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# MERCAPTAN ADDITION TO 1-*O*-ALLYL-2,3,4,6-TETRA-*O*-ACETYL-*β*-D-GALACTOPYRANOSE

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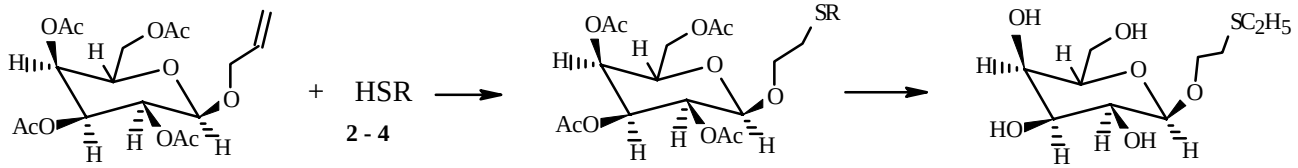
*Addition of ethyl-, propyl-, and* n-*butylmercaptans to 1-*O*-allyl-2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranose in the presence of benzoyl peroxide catalyst was studied for the first time. The products were 1-*O*-(3-ethylthiopropyl)-2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranose, 1-*O*-(3-propylthiopropyl)-2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranose, and 1-*O*-(3-butylthiopropyl)-2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranose. Deacetylation of 1-*O*-(3-ethylthiopropyl)-2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranose produced 1-*O*-(3-ethylthiopropyl)-β-D-galactopyranose.*

**Key words:** mercaptan addition, allylgalactopyranoside, mercaptans, *S*-containing glycosides, benzoyl peroxide, deacetylation.

Organosulfur compounds play an important role in the life processes of living organisms. This type of compounds is widely used in medicine, agriculture, and other industries [1, 2].

Herein we propose a convenient method for synthesizing new types of S-containing glycosides.

Reaction of 1-*O*-allyl-2,3,4,6-tetra-*O*-acetyl-*β*-D-galactopyranose (**1**) with ethyl-, propyl-, and *n*-butylmercaptans (**2**-**4**) in the presence of benzoyl peroxide catalyst under $N_2$ at 70-75°C synthesized 1-*O*-(3-ethylthiopropyl)-2,3,4,6-tetra-*O*-acetyl-*β*-D-galactopyranose (**5**), 1-*O*-(3-propylthiopropyl)-2,3,4,6-tetra-*O*-acetyl-*β*-D-galactopyranose (**6**), and 1-*O*-(3-butylthiopropyl)-2,3,4,6-tetra-*O*-acetyl-*β*-D-galactopyranose (**7**), respectively.




**2, 5:** R = $C_2H_5$; **3, 6:** R = $C_3H_7$; **4, 7:** R = $C_4H_9$

The course of the reaction was monitored by TLC. The products were crystalline yellow compounds that were very soluble in $CHCl_3$, tetrachloroethane, and ethanol. The yields decreased as the chain grew, possibly due to steric factors.

These mercaptan additions followed mainly the Farmer rule, although a small amount (6-9%) of the Markovnikov addition product **9** was also produced. This was confirmed by GC performed using three carrier-gas flow rates (20, 40, and 60 mL/min). The HETP (height equivalent to a theoretical plate) and separation factor (Kd) showed that the optimal carrier-gas flow rate was 40 mL/min.

Mercaptan addition produced a mixture of products 1-*O*-(3-ethylthiopropyl)-2,3,4,6-tetra-*O*-acetyl-*β*-D-galactopyranose and 1-*O*-(2-ethylthiopropyl)-2,3,4,6-tetra-*O*-acetyl-*β*-D-galactopyranose in a 11:1 ratio. The chromatographically pure main product (**5**) was obtained after separation over a column ($C_6H_6$:$CHCl_3$, 2:1, silica gel L 50/100).

