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SYNTHESIS AND BIOLOGICAL ACTIVITY OF CERTAIN DERIVATIVES OF SELENOGLUCOSIDES

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The condensation of 1-Se-2,3,4,6-tetra-O-acetyl-β-D-glucopyranose with trimethylchlorosilane, triphenylchlorosilane, dibutylchloroarsine, and diphenylchloroarsine has been studied. New derivatives of selenoglucosides have been synthesized. The biocidal properties of the synthesized compounds have been studied.

Keywords: Se-glucose, dibutylchloroarsine, diphenylchloroarsine, trimethylchlorosilane, triphenylchlorosilane.

For some time past wide opportunities have arisen for the use of organic compounds containing sulfur, selenium, arsenic, and other heteroatoms in agriculture, medicine, and industry. It is known that organosilicon compounds serve for the prophylaxis of the formation and growth of tumors (various forms of leukemia, Ehrlich's tumor, sarcoma 180, etc.) [1, 2]. At the present time various organic and inorganic arsenic-containing compounds have been approved. These possess bactericidal and fungicidal properties and are successfully applied against a series of pathogenic microorganisms participating in biodegradation [3, 4]. The biocidal properties of selenium-containing organic compounds have been studied comparatively little.

The application of glycosides for the modification of biologically active organic compounds of silicon, selenium, and arsenic may, on the one hand, change their biological and physiological action, and on the other, may reduce their toxicity.

The synthesis of derivatives of selenoglucosides has been carried out and their bactericidal action has been investigated in the present work.

1-Selenotrimethylsilyl-2,3,4,6-tetra-O-acetyl-β-D-glucopyranose (**2**), 1-selenotriphenylsilyl-2,3,4,6-tetra-O-acetyl-β-D-glucopyranose (**3**), 1-selenodibutylarsinyl-2,3,4,6-tetra-O-acetyl-β-D-glucopyranose (**4**), and 1-selenodiphenylarsinyl-2,3,4,6-tetra-O-acetyl-β-D-glucopyranose (**5**) have been synthesized by the condensation of 1-Se-2,3,4,6-tetra-O-acetyl-β-D-glucopyranose (**1**) with chlorotrimethylsilane, chlorotriphenylsilane, dibutylchloroarsine, and chlorodiphenylarsine.

To clarify the bactericidal properties of the compounds **2-5** synthesized by us their effect was tested on the growth and development of certain microorganisms.

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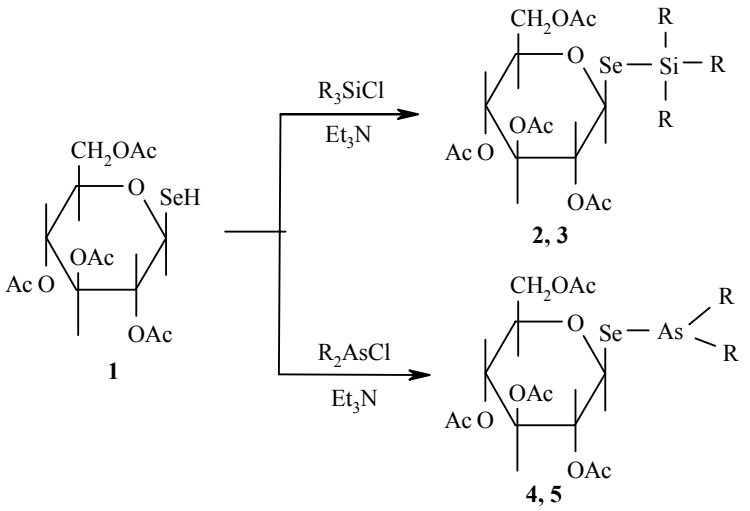
The synthesized compounds displayed a selective effect on the growth and development of various microorganisms. Thus, at concn. = 1.0 g/liter compounds **3** and **5** possess high activity in relation to *Actinomyces griseus* (suppression zones 7.0 and 10.0 mm respectively).



2 R = Me, **3**, **5** R = Ph, **4** R = Bu

Moderate activity in relation to *Actinomyces streptomicini* was detected for compounds **2, 4**, and **5** (suppression zone 4.0 mm). In relation to the phytopathogenic bacterium *Xanthomonas compestris* only compound **5** proved to be active, although the activity was low (suppression zone 2 mm). Compounds **3** and **5**, possessing high activity, contain phenyl groups in their molecules.

The results of the investigation make it possible to show the biologically active groups in the compounds investigated and to establish a certain correlation between structure and biological activity, which is promising for the purpose-directed search for new compounds with their biological properties previously designed.

EXPERIMENTAL

The IR spectra were obtained on an AVAKA 250 spectrometer in KBr disks. Optical rotation was measured on a SU-3 universal saccharimeter. ^{13}C NMR spectra were recorded on a Bruker AM-300 (75 MHz) in $CDCl_3$, internal standard was TMS.

TABLE 1. Effect of Compounds **2-5** on the Growth and Development of Microorganisms

Test microorganism	**2**		**3**		**4**		**5**		Control
	Suppression zone of microorganism, mm at concn., g/liter								
	1.0	0.1	1.0	0.1	1.0	0.1	1.0	0.1	0.0
Actynomyces griseus	3.0	2.0	7.0	4.0	3.0	1.0	10.0	7.0	0.5
Actynomyces streptomicini	4.0	1.5	3.5	2.5	4.0	1.5	4.0	2.5	0.4
Xanthomonas compestris	0.5	0	1.0	0.5	0	0	2.0	0.0	0.1

1-Seleno-2,3,4,6-tetra-O-acetyl-β-D-glucopyranose (1). Yield was 67.5%, mp 94-95°C, R_f 0.9 (hexane–ethyl acetate, 6:4), $[\alpha]_D$ +21° (*c* 0.62, chloroform). IR spectrum, ν, cm^{-1}: 2580 (Se-H); 1720 (C=O); 1010, 1040 (C–O–C). Found, %: C 40.02; H 5.11. $C_{14}H_{20}O_9Se$. Calculated, %: C 40.87; H 4.6.

