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N, N¹ - TETRAMETHYLENE BIS - [(n- HEXANOYL) -CARBAMATE]: Synthesis, Properties and Its Application

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ABSTRACT: The proposed article relates to organic chemical synthesis and the study of derivatives of N, N¹-tetramethylene bis - [(n-hexanoyl) carbamate]. Chemical properties and reactions of N, N¹- dinitrozosation, N, N¹ – dichlorination, and N, N¹ – dialkylation were studied. The results of the biological activity of derivatives of N, N¹-tetramethylene bis - [(n-hexanoyl) carbamate] were obtained. The preparation, recommended by us in a solution, surpasses many known drugs in biostimulating activity and is even less toxic. The ways of practical application of derivatives N, N¹-tetramethylene bis - [(n-hexanoyl) carbamate] are outlined.

KEY WORDS: Organic synthesis, Derivatives, Carbamate, Hexamethylene, Reactive centers, Electrophilic substitution mechanism, N,N¹- dichlorination, dinitrozosation, dibenzylation, Field test.

I. INTRODUCTION

Research in the field of derivatives of carbamates and bis-carbamates, currently conducted, has gained particular development in the chemistry of synthetic organic compounds. A significant role is given to derivatives of carbamate and bis-carbamate, which have various technical, biological and pharmacological activity, which are of undoubted interest from a practical point of view.

II. SIGNIFICANCE OF THE SYSTEM

The paper mainly focuses on how the chemistry derivatives of tetramethylenebis -(n-hexanoyl)-carbamates compounds. 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.

III. LITERATURE SURVEY

A modern search in almost all areas of technology, especially in agriculture, has revealed some carbamate derivatives that have diverse activity and are used, for example, as foam [1]; as high melting compounds [2]; as antifouling agents [3]; in emulsions for photographic films [4]; as a resistant adhesive [5]; good surface coverage [6]; It is known that carbamate derivatives increase the photosensitivity of polymers by 20-50 times [7]. In addition, carbamates derivatives were used as fungicidal agents for processing textiles, hides, furs, leather, as well as in detergents and cleaners [8-15]; and especially as a biostimulant, in cotton growing, crop production, industrial crops and many other crops [16-23]. This list can be continued, since the scope of derivatives of carbamates, polyurethanes, enamels is very wide.

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

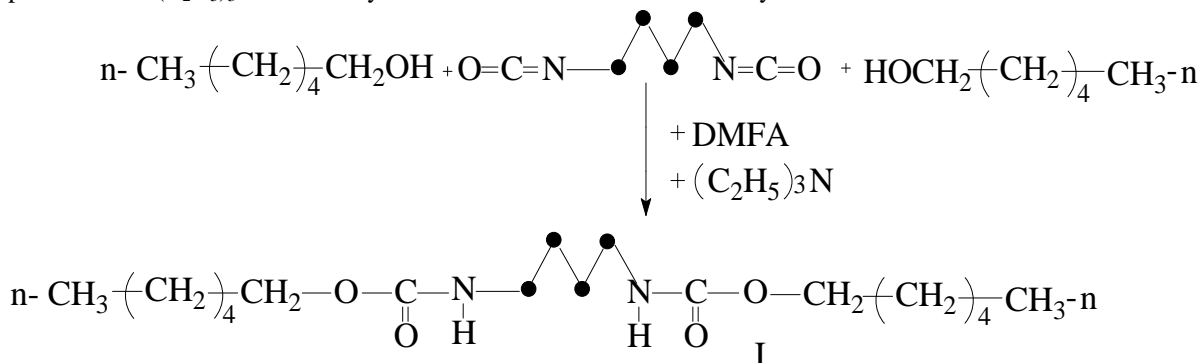
Our method of obtaining N, N¹-tetramethylene bis - [(n-hexanoyl) carbamate] consists in the nucleophilic addition of (A_N) n-hexanol to tetramethylenediisocyanate at temperatures of 26-45 °C in the presence of a solvent and a catalyst (base), filtering and drying at a temperature of 148-150 °C.

In the process of obtaining N, N¹ -tetramethylenebis - [(n-hexanoyl) carbamate] gaseous and solid wastes are not formed, and the catalyst after regeneration is used in the following operations.

