SYNTHESIS AND STUDY OF THE PROPERTIES OF BIS-CARBAMATE MEE-2 AND ITS DERIVATIVES

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ABSTRACT

This scientific work discusses synthesis methods and development of waste-free, energy-saving, environmentally friendly and resource-saving technology for the production of N, N’-hexamethylene bis [(m-cresol)-carbamate], i.e. MEE-2 and its derivatives. And also, the study of the N-H center of the MEE-2 molecule where the chemical transformation occurs according to the mechanism of S_N nucleophilic addition. As a result, a new, previously little studied area of chemistry of bis-carbamate compounds based on cresol and hexamethylene diisocyanate has emerged.

Keywords: Bis-carbamate, virtual, screening, structure, simulation, activity, biological, pharm, therapeutic, agriculture.

INTRODUCTION

Carbamates, or urethanes, are organic compounds derived from carbamic acid (carbonic acid amide). Carbamates and bis-carbamates are used in many industries: agriculture, medicine, technology, chemistry, fuel industry, rubber industry, pharmaceuticals, petrochemical industry, and on their basis a variety of drugs are obtained for the needs of the national economy.

Recent studies of carbamate and bis-carbamate derivatives carried out at the present time are motivated not only by theoretical, but also by practical needs. From this point of view, carbamate derivatives are of undoubted interest as substances with various biological activities. They are widely used; in agriculture they are used as bactericides, herbicides, fungicides, insecticides, growth stimulants, and many others [1-4]. Of particular interest is the use of these compounds in medicine as antiviral, antitumor, anti-inflammatory, antidiabetic, antiarrhythmic, vasodilator and other pharmaceuticals [5-8]. Syntheses of new compounds based on derivatives of

replacement cresols and isocyanates, as well as their practical application, have broad prospects in solving priority development problems, primarily in the petrochemical industry for the production of various chemicals, reagents, new drugs for the needs of the entire national economy and the growth of the well-being of the people of the Republic of Uzbekistan [9-13]. The chemistry, mechanism, technology and properties of bis-alkylphenol-carbamate derivatives attract the attention of the world's oil and gas workers, petrochemical synthesis specialists, organic researchers, chemists, technologists and pharmacists searching for new promising substances. Also, a number of international and domestic scientific works are devoted to this area [14-18]. Nevertheless, there is still no information in the world literature about the development of the synthesis of N,N'-hexamethylene bis-[(meta-cresol)-carbamates] i.e. MEE-2 and its derivatives.

The purpose of this research work is the development of theoretical and applied aspects of the nucleophilic addition of derivatives, the search and development of technology for the synthesis of waste-free, energy-saving, highly efficient and low-toxic methods for the synthesis and production of MEE-2 bis-carbamate compounds and its derivatives. Previously, the authors of this article synthesized bis-carbamates of the MEE-1 series and its derivatives. The mechanisms and parameters influencing the reactions were studied. Some of them were introduced into the chemical, petrochemical and agricultural industries [19-24].

MATERIALS AND METHODS

Synthesis of N,N'-hexamethylene bis-[(m-cresol)-carbamate] i.e. MEE-2: In a three-neck flask equipped with a reflux condenser, a thermometer, and a stirrer, place 7.70 g (0.02 mol) of meta-cresol, add 30 ml of triethylamine (TEA), 60 ml of dimethylformamide (DMF), add drops at a temperature of 40-42 °C with stirring 2.6 ml hexamethylene diisocyanate (HMDI) dissolved in 8 ml DMF. The reaction mixture is stirred for 3 hours at a reaction mixture temperature of 45-48°C. After the time has passed, the contents of the flask are transferred to a glass and water is added. The deposited precipitate is washed with those. After drying, a colorless powder is obtained with a yield of 9.6 g (93.7% of theoretical). T_{melt} = 201–202°C; R_f = 0.74; M_M = 468.64; Found, %: C – 71.74; H – 8.51; N – 5.98; Calculated, %: C – 71.76; H – 8.60; N – 5.97.