1-Seleno-R_3Si-2,3,4,6-tetra-O-acetyl-β-D-glucopyranoses 2, 3 and 1-Seleno-R_2As-2,3,4,6-tetra-O-acetyl-β-D-glucopyranoses 4, 5 (General Method). An ether solution of the appropriate R_3SiCl or R_2AsCl (1.8 mmol) was added dropwise with stirring and heating (50-60°C) to a solution of selenoglucose **1** (0.62 g, 1.4 mmol) in chloroform (25 ml) and triethylamine (0.32 ml). Stirring was continued for 2 h (compound **2**) or 1 h (compound **3**) and left for 18 h at ~20°C (compounds **4** and **5** were left without additional stirring). The separated solid triethylamine hydrochloride was filtered off, and washed with ether. The combined filtrates were treated with activated carbon, and concentrated in vacuum until the start of crystallization. The precipitated crystals were filtered off and recrystallized twice from ethanol. Chromatographically pure compounds were obtained.

1-Selenotrimethylsilyl-2,3,4,6-tetra-O-acetyl-β-D-glucopyranose (2). White crystals, yield 0.44 g (60%); mp 96-97°C, $[\alpha]_D$ +13.4° (*c* 0.32, chloroform), R_f 0.51 (benzene–dioxane, 3:1). ^{13}C NMR spectrum, δ, ppm: 91.8 (C-1); 84.7 (C-2); 74.5 (C-3); 70.8 (C-4); 71.9 (C-5); 69.2 (C-6); 168.2-170.6 (C=O); 10.2-27.5 (CH_3). Found, %: C 42.60; H 6.00; Si 6.10. $C_{17}H_{28}O_9SeSi$. Calculated, %: C 42.20; H 5.80; Si 5.80.

1-Selenotriphenylsilyl-2,3,4,6-tetra-O-acetyl-β-D-glucopyranose (3). Yield 0.63 g (63%); mp 192-193°C, R_f 0.63 (chloroform–methanol, 4:1), $[\alpha]_D$ +22.7° (*c* 0.4, chloroform). ^{13}C NMR spectrum, δ, ppm: 95.5 (C-1); 71.2 (C-2); 73.6 (C-3); 66.8 (C-4); 77.0 (C-5); 62.5 (C-6); 170.4-175.6 (C=O); 20.6-29.7 (CH_3); 127.1-133.6 (C_6H_5). Found, %: C 57.40; H 5.10; Si 4.23. $C_{32}H_{34}O_9SeSi$. Calculated, %: C 57.40; H 5.08; Si 4.20.

1-Selenodibutylarsinyl-2,3,4,6-tetra-O-acetyl-β-D-glucopyranose (4). Yield 0.82 g (55%); mp 114-115°C, R_f 0.82 (petroleum ether–benzene, 1:1), $[\alpha]_D$ +20.1° (*c* 0.3, chloroform). ^{13}C NMR spectrum, δ, ppm: 92.5 (C-1); 71.2 (C-2); 73.4 (C-3); 69.0 (C-4); 76.8 (C-5); 62.8 (C-6); 167.5-172.5 (C=O); 35.4-42.0 (CH_2); 13.6-22.2 (CH_3). Found, %: C 44.35; H 6.20; As 14.11. $C_{22}H_{37}AsO_9Se$. Calculated, %: C 44.10; H 6.18; As 12.50.

1-Selenodiphenylarsinyl-2,3,4,6-tetra-O-acetyl-β-D-glucopyranose (5). Yield 0.49 g (51%); mp 131-132.5°C, R_f 0.31 (petroleum ether–benzene, 1:1), $[\alpha]_D$ +15.7° (*c* 0.47, chloroform). ^{13}C NMR spectrum, δ, ppm: 95.5 (C-1); 71.2 (C-2); 73.5 (C-3); 68.8 (C-4); 73.7 (C-5); 62.5 (C-6); 168.0-171.0 (C=O); 20.0-21.9 (CH_3); 136.0-137.0 (C_6H_5). Found, %: C 49.20; H 4.90; As 12.40. $C_{26}H_{29}AsO_9Se$. Calculated, %: C 48.80; H 4.50; As 11.70.

Determination of Bactericidal Activity. As test microorganisms actinomycetes producing physiologically active substances were used, *viz. Actinomyces griseus*, *Actinomyces streptomicini*, and the phytogenic bacterium *Xanthomonas compestris*. Solid nutrient media were used for incubating test organisms: Krasil'nikov medium (1 g KNO_3, 0.5 g K_2HPO4, 0.5 g NaCl, 0.5 g $MgSO_4$, traces of $FeSO_4$, 1 g $CaCO_3$, 20 g starch, water) was used for actinomycetes and meat-peptone agar (MPA) for bacteria. The effect of the synthesized compounds on the growth and development of microorganisms was studied by the Egorov method (alveolar method) [5]. The size of the toxic action was determined from the sterility zone around a hole. A solvent mixture of ethyl alcohol–chloroform, 1:1 served as control. Substances of concentration 1.0 and 0.1 g/l were placed in the hole. The results of the investigations are given in Table 1.

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