

SYNTHESIS, PROPERTIES AND BIOLOGICAL ACTIVITY OF L-BORNEOLA CARBHAMATE DERIVATIVE

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Abstract

The chemical properties of the L-borneola carbamate derivative have been synthesized and studied. It is given description of the technological process and its scheme, chemical transformations of N,N¹-tetramethylene bis [(L-borneoylo) carbamate], reactions of N,N¹-chlorination, nitrozoation, metallation and alkylation, the growth-stimulating activity of N, N¹-tetramethylene bis [(L-borneoyl) carbamate] are studied.

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1. Introduction

A new search in almost all fields of technology, especially in agriculture, revealed some derivatives of carbamates, which have various activities and are used, for example: as a foam plastic [1]; as high-melting compounds [2]; as an antifouling agent [3]; in emulsions for photographic films [4]; as a stable adhesive [5]; good surface coverage [6]; It is known that carbamate derivatives increase the photosensitivity of polymers in 20-50 times [7]. In addition, carbamates were used as fungicidal agents for the processing of textiles, hides, furs, skins, and also in detergents and cleaning agents [8-12]; and especially as a biostimulant in cotton growing, plant growing, technical crops and many other cultures [13-20].

This list can be continued, since the field of application of derivatives of carbamates, polyurethanes, enamels is wide.

Therefore, the search and synthesis, as well as the technologies for obtaining derivatives of carbamates, bis-carbamates, are an actual task of modern organic, bioorganic and physiological activity chemistry.

2. Research Method

The object of the study was the derivatives of N,N¹-tetramethylene bis [(L-borneoylo)-carbamate]. Their physical and chemical properties, biostimulating activity were studied. IR spectra recorded on a VR-20 spectrometer in KBr tablets. The identity of N,N¹-dinitrozo-N,N¹-tetramethylene bis [(L-borneoylo)-carbamate] was established by TLC on "Silifol" plates.

3. Results and Analysis

The method we developed for the preparation of N,N¹-tetramethylene bis [(L-borneoyl) carbamate] consists in the nucleophilic addition of (A_N) L-borneol to tetramethylene diisocyanate at temperatures of 26-42 °C in the presence of a solvent and catalyst (base), filtration and drying at temperature 150-155 °C.

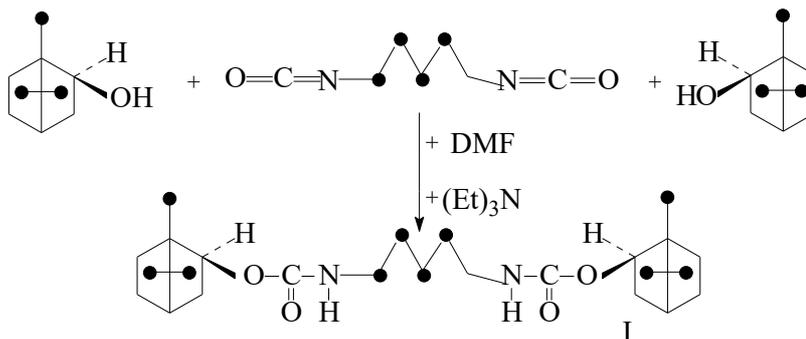
During the preparation of N, N¹-tetramethylene bis [(L-borneoylo) carbamate], gaseous and solid wastes are not formed, and the catalyst after regeneration is used in the following operations.

The final finished compound N, N¹-tetramethylene bis [(L-borneoylo) carbamate] is a colorless powder with a melting point of 167-168 °C, is soluble in DMSO, DMF, DMAS and other organic solvents.

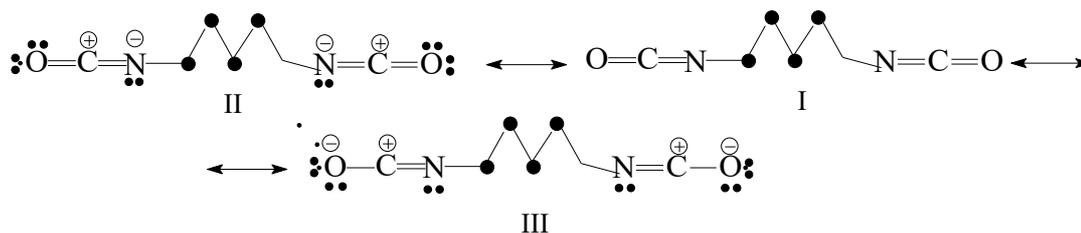
Description of the technological process and its scheme.

