the cell culture and the duration of action. When a HEF culture is used the inhibition ranged from 5.5% to 22.5% after 1 h of incubation, whereas no inhibition was detectable after 20 h of incubation. With a human fibroblast cell culture (M-19), no inhibition could be detected after 1 h, but after 20 h of incubation a degree of inhibition of cellular DNA biosynthesis ranging from 2.6% to 79.7% was observed.

The biologically inactive compound XXXIV inhibits the DNA biosynthesis in HEF and M-19 cell cultures to 79% and 23%, respectively, which indicates its potential toxicity. Compounds Ia, Ib, and XXXIV, which have antiviral activity, show very low inhibition of cellular DNA biosynthesis. Most significantly, these compounds have different inhibitory effects on the DNA biosynthesis in the different cell cultures tested. Thus, both the toxicity and specificity of these compounds are dependent on the type of viral infection and the metabolic characteristics of the particular cell culture.

Compound XX, which possesses antiviral activity and is capable of complex formation with DNA, shows a weak inhibition of cellular DNA biosynthesis (3-12%). It can be assumed that its antiviral activity against DNA viruses is due to an inhibition of viral DNA synthesis.

The data presented in this paper on the antiviral activity, low toxicity, and capability of complex formation with DNA of the compounds tested show that this is a promising class of compounds for the search for biologically active substances.

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SYNTHESIS AND ANTIMICROBIAL ACTIVITY OF A NUMBER OF 1,2,3-TRIAZOLE DERIVATIVES

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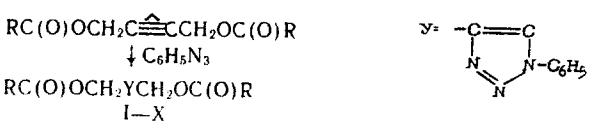
The reaction of 1,3-dipolar ring-attachment of organic azides to compounds containing an acetylene bond forms a variety of 1,2,3-triazole derivatives [2, 5].

We have synthesized a number of new triazole derivatives based on acetylene esters, i.e., derivatives of benzic acid and phenylazide (PA).

The syntheses were carried out according to the following scheme:



R=Ph (I), 2-ClC$_6$H$_4$ (II); 2,4-Cl$_2$C$_6$H$_3$ (III); 2-BrC$_6$H$_4$ (IV), 3-BrC$_6$H$_4$ (V), 2-IC$_6$H$_4$ (VI), 3-IC$_6$H$_4$ (VII), 2-NO$_2$C$_6$H$_4$ (VIII), 3-NO$_2$C$_6$H$_4$ (IX), 4-NO$_2$C$_6$H$_4$ (X).

The resulting products are stable in normal conditions, and are crystalline substances, soluble in organic solvents and insoluble in water.

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The structures of these compounds were confirmed by IR and PMR spectroscopy, and by elemental analysis.

The IR spectrum contained absorption peaks characteristic of the triazole ring (3070, 2960, 1590, 1050, and 970 cm^{-1}), for the C=C bond in the 1650-1700 cm^{-1} region, for the C=O bond in the 1710-1720 cm^{-1} region, for the C–O–C bond in the 1220-1280 cm^{-1} region, and for the C-Ar bond in the 730-750 cm^{-1} region.

The PMR spectral data (ppm) were: 6.72-7.74, 4H – aromatic protons; 4.2-5.92 $-CH_2-O-$, 5H, 8.04.

The physicochemical constants for the compounds synthesized are shown in Table 1.

Chemical Studies

IR spectra were taken on a Specord-75 apparatus in KBr. PMR spectra were taken on a Varian-100 apparatus with a working frequency of 100 MHz at room temperature, using hexamethyldisilazane as internal standard and CD_3OH as solvent. Chemical shifts are given in ppm(δ-scale). The purity of preparations and reaction routes were checked by TLC on Silufol UV-254 plates (Czechoslovakia) in a solvent system consisting of ether:hexane (5:3), and compounds were detected with iodine vapor. Elemental analysis results agreed with calculated values

1-Phenyl-4,5-bis(benzoyloxymethyl)-1,2,3-triazole (I)

