The results of the investigation of the tuberculostatic activity of the synthesized compounds are given in Table 2.

Of all the compounds studied, the highest tuberculostatic activity with respect to the $H37R_V$ strain was exhibited by compounds IVc-e, i.e., 4-amino-3-benzoylvinylthio-1,2,4-triazoles, unsubstituted at the 5-position (R^2 = H).

Thus, it was found from our investigations that compounds IVc-e have a tuberculostatic activity comparable with that of conventional antitubercular preparations.

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SYNTHESIS AND ANTIMICROBIAL ACTIVITY OF 1,1,2-TRIIODO-1-PROPEN-3-YL BENZOATES

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The problem of the search for and study of new antimicrobial preparations is a timely task; this is associated with the increasing resistance of microorganisms to previously used antimicrobial preparations.

In order to search for new, more active antimicrobial agents we tested six compounds obtained by the reaction of the acid chlorides of benzoic acid derivatives with 1,1,2-triiodo-1-propen-3-ol. (See scheme on next page.)

The physicochemical characteristics of the synthesized compounds are presented in Table 1.

The individuality was verified by TLC on activity II Al_2O_3 in a benzene–methanol (9:1) and chloroform–hexane (9:1) systems.

TABLE 1. Physicochemical Characteristics of 1,2,2-Triiodo-1-propen-3-yl Benzoates

Compound	Yield, %	mp, °C	Empirical formula
I	83,2	78—80	$C_{10}H_7I_3O_2$
II	85,6	147—145	$C_{10}H_6I_3NO_4$
III	81,2	151—153	$C_{10}H_6I_3NO_4$
IV	80,1	148—150	$C_{10}H_5I_3N_2O_6$
V	83,5	149—151	$C_{10}H_6BrI_3O_2$
VI	84,3	130—132	$C_{10}H_6BrI_3O_2$

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TABLE 2. Bacteriostatic and Bactericidal Activity of the Preparations

Compounds*	Forms and serotypes of bacteria																		
	Pseudomonas aeruginosa	Y. enterocolitica	S. typhi murium	Citrobacter freundii	Par. A	Prot. mirabilis	Staph. 209	Sh. stutzerishmitzii	Sh. flex. — 2a	Par. B	Sh. Boydii—1	Sh. newcastle	Sh. flex. — 2a	Sh. boydii=1	Sh. flex. — 4a	Sh. flex. — 1a	Sh. Sonnei	Sh. flex. — 4a	Sh. newcastle	Sh.
I	nl	28	25	18	12 sg	20 sg	15	18	18	7 sg	27	30	13	26	20 sg	13	28	13	28	25
II	nl	25	25	19	14	15 sg	7 sg	15	20	15	30	15	20	15	16	25	20	17	13	20
III	nl	25	23	22	20	20 sg	10 sg	20	17	20	20	30	25	20	17	18	13	20	28	25
IV	nl	25	25	19	14	20 sg	10 sg	16	20	10sg	30	25	20	12	10	25	20	30	25	16
V	nl	25	20	20	20	20 sg	10 sg	20	22	10sg	20	25	23	15	10	20	20	20	16	20
VI	nl	20	20	21	10	17 sg	10 sg	15	20	10sg	22	20	20	20	13	25	13	20	20	17

*1-Billion suspension — 1 ml, 0.2 mg of the preparation, 0.1 ml of DMSO + 0.9 n.b. (n.b. — neutral buffer) (nl stands for no lysis, and sg stands for secondary growth).

TABLE 3. Action of Various Dilutions of I-VI on Strains of Bacteria

Compound	Strain	No. of colonies grown in the corresponding dilutions of I-VI, mg				
		100	50	25	12.5	6.25
I	Sh. flexneri-2a	—	—	6	50	81
II	St.-209	—	2	20	30	90
III	Par. A	—	—	—	—	—
IV	Sh. stutzeri-shmitzii	—	—	—	—	—
V	Sh. boydii-1	—	—	2	6	1
VI	Prot. mirabilis	—	—	—	—	1

Note: 18 h cultures of the 10-million suspension were used in the research.

$$RCOCl + HOCH_2CI = CI_2 \xrightarrow{-HCl} RCOOCH_2CI = CI_2$$

I—IV

R = C_6H_5 (I), 3-$NO_2C_6H_4$ (II); 4-$NO_2C_6H_4$ (III), 3,5-$(NO_2)_2C_6H_3$ (IV); 2-BrC_6H_4 (V); 4-BrC_6H_4 (VI)

The structures were proved by data from the IR spectra and the results of elementary analysis. The results of elementary analysis satisfied the calculated values.

Thus absorption bands that are characteristic for stretching vibrations of the −C=C− bond are present in the IR spectra of all of the compounds at 1625 cm^{-1}; an absorption band that is characteristic for the stretching vibrations of an ester grouping is present at 1720 cm^{-1}.

EXPERIMENTAL (CHEMICAL)

The IR spectra of KBr pellets of the compounds were recorded with a UR-20 spectrometer.