The non-waste method for obtaining a plant growth regulator involves the synthesis of N, N¹-tetramethylene bis [(L-borneoylo) carbamate] by reacting tetramethylene diisocyanate with L-borneol in the presence of the (Et)₃N base catalyst and the universal dimethylformamide solvent:

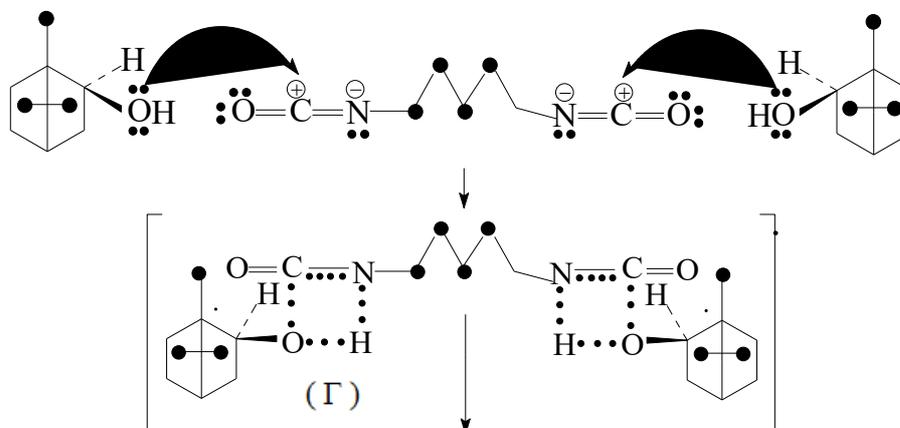
Chemistry process:

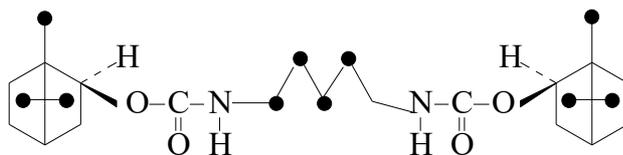


The chemical behavior of N, N¹-tetramethylene diisocyanate most fully agrees with such a distribution of electron densities in the $\text{—N}=\overset{\oplus}{\text{C}}=\overset{\ominus}{\text{O}}$ group, which is described by the conjugation of the following structures:



Nitrogen and oxygen in the $\text{—N}=\overset{\oplus}{\text{C}}=\overset{\ominus}{\text{O}}$ group carry mainly a negative charge and possess electron-donating and electrophilic attacks. In some cases, diisocyanates can also play the role of electrophilic agents. The most typical reactions for them are nucleophilic additions with the participation of oxygen- and nitrogen-containing substances. The HO-group of the L-borneol, having a free electron pair, attacks the electrophilic center in the molecule of tetramethylene diisocyanate to form an intermediate process (Γ), which is rearranged into bis-carbamate:





Description of the technological process for N,N'-tetramethylene bis [(L-borneoylo) carbamate].

The technological scheme of the production of N,N'-tetramethylene bis [(L-borneoylo) carbamate] is shown in the figure 1.