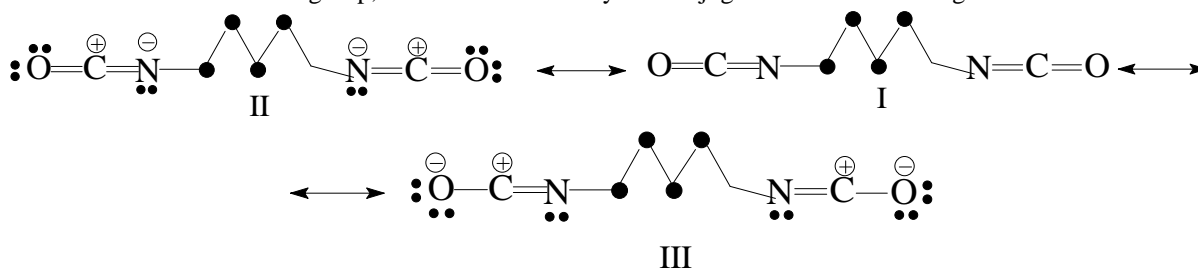
The final finished compound N, N¹-tetramethylene bis - [(n-hexanoyl) carbamate] is a colorless powder with a melting point of 256-258 °C, it is soluble in DMF, DMAS, DMSO, dioxane, nitrobenzene and other organic solvents.

Description of the technological process and its scheme.

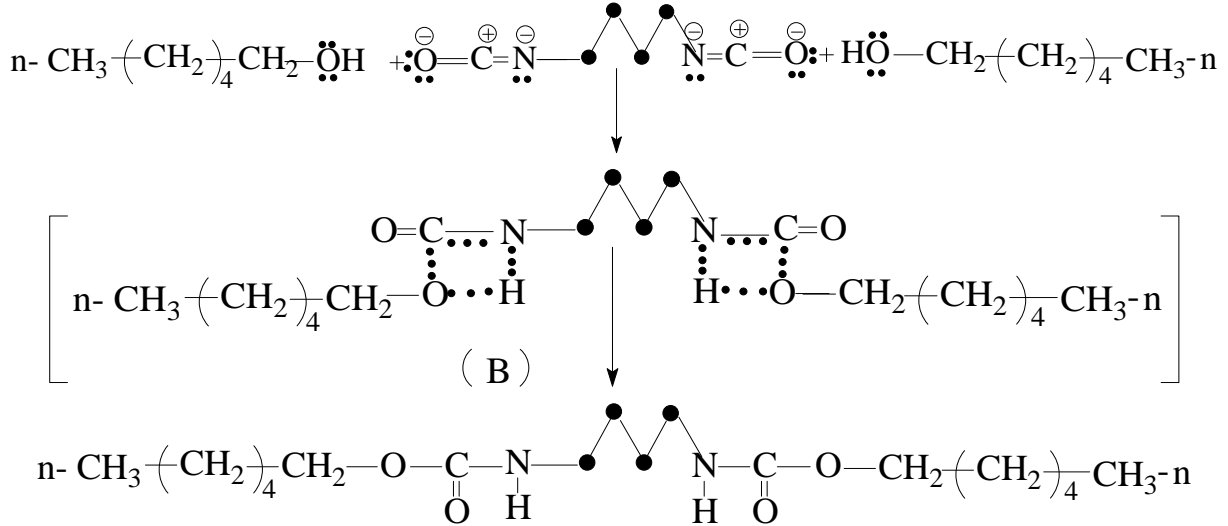
A non-waste method of obtaining a growth stimulator of industrial plants involves the synthesis of N,N¹-tetramethylenebis - [(n-hexanoyl) carbamate] by the interaction of tetramethylene di-isocyanate with n-hexanol in the presence of a (C₂H₅)₃N base catalyst and a universal solvent of dimethylformamide:



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



Nitrogen and oxygen in the group carry mainly a negative charge and have an electron-donating and an electrophilic atom. In some cases, diisocyanates can also play the role of electrophilic agents. The reactions of nucleophilic addition with the participation of oxygen and nitrogen containing substances are most typical (characteristic) of them. The HO-group of n-hexanol, having a free electron pair, attacks the electrophilic center in the tetramethylenediisocyanate molecule, with the formation of an intermediate process (B), which regroups into bis-carbamate:



Description of the technological process for the production of N, N¹-tetramethylene bis - [(n-hexanoyl) carbamate]

The technological scheme for the production of N, N¹-tetramethylene bis - [(n-hexanoyl) carbamate] is shown in the figure 1.

