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BRIEF COMMUNICATIONS

Synthesis and Fungicidal Activity of Alkaloid-Containing Carbohydrates

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Abstract—*N*-Glycosylamines, triethylammonium salt of xylosyl- and glucosylbenzyldithiocarbamates, and their derivatives containing fragments of alkaloids were synthesized; some of these substances exhibit fungicidal activity.

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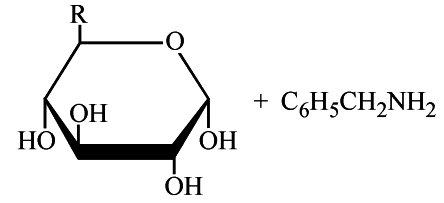
Among numerous substances comprising the environment, carbohydrates and their derivatives occupy an extremely important place and have enormous significance in technology and everyday human activity. Carbohydrates in the form of various derivatives enter into the cell composition of any living body, playing the role of structural material, energy source, substrates, and regulators of specific and biochemical processes [1].

Modified derivatives of monosaccharides are of great scientific and practical interest, since many of these have pronounced biological activity with a wide spectrum of effect. A number of derivatives of monosaccharides find wide use in medicine, e.g., as effective anticancer and antiviral agents [2]. All this stimulates an interest in synthetic chemistry of modification of monosaccharides.

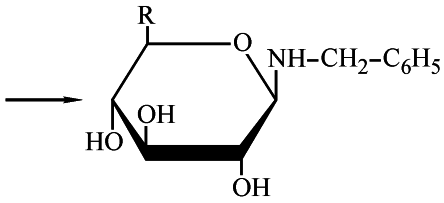
In recent years, *N*-glycosylamides (*N*-glycosides) find expanding application for synthesis of natural glycopeptides, their analogs, and glycoconjugates used in various biological studies. *N*-Glycosylamines are considered as potential pharmaceuticals, since introduction of carbohydrate group into a molecule not only increases the solubility but in some cases alters the biological effect as well [3].

We obtain a series of new carbohydrate-containing derivatives based on xylose and glucose for subsequent study of their reactivity and biological activity.

Condensation of *D*-xylose (**1**) and *D*-glucose (**2**) with benzylamine was performed in alcoholic solution under heating by the procedure described in [4]:



1, **2**



3, **4**

where R is H (**1, 3**), CH_2OH (**2, 4**).

The synthesized xyloxylbenzylamine (**3**) and glucosylbenzylamine (**4**) are hygroscopic white crystalline substances darkening in air. Depending on the synthesis conditions, *N*-glycosides can crystallize with 1 or 0.5 mol of water. When stored in a desiccator over P_2O_5, they become anhydrous.

The IR spectra of the compounds contain an absorption band at 891 ± 7 cm^{-1}, suggesting β-conformation at the anomeric center. Vibrations of the NH group appear in the range 2880–2920 cm^{-1}, and out-of-plane bending modes of the CH group of the aromatic ring, in the ranges 745–755 and 695–705 cm^{-1}. The IR spectra of **3** and **4** show that they contain no C=N bonds, i.e., they are not Schiff bases.

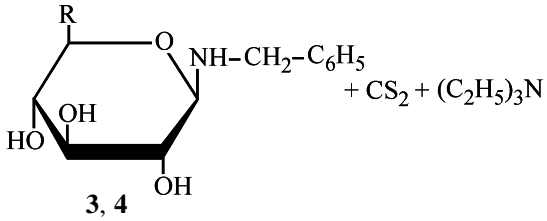
According to published data [5], the absorption in