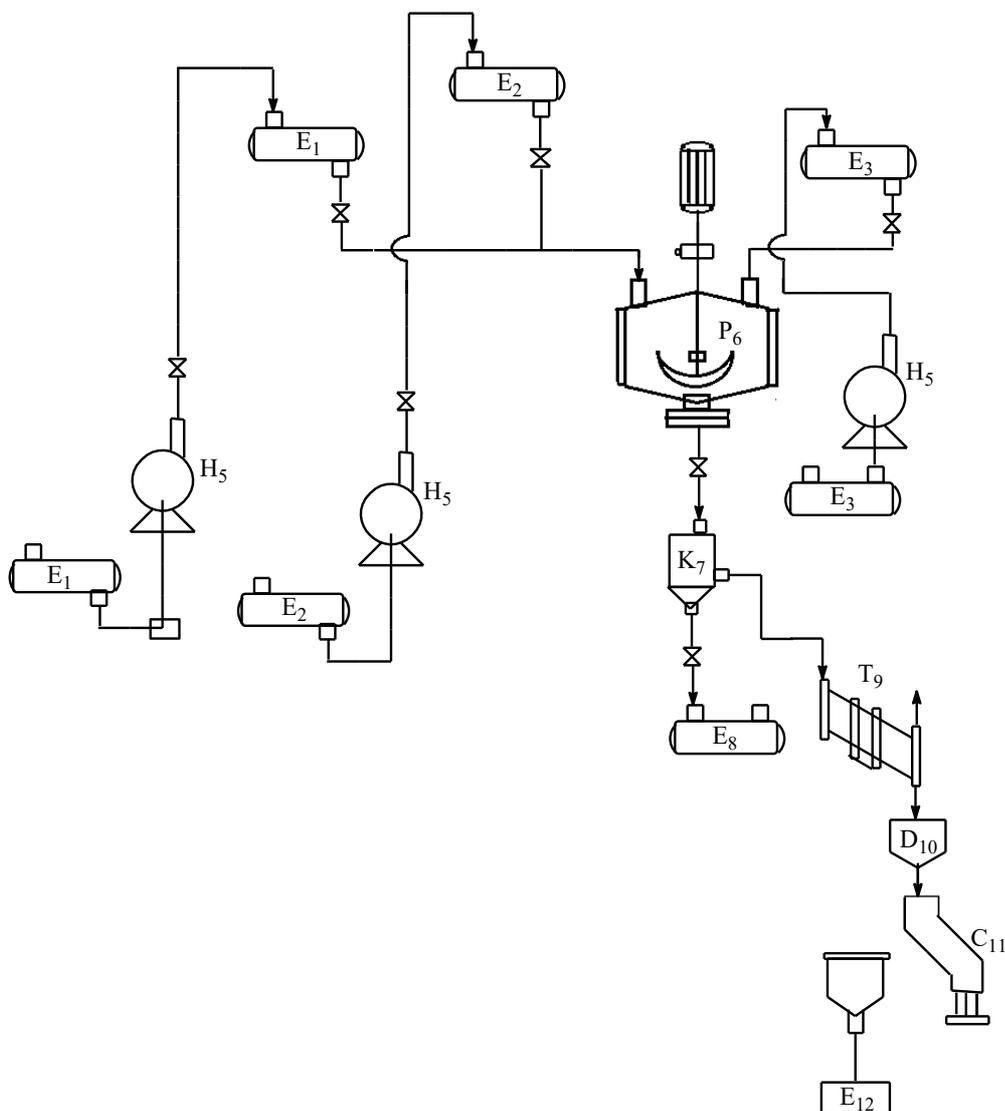


Figure 1. Technological scheme of production of tetra methylene bis - [(L-borneoylo) carbamate]: E₁, E₂, E₃-capacities for TMDI, L-borneoyl, DMF and (C₂H₅)₃N; H₅-pump; P₆-reactor; K₇-nutch filter; E₈-capacity for spent solvent and catalyst; T₉-drum dryer; D₁₀ is a crusher; C₁₁-vibrating screen; E₁₂-the capacity for the finished product.

The operational quantities of L-borneol, TMDI, DMF and (C₂H₅)₃N are loaded into the reactor P₆ from the capacities E₁ to E₃. The mixture was stirred at room temperature for 3,5-4 hours. The precipitated white crystals are filtered off in a K₇ filter. A mixture of DMF and catalyst [(C₂H₅)₃N or P_y] is collected in a vessel of E₈. The final reaction product and the snow-white crystals are dried in a T₉ drum dryer, then fed to a D₁₀ crusher and screened for C₁₁. The finished product is packed in polyethylene barrels with a capacity of 20-200 dm³.

We need to emphasize that during the technological process of obtaining N,N'-tetramethylene bis [(L-borneoylo) carbamate], the interaction of N,N'-tetramethylene diisocyanate with L-borneol proceeded

without the release of harmful by-products (CO, NO, Cl₂, HCl, HCN, H₂S, etc.). The synthesis technology was carried out in a medium of dimethylformamide at a temperature of 28 °C (without heating) for 3,5- 4 hours. It should be noted that new derivatives of N,N¹-tetramethylene bis [(L-borneoylo) carbamate], ecologically clean, white crystals with rather high yields were obtained without waste.

Physico-chemical parameters of N,N¹-tetramethylene bis [(L-borneoylo) carbamate] (I) are given in Table 1.

Table 1. Physico-chemical parameters of the preparation (I)

Structural formula	Output, %	T _{pl} , °C	R _f	Gross formula	Elemental analysis, %		M _M
					Calculated	Found	
					N	N	
	97,2	167-168	0,72	C ₂₆ H ₄₆ N ₂ O ₄	6,22	6,06	450

The structure of N,N¹-tetramethylene bis [(L-borneoylo)-carbamate] was confirmed by elemental analysis data, as well as by IR spectroscopy.