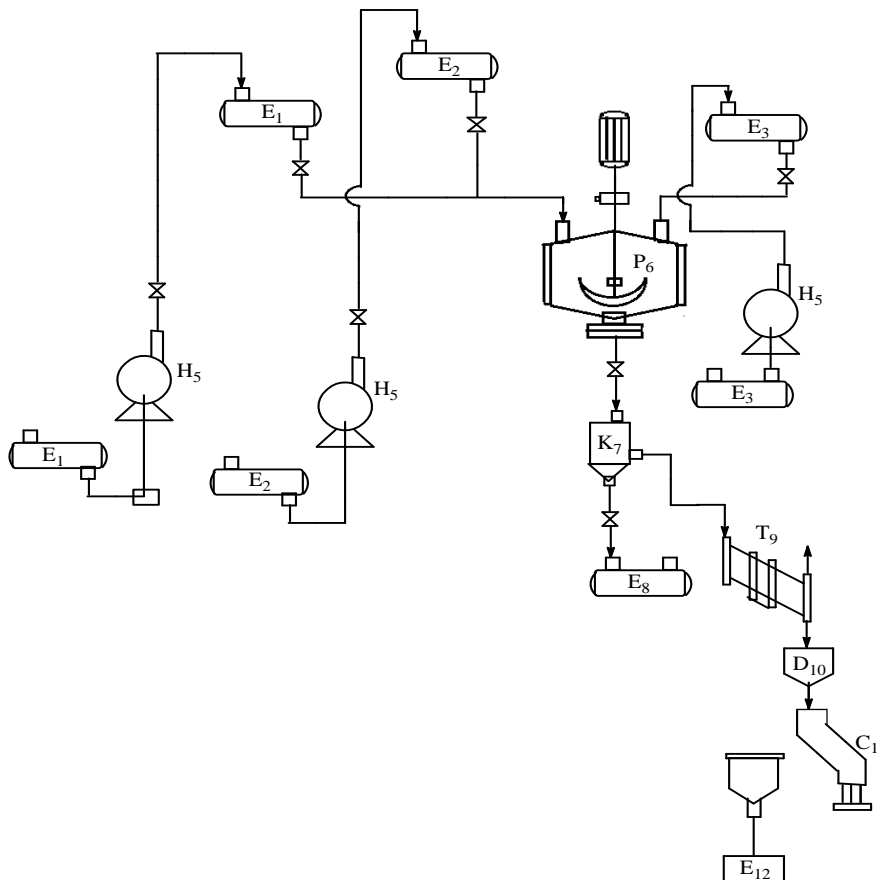


Fig1. Technological scheme for the production of N, N¹-tetramethylene bis - [(n-hexanoyl) carbamate].
 E₁-E₃ - containers for TMDI, n-hexanol, DMF and (C₂H₅)₃N; H₅ - pump; P₆ - reactor; K₇ – inch filter;
 E₈ - capacity for waste solvent and catalyst (base); T₉ - drum dryer; D₁₀ - crusher;
 C₁₁ - vibrating screen; E₁₂ - capacity for the finished product.

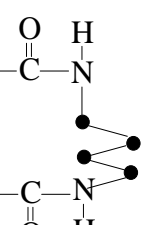
Operational amounts of n-hexanol, TMDI, DMF and $(C_2H_5)_3N$ are loaded into the P_6 reactor from E_1 - E_3 tanks. The mixture was stirred at room temperature for 4,0 hours. The precipitated white crystals are filtered off in an F_7 filter. A mixture of DMF and a catalyst base $(C_2H_5)_3N$ or pyridine is collected in a container E_8 . The final reaction product and snow-white crystals are dried in a T_9 drum dryer, then sent to a D_{10} crusher and screened on a C_{11} vibrating screen. The finished product is packaged in plastic barrels with a capacity of 20-200 dm^3 .

We need to emphasize that during the technological process for the production of N, N^1 - tetramethylenebis - [(n-hexanoyl) carbamate], the reaction of the interaction of N, N^1 - tetramethylenediisocyanate with n-hexanol proceeded without emission of harmful gases ($CO, NO, Cl_2, HCl, HCN, H_2S$, etc.). The synthesis technology was carried out in dimethylformamide at a temperature of 28 °C (without heating) for 4,0 hours.

It should be noted that ecologically pure waste-free new derivatives of N, N^1 - tetramethylenebis - [(n-hexanoyl) carbamate], snow-white crystals with rather high yields were obtained.

The physicochemical parameters of N, N^1 - tetramethylenebis - [(n-hexanoyl) carbamate] (I) are given in Table 1.


