

# SYNTHESIS AND PROPERTIES OF THE DERIVATIVE N, N<sup>1</sup>-TETRAMETHYLENE BIS (P- FERROCENYLPHENOXY) -KARBAMATE AND ITS APPLICATION

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## Abstract

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The chemical properties of N, N<sup>1</sup>-tetramethylene bis (p-ferrocenylphenoxy) carbamate have been synthesized and studied. synthesis of new, previously unknown derivatives of bis (p-ferrocenylphenoxy) carbamates, the chemical properties of N-H reaction centers by the reactions of chlorination, nitrozoation, metallation and alkylation, the growth-stimulating activity of tetramethylene bis (p-ferrocenylphenoxy) carbamate are studied.

## Keywords:

derivatives;  
bis (p-ferrocenylphenoxy)  
carbamate;  
electrophilic substitution;  
biological activity;

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## 1. Introduction

In the chemistry of synthetic organic compounds a special development has been taken by the direction of fine organic synthesis of substances, among which a significant role is played by the carbamate and bis-carbamate derivatives obtained on the basis of isocyanate and diisocyanate.

Numerous studies in the field of derivatives of carbamates and bis-carbamates, conducted at the present time, are prompted not only by theoretical, but also by practical needs. From this point of view, derivatives of carbamates and bis-carbamates are of undoubted interest as substances possessing various technical, biological and pharmacological activities. They are successfully used in almost all branches of the national economy, in particular, in engineering as accelerators for rubber vulcanization, additives for lubricating oils, they are also used as raw materials for the production of polymers, and as inhibitors of corrosion [1-6].

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In agriculture, they have found application as pesticides, herbicides, fungicides, defoliants, insecticides, nematicides, bactericides, growth stimulators, etc. The use of these substances in medicine as antitumor, antiviral, anti-inflammatory, antiarrhythmic and other drugs is of particular interest [7-12].

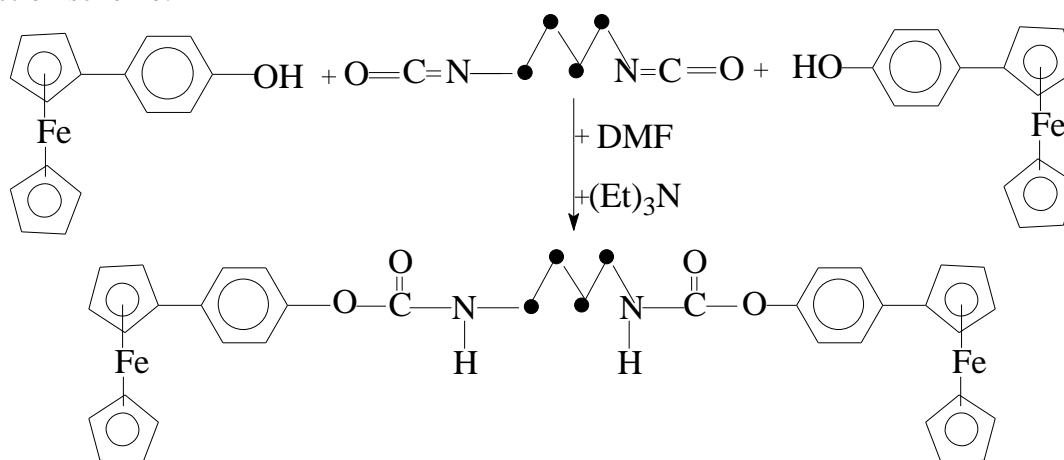
In this regard, we presented earlier studies in the synthesis of new bis-p-ferrocenylphenoxy-carbamate derivatives and studied their chemical properties.

## 2. Research Method

The object of the study was the derivatives of of N, N<sup>1</sup>-tetramethylene bis (p-ferrocenylphenoxy) carbamate. Their physical and chemical properties, biostimulating activity were studied. IR spectra recorded on a VR-20 spectrometer in KBr tablets.