In the IR spectrum of N,N¹-tetramethylene bis [(L-borneoylo)-carbamate], there is a broad absorption

band in the 1717 cm⁻¹ region, characteristic for the groups, and the absorption band in the 1616-1575 cm⁻¹ region corresponds to the absorption of the NHCOO- bond, a strong absorption band in the 3248 cm⁻¹ region is characteristic for N-H groups.

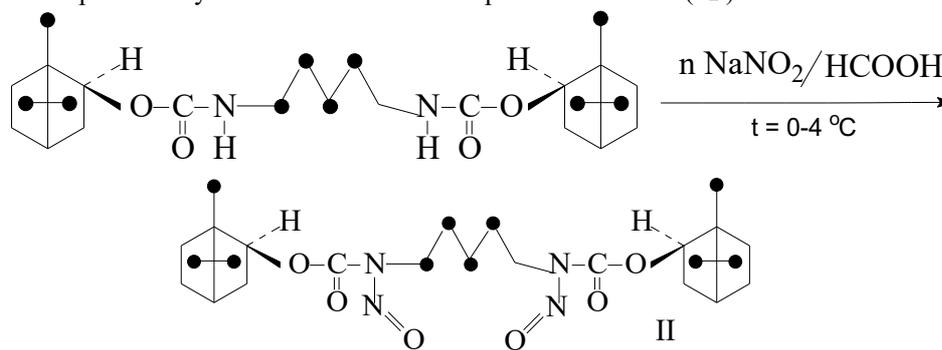
To study the reactivity of the N, N¹-tetramethylene bis [(L-borneoylo)-carbamate] reaction centers, we performed rare reactions: N, N¹-dinitrozozirovaniya, N, N¹-dichlorination and N, N¹-dialkylation.

Chemical transformations of N,N¹-tetramethylene bis [(L-borneoylo)- carbamate].

The reactions of N, N¹-dinitrozoization of bis [(alkyl, aryl-, cycloalkyl)-carbamate] derivatives have been relatively poorly studied in the world literature [23-27].

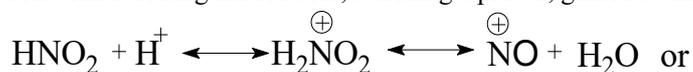
According to the published data and the data of our own studies, N-nitrozozirovaniya reacts with nitrogen atoms directly bound to the polymethylene $(-CH_2)_n$ chain.

As a result of the reaction of N, N¹-dinitrozozirovaniya of N,N¹-tetramethylene bis [(L-borneoylo)-carbamate] (I) with NaNO₂ (in excess) in 98% HCOOH at 0-4 °C there were obtained N, N¹-dinitrozo-replaced by N, N¹-tetramethylene bis [(L-borneoylo)-carbamate] in a high yield of 81.3%. N,N¹-dinitrozozirovaniya proceeds by the mechanism of electrophilic substitution (S_E).



The attacking agent is the nitrosonium —NO^+ ion. Since nitrous acid, which is the most common nitrosizing agent, does not exist in a free form, sodium nitrite and a strong acid (HCOOH) are used for the

process. The resulting nitrous acid, attaching a proton, generates an —NO^+ ion:



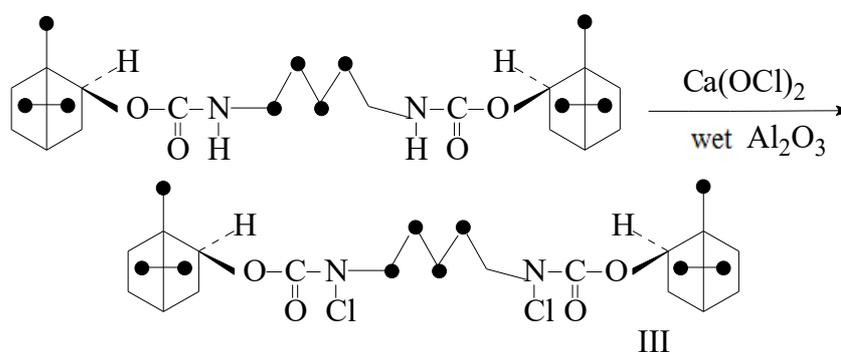


N_2N^1 -dinitrozoation is conducted while cooling the reaction mixture. The increase in temperature is undesirable, since this reduces the yield of the desired product, and sometimes affects the direction of the reaction. Identification of N_2N^1 -dinitrozo compounds is carried out on the band absorption $\text{N}=\text{N}=\text{O}$ bands. A strong band in the $1500\text{-}1420\text{ cm}^{-1}$ region is typical for $\text{N}=\text{N}=\text{O}$ groups.

