

Review Article

SYNTHESIS OF NEW BROMINE ACETYLENE DITHIOCARBAMATES DERIVATIVES AND THEIR GROWTH-STIMULATING ACTIVITY.

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Abstract

The proposed article relates to organic chemical synthesis and the study of new bromo-acetylene dithiocarbamates, the chemical properties of 1-isothiocyanate and 1-thiolacetylene esters of bromo-substituted benzoic acid, which are crystalline substances that are readily soluble in many organic solvents and insoluble in water. The structure of the bromine derivatives of acetylene dithiocarbamates was established by elemental analysis, IR and PMR spectroscopy. A probable mechanism of the interaction of 1-thiolpropargyl ethers with 1-isothioisocyanatepropargyl ethers is presented. With an increase in the nucleophilicity of the $-SH$ groups, the rates of addition and the yields of the final products increase, with a decrease in basicity and an increase in steric factors of the radicals, the rates of yield of the reaction products decrease slightly.

Comparative tests show that the test derivative of the drug 1 - [(ortho-bromobenzoate-propynyl) -1⁻ (ortho-bromobenzoate-propynyl) dithiocarbamate] showed a higher growth-promoting activity.

Key Words: derivatives, acetylene, carbamates, dithiocarbamates, esters, isothiocyanate, thiolacetylene, propargyl ethers, analysis, spectroscopy, mechanism, growth-stimulating activity.

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INTRODUCTION

In recent years, work has been carried out to find new, more effective low-toxic drugs among sulfur compounds, since the presence of a sulfur atom in the molecules of organic compounds increases pharmacological, physiological, biological activity, while reducing toxicity, and also displays antiulcer, antimicrobial, antifungal, anti-tuberculosis and other properties [1-6].

SIGNIFICANCE OF THE SYSTEM

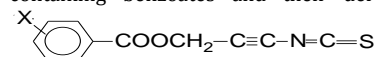
The paper mainly focuses on how the chemistry derivative of bromine acetylene dietcarbamates. The study of literature survey is presented in section III, Proposed methodology and discussion is explained in section IV, section V covers the experimental results of the study, and section VI discusses the future study and Conclusion.

LITERATURE SURVEY

It is known that acetylene, diacetylene derivatives have various types of biological activity. So, acetylene, diacetylene, thiolacetylene, thioisocyanatoacetylene esters containing aromatic and heteroatom substituents possess pesticidal,

herbicidal, fungicidal, insecticidal, growth-promoting, antitumor, anticholinergic and many other activities. [7-12].

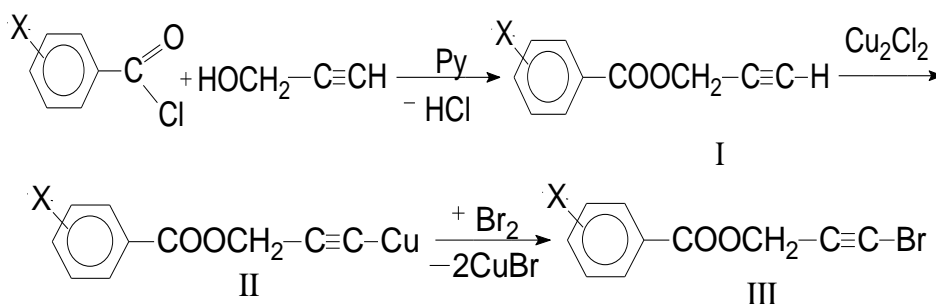
The literature [13-19] describes the synthesis of various acetylene sulfides, sulfoxides with an end triple bond. However, information on the synthesis of 1-thiolacetylene containing benzoates and their derivatives of the type