## 3. Results and Analysis

Thus, by the interaction of para-ferrocenylphenol with diisocyanates, bis-p-ferrocenylphenoxy-carbamate derivatives were prepared according to the following reaction scheme:



The reaction of diisocyanate with p-ferrocenylphenol was carried out at a molar ratio of reactants of 1: 2 at room temperature of 26-36 °C for 3,5-4 hours. As a result of the reaction, N, N<sup>1</sup>-tetramethylene bis [(p-ferrocenylphenoxy) carbamate] (I) is formed which is a weakly colored high-melting powder, which is difficult to solubilize in water and other readily available solvents, which confirms the presence of two carbamate ( $-\text{NHCOO}$ ), as well as ferrocenyl phenoxy and tetramethylene hydrocarbons.

The physicochemical characteristics of the obtained product are shown in Table 1.

**Table 1. Physico-chemical characteristics of N, N<sup>1</sup>-tetramethylene bis [(p-ferrocenylphenoxy) carbamate]**

Structural formula	Output, %	Tm, °C	R <sub>f</sub>	Gross formula	Elemental analysis, %		M <sub>M</sub>
					Calculate	Found	
					N	N	
	92,3	213-214	0,66	C <sub>38</sub> H <sub>36</sub> Fe <sub>2</sub> N <sub>2</sub> O <sub>4</sub>	4,02	3,94	695,7

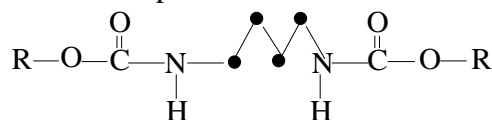
As can be seen from table 1, the yield of N,N<sup>1</sup>-tetramethylene bis [(p-ferrocenylphenoxy) carbamate] is rather high. The high yield of the resulting bis (p-ferrocenylphenoxy) carbamate derivative is apparently due to the high density and easy

mobility of the electron cloud of the conjugated ( $-\text{N}=\overset{\oplus}{\text{C}}=\text{O}$ ) group, which leads to an increase in the positive charge on the carbon atom of the isocyanate group, attacking this atom with a nucleophilic agent, as well as the absence of steric obstacles.

The structure of the synthesized compound (I) was determined by the IR spectrum and elemental analysis data (Table 2).

To determine the reactivity of N-H groups of bis (p-ferrocenylphenoxy) carbamate, we carried out N, N<sup>1</sup>-dinitrozoation, metallation, alkylation, and halogenation reactions.

Table 2. The IR spectral data of the derivative (I)