1,4-Bis(benzoyloxy)butene-2 (2.4 g, 0.01 mole) and toluene (20 ml) were placed in a flask fitted with a reflux condenser, along with 1.3 g (0.0011 mole) of freshly prepared PA. PA was prepared from phenylhydrazine as described in [4]. The mixture was heated to the solvent boiling point. After the reaction had been carried out, the solvent was removed by evaporation,

TABLE 1. Physicochemical Constants of Compounds I-X

Compound	Yield, %	Melting point, °C	R_f	Molecular formula	IR spectrum, cm^{-1} Frequencies characteristic for the triazole ring				
I	82	100—102	0,20	$C_{24}H_{19}N_3O_4$	3070	2960	1590	1050	970
II	84	118—120	0,37	$C_{24}H_{17}Cl_2N_3O_4$	3060	2950	1580	1055	975
III	90	101—102	0,16	$C_{24}H_{15}Cl_4N_3O_4$	3075	2965	1575	1060	965
IV	75	137—139	0,38	$C_{24}H_{17}Br_2N_3O_4$	3065	2955	1585	1065	970
V	79	142—144	0,47	$C_{24}H_{17}Br_2N_3O_4$	3060	2965	1570	1055	965
VI	81	141—143	0,45	$C_{24}H_{17}I_2N_3O_4$	3065	2960	1575	1060	960
VII	88	173—175	0,35	$C_{24}H_{17}I_2N_3O_4$	3060	2965	1585	1055	965
VIII	72	120—122	0,15	$C_{24}H_{17}N_5O_8$	3065	2970	1580	1060	970
IX	81	115—116	0,17	$C_{24}H_{17}N_5O_8$	3070	2960	1575	1055	965
X	86	188—190	0,21	$C_{24}H_{17}N_5O_8$	3065	2955	1585	1045	970

TABLE 2. Antimicrobial Activities of Compounds I-X (zone diameters, in mm)

Compound	S. aureus 209	Micrococcus	S. typhimurium	S. typhi	Sh. flexneri 2a	Serratia
I	6	15	13	8	8	6
II	10	4	10	6	—	—
III	15	10	—	4	20	4
IV	12	18	10	6	—	10
V	18	15	8	—	18	10
VI	10	8	10	—	16	—
VII	17	15	6	8	15	20
VIII	15	12	4	—	20	15
IX	—	10	—	22	15	—
X	4	—	15	—	20	—
Control:						
Penicillin	10	—	—	—	—	—
Levomycetin	—	—	8	—	—	—
Polymyxin	10	—	—	—	—	—

and the product was recrystallized from hexane, giving a white crystalline substance with a yield of 2.6 g (84%). The melting temperature was 118-120°C, and the R_f was 0.2.

Compounds II-X were prepared in similar conditions.

Biological Studies

The presence of halogens, nitro groups, and triazole rings in the compounds synthesized here should produce biological activity [1, 3]. The antimicrobial activity of these compounds was tested in the Department of Microbiology, Tashkent Medical Institute.

Antimicrobial activity was assessed using a well method or in suspension. Wells were cut in the surface of meat peptone agar plates, bacterial test suspensions (10^9 cells/ml) were spread on the plates, and 0.2-1 mg of compounds were placed in the wells to allow diffusion into the agar. Growth inhibition zone diameters were measured in mm after incubation at 37°C for 13-24 h.

The results of these studies are shown in Table 2.

All compounds investigated had at least some antimicrobial activity.

The most active were compounds V and VII. Activity decreased among halogen-containing compounds in the following order: Br > I > Cl, i.e., bromine-containing compounds were the most active. The presence of bromine in the m-position produced selective activity.

Activity decreased among nitro-containing compounds in the order o > m > p. Nitro groups in the o-position gave the highest levels of activity (Compound VIII).

The activities of the compounds synthesized here were comparable with those of some widely recognized antimicrobial compounds, such as the penicillins, levomycetin, and polymyxin.

The results obtained here show that some of the compounds were more active than well known antimicrobials: e.g., penicillin and polymyxin against *Staphylococcus aureus* 209, and levomycetin against *Salmonella typhimurium*.

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