Preparation of N_2N^1 -dichlorination of the preparation (I).

Derivatives bis- borneoylocarbamate are the most valuable raw material for the further synthesis of various biologically active compounds used in engineering, agriculture, and also have a high reaction center ($\text{N}-\text{H}$ groups) for the reactions of nucleophilic and electrophilic substitutions.

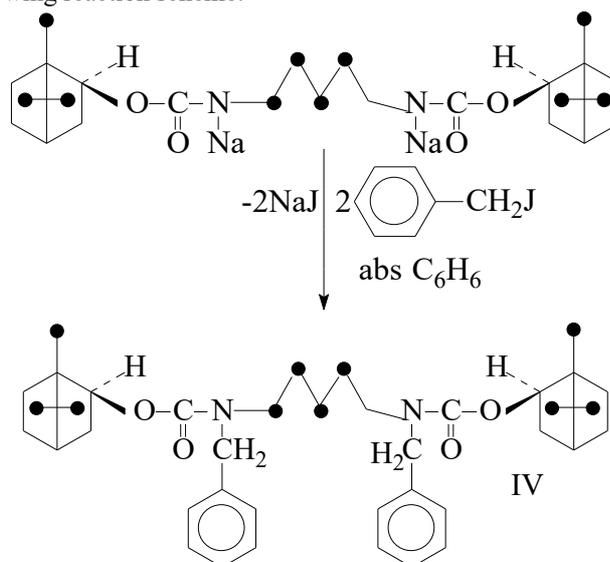
We have developed an effective, affordable, cheap, stable and environmentally friendly method for the N_2N^1 -dichlorination of bis-carbamate with calcium hypochlorite on wet aluminum oxide:



The yield of compounds (III) is 91,5%; $T_m = 184\text{-}185\text{ }^\circ\text{C}$.

Preparation of N_2N^1 -dibenzyl substituted of the derivatives of the preparation (I).

Dibenylation on $\text{N}-\text{H}$ groups in biscarbamates (I) with benzyliodides is of undoubted interest for establishing the reactivity of the compounds containing (I). Benzylation reactions were carried out by the reaction of N_2N^1 -disodium derivatives of N_2N^1 -tetramethylene bis [(L- borneoylo)-carbamate] with benzyl iodide in anhydrous benzene at $28\text{-}32\text{ }^\circ\text{C}$ and benzyl iodide was added dropwise with stirring during 3,0-3,5 hours according to the following reaction scheme:



The flow of the benzylation reaction solely at the nitrogen atom N_2N^1 is apparently due to the relatively easy dissociation of sodium in this atom due to the presence of neighboring carbonyl groups. The yield of the preparation (IV) was 95,6 %. Physico-chemical parameters IV are given in Table 2.

Table 2. Physico-chemical parameters of compounds (IV)

Structural formula	Output, %	T _{P1} , °C	R _f	Gross formula	Elemental analysis, %		M _M
					Calculated	Found	
					N	N	
	95,6	203-204	0,64	C ₄₀ H ₅₆ N ₂ O ₄	4,45	4,29	628

EXPERIMENTAL PART

Synthesis of N, N¹-tetramethylene bis [(L-borneoylo) carbamate] (I).

30,8 g (0,2 mol) of L-borneol was added to a three-necked flask equipped with a reflux condenser, a thermometer, a stirrer, 14 ml of trimethylamine, 60 ml of DMF is added there at room temperature 28-30 °C, 14,0 g (0,1 mole) of tetramethylene diisocyanate dissolved in 20 ml of DMF is added with stirring, dropwise. The reaction mixture is stirred for 3 hours at a reaction mixture temperature of 36-41 °C. After the time has passed, the contents of the flask are transferred to a glass, water is added. The precipitate was washed with TLC. After drying, a colorless powder is obtained, the yield (I) is 43,55 g (97,2 % of theoretical); T_m = 167-168 °C; R_f = 0,72. Found, %: C 69,16; H 9,84; N 6,06. Calculated for C₂₆H₄₆N₂O₄, %: C 69,35; H 10,02; N 6,22



Synthesis of N, N¹-dinitrozo-N, N¹-tetramethylene bis [(L-borneoylo) carbamate] (II).