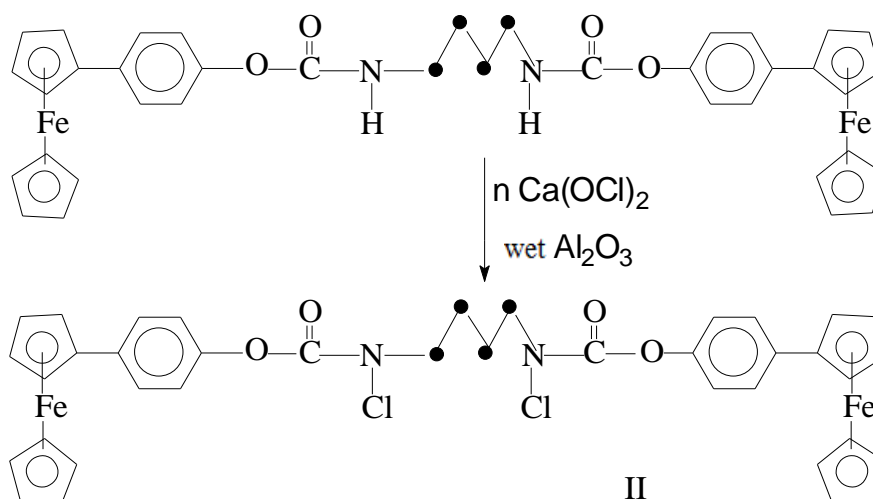


R	IR spectr, $\nu$ , $\text{cm}^{-1}$						
	$-\text{N}-\overset{\text{O}}{\parallel}{\text{C}}-\text{O}$ $\text{H}$	$-\text{N}-\text{H}$	$-\overset{\text{O}}{\parallel}{\text{C}}-\text{O}$	$-(\text{CH}_2)_4$		$-\text{NH}-\text{CH}_2-$	$\text{O}-\text{CH}_2$
	1592	3314	1680	756-729	860-800	1432	1280

### Preparation of N, N<sup>1</sup>-dichlorosubstituted -N, N<sup>1</sup>-tetramethylene bis [(p-ferrocenylphenoxy) carbamate]

We have developed an efficient, affordable, cheap, environmentally friendly method for the N, N<sup>1</sup>-dichlorination of the bis-carbamate derivative by calcium hypochlorite on wet  $\text{Al}_2\text{O}_3$ .

The scheme of the chemical reaction is as follows:



These reactions are of interest to many specialists in chemistry, pharmacology, biology, biochemistry, bioorganics, microbiology and many others, because of the existence of a vital, highly reactive center (N-H group) consisting of the derivative of bis-carbamate, that is required for nucleophilic and electrophilic substitution.

The yield of product II and the physicochemical parameters are given in Table 3.

To prove the structure of the newly synthesized N, N<sup>1</sup>-dichlorosubstituted -N, N<sup>1</sup>-tetramethylene bis [(p-ferrocenylphenoxy) carbamate], IR spectra were taken, elemental analysis and qualitative reactions with AgNO<sub>3</sub> were carried out.

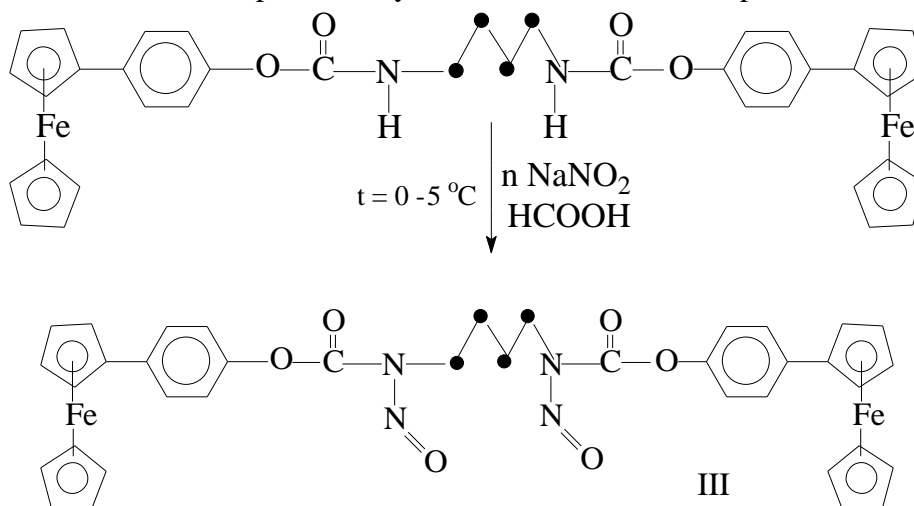
**Table 3. Physicochemical parameters of preparation II**

Structural formula	Output, %	Tm, °C	R <sub>f</sub>	Gross formula	Elemental analysis, %				M <sub>M</sub>
					Calculated		Found		
					N	Cl	N	Cl	
	92,3	198-194	0,71	C <sub>38</sub> H <sub>34</sub> Cl <sub>2</sub> Fe <sub>2</sub> N <sub>2</sub> O <sub>4</sub>	4,02	9,28	3,94	9,11	764,7

**Preparation of N, N<sup>1</sup>-dinitrozo-substituted -N, N<sup>1</sup>-tetramethylene bis [(p-ferrocenylphenoxy) carbamate]**

As a result of the reaction of N,N<sup>1</sup>-dinitrozoization of the bis [(p-ferrocenylphenoxy) carbamate derivative] with sodium nitrite (in excess) in formic acid, the corresponding N,N-dinitrozo-substituted bis [(p-ferrocenylphenoxy) carbamate] % (table 4).

