SYNTHESIS AND ANTIMICROBIAL ACTIVITY OF 3,3′-BIS-(PROPYN-1,1′-BENZOATO)DIMETHYLSILANES

Kh. Yuldasheva, A. D. Dzhuraev, A. G. Makhsumov, and N. Amanov

UDC 615.281:547.77].012.1.07

During our investigations of the synthesis of compounds that have antimicrobial properties, we have obtained novel silicon-containing compounds (I-X). The synthesis of these compounds was carried out by reacting propargyl esters of substituted benzoic acids with dimethyldichlorosilane in benzene according to the scheme:

$$2RCOOCH_2C{\equiv}CH + Cl{-}Si(CH_3)_2Cl \xrightarrow[2HCl]{} RCOOCH_2C{\equiv}C{-}Si(CH_3)_2{-}C{\equiv}CCH_2OCOR$$

where R = Ph (I), 2-ClC_6H_4 (II), 2,4-$Cl_2C_6H_3$ (III), 2-BrC_6H_4 (IV), 3-BrC_6H_4 (V); 2-IC_6H_4 (VI); 3-IC_6H_5 (VII); 2-$NO_2C_6H_4$ (VIII); 4-$NO_2C_6H_4$ (IX); 2, 4-$(NO_2)_2C_6H_3$ (X).

The prepared compounds (Table 1) are crystalline substances that are soluble in organic solvents. The purity of the compounds was verified by TLC on Al_2O_3 of activity stage II in the system toluene–acetic acid; spots were visualized in iodine vapor. Their structure was confirmed by elemental analyses and IR spectroscopy.

The IR spectrum contains absorption bands in the region 1710-1750 cm^{-1} characteristic of the COO group, in the region 1500-1600 cm^{-1} characteristic of the benzene ring; in the regions 600, 650, and 670 cm^{-1} are bands that are characteristic of the Si-C bond, valence vibrations of the -C≡C- bond are found in the region 2100-2210 cm^{-1}, and the $Si-CH_3$ bond is found in the regions 740, 800, and 1250 cm^{-1}. Absorption bands that are characteristic of the -C≡C- bond are evidence of the formation of a propynyl derivative. The absence of bands in the regions 1930 and 1030-1060 cm^{-1}, corresponding with valence vibrations of the C=C=C group, indicates that as a result of the reaction of propargyl esters of substituted benzoic acids with dimethyldichlorosilane an acetylene-allene isomerization, which has been found in monopropargyl derivatives of Si, Ge, Sn, and Pb, is not observed.

We have studied the antimicrobial properties of the prepared compounds and attempted to find a relationship between their activity and chemical structure.

EXPERIMENTAL (CHEMICAL)

IR spectra were taken on a Specord-75 spectrometer (KBr). Data of elemental analyses were in agreement with calculated values.

3,3′-Bis(propyn-1,1′-benzoyloxy)dimethylsilane (I). A flask equipped with a reflux condenser is charged with 1.6 g (0.01 mole) of propargyl benzoate, 2.35 ml of dimethyldichlorosilane, and 100 ml of benzene. The reaction mixture is stirred at 30-40°C for 6 h and the product is reaction mixture is stirred at 30-40°C for 6 h and the product is extracted with ether. The solvents are evaporated and the product is purified by TLC on Al_2O_3 of activity II in the system toluene–acetic acid, 4:10. R_f 0.67. The prepared compound is a white crystalline substance melting at 88-89°C. Yield 70.5%.

Compounds II-X were prepared in much the same way.

EXPERIMENTAL (BIOLOGICAL)

The presence of antimicrobial activities in the prepared compounds was determined by the "alveolar" or dispersion method. The method consists of preparing a hole in the surface of beef-extract agar (BEA), applying a microbial suspension of the test culture (1 billion/ml) on the BEA surface, and introducing into the hole an amount of 0.2 to 1 mg of the compound to be tested, which diffused into the agar. After incubation in a thermostat at 37°C for 18-24 h the result was judged by diameter of zone of action (in mm).

First Tashkent Medical Institute. Translated from Khimiko-Farmatsevticheskii Zhurnal, Vol. 26, No. 3, pp. 53-54, March, 1992. Original article submitted January 28, 1991.

6091-150X/92/2603-0250$12.50

TABLE 1. Physicochemical Properties of 3,3′-Bis(propyn-1,1′-benzoato)dimethylsilanes

Compound	Yield, %	mp, °C	R_f	Empirical formula
I	70,5	101—102	0,57	$C_{22}H_{20}O_4Si$
II	73,4	122—123	0,45	$C_{22}H_{18}O_4Cl_2Si$
III	72,3	139—140	0,67	$C_{22}H_{16}O_4Cl_4Si$
IV	75,6	108—109	0,39	$C_{22}H_{18}O_4Br_2Si$
V	80,1	120—121	0,77	$C_{22}H_{18}O_4Br_2Si$
VI	79,4	153—154	0,88	$C_{22}H_{18}O_4I_2Si$
VII	85,3	149—150	0,63	$C_{22}H_{18}O_4I_2Si$
VIII	84,2	96—97	0,73	$C_{22}H_{18}N_2O_8Si$
IX	81,7	179—180	0,43	$C_{22}H_{18}N_2O_8Si$
X	87,3	162—163	0,48	$C_{22}H_{16}N_4O_{12}Si$

TABLE 2. Antimicrobial Activity of the Prepared Compounds (weighed portion of the preparation 0.5 mg)

Compound	Test organism							
	S. aureus	Micrococcus	E. coli O_{29}	S. typhimurium	S. typhi	Sh. flexneri 2a	Proteus vulgaris	Bacilla
I	25	25	35	15	15	15	15	10
II	15	10	10	10	g.s.	10	8	10
III	n/a	n/a	g.s.	n/a	n/a	n/a	n/a	n/a
IV	20	15	10	g.s.	10	n/a	n/a	8
V	n/a	g.s	n/a	n/a	n/a	n/a	n/a	n/a
IV	g.s.	8	n/a	n/a	n/a	n/a	n/a	n/a
VII	n/a	g.s.	n/a	8	n/a	n/a	n/a	n/a
VIII	15	15	10	10	10	15	8	10
IX	15	2	n/a	5	n/a	5	n/a	n/a
X	12	8	g.s.	8	n/a	8	10	n/a
Control:								
penicillin	5	n/a	n/t	n/t	n/t	n/t	n/t	n/t
levomycetin	n/t	n/a	n/t	n/t	12	n/t	11	n/t
polymyxin	n/t	n/t	n/t	5	n/t	15	n/t	n/t

Notes. g.s.) growth suppression of the test microbes; n/a) no activity on the mentioned microbe; n/t) not tested on the mentioned microbe.

Results of the investigations are listed in Table 2.

It is seen from the given data that the test compounds, with the exception of III and V, have antimicrobial activity. Among them the best activity is displayed by compound I. On introduction of halogens into the benzene ring the nature of the activity is changed. Compound IV shows selective activity against cocci. Replacing halogens by a nitro group leads to an increase in antimicrobial activity, the highest activity is found in compound VIII. The presence of a nitro group at the para position leads lowering of the activity. Introduction of two nitro groups also lowers the activity.

Thus, it has been found that the highest activity is displayed by compound I.

The reported structure-activity regularity makes in possible to carry out purposeful syntheses of chemical compounds later on.

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