (350 mg, 0.62 mmol), reaction time 30 min. Yield: 167 mg (69%), white crystals from water, mp 180–182 °C ($R_f$ 0.47, 7:3 $CHCl_3$–MeOH); $[\alpha]_D$ +92 (*c* 0.1, $Me_2SO$). Anal. Calcd for $C_{13}H_{14}BrNO_6S$ (392.22): C, 39.81; H, 3.60, Br 20.37; N, 3.57; O, 24.47; S, 8.18. Found: C, 38.01; H, 3.85, Br 20.98; N, 3.65; O, 25.36; S, 8.76.

### 1.19. (1*S*)-2,3,4,6-Tetra-*O*-acetyl-1,5-anhydro-D-galactitol-spiro[1.5]-3-(2-naphthyl)-1,4,2-oxathiazole (9a)

According to General method II from **5a** (700 mg, 1.30 mmol), reaction time 15 min. Yield: 515 mg (74%), foam ($R_f$ 0.68, 1:1 EtOAc–hexane); $[\alpha]_D$ +87 (*c* 1, $CHCl_3$). Anal. Calcd for $C_{25}H_{25}NO_{10}S$ (531.53): C, 56.49; H, 4.74; N, 2.64; O, 30.10; S, 6.03. Found: C, 56.45; H, 4.81; N, 2.59; O, 30.16; S, 5.99.

### 1.20. (1*S*)-1,5-Anhydro-D-galactitol-spiro[1.5]-3-(2-naphthyl)-1,4,2-oxathiazole (9b)

According to General method III from **9a** (530 mg, 1.0 mmol), reaction time 25 min. Yield: 262 mg (72%), white crystals from water, mp 176–178 °C ($R_f$ 0.71, 7:3 $CHCl_3$–MeOH); $[\alpha]_D$ +57 (*c* 0.5, $Me_2SO$). Anal. Calcd for $C_{17}H_{17}NO_6S$ (363.39): C, 56.19; H, 4.72; N, 3.85; O, 26.42; S, 8.82. Found: C, 56.25; H, 4.81; N, 3.75; O, 26.50; S, 8.78.

Enzymatic tests were carried out as described earlier.[17]

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