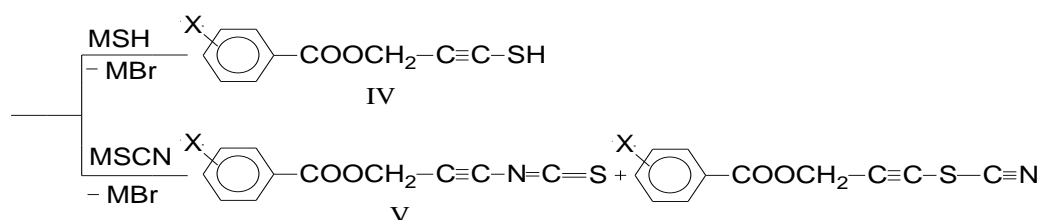


has been little studied in the literature. These little-known compounds essentially represent a new kind of compounds whose properties are hardly studied.

PROPOSED METHODOLOGY AND DISCUSSION

In this regard, we obtained 1-isothiocyanato- and 1-thiolacetylene esters of bromo-substituted benzoates. For the synthesis of this kind of isothiocyanates, thiols by reaction with thiocyanate, hydrosulfide of alkali metal, we used bromo-substituted benzoates obtained from 1-bromoacetylene esters according to the scheme:





where $X = \text{Br}$; $M = \text{Na}$; K ; NH_4^+ ; Pb^{+2} ; Ca^{+2} ;

The IV reaction was carried out in anhydrous ethyl alcohol at a temperature of 76-80 °C in an atmosphere of dry nitrogen with a yield of 79-86%.

The reaction V of the product was carried out by reacting 1-bromopropargyl ether of orthobromobenzoic acid with sodium thiocyanate at a temperature of 52-54 °C for two hours with stirring in the presence of organic solvents (acetone, ethanol).

It was found that in a dilute sodium hydrosulfide solution, the reaction mixture is weak and the yield of the target products is negligible. When using a saturated solution, the reaction proceeds selectively, easily, smoothly and the yield of the target product is much larger, the products of which have a weak characteristic odor of 1-thiols. Derivatives of 1-

isothiocyanate and 1-thiolacetylene esters of bromosubstituted benzoates are crystalline substances that are readily soluble in many organic solvents and insoluble in water.

Physico-chemical parameters of the derivatives of brominated 1-thiol and 1-isothiocyanate acetylene esters of benzoates (IV and V) are shown in table 1.

Purification of 1-isothiocyanate and 1-thiolacetylene esters, bromine-substituted benzoates was carried out using preparative thin-layer chromatography on Al_2O_3 in a benzene-hexane system (24:1). To prove the structure of 1-isothiocyanate and 1-thiol-acetylene esters of bromo-substituted benzoates, the method of IR and PMR spectroscopy was used (table 2.)

The following absorption bands are present in the IR spectrum:

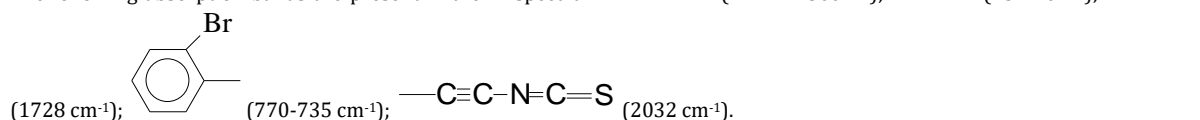
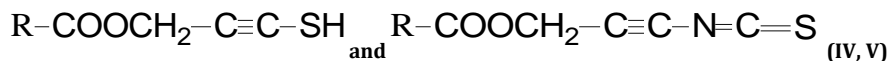


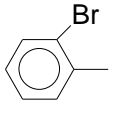
Table 1. Physicochemical parameters of preparations IV and V

№	Structural formula	Yield, %	MT, °C	R _f	Bruttoformula	Elemental analysis, %				M _M
						Calculated		Found		
						N	S	N	S	
IV		83,7	60-61	0,64	$\text{C}_{10}\text{H}_7\text{SBrO}_2$	-	11,78	-	11,79	271,46
V		80,4	119-120	0,71	$\text{C}_{11}\text{H}_6\text{SNBrO}_2$	4,73	10,83	4,57	10,77	295,6