4,50 g (0,01 mol) of N, N¹-tetramethylene bis [(L-borneoylo)-carbamate] dissolved in 100 ml of formic acid are placed in a three-necked flask equipped with a reflux condenser, thermometer, and stirrer. With constant stirring at 0-4 °C, 0,5 g of sodium nitrite is added in portions over a period of 3,5-4,0 hours. After the end of the reaction, the contents are poured into a liter jar, 250 ml of cold water are added, and a precipitate begins to precipitate. The precipitate is filtered off, washed with benzene and dried. The identity of N, N¹-dinitrozo-N, N¹-tetramethylene bis [(L-borneoylo)-carbamate] was established by TLC on "Silifol" plates. Yield: II - 4,13 g (81,3 %); T_m = 223-225 °C (dec), R_f = 0,68. Found, %: C 61,48; H 7,93; N 11,01. Calculated for C₂₆H₄₆N₄O₆, %: C 61,66; H 8,03; N 11,06.

Synthesis of N, N¹-dichloro-N, N¹-tetramethylene bis [(L-borneoylo)-carbamate] (III).

4,50 g (0,01 mol) of N, N¹-tetramethylene bis [(L-borneoylo)-carbamate], 40 ml of CCl₄, 22 g of wet alumina are placed in a three-necked flask equipped with a reflux condenser with a chloroalkate tube, an autosolver, a thermometer, and 4,5 g of calcium hypochlorite are added dropwise at a temperature of 40 °C for 1 hour. The reaction mixture is then allowed to stand for 20 hours, filtered, and the residue is washed with ether and with an alcohol. Then the mixture is dried and N, N¹-dichloro-N, N¹-tetramethylene bis [(L-borneoylo)-carbamate] is obtained. The yield is (III).- 4,75 g (91,5% of theory). T_m = 184-185 °C; R_f = 0,71. Found, %: C 59,93; H 8,31; N 5,28; Cl 13,48. Calculated for C₂₆H₄₆Cl₂N₂O₄, %: C 60,11; H 8,47; N 5,39; Cl 13,68.

To prove the structure of N, N¹-dichloro-substituted N, N¹-tetramethylene bis [(L-borneoylo)-carbamate], an elemental analysis of silver salts (AgNO₃ solution) was carried out.

Synthesis of N, N¹-disodium of substituted (I).

In CH₃ONa (from 0,031 g / mol Na and 30 ml abs. CH₃OH) 4,5 g (0,01 mol) of I are added. The mixture is stirred for 2 hours at 20 °C and 2 hours at 40 °C, the precipitate is filtered off and washed with abs. CH₃OH to give the product. The yield is 86,4%; T_m = above 330 °C (dec.)

Synthesis of N, N¹-dibenzyl substituted (I) (IV).

4,91 g (0,01 mole) of N, N¹-disodium substituted (I) in 14 ml of DMF are charged with 4,4 ml (0,02 moles) of benzyl iodide dropwise with stirring. The mixture is stirred for 10 hours with heating in a boiling water bath, cooled and added with 25 ml of water, the precipitate is separated, recrystallized from 30 % alcohol, dried and yielded (IV) in a yield of 95,6 % (theoretical) = 203-204 °C, R_f = 0,69. Found, %: C 76,33; H 8,71; N 4,29. Calculated for C₂₆H₅₆N₂O₄, %: C 76,43; H 8,91; N 4,45.

Field tests for the growth-stimulating activity of the preparation (I)

After the initial tests for the growth-stimulating activity of the preparation (I), field tests were conducted on S.Azamov's farm in the Kasbinsk fog of the Kashkadarya region, as well as in a number of farms in the Andijan and Navoi regions of Uzbekistan: from April to November 2017.

The first bioregulator (I), in particular N, N¹-tetramethylene bis [(L-borneoyl) carbamate] (I) was tested at a concentration of 0,001% (i.e., diluted 750). Cucumbers of "Uzbekistan-740" variety, "Temp" varieties, medium-fiber cotton "6524", as well as various varieties of maize, sunflower and melons on an area of 2849 hectares were used in the farm. An additional 11205 tons of cotton was received, which is about 4,2 billion soums only for cotton growing. Similarly interesting results were obtained on cucumbers, sunflowers, soybeans, corn and tomatoes.

Thus, the drug (I), recommended by us in a solution of 0,001% concentration, exceeds many known preparations in biostimulating activity and is even less toxic (LD₅₀ = 3749 mg / kg).

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