Chemistry

Yu. A. ZHDANOV, T. V. BOGDANOVA, V. G. ZOLOTUKHINA

1964

SovietRxiv

Abstract

Full Text

Chemistry

Yu. A. ZHDANOV, T. V. BOGDANOVA, V. G. ZOLOTUKHINA

CONDENSATION OF AL-FORMS OF SUGARS WITH 4-HYDROXYCOUMARIN

(Presented by Academician B. A. Kazanskii, 10 IV 1964)

Taking into account the anticoagulant action of coumarin derivatives and the insufficient solubility in water of its commonly used preparations, we attempted the synthesis of 4-hydroxycoumarin containing a carbohydrate substituent in position 3. By their chemical nature, such derivatives are close to the class of C-glycosides; however, they cannot be obtained by the organomagnesium synthesis used for this class. Convenient starting substances for carrying out the condensation reaction with compounds containing sufficiently mobile C—H bonds are the al-forms of sugars ([1,2]).

We studied the condensation of 4-hydroxycoumarin with the complete acetates of al-*D*-glucose, al-*D*-galactose, and al-*D*-mannose. As the investigations showed, 4-hydroxycoumarin, upon heating in ethanol, forms with al-forms of sugars products arising by the type of a crotonic condensation:

$$\text{4-hydroxycoumarin} + \begin{array}{c}\text{CHO}\\|\\(\text{CHOAc})_4\\|\\\text{CH}_2\text{OAc}\end{array} \xrightarrow[-\text{H}_2\text{O}]{} \text{3-CH(CHOAc)}_4\text{CH}_2\text{OAc-coumarin derivative}$$

The reaction scheme given is confirmed by data of elemental analysis, by quantitative addition of bromine at the double bond, and by determination of the number of acetyl groups by hydrolysis ([3]). The condensation products are readily deacetylated in absolute methanol in the presence of catalytic amounts of hydrochloric acid ([4]).

$$\text{3-CH(CHOAc)}_4\text{CH}_2\text{OAc-coumarin derivative} \xrightarrow{\text{HClO}_4} \text{3-CH(CHOH)}_4\text{CH}_2\text{OH-coumarin derivative}$$

The structure of the deacetylated products was proved by data of elemental analysis, by quantitative addition of bromine, and by periodate oxidation of

the carbohydrate part of the molecule ([5]). The 3-glycosylidenecoumarandiones-2,4 obtained by us are readily soluble in water, ethanol, and methanol, and are insoluble in most organic solvents. As shown by investigations carried out at the Department of Pharmacology of the Rostov Medical Institute, the synthesized substances possess anticoagulant activity.

Experimental part

3-(Penta-*O*-acetyl)-glycosylidenecoumarandione-2,4. To carry out the condensation, 0.7 g (0.004 mole) of the fully acetylated al-hexose (*D*-glucose, *D*-galactose, or *D*-mannose) and 1.56 g (0.004 mole) of 4-hydroxycoumarin are taken. The alcoholic solution of the indicated substances is heated in a flask with a reflux condenser on a boiling water bath for 25 hr.

The alcohol is distilled off in the vacuum of a water-jet pump. The residue is dissolved in chloroform, the solution is clarified with activated charcoal and dried over anhydrous sodium sulfate. After filtration, the chloroform is distilled off under vacuum.

When the resulting syrup is dissolved in absolute methanol and dry ether is added, the pure final product is isolated. The results of the syntheses are given in Table 1.

The product is soluble in chloroform, methanol, ethanol, and acetone; it does not dissolve in water, benzene, toluene, sulfuric ether, or petroleum ether. The substances are described for the first time.

Table 1

Sugar residue	Yield, %	M.p., °C	C, %[1]	H, %[1]	Bromine absorption in mol[2]	Number of acetyl groups[3]
D-glucose	33	252 with decomp.	56.48	4.49	0.93	4.85
D-galactose	48	syrup	56.34	4.56	0.96	4.85
D-mannose	43	syrup	56.38	4.67	0.98	4.89

[1] ($C_{25}H_{28}O_{13}$). Calculated, %: C 56.18; H 4.87. [2] Theoretical 1 mol. [3] Theoretical 5 groups.

3-Glycosylidenecoumarandione-2,4. 0.7 g of the acetylated product is dissolved in absolute methanol. Three drops of 60% hydrochloric acid are added to

the solution. After heating for 1.5 h on a gently boiling water bath, the reaction mixture is neutralized with sodium bicarbonate, the solution is filtered, and the methanol is removed in the vacuum of a water-jet pump while heating on a water bath. The resulting syrup is again dissolved in methanol, the solution is purified with activated charcoal, and dried with anhydrous sodium sulfate. The filtered solution is evaporated in vacuo to a syrup, after which, upon dissolving it in absolute methanol and adding dry ether, a crystalline final product, yellow in color, is isolated.

Table 2

Sugar residue	Yield, %	M.p., °C	C, %[1]	H, %[1]	Bromine addition in mol[2]	Periodate oxidation: sodium periodate absorbed, mol[3]	Periodate oxidation: formic acid obtained, mol[4]
D-glucose	70	176–178	55.40	4.38	1.008	3.98	2.98
D-galactose	60	164–168	55.36	4.42	1.09	3.99	2.98
D-mannose	66	120–125	55.56	4.45	1.001	3.98	2.98

[1] $C_{15}H_{16}O_8$. Calculated, %: C 55.72; H 4.65. [2] Theoretical 1 mol. [3] Theoretical 4 mol. [4] Theoretical 3 mol.

The product dissolves in water, ethanol, and methanol, and is insoluble in most organic solvents. The substances are described for the first time. The results of deacetylation are given in Table 2.

Rostov-on-Don
State University

Received
10 I 1964

CITED LITERATURE

[1] H. Zinner, E. Wittenburg, Ber., **92**, 1614 (1959). [2] N. K. Kochetkov, B. A. Dmitriev, *Izv. AN SSSR, Ser. Khim.*, No. 7, 262 (1962). [3] *Methods in Carbohydrate Chemistry*, **1**, 1962, p. 449. [4] Yu. A. Zhdanov, G. A. Korol' chenko, G. N. Dorofeenko, DAN, **143**, 852 (1962). [5] I. Guben, F. Veil' , *Metody organicheskoi khimii*, **2**, 348 (1963).

Note: Figure translations are in progress. See original paper for figures.

Source: Math-Net.Ru and CyberLeninka. Machine translation. Verify with the original.