Table 2. IR and PMR spectra



№	R-	IR spectra, cm ⁻¹					PMR spectra - δ, m.d.			
		-SH	-C≡C-	-N=C=S	-S-C≡N		-SH	-O-CH2-	Ar	
IV		2544	2222	-	-	1728	770-735	2,13	4,65	6,2-7,4

V		-	2230	2032	2145	1730	770-742	-	4,63	6,1-7,5
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The following absorption bands are present in the IR spectrum: $\text{—C}\equiv\text{C—}$ (2222-2230 cm^{-1}); —SH (2544 cm^{-1}); —C—O— (1728 cm^{-1});

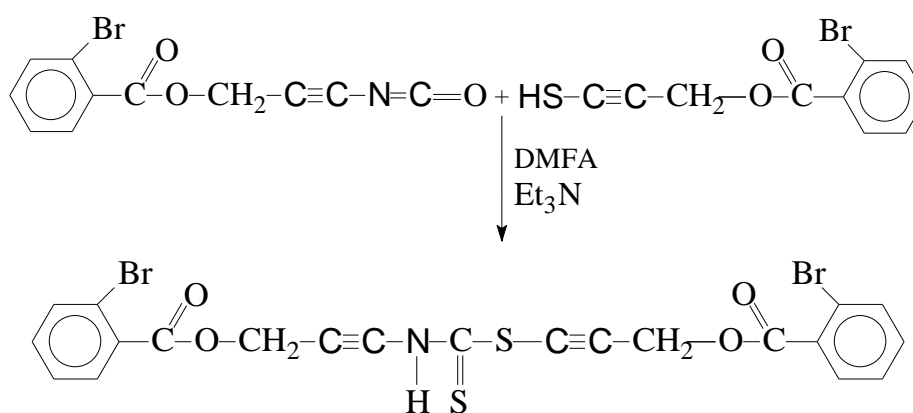
$\text{—C}\equiv\text{C—N=C=S}$ (2032 cm^{-1}); $\text{—C}\equiv\text{C—}$ (770-735 cm^{-1});

In the 1-thiolacetylene ester PMR spectra, signals that are in the range of 6,2-7,4 and 6,1-7,5 m.d. belong to the protons of the o-bromo-substituted benzene ring. signals from protons of groups $\text{—O—CH}_2\text{—}$ and —SH are at 4,65 and 2,13 m.d. respectively.

In addition, the chemical properties of 1-isothiocyanate and 1-thiolacetylene esters of bromo-substituted benzoic acid have been studied.

It was established that group —N=C=S and —SH easily react according to the A_N mechanism in the presence of dimethylformamide and triethylamine at a temperature of 78-85 °C for 5 hours with the formation of [1-(ortho-bromobenzoate-propynyl)-1-(ortho-bromobenzoate-propynyl)] - dithiocarbamate.

Chemical reaction of 1-isothiocyanate-propargyl esters of substituted benzoic acids with 1-thiol of propargyl esters of orthobromobenzoic acid was carried out as follows:



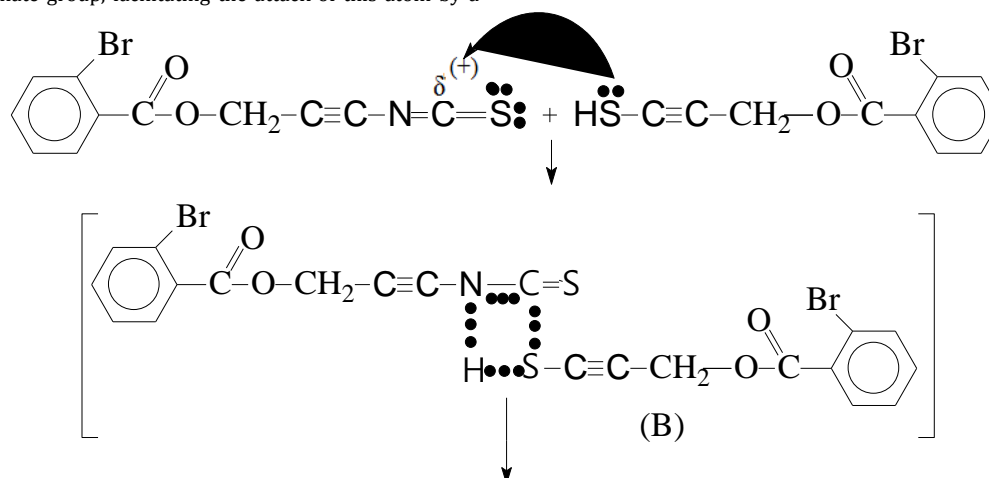
The high density, selectivity and easy mobility of the electron cloud of group $\text{—C}\equiv\text{C—N=C=S}$ determine its high reactivity. Yields of products amounted to 85%. As expected, products with good A_N reaction yields were obtained.

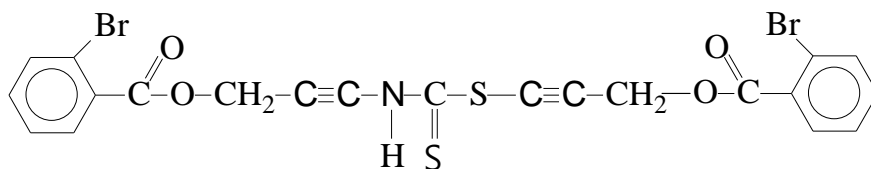
The physicochemical characteristics of the derivatives of bis-propynyl dithiocarbamates are apparently due to the high density and easy mobility of the electron cloud of the super-

conjugated ($\text{—C}\equiv\text{C—N=C=S}$) group, which leads to an increase in the positive charge on the carbon atom of the isothiocyanate group, facilitating the attack of this atom by a

nucleophilic agent, and also regarding the question is whether this occurs due to an increase in the positive charge on the carbon atom or due to the stabilization of the transition state.

However, in our cases, the —SH thiol group, having a free pair, attacks the electrophilic center in the 1-isothiocyanate molecule of propargyl ethers with the formation of intermediate product (B), which then regroups into the final reaction product. Based on our assumptions and published data, the probable mechanism for the interaction of 1-thiolpropargyl ethers with 1-isothioisocyanate propargyl ethers can be represented by the scheme:




Table 3. Physico-chemical parameters of the dithiocarbamate derivative (V)

Nº	Structural formula	Yield, %	MT, °C	R _f	M _n
V	 [1-(ortho-bromobenzoate-propynyl)-1-(ortho-bromobenzoate-propyn)]-dithiocarbamate.	84,5	177-178	0,71	554,92

The structure was established by IR spectroscopy and elemental analysis.

Some characteristics and spectral data of the derivative of bis- (propynylbenzoates) substituted dithiocarbamates (V) are shown in table 4.

Table 4. IR and PMR spectra

Nº	IR spectra, cm ⁻¹						Brutto formula	PMR spectra - δ, m.d.			
								Calculated		Found	
								N	S	N	S
V	1126	2220	1730	770-735	1112	1008	C ₂₁ H ₁₃ S ₂ Br ₂ NO ₄	2,46	11,31	2,34	11,25

With an increase in the nucleophilicity of -SH groups (in the presence of Et₃N or Py), the addition rates and yields of the final products increase; with a decrease in basicity and an increase in steric factors of the radicals, final product yields rates decrease slightly.

The structure of the first synthesized derivative of bis-[(propynyl-benzoate)-substituted dithiocarbamate] (V) was established by IR spectroscopy and confirmed by elemental analysis.

In the IR spectra of the derivative of bis [(propynyl bromobenzoates) dithiocarbamates], the absorption band of the stretching vibrations of the -NHCS groups (1126 cm⁻¹) is

characteristic; groups (1720 cm⁻¹); groups (1008 cm⁻¹); and groups (2220 cm⁻¹).