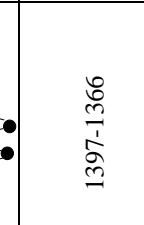
Table 1. Physico-chemical parameters of the drug (I)

Structural formula	Yield, %	MT, °C	R_f	Bruttofor mula	Elemental analysis, %		M_M
					Calculated	Found	
					N	N	
$n-CH_3-(CH_2)_4-CH_2-O-C(=O)-N$ 	92,3	256-258	0,74	$C_{18}H_{36}N_2O_4$	8,14	8,01	344

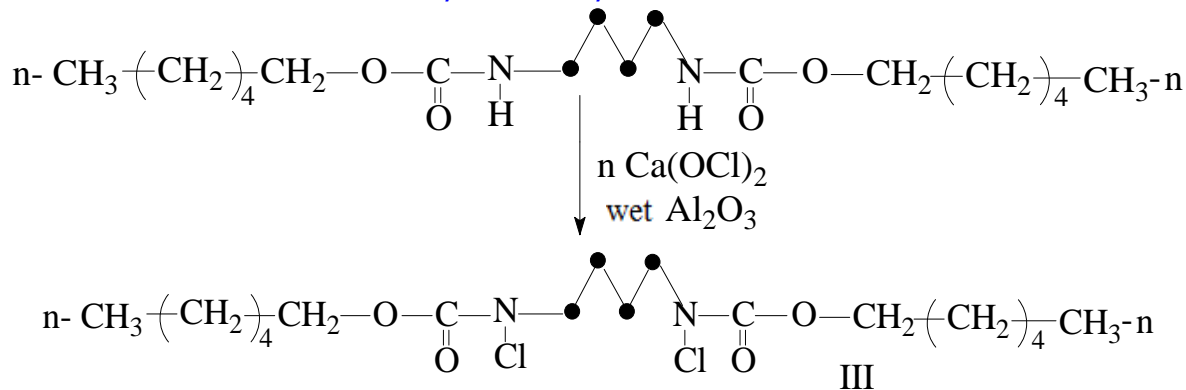
The structure of N, N^1 - tetramethylenebis - [(n-hexanoyl) carbamate] was confirmed by elemental analysis, as well as by IR and PMR spectroscopy.

In the IR spectrum of N, N^1 - tetramethylenebis - [(n-hexanoyl) carbamate] there is a wide absorption band in the region of 1670 cm^{-1} , characteristic of groups, and the absorption band in the region of 1484 cm^{-1} corresponds to the absorption of the bond, a strong absorption band of 3190 cm^{-1} is characteristic of groups. (Table 2).

Table 2. IR and PMR spectra of the drug (I)

Compound I	IR-spectra, ν, cm^{-1}					PMR spectrum, $\delta, m.g.$		
	-NH - CH ₂ -	-C=O	-N-H	-N-C-O-		-CH ₂ -N	CH ₃ -	-CH ₂ -
$n-CH_3-(CH_2)_4-CH_2-O-C(=O)-N$ 	1397-1366	1670	3190	1284	756-724	3,35	2,21	1,27-1,21

To study the reactivity of N, N^1 - tetramethylenebis - [(n-hexanoyl) carbamate] N-H reactive centers, we performed rare reactions of N, N^1 -dinitrososation, N, N^1 - dichlorination, and N, N^1 - dialkylation.



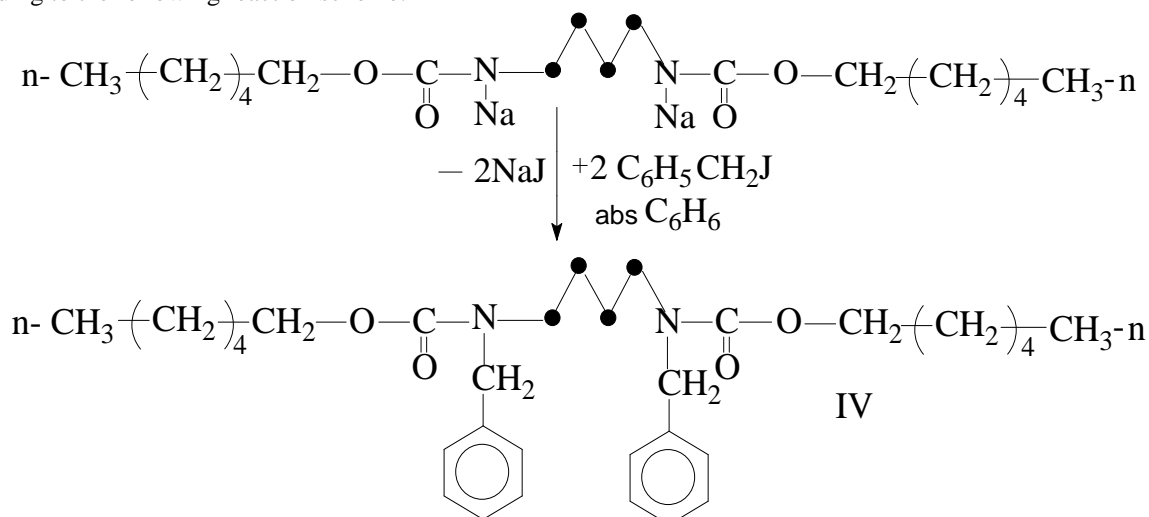
Physico-chemical parameters of the drug (III) are shown in table 3.

