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Note

Simple synthesis of 6-thio glycopyranoses. Synthesis of 1,2,3-tri-*O*-acetyl-6-*S*-acetyl-4-*O*-benzoyl-6-thio-α-D-galactopyranose

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In connection with other work underway in our laboratory, we needed a 6-thio-D-galactopyranose derivative. A literature search produced only two references describing the syntheses of 6-thio-D-galactose derivatives [1,2]. Unfortunately, neither one was suitable for our purpose. One paper described the synthesis of a 6-thio-D-galactoseptanose derivative in a rather long reaction sequence and with an undetermined yield [1], whereas the other [2] described the synthesis of a peracetylated 6-thio-D-galactopyranose derivative with an unacceptably low yield.

1. Results and discussion

The starting material for our synthesis was 1,2,3-tri-*O*-acetyl-4,6-*O*-benzylidene-α-D-galactopyranose (**1**) which was obtained as previously described [3,4].

Reaction of **1** with *N*-bromosuccinimide in anhydrous carbon tetrachloride, at reflux [5], gave a quantitative yield of 1,2,3-tri-*O*-acetyl-4-*O*-benzoyl-6-bromo-6-deoxy-α-D-galactopyranose (**2**). Nucleophilic displacement of the C-6 bromine of **2** with potassium

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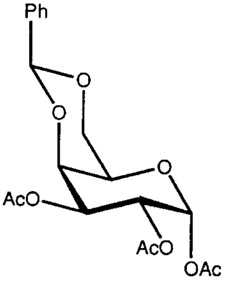
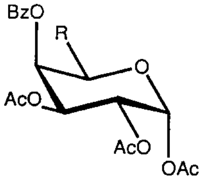
thioacetate at room temperature in anhydrous dimethyl sulfoxide afforded 1,2,3-tri-*O*-acetyl-6-*S*-acetyl-4-*O*-benzoyl-6-thio-α-D-galactopyranose (**3**) in 72% yield.



1



2, R = Br
3, R = SAc

2. Experimental

General methods.—All chromatography was performed on Silica Gel 60 for flash chromatography (Fluka Chemie, AG, Buchs, Switzerland). Melting points were determined with a Büchi apparatus and are uncorrected. The NMR spectra were recorded in chloroform-*d* solution using a Bruker AMX-2-500 NMR spectrometer operating in quadrature mode at 298 K. Tetramethylsilane was used as the internal standard. Chemical shifts (δ) are expressed in ppm.

1,2,3-Tri-O-acetyl-4-O-benzoyl-6-bromo-6-deoxy-α-D-galactopyranose (**2**).—To a solution of peracetylated 4,6-*O*-benzylidene-α-D-galactopyranose derivative **1** (5.0 g; 12.68 mmol) in anhydrous CCl_4 (100 mL) were added $BaCO_3$ (5.0 g) and *N*-bromosuccinimide (2.50 g, 14.04 mmol). The mixture was refluxed for 90 min and then cooled to room temperature. The solids were removed by filtration through a Buchner funnel and the precipitate was washed with a small amount of $CHCl_3$. The combined filtrate was evaporated on a rotary evaporator to dryness and the residue was dried in high vacuum. A colourless glassy product was obtained (6.0 g, 100%) that was chromatographically pure, $[\alpha]_D$ +149.5° (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 8.1–7.2 (m, 5 H, aromatic protons), 6.467 (d, 1 H, $J_{1,2}$ 3.53, $J_{1,5}$ 0.3 Hz, H-1), 5.950 (dd, 1 H, $J_{3,4}$ 3.15, $J_{4,5}$ 1.17 Hz, H-4), 5.462 (dd, 1 H, $J_{2,3}$ 10.92, $J_{3,4}$ 3.15 Hz, H-3), 5.402 (dd, 1 H, H-2), 4.417 (dd, 1 H, $J_{5,6a} = J_{5,6b} = 7.00$ Hz, H-5), 3.39 (dd, 1 H, $J_{6a,6b}$ 10.4 Hz, H-6), 3.34 (dd, 1 H, H-6), 2.19 (s, 3 H, C-1 acetate), 2.02 and 1.98 (2 s, 6 H, C-2 and C-3 acetates). Anal. Calcd for $C_{19}H_{21}BrO_9$ (473.28): C, 48.22; H, 4.47; Br, 16.88. Found: C, 47.98; H, 4.65; Br, 18.32.

1,2,3-Tri-O-acetyl-6-S-acetyl-4-O-benzoyl-6-thio-α-D-galactopyranose (**3**).—To a solution of the 6-deoxy-6-bromo-D-galactopyranose derivative **2** (1.00 g; 2.11 mmol) in anhydrous Me_2SO, KSAc (1.00 g, 8.76 mmol) was added and the mixture was stirred at room temperature for 21 h. Brine (150 mL) was then added and the mixture was extracted with two 150-mL portions of $CHCl_3$. Each extract was washed with brine and the combined extract was dried ($CaCl_2$) and evaporated. The residue was purified by chromatography on silica gel using 3:1 (v/v) hexane–EtOAc and 98:2 $CHCl_3$–2-propanol as eluants. Pure **3** was obtained as a colourless glassy product (0.72 g, 72%). $[\alpha]_D$ + 141.4° (*c* 1.0, $CHCl_3$); ^1H NMR: δ 8.10–7.25 (m, 5 H, aromatic protons), 6.45 (d, 1 H, $J_{1,2}$ 3.11, $J_{1,5}$ 0.39 Hz, H-1), 5.782 (dd, 1 H, $J_{3,4}$ 2.8, $J_{4,5}$ 1.25 Hz, H-4), 5.407 (m, 1 H, $J_{2,3}$ 6–7, $J_{3,4}$ 2.8 Hz, H-3), 5.399 (dd, 1 H, H-2), 4.257 (dd, $J_{5,6a} = J_{5,6b}$ = 7.0 Hz, H-5), 3.056 (d, 2 H, H-6), 2.312 (s, 3 H, thioacetate), 2.168, 2.007, and 1.964 (3 s, 9 H, C-1, C-2, and C-3 acetates). Anal. Calcd for $C_{21}H_{24}O_{10}S$ (468.47): C, 53.84; H, 5.16; S, 6.84. Found: C, 53.73; H, 5.28; S, 6.93.

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