EXPERIMENTAL PART

Synthesis of propargyl ether 0-bromobenzoate

2,15 g (0,01 mol) of orthobromobenzoic acid and 10 ml of absolute propinol are placed in a flask. Then 1,58 g of tetrachlorosilicon is added, the reaction mixture is heated to boiling for 30 minutes.

Propargyl ether of orthobromobenzoic acid is obtained with a yield of 2,17 g (91 % of theory); M_p = 74-75 °C

Found, %: C 50,21; H 2,87; Br 33,19.

Calculated for C₁₀H₇BrO₂, %: C 50,23; H 2,92; Br 33,30.

Synthesis of 1-bromopropargyl ether of ortho-bromobenzoate (a)

1-copper of orthobromobenzoic acid propargyl ether was placed in a two-necked flask equipped with a stirrer and 100

ml of dry diethyl ether was added dropwise. 1,6 g (0,01 g mol) of liquid bromine was added dropwise added with vigorous stirring. Then the reaction mixture was still stirred for 2 hours at room temperature. After this time, the contents of the flask were filtered off and the filtrate was evaporated. 1-bromo propargyl ether of orthobromobenzoic acid is a crystalline substance of light cream color.

The product yield is 2,84 g (89,4% of theory). M_p = 54-55°C.

Found, %: C 37,63; H 1,76; Br 50,09.

Calculated for C₁₀H₆Br₂O₂, %: C 37,74; H 1,88; Br 50,26.

1-bromo PE ortho-bromobenzoate (b)

2,15 g (0,01 mol) of orthobromobenzoatepropargyl ether in 50 ml of dioxane and a freshly prepared solution of sodium hypobromite (8 g of sodium hydroxide, 40 ml of water, 75 g of crushed ice, 2,5 g of bromine) were stirred for 9 hours. Orthobromobenzoate 1-bromopropargyl ether was synthesized at 20-25 °C according to the known method [20] with a melting point of 54-55 °C.

The yield is 2,84 g (89,4% of theory).

Found, %: C 37,63; H 1,76; Br 50,09

Calculated for C₁₀H₆Br₂O₂, %: C 37,74; H 1,88; Br 50,26

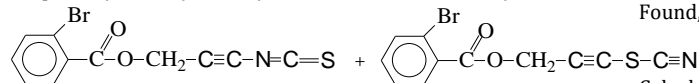
1-isothiocyanate of propargyl ether of ortho-bromobenzoate

3,2 g (0,01 mol) of 1-bromo-propargyl ether of ortho-bromobenzoate with 108 ml of absolute acetone is placed in a three-necked flask with a capacity of half a liter, equipped with a mechanical stirrer, reflux condenser and dropping funnel; alcohol solution of sodium thiocyanate 10,53 g (0,13 mol) and 100 ml of absolute ethanol are added dropwise gradually with stirring. The reaction mixture is heated to a temperature of 52-54 °C in a water bath for 2 hours with stirring.

Then the contents of the flask are transferred to a separatory funnel, diluted with 100 ml of water and extracted twice with

ether. The extracts were combined, dried over $MgSO_4$ and the ether was evaporated. The product recrystallized from methanol has a mp. = 117-118 °C. The obtained target (V) product after TLC on Al_2O_3 has a melting point of 119-120 °C. The yield of 1-isothiocyanate is 80,4 % and 10,6 % of the isomer.

IR spectra(ν , cm^{-1}): 2032 ($-C\equiv C-N=C=S$).



	80,4%					10,6%				
Found, %:	C	N	H	S	Br	C	N	H	S	Br
	44,4	4,5	2,0	10,6	26,8	4,7	8;	1;	9;	8.
Calculated for $C_{11}H_6BrS$	C	N	H	S	Br					
NO_2 , %:	44,6	4,7	2,0	10,8	27,0	0;	3;	6;	3;	1.