1,1,2-Triiodo-1-propen-3-yl Benzoate. A solution of 4.36 g of 1,1,2-triiodo-1-propen-3-ol in 10 ml of pyridine was added to a solution of 1.4 g of benzoyl chloride in 20 ml of benzene, after which the mixture was stirred at 70-80°C for 4 h. The cooled mixture was treated with a saturated solution of Na_2CO_3 and extracted with ether. The solvent was evaporated with ether. The solvent was evaporated to give 1.16 g (83%) of a crystalline yellow compound with mp 78-80°C.

The remaining compounds were similarly obtained.

EXPERIMENTAL (BIOLOGICAL)

Taking into account the fact that the new substances contain iodine atoms, we decided to test them for antimicrobial activity on test microbes that induce intestinal infections (Salmonella, Shigella) and quasi-pathogenic bacteria (Proteus, Pseudomonas, Citrobacter, Staphylococcus, etc.), which under certain conditions, cause illness in both humans and animals.

The existence of antimicrobial properties in the investigated compounds was revealed by the "hole" or the method of weighed samples. The essence of the method consists in the preparation of holes on the surface of meat-peptone agar (MPA), treatment of the surface of the MPA with a microbial suspension of the test culture (1 billion/ml), and introduction into the holes in amounts from 0.2 to 1 mg of the investigated compound, which diffused into the agar. After incubation in a thermostat at 37°C for 18-24 h, the result was reckoned from the diameter of the zone of bactericidal activity (in millimeters).

The study of the bacteriostatic properties was determined by the method of serial dilutions in nutritive agar, which makes it possible to establish the MIC (minimal inhibiting concentration) in micrograms per milliliter.

The investigated test culture was seeded after pouring successive dilutions of the preparation in liquefied nutritive agar into Petri dishes and coagulation on the surface of agar with respect to sectors by crosshatching with a bacteriological loop. The results were

evaluated from the absence or presence of growth of the microbe after incubation at 37°C for 18-48 h. The last concentration of the preparation at which growth is not observed is its MIC (the method was recommended by order of the Ministry of Public Health of the USSR from March 13, 1975, "Unification of methods for the determination of the sensitivity to chemotherapeutic preparations").

The results obtained are presented in Tables 2 and 3.

An analysis of the data presented in Tables 2 and 3 shows that all of the preparations used for the tests have antimicrobial activity with respect to all of the test microbes used for the investigation. The compounds have the most pronounced action on inducers of intestinal infections (Shigella, Salmonella) and some representatives of quasi-pathogenic bacteria. In addition, they have no effect on Bacillus pyocyaneus and cause a lag in the growth of Sh. stutzeri-shmitzii and Staph. aureus 209. For most of the test microbes the MIC ranges from 50 to 100 μg/ml, while for some it ranges from 6.25 to 12.5 μg/ml (S. paratyphi A, Proteus mirabilis).

Thus it was established that all of the tested preparations have approximately the same antimicrobial properties against most of the test microbes used for the investigations, although S. enterocolitica, Citrobacter, S. paratyphi A and B, and some forms of Shigella proved to be more sensitive to them.

SYNTHESIS AND ANTIMICROBIAL ACTIVITY OF DERIVATIVES OF AMINOBENZOCROWN ETHERS

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We have previously shown [5, 6] that some aliphatic derivatives of crown ethers (CE) display high antimicrobial activity (AMA). Biological activity of a number of other CE is also known [1, 7]. However, the structure–function interrelationship for such compounds has not been adequately studied; the reason for this is the relatively small number of investigated representatives of CE.

The aim of the present research was to study the AMA of derivatives of aminobenzocrown ethers (ABC). We have developed general and convenient methods for the synthesis of some derivatives of ABC and have studied their AMA.

The corresponding N-acyl derivatives III, IV, and Va, b were synthesized in high yields by acylation of 4'-aminobenzo-15-crown-5 (I) and the isomers of diaminodibenzo-18-crown-6 [trans (IIa) and cis (IIb)] with acetic anhydride and benzoyl chloride.

The corresponding formamidinocrown ethers (FCE) VII-XI and acetamidinocrown ether XII were obtained in high yields (up to 95%) by the reaction of I, IIa, b, and diaminodibenzo-24-crown-8 (VI) with dimethylacetals of dimethylformamide, N-formylpiperidine, N-formylmorpholine, and dimethylacetamide.

It was also established that VII, VIIIa, b, and XI are transaminated extremely readily by various amines with the formation of the corresponding FCE. Thus amidines IXa, b and Xa, b were also obtained by transamination of VIIIa, b by, respectively, piperidine and morpholine [2], while amidoxime XIII was obtained by transamination of VIIIa with hydroxylamine hydrochloride at 20°C. Thus the proposed method for the synthesis makes it possible to readily obtain an extensive set of compounds of this type in high yields.

The synthesis and investigation of N,N'-bis(crown ether)-amidines, which have not been previously described in the literature, are of great interest in this respect. We have developed a convenient general method for obtaining bis-CE of this type in yields greater than 75% that does not require column chromatography for their isolation. Thus, for example,

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