N, N<sup>1</sup>-dinitrozoization proceeds by the mechanism of electrophilic substitution:



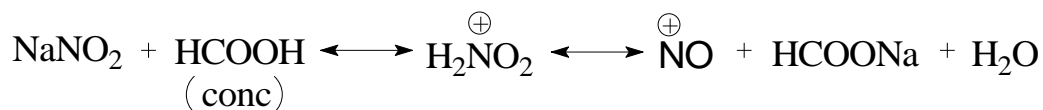
N, N<sup>1</sup>-dinitrozo-substituted bis [(p-ferrocenylphenoxy) carbamate]

**Table 4. Physicochemical parameters of preparation III**

Structural formula	Output, %	Tm, °C	R <sub>f</sub>	Gross formula	Elemental analysis, %		M <sub>M</sub>
					Calculated	Found	
					N	N	
	88,2	348(dec.)	0,61	C <sub>38</sub> H <sub>34</sub> Fe <sub>2</sub> N <sub>4</sub> O <sub>6</sub>	7,43	7,46	753,7

The attacking agent is nitrosonium ion  $\text{NO}^{\oplus}$ . Since nitrous acid, which is the most common 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 ion  $\text{NO}^{\oplus}$ :

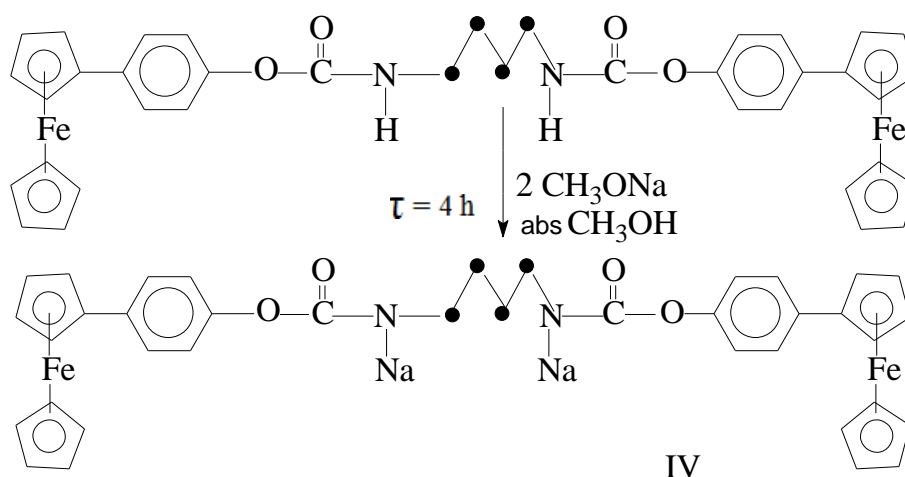


N, N<sup>1</sup>-dinitrozoation is carried out with cooling (0-5 ° C) of the reaction mixture. The increase in temperature is undesirable, since this reduces the yield of the desired product, and sometimes affects the direction of the reaction. Identification of N, N<sup>1</sup>-dinitrozo compounds is carried out on the absorption bands of N-nitroso groups. A very strong absorption band in the region of 1530-1440 cm<sup>-1</sup> for  $\text{N}-\text{N}=\text{O}$  groups is characteristic.

### Preparation of N, N<sup>1</sup>-disodium-substituted N, N<sup>1</sup>-tetramethylene bis [(p-ferrocenylphenoxy) carbamate]

One of the methods of metallization, which can be carried out using N-metalation, is the replacement of sodium by hydrogen atoms in the N-H group. N, N<sup>1</sup>-tetramethylene-bis [(p-ferrocenylphenoxy) carbamate] are subjected to directional metallation on N-H groups by means of CH<sub>3</sub>ONa.