1-thiolpropargyl ether of ortho-bromobenzoate

3,18 g (0,01 mol) of 1-bromopropargyl ether of ortho-bromobenzoate with 55 ml of absolute ethanol and 0,56 g (0,01 mol) of freshly prepared NaSH are mixed with vigorous stirring in a nitrogen atmosphere at 30-35 °C in a four-necked flask with a capacity of 300 ml equipped with a stirrer, thermometer, gas pipe and a reflux condenser with a calcium chloride pipe. To obtain high yields, the reaction mixture is kept at 70 °C for three hours. The mixture was cooled, acidified with 5% HCl and extracted with sulfuric ether and dried. The yield of 1-thiol PE ortho-bromobenzoate is 2,25 g (80,7%). Mp. = 40-41 °C.

Found, %:	C	H	S	Br
	44,04	2,48	11,68;	Br29,34
	;	;		
Calculated for $C_{10}H_7SBr$	C <td>H <td>S</td> <td>Br</td> </td>	H <td>S</td> <td>Br</td>	S	Br
O, %:	44,19	2,57	;	Br29,43
	;	;		

[1- (ortho-bromobenzoate-propynyl) -1¹- (ortho-bromobenzoate-propynyl) -dithiocarbamate]

2,4 g (0,01 mol) of 1-thiolpropargyl ether of ortho-bromobenzoate in 30 ml of DMF are placed in a 0,25 L four-necked flask equipped with a stirrer, thermometer, dropping funnel and a reflux condenser with a calcium chloride tube. The reaction mixture is heated in a glycerin bath to 38-45 °C. 3,12 g (0,01 mol) of 1-isothiocyanate of propargyl ether of orthobromobenzoate in 35 ml of DMF is added in small

portions with continuous stirring. The reaction mixture was kept at 86-87 °C for 5 hours. At the end of the reaction, the mixture is cooled, 115 ml of water are added and extracted with sulfuric ether (2-3 times). The ether extract is washed several times with water and dried over anhydrous $CaCl_2$, the obtained target product after TLC on Al_2O_3 has a melting point of 157-158 °C.

The yield of the product is 4,88 g (90,1% of theoretical).

Found, %:	C	H	N	S	Br
	44,3	2,8	2,3	11,2	28,2
	4;	6;	3;	5;	1.
Calculated for $C_{21}H_{13}S_2N$	C <td>H <td>N <td>S <td>Br</td> </td></td></td>	H <td>N <td>S <td>Br</td> </td></td>	N <td>S <td>Br</td> </td>	S <td>Br</td>	Br
Br_2O_4 , %:	44,4	2,9	2,4	11,3	28,1
	5;	9;	6;	1;	8.

CONCLUSION AND FUTURE WORK

To identify the growth-promoting activity of compounds 1 - [(ortho-bromobenzoate-propynyl) -1¹- (ortho-bromobenzoate-propynyl) dithiocarbamate] with the provisional name (AGM-96), tests were carried out in the laboratory of the Institute of Plant Chemistry of the Academy of Sciences of the Republic of Uzbekistan in laboratory conditions, vegetable seeds and cotton seeds served as biotests.

The experiments used cucumbers of the Uzbekistan-740 variety, tomatoes of the Temp variety and medium-fiber cotton of the S-6524 variety. The preparations were dissolved in DMF, the presowing method of seed sowing was used for 18-20 hours. The concentrations used were 0,1; 0,01; 0,001; 0,0001 and 0,00001 %%. The repetition of the experiments is 4-fold. The counts were carried out by measuring the length of the stem and root of 10-day-old seedlings of cotton. It was noted that all preparations tend to stimulate the growth of the root system of young seedlings, both vegetable crops and cotton.

Primary screening was performed according to the method of Yu.V. Rakitina. This method allows you to quickly determine the degree of physiological activity of new chemical compounds, which is detected by stimulation or inhibition of germination of plant seeds, as well as by changing the length of the roots and the length of the stem part. The preparations were tested by seed locking in solutions of various concentrations, followed by germination in Petri dishes. Control seeds were soaked in distilled water.