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TABLE 1. Effect of S-Containing Glycosides **5-7** on Growth of Certain Microorganisms

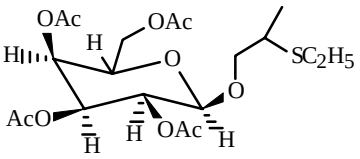
| Microorganism | Control | Compound | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | **5** | | | **6** | | | **7** | | |
| | | concentration, % (g/L) | | | | | | | | |
| | | 0.001 | 0.01 | 0.1 | 0.001 | 0.01 | 0.1 | 0.001 | 0.01 | 0.1 |
| | | inhibition area of microorganisms, mm | | | | | | | | |
| *Actinomyces griceus* | 0.1 | 2.0 | 3.5 | 12.5 | 1.5 | 2.0 | 12.0 | 1.5 | 2.5 | 11.0 |
| *Actinomyces streptomycine* | 0.2 | 0.5 | 5.0 | 8.0 | 1.5 | 3.0 | 7.5 | 2.5 | 4.0 | 5.0 |
| *Xantomonas campestris* | 0.1 | 1.5 | 1.0 | 2.0 | 2.0 | 0.5 | 1.0 | 0 | 0.5 | 0.5 |

Deacetylation of **5** in the presence of sodium methoxide in absolute methanol produced 1-*O*-(3-ethylthiopropyl)-*β*-D-galactopyranose (**8**).

The theoretical basis for the ratio of final products from mercaptan addition to allylgalactoside was developed using quantum-chemical calculations carried out using CS MOPAC (Chem 3D Ultra-version 8.03). The compound was optimized by minimizing the energy using both molecular mechanics (MM) and quantum-chemical methods before each calculation using AM1 (Austin Model 1) [3].

Addition of ethylmercaptan (**2**) to 1-*O*-allyl-2,3,4,6-tetra-*O*-acetyl-*β*-D-galactopyranose (**1**) was selected as the model reaction and was examined in two directions, Farmer and Markovnikov additions.

Farmer addition produced 1-*O*-(3-ethylthiopropyl)-2,3,4,6-tetra-*O*-acetyl-*β*-D-galactopyranose (**5**); Markovnikov addition, 1-*O*-(2-ethylthiopropyl)-2,3,4,6-tetra-*O*-acetyl-*β*-D-galactopyranose (**9**).




**9**

The calculated heats of formation of the products showed a high probability for formation of **5** with $\Delta H_f$ = -450.12 kcal/mol and $\Delta H_r$ = -20.82 kcal/mol (for **9**, $\Delta H_f$ = -416.09 kcal/mol, $\Delta H_r$ = -4.23 kcal/mol).

The structures of the compounds were confirmed by elemental analyses and $^{13}C$ NMR and PMR spectroscopy.

The $^{13}C$ NMR spectra of **5-7** produced by mercaptan addition to allylgalactopyranoside showed that signals corresponding to *β*- and *γ*-C atoms of the allyl double bond (–CH=$CH_2$) disappeared at 133.2 and 117.5 ppm and that two new signals at 22.7-27.4 (*β*-C) and 16.6-21.08 (*γ*-C) corresponding to the C atoms of the methylene group appeared. There were also new corresponding peaks. All other signals of the galactoside moiety underwent only insignificant shifts.

We tested the bactericidal activity of S-containing **5-7** synthesized by us.

The bactericidal activity of the compounds was determined using wells. The test microorganisms were bacteria and actinomycetes *Xantomonas campestris*, *Actinomyces griceus*, and *A. streptomycine*. The control was the solvent $C_2H_5OH$:$CHCl_3$ (1:1).

The tests showed that the compounds were toxic and inhibited development of the test microorganisms.

Table 1 shows that **5-7** selectively affect growth and development of the microorganisms. Compound **5** had the highest bacteridical activity.

## EXPERIMENTAL

PMR spectra were recorded on a Bruker WM-250 spectrometer (250 MHz, $CDCl_3$) with TMS internal standard; $^{13}C$ NMR spectra, on a Bruker AM-300 spectrometer (75 MHz, $CDCl_3$). The purity of the products and the $R_f$ values were determined on Silufol UV-254 plates using $CH_3OH$:$CHCl_3$ (system a, 1:5) and $C_6H_6$:$CHCl_3$ (system b, 3:2; system c, 2:1). Optical rotation was measured on a SU-3 universal saccharimeter.

GC was performed on a LKhM-8MD chromatograph (column length, 2 m; diameter, 3 mm). The column was packed with Chromaton NAW-DMCS (Czech Rep.) consisting of solid support Chromaton-N and added liquid phase SE-30 (5% of the support mass). The column temperature was 200°C; vaporizer, 250°C; carrier gas, He.