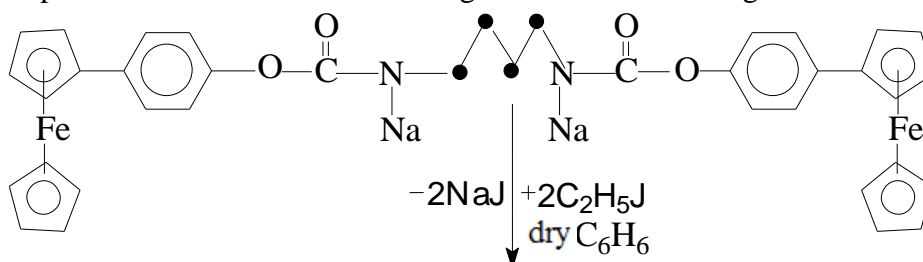
The reaction of N, N<sup>1</sup>-dimetallation proceeds according to the following scheme:

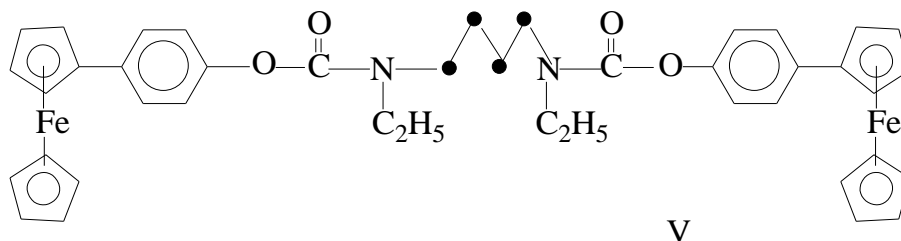


### Preparation of N, N<sup>1</sup>-diethyl-substituted N, N<sup>1</sup>-tetramethylene bis [(p-ferrocenylphenoxy) carbamate]

Alkylation  $\text{N}-\text{H}$  in carbamates with alkyl halides is of undoubted interest when it comes to elucidate the reactive capacity of the compounds containing  $\text{N}-\text{H}$ .

We carried out alkylation reactions, the interaction of N, N<sup>1</sup>-disodium derivatives of N, N<sup>1</sup>-tetramethylene bis [(p-ferrocenylphenoxy) carbamate] with ethyl iodide in abs. benzene at room temperature of 26-28 °C with stirring for 3 hours according to the scheme:





The flow of the alkylation reaction solely at the nitrogen atom N, N<sup>1</sup> - is probably due to the relatively easy dissociation of sodium in this atom due to the presence of neighboring carbonyl groups. The yield of product V is 90,4 %, T<sub>m</sub> = 221-222 ° C.

Thus, methods for the preparation of N, N<sup>1</sup>-tetramethylene bis [(p-ferrocenylphenoxy) carbamate] have been developed and its chemical properties at N-H reaction centers have been studied: the chlorination, nitrozoation, metallation and alkylation reactions.

### Experimental part

The course of the reaction and the individuality of the compounds are monitored by TLC method on aluminum oxide of the II degree of active capability with the appearance of spots by iodine vapor. IR spectra recorded on a spectrometer UR-20.

#### Synthesis of N, N<sup>1</sup>-tetramethylene bis [(p-ferrocenylphenoxy) carbamate] (I)

It is added 15 ml of triethylamine, 80 ml of DMF, 14 g (0,1 mol) of TMDI dissolved in 25 ml of DMF to 15,6 g (0,2 mol) of para-ferrocenylphenol, the addition is proceeded dropwise with stirring at room temperature. The reaction mixture is stirred for 3 hours at a temperature of 35-40 ° C. At the end of the time, the contents of the flask are transferred to a glass, water is added. The formed precipitate is washed with TLC. After drying, a colorless powder is obtained, yield (I) is 92,3 %; T<sub>m</sub> = 213-214 ° C.