Table 3. Physico-chemical parameters of the drug (III).

Structural formula	Yield, %	MT, °C	R _f	Bruttoformula	Elemental analysis, %				M _M
					Calculated		Found		
					N	Cl	N	Cl	
$ \begin{array}{c} \text{n-CH}_3\text{-(CH}_2\text{)}_4\text{CH}_2\text{-O-C(=O)-N(Cl)-} \bullet \bullet \text{N(Cl)-C(=O)-O-CH}_2\text{-(CH}_2\text{)}_4\text{CH}_3\text{-n} \\ \text{III} \end{array} $	95.6	141-142	0.71	C ₁₈ H ₃₄ Cl ₂ N ₂ O ₄	6.78	17.19	6.57	17.06	413

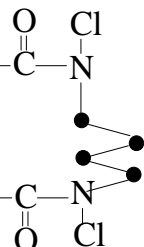
3. Obtaining N, N¹ – dibenzyl substituted derivatives of the drug (I)

Dibenzylation at the N-H groups in bis-carbamates (I) with benzyl iodide is of undoubted interest for establishing the reactivity of compounds containing (I). Benzylation reactions were carried out by the interaction of N, N¹ – disodium derivatives of N, N¹ – tetramethylenebis (n-hexanoyl) carbamate] with benzyl iodide in anhydrous benzene at a temperature of 28-35 °C and benzyl iodide was added dropwise with stirring over 3,5 hours according to the following reaction scheme:



The occurrence of the benzylation reaction exclusively at the nitrogen atom N, N¹- is apparently explained by the relatively easy dissociation of sodium at this atom due to the presence of neighboring carbonyl groups. The yield of the drug (IV) was 88,3%. Physico-chemical parameters (IV) are shown in table 4.

Table 4. Physicochemical parameters of compounds (IV).

Structural formula	Yield, %	MT, °C	R _f	Bruttoformula	Elemental analysis, %						M _M
					Calculated			Found			
					C	H	N	C	H	N	
$n\text{-CH}_3\text{-(CH}_2\text{)}_4\text{CH}_2\text{-O-C(=O)-N(Cl)-}$ 	92,5	176-177	0,69	C ₃₂ H ₄₈ N ₂ O ₄	73,28	9,16	5,34	73,12	9,01	5,19	524

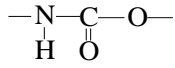

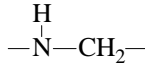
V. EXPERIMENTAL RESULTS

A. Synthesis of N, N¹ - tetramethylenebis - [(n-hexanoyl) carbamate] (I).

20,4 g (0,2 mol) of n-hexanol are placed in a three-necked flask equipped with a reflux condenser, thermometer, stirrer, 15 ml of triethylamine, 60 ml of DMF are added, 14,0 g (0,1 mol) of tetramethylenediisocyanate dissolved in 22 ml of DMF at room temperature 30-32 °C are added with stirring and dropwise. The reaction mixture is stirred for 3 hours at a temperature of the reaction mixture of 36-43 °C. After a time, 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 of product (I) is 31,75 g (95,5% of theoretical); Mp = 256-257 °C. R_f = 0,74;

Found, %: C 62,62; H 10,32; N 8,01

Calculated for C₁₈H₃₆N₂O₄, % : C 62,79; H 10,46; N 8,14

IR-spectra, ν, cm⁻¹ :  (1284); N-H (3190);  (1670); $\text{-(CH}_2\text{)}_4\text{-}$ (756-724);  (1397-1366).