**1-*O*-Allyl-2,3,4,6-tetra-*O*-acetyl-$\beta$-D-galactopyranose (1)**, mp 103-104°C, $[\alpha]_D^{20}$ -9.8° (*c* 0.65, $CHCl_3$), $R_f$ -0.41 (system c), $C_{19}H_{30}O_{10}S$ {lit. [4] mp 102-103°C, $[\alpha]_D^{20}$ -10.9° (*c* 0.85, $CHCl_3$)}.

$^{13}C$ NMR spectrum (δ, ppm): 20.7-20.3 (RO–CO–$\underline{C}H_3$), 69.9 (RO–$\underline{C}H_2$–$CH_2$–), 133.2 (RO–$CH_2$–$\underline{C}H_2$=$CH_2$), 117.5 (RO–$CH_2$–$CH_2$=$\underline{C}H_2$), 100.6 (C-1), 75.8 (C-2), 72.8 (C-3), 74.6 (C-4), 67.9 (C-5), 61.6 (C-6), 170.8-168.95 (4RO–$\underline{C}O$–$CH_3$).

**1-*O*-(3-Ethylthiopropyl)-2,3,4,6-tetra-*O*-acetyl-$\beta$-D-galactopyranose (5).** A mixture of ethylmercaptan (0.62 g, 0.01 mol) in dry $CHCl_3$ (10 mL) and benzoyl peroxide (0.1 g) was treated with a solution of **1** (3.88 g, 0.01 mol) in dry $CHCl_3$ (20 mL). The reaction was carried out under $N_2$ with constant stirring for 5 h (70-75°C). The mixture was cooled and separated over a column (system c, silica gel L 50/100) to afford chromatographically pure product (2.79 g, 62%), $R_f$ 0.51 (system a), mp 105-106°C, $[\alpha]_D^{17}$ +17.2° (*c* 0.41, $CHCl_3$), $C_{19}H_{30}O_{10}S$.

$^{13}C$ NMR spectrum (δ, ppm): 20.7-16.3 (RO–CO–$\underline{C}H_3$), 72.3 (RO–$\underline{C}H_2$–$CH_2$–), 27.4 (RO–$CH_2$–$\underline{C}H_2$–), 21.08 (RO–$CH_2$–$CH_2$–$\underline{C}H_2$–S–), 20.6 [RO–$(CH_2)_3$–S–$\underline{C}H_2$–], 12.9 [RO–$(CH_2)_3$–S–$CH_2\underline{C}H_3$], 103.2 (C-1), 71.6 (C-2), 72.1 (C-3), 74.6 (C-4), 77.9 (C-5), 62.2 (C-6), 168.5-170.2 (4RO–$\underline{C}O$–$CH_3$).

PMR spectrum (δ, ppm, J/Hz): 4.43 (1H, d, $J_{1,2}$ = 8.05, H-1), 5.18 (1H, dd, $J_{2,1}$ = 8.05, $J_{2,3}$ = 10.4, H-2), 4.98 (1H, dd, $J_{3,2}$ = 10.5, $J_{3,4}$ = 3.3, H-3), 5.36 (1H, dd, $J_{4,3:4,5}$ = 9.3, H-4), 3.40-3.36 (1H, m, H-5), 4.08-4.15 (2H, dd, $J_{5,6}$ = 3.2, $J_{5,6'}$ = 1.9, $J_{6,6'}$ = 12.3, $C\underline{H}_2OCOCH_3$, H-6′), 2.11, 2.02, 2.01, 1.95 (12H, m, 4CO–$CH_3$), 3.88-3.79 (2H, m, RO–$\underline{C}H_2$–$CH_2$–), 1.61-1.57 (2H, m, RO–$CH_2$–$C\underline{H}_2$–), 0.48-0.41 (2H, m, RO–$CH_2$–$CH_2$–$C\underline{H}_2$–S–), 0.98-0.72 (2H, m, RO–$CH_2$–$CH_2$–$CH_2$–S–$C\underline{H}_2$–), 0.18-0.00 (3H, m, RO–$CH_2$–$CH_2$–$CH_2$–S–$CH_2$–$C\underline{H}_3$).