Physicochemical constants and elemental analyses of compounds **3**–**12**

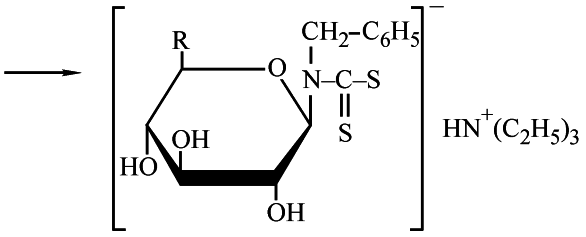
Compound	Yield, %	mp, °C	Found, %			Empirical formula	Calculated, %		
			C	H	N		C	H	N
3	90.2	105–106	60.35	7.18	5.85	$C_{12}H_{17}NO_4$	60.20	7.09	5.80
4	91.8	69–70	58.09	7.02	5.29	$C_{13}H_{19}NO_5$	57.98	7.11	5.20
5	39.7	94–95	54.82	7.79	6.76	$C_{19}H_{32}N_2O_4S_2$	54.76	7.65	6.70
6	41.6	62–63	53.98	7.60	6.33	$C_{20}H_{34}N_2O_5S_2$	53.78	7.67	6.27
7	40.5	129–130	57.26	5.96	8.37	$C_{24}H_{29}N_3O_5S_2$	57.00	5.72	8.32
8	45.3	106–107	56.18	6.12	7.90	$C_{25}H_{33}N_3O_6S_2$	56.05	6.21	7.84
9	57.5	142–143	57.53	6.69	5.93	$C_{23}H_{32}N_2O_5S_2$	57.10	6.63	5.80
10	70.9	68–69	56.55	6.68	5.58	$C_{24}H_{34}N_2O_6S_2$	56.45	6.71	5.49
11	41.8	99–100	57.51	6.79	5.88	$C_{23}H_{32}N_2O_5S_2$	57.10	6.63	5.80
12	51.1	73–74	56.57	6.86	5.59	$C_{24}H_{34}N_2O_6S_2$	56.45	6.71	5.49

the range of 1120–1170 cm^{-1} is characteristic of cyclic forms of carbohydrates, since sugar alcohols having the open-chain structure do not absorb in this range, which is in good agreement with the data obtained.

The synthesized xylosylbenzylamine (**3**) and glucosylbenzylamine (**4**) are fairly reactive compounds. Triethylammonium salts of xylosyl- and glucosylbenzyldithiocarbamates (**5, 6**) were synthesized by the reaction of the corresponding *N*-glycosides with carbon disulfide in ethanol in the presence of triethylamine:



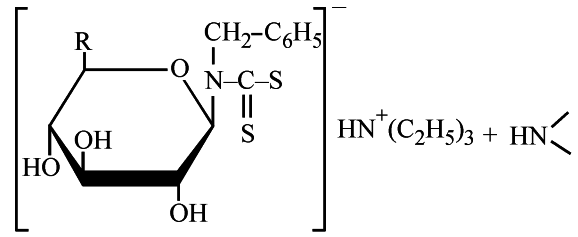
3, **4**



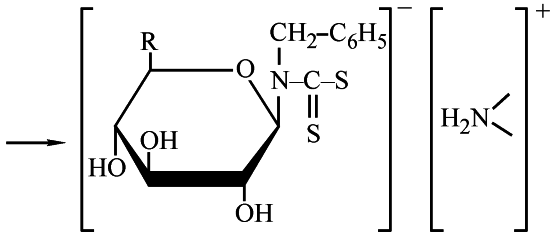
5, **6**

where R is H (**3, 5**), CH_2OH (**4, 6**).

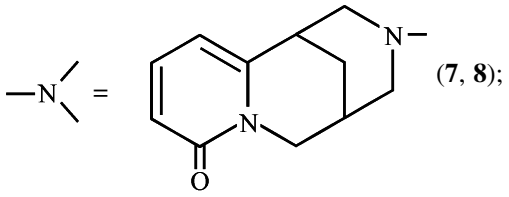
The next stage is substitution of alkaloid fragment for triethylamine by the reaction of triethylammonium xylosyl- and glucosylbenzyldithiocarbamate with alkaloids cytisine, 1-ephedrine, and *d*-pseudoephedrine in alcohol:



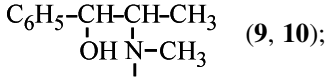
5, **6**



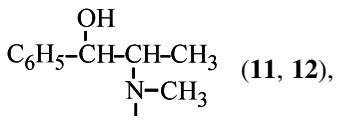
7–**12**



(**7**, **8**);



(**9**, **10**);



(**11**, **12**),

where R is H (**5, 7, 9, 11**); CH_2OH (**6, 8, 10, 12**).