B. Synthesis of N, N¹-dinitrozo-N, N¹-tetramethylene bis - [(n-hexanoyl) carbamate] (II)

3,44 g (0,01 mol) (I) of N, N¹-tetramethylene bis - [(n-hexanoylo) carbamate] dissolved in 100 ml of formic acid was placed in a three-necked flask equipped with a reflux condenser, thermometer, stirrer. 0,6 g of sodium nitrite is added in excess within 4,0 hours. With constant stirring at a temperature of 0-4 °C, in portions. After 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 was filtered off, washed with benzene and dried. The identity of N, N¹-dinitrozo-N, N¹-tetramethylene bis - [(n-hexanoyl) carbamate] was established by TLC on Silifol plates, yield (II) - (83,6% of theoretical); Mp = 240 °C (dec).

Found, %: C 53,59; H 8,38; N 13,76

Calculated for C₁₈H₃₄N₄O₆, % : C 53,73; H 8,45; N 13,93

C. Synthesis of N, N¹-dinitrozo-N, N¹-tetramethylene bis - [(n-hexanoyl) carbamate] (III).

3,44 g (0,01 mol) of N, N¹-tetramethylene bis - [(n-hexanoyl) carbamate], 40 ml of CCl₄, 22 ml of wet alumina are placed in a three-necked flask equipped with a reflux condenser with a chlorine tube, a stirrer, a thermometer. 4,5 g of calcium hypochlorite is added dropwise at a temperature of 4 °C, over 1,0 hour. Then the reaction mass is left for 20 hours, filtered off, the residue is washed with ether, alcohol, dried and N, N¹-dichloro-N, N¹-tetramethylene bis - [(n-hexanoylo) carbamate] is obtained. Yield (III) - 3,96 g (95,6% of theoretical), Mp = 141-142 °C; R_f = 0,71;

Found, %: C 52,19; H 8,16; N 6,57; Cl 17,06

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Calculated for $C_{18}H_{34}Cl_2N_2O_4$, % : C 52,30; H 8,23; N 6,78; Cl 17,19

To prove the structure of N, N¹-dichloro-substituted N, N¹-tetramethylene bis - [(n-hexanoyl) carbamate], a qualitative elemental analysis of silver salts (AgNO₃ solution) was performed.

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

3,44 g (0,01 mol) (I) are added To CH₃ONa (from 0,031 mol) Na and 30 ml abs. CH₃OH). The mixture is stirred for 2 hours at a temperature of 20 °C and 2 hours at a temperature of 40 °C, the precipitate is filtered off, washed with abs. CH₃OH to give product (IIIa). Yield - 84-85% (of theoretical); Mp = above 345 °C (dec).

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

3,23 g (0,01 mol) of N, N¹ disodium substituted (I) are placed in 15 ml of DMF, 4,4 ml (0,02 mol) of benzyl iodide are added drop wise with stirring. The mixture is stirred for 10 hours while heating in a boiling water bath, cooled and poured 25 ml of water, the precipitate is separated, recrystallized from 30% alcohol, dried and obtained (IV) with a yield of 92,5% (from theoretical); Mp = 176-177 °C. Rf = 0,69;

Found, %: C 73,12; H 9,01; N 5,19;

Calculated for $C_{32}H_{48}N_2O_4$, % : C73,28; H 9,16; N 5,34;

VI. CONCLUSION AND FUTURE WORK

Field tests for growth-promoting activity of the N,N¹-tetramethylene bis-[(n-hexanoyl) carbamate] preparation (I)

After the initial tests for growth-promoting activity of the drug (I), field trials were recommended on the farm of S. Azamov in the Kasbinsky 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 bioregulator (I) obtained for the first time, in particular, N, N¹-tetramethylene bis - [(n-hexanoyl) carbamate] (I), was tested at a concentration of 0,001 % (i.e., diluted 750 times). The farm used Uzbekistan-740 cucumbers, Temp tomatoes, 6524 medium-fiber cotton, and various varieties of corn, sunflower, and gourds on an area of 1,134 hectares. An additional 5030 tons of cotton was received, which is about 2 billion soums in cotton growing alone. Similarly interesting results were obtained on cucumbers, sunflowers, corn and tomatoes.

Thus, the preparation (I), recommended by us in a solution of 0,001 % concentration, surpasses many known drugs in biostimulating activity and is even less toxic (LD50 ~ 4633 mg / kg).

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