#### Synthesis of N, N<sup>1</sup>-tetramethylene-N, N<sup>1</sup>-dichloro-bis [(p-ferrocenylphenoxy) carbamate] (II)

7,0 g (0,01 mole) of I, 60 ml of CCl<sub>4</sub>, 25 g of wet alumina are placed and 4,5 g of calcium hypochlorite are added dropwise at a temperature of 40 ° C for 1 hour. The reaction mixture is left for 19 hours. It is filtered off, washed with ether, with an alcohol, dried and then it can be (II) obtained a yield of 93,2 %; T<sub>m</sub> = 198-199 ° C. Found: Cl 9,28; N 3,66. Calculated for C<sub>38</sub>H<sub>34</sub>Cl<sub>2</sub>Fe<sub>2</sub>N<sub>2</sub>O<sub>4</sub>, %: Cl 9,11; N 3,68.

To prove the structure of N, N<sup>1</sup>-dichlorosubstituted I (II) an elemental analysis of silver salts (AgNO<sub>3</sub> solution) was carried out.

#### Synthesis of N, N<sup>1</sup>-dinitroso-substituted I (III)

To 7,0 g (0,01 mol) of I dissolved in 110 ml of formic acid, continuously stirring at a temperature of 0-5 ° C, 0,6 g of sodium nitrite is added in batches in excess for 3,5-4 hours. After the end, the substance is poured into a glass, water is add, the precipitate is filtered off, washed with benzene and dried, TLC on "Silifol" plates; output – 88,2 %; T<sub>m</sub> = 348 ° C (dec.)

#### Synthesis of N, N<sup>1</sup>-disodium-substituted I (IV)

In CH<sub>3</sub>ONa (from 0,031 g / mol and 80 ml abs. CH<sub>3</sub>OH), 7,0 g (0,01 mole) of I is added. The mixture was stirred for 2 hours at 20 ° C and 2 hours at - 40 ° C. The precipitate is filtered off, washed with abs CH<sub>3</sub>OH, and IV is obtained, yield: 87,4 %; T<sub>m</sub> = above 360 ° C (dec.)

#### Synthesis of N, N<sup>1</sup>-diethyl-substituted I (V)

7,19 g (0,01 mole) of IV are placed in 15 ml of DMF, 3,12 ml (0,02 mol) of ethyl iodide are added dropwise with stirring. The mixture is stirred for 10 hours with heating in a boiling water bath, cooled and washed with 25 ml of water, the precipitate is separated, recrystallized from 50% alcohol, dried and yielded (V) in 89,6 % yield; T<sub>m</sub> = 203-204 ° C.

**Field tests for the growth-stimulating activity of the drug SSJ-5 (I).**

After the initial tests for the growth-stimulating activity of the drug SSJ-5 (I), field trials were tested on the farm of S. Agzamov in the Kasbinsk fog of the Kashkadarya region in the period from April to October 2017.

For the first time, the obtained SSJ -5 growth stimulator, in particular N, N<sup>1</sup>-tetramethylene bis [(p-ferrocenylphenoxy) carbamate] (I) was tested at a concentration of 0.001% (i.e., diluted 750). Cucumbers of "Uzbekistan-740" variety, "Temp" varieties, medium-fiber cotton of "C-6524" variety, corn and sunflower on the area of 24669 hectares were used in the farm. An additional 10,361 tons of cotton was received, which represents an estimated economic effect of about 4 billion sums only for cotton growing. Similarly, good results were obtained on tomatoes, cucumbers, sunflower and corn. Thus, the drug SSJ-5 (I), recommended by us in a solution of 0,001 % concentration, exceeds many of the known drugs in stimulating activity and is less toxic (LD<sub>50</sub> = 4130 mg / kg).

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