**1-*O*-(3-Propylthiopropyl)-2,3,4,6-tetra-*O*-acetyl-$\beta$-D-galactopyranose (6)** was prepared analogously by addition of propylmercaptan (0.76 g, 0.01 mol) to **1** (3.88 g, 0.01 mol) in the presence of benzoyl peroxide (0.1 g). Yield 2.53 g (55.2%), $R_f$ 0.42 (system b), mp 111-112°C, $[\alpha]_D^{17}$ +9.8° (*c* 0.35, $CHCl_3$), $C_{20}H_{32}O_{10}S$.

$^{13}C$ NMR spectrum (δ, ppm): 20.6-20.8 (RO–CO–$\underline{C}H_3$), 72.2 (RO–$\underline{C}H_2$–$CH_2$–), 24.9 (RO–$CH_2$–$\underline{C}H_2$–$CH_2$–S–), 17.5 [RO–$(CH_2)_2$–$\underline{C}H_2$–S–], 12.5 [RO–$(CH_2)_3$–S–$\underline{C}H_2$–], 60.9 [RO–$(CH_2)_3$–S–$CH_2$–$\underline{C}H_2$–$CH_3$], 8.2 [RO–$(CH_2)_3$–S–$CH_2$–$CH_2$–$\underline{C}H_3$], 100.8 (C-1), 80.5 (C-2), 84.6 (C-3), 78.2 (C-4), 77.5 (C-5), 72.6 (C-6), 168.7-170.4 (RO–$\underline{C}O$–$CH_3$).

**1-*O*-(3-Butylthiopropyl)-2,3,4,6-tetra-*O*-acetyl-$\beta$-D-galactopyranose (7)** was prepared analogously by addition of butylmercaptan (0.9 g, 0.01 mol) to **1** (3.88 g, 0.01 mol) in the presence of benzoyl peroxide catalyst (0.1 g). Yield 3.36 g (51.5%), $R_f$ 0.64 (system a), mp 142-143°C, $[\alpha]_D^{17}$ +12.7° (*c* 0.53, $CHCl_3$), $C_{21}H_{34}O_{10}S$.

$^{13}C$ NMR spectrum (δ, ppm): 20.6-20.8 (RO–CO–$\underline{C}H_3$), 72.8 (RO–$\underline{C}H_2$–$CH_2$–), 22.7 (RO–$CH_2$–$\underline{C}H_2$–$CH_2$–S–), 16.6 [RO–$(CH_2)_2$–$\underline{C}H_2$–S–], 13.9 [RO–$(CH_2)_3$–S–$\underline{C}H_2$–], 11.5 [RO–$(CH_2)_3$–S–$CH_2$–$\underline{C}H_2$–$CH_3$], 16.0 [RO–$(CH_2)_3$–S–$CH_2$–$CH_2$–$\underline{C}H_2$–$CH_3$], 7.5 [RO–$(CH_2)_3$–S–$(CH_2)_3$–$\underline{C}H_3$], 104.4 (C-1), 70.5 (C-2), 71.6 (C-3), 74.9 (C-4), 77.1 (C-5), 66.8 (C-6), 168.4-170 (RO–$\underline{C}O$–$CH_3$).

**Deacetylation.** A suspension of **5** (0.45 g, 0.001 mol) in absolute methanol (20 mL) was heated for 10 min on a water bath with sodium methoxide solution (1.5 mL, 0.1 N), left overnight, and filtered. The filtrate was concentrated under reduced pressure (water aspirator). The residue was treated with ether until crystals separated. Crystals were filtered off and recrystalized from hexane. Yield of **8**, 0.13 g (48.9%), $[\alpha]_D^{17}$ +8° (*c* 0.31, $CHCl_3$), mp 97-98°C, $R_f$ 0.39 (system c), $C_{11}H_{22}O_6S$.

$^{13}C$ NMR spectrum (δ, ppm): 72.4 (RO–$\underline{C}H_2$–$CH_2$–), 28.2 (RO–$CH_2$–$\underline{C}H_2$–$CH_2$–S–), 24.6 (RO–$CH_2$–$CH_2$–$\underline{C}H_2$–S–), 21.5 (RO–$CH_2$–$CH_2$–$CH_2$–S–$\underline{C}H_2$–), 13.0 [RO–$(CH_2)_3$–S–$\underline{C}H_2$–$CH_3$], 104.9 (C-1), 71.8 (C-2), 73.4 (C-3), 69.2 (C-4), 76.5 (C-5), 62.3 (C-6).

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