Each series of experiments is accompanied by control. In control variants, only a pure solvent is added to the nutrient medium. The result of the experiments is recorded after 3,5,7 and 10 days after inoculation (tables 5-7).

Table 5. The effect of the preparation AGM-96 on the germination of seeds and the growth of seedlings of cotton variety "S-6524"

Experiences A drug	Concentration, %	Germination, %	Cotton	
			Rootgrowth	Stem growth
Control - water	without	80,0	100,0	100,0
[1- (ortho-bromobenzoate-propynyl) -1 ¹ - (ortho-bromobenzoate-propynyl)] - dithiocarbamate.	0,1	86,8	112,0	109,0
	0,01	84,3	111,0	111,3
	0,001	87,4	128,7	116,4
	0,0001	81,0	116,5	109,0
	0,00001	80,0	120,7	113,4
«Rostlin» (famous)	0,75-1,0	80,0	104,1	102,4

Table 6. The effect of the drug AGM-96 on the germination of seeds and the growth of seedlings of cucumbers varieties "Uzbekistan-740"

Experiences A drug	Concentration, %	Germination, %	Cucumbers	
			Rootgrowth	Stem growth
Control - water	without	100,0	100,0	100,0
[1- (ortho-bromobenzoate-propynyl) -1 ¹ - (ortho-bromobenzoate-propynyl)] - dithiocarbamate.	0,1	100,0	105,5	107,4
	0,01	100,0	108,3	111,6
	0,001	100,0	116,7	110,6

	0,0001	100,0	119,6	113,4
	0,00001	100,0	127,7	115,6
«Rostlin» (famous)	0,75-1,0	100,0	103,4	101,4

Table 7. The effect of the drug AGM-96 on seed germination and growth of seedlings of tomato varieties "Temp".

Experiences A drug	Concentration, %	Germination, %	Tomatoes	
			Rootgrowth	Stem growth
Control - water	without	50,0	100,0	100,0
[1- (ortho-bromobenzoate-propynyl) -1 ¹ - (ortho-bromobenzoate-propynyl)] - dithiocarbamate.	0,1	50,0	106,3	116,6
	0,01	56,4	115,3	121,7
	0,001	57,3	139,6	125,4
	0,0001	49,8	114,5	107,7
	0,00001	53,3	119,3	106,4
«Rostlin» (famous)	0,75-1,0	52,1	101,7	100,4

Comparative tests also show that the test drug AGM-96, i.e. derivative 1 - [(ortho-bromobenzoate-propynyl) -1¹- (ortho-bromobenzoate-propynyl) -dithiocarbamate], showed higher growth-promoting activity at a lower concentration (from 7,5 to 75000 times) than currently used in many agriculture industries of Uzbekistan, the drug "Rostlin".

The drug AGM-96 on cotton culture showed biological activity at a concentration of 0,00001 % (diluted 75,000 times), stimulated root growth of 120,7 %, and stem growth of 113,4 % higher than the control and the well-known drug Rostlin (concentration 0,75 -1,0).

The drug AGM-96 on tomatoes, similar to previous cultures, showed a very high biological activity of 119,3 % at a concentration of 0,00001 % (even 75,000 times diluted).

The drug AGM-96 on cucumber culture also showed biological activity at a concentration of 0,00001 % (i.e. 75,000 times diluted), promoted root growth by 127,7 %, somewhat lower - stem growth 115,6 % higher than control and the well-known drug "Rostlin" (concentration 0,75-1,0 %).

Thus, the low-toxic (LD₅₀ = 2450 mg / kg) preparation AGM-96 showed high stimulating properties on the seeds of tomato, cucumbers and cotton at 0,00001% concentration.

The results of determining the growth-promoting activity of compound 1 - [(ortho-bromobenzoate-propynyl) -1¹- (ortho-bromobenzoate-propynyl) dithiocarbamate] are presented in tables 5,6,7.

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