Compounds **7**–**12** are white powders readily soluble in water, ethanol, and DMF and insoluble in hydro-

carbons. The composition and structure of **7**–**12** were confirmed by elemental analysis and IR spectroscopy. The IR spectra of **7**–**12** contain no absorption bands at 844 ± 8 cm^{-1}, which suggests β-conformation of pyranose ring of the compounds synthesized. In the range 2900–2930 cm^{-1}, there are stretching vibration bands of the N–H bond; at 1640–1650 cm^{-1}, the >N–C=O bands; and at 1070–1100 cm^{-1}; the thiocarbonyl group (C=S) bands.

There are contradictory opinions on how the important structural feature of carbohydrates, the presence of pyranose or furanose ring, is manifested in the IR spectrum [6]. The presence of several peaks in the range 1010–1090 cm^{-1} suggests the pyranose form of the glycoside fragment.

The characteristics of **3**–**12** are listed in the table. The spectra of all the compounds studied are characterized by broad strong bands in the range 3250–3400 cm^{-1}, caused by stretching vibrations of OH groups.

Two synthesized compounds **7** and **8** were tested for fungicidal activity. Phytopathogenic fungi *Fusarium oxysporum* and *Botrytis cinerea* were used as test cultures. The fungicidal activity was estimated from the intensity of microorganism development in a nutrient medium in comparison with the reference tests without addition of the compounds studied.

We found that cytisine salts of xylosyl- and glucosylbenzyldithiocarbamates tested *in vitro* have pronounced fungicidal activity against phytopathogenic fungi *Fusarium oxysporum* (72–78 and 69–74% suppression of development, respectively).[1]

The results obtained were recorded in a statement of biological tests.

EXPERIMENTAL

The IR spectra were recorded on an Avatar-320 spectrometer in KBr pellets. Melting points were determined on a Boetius device. The reaction course and purity of the resulting compounds were monitored by thin-layer chromatography on Silufol UV-254 plates in the system isopropanol : ammonia : water = 7 : 2 : 1. The plates were developed with iodine vapor.

Xylosyl- and glucosylbenzylamine (3, 4). To a 0.05 M solution of benzylamine and 8 ml of alcohol, 0.05 M of anhydrous finely ground carbohydrate was added. The mixture was heated on a water bath at 60–65°C for 20 min, then 10 ml of alcohol was added, and the solution was left to crystallize in a refrigerator. In a few hours, the substance completely crystallized. The product was washed with anhydrous ethanol and then with ether and dried in a desiccator upon P_2O_5.

Triethylammonium xylosyl- and glucosylbenzyldithiocarbamates (5, 6). To a 0.01 M solution of xylosyl- or glucosylbenzylamine in 5 ml of ethanol, 0.01 M of triethylamine was added with stirring, after which 0.01 M of carbon sulfide in 10 ml of alcohol was slowly added with cooling (3–5°C), and the mixture was stirred for 60 min at room temperature. After slight cooling, a precipitate formed. The precipitate was washed with anhydrous ethanol and then with anhydrous ether and dried in a desiccator upon P_2O_5.

Cytisine xylosyl- and glucosylbenzyldithiocarbamates (7, 8). To a stirred 0.001 M solution of compound **5** or **6** in 3 ml of ethanol, a 0.001 M solution of cytosine in 5 ml of ethanol was added at room temperature, and the mixture was stirred for 60 min. Then the mixture was heated at 55–58°C for 3 h. The solvent was removed on a water bath. The oily product was triturated with petroleum ether. The resulting powder was washed with diethyl ether.

Compounds **9**–**12** were obtained similarly (see table).

CONCLUSIONS

(1) *N*-Glycosylamines based on xylose and glucose were synthesized.

(2) Triethylammonium xylosyl- and glucosylbenzyldithiocarbamates and their derivatives containing fragments of alkaloids cytisine, 1-ephedrine, and *d*-pseudoephedrine were synthesized.

(3) Cytisine xylosyl- and glucosylbenzyldithiocarbamates exhibit pronounced fungicidal activity.

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[1] The studies were carried out at the Research Institute of Plant Protection (Almaty, Kazakhstan).