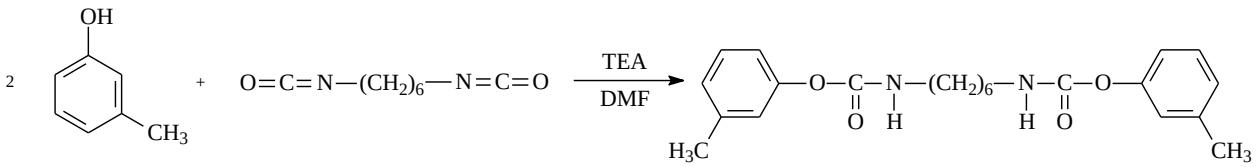
Synthesis of N,N'-dichloro-N,N'-hexamethylene bis-[(m-cresol)-carbamate] i.e. MEE-2g: In a three-neck flask equipped with a reflux condenser with a calcium chloride tube, a stirrer, and a thermometer, place 3.85 g (0.01 mol) of N,N'-hexamethylene bis-(m-cresol)-carbamate, 55 ml of CCl_4, 25 g of wet alumina and add 60 g of calcium hypochlorite drop by drop at a temperature of 40 degrees, then the reaction mass is left for 32 hours, the residue is filtered off, washed with ether, alcohol and dried. Product yield – 4.37 g (96.6% of theoretical); T_{melt} = 91–92°C; R_f = 0.69;

Found, %: C – 58.17; H – 5.66; N – 6.06; Cl – 15.47; Calculated, %: C – 58.28; H – 5.77; N – 6.18; Cl – 15.64.

Synthesis of N,N’-dinitroso-N,N’-hexamethylene bis-[(m-cresol)-carbamate] i.e. MEE-2a: 3.85 g (0.01 mol) of N,N’-hexamethylene bis-[(m-cresol)-carbamate], dissolved in 100 ml of formic acid, is placed in a three-neck flask equipped with a reflux condenser, a thermometer, and a stirrer. With constant stirring at a temperature of 0–5°C, add 0.5 g of sodium nitrite (in excess) in portions over 4.0 hours. After the reaction is completed, the contents are poured into a liter jar, 250 mg of cold water is added, and a precipitate begins to form. The precipitate is filtered off, washed with benzene and dried. The identity of N,N’-dinitroso-N,N’-hexamethylene bis-[(m-cresol)-carbamate] was determined by thin layer chromatography (TLC) on Silifol plates. Yield of compound – 4.13 g (93.4% of theoretical); T_{melt} = 235°C (decomposed); R_f = 0.69; M_M = 442.46; Found, %: C – 59.59; H – 5.87; N – 12.53; Calculated, %: C – 59.72; H – 5.92; N – 12.66.

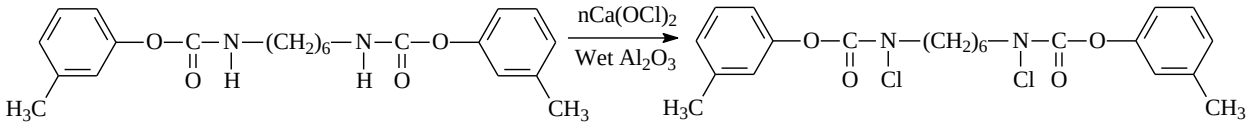
RESULTS AND DISCUSSIONS

New derivatives of N,N’-hexamethylene bis-(m-cresol)-carbamate were obtained by reacting meta-cresol with hexamethylene diisocyanate. Cost-effective, waste-free, energy-saving synthesis was carried out according to the following scheme:



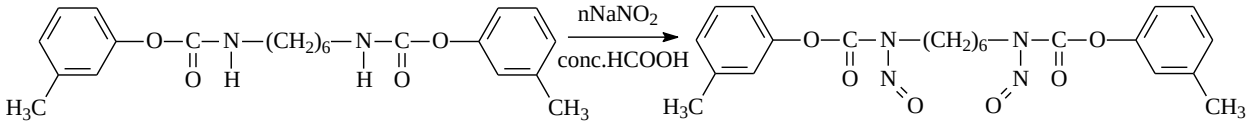
The reaction is carried out in a medium of dimethylformamide and the organic base triethylamine at room temperature for 4 hours. The high density, selectivity and easy mobility of the electron cloud of the group N=C=O determine its high reactivity. The product yield was 94.6% as expected and compounds were obtained in good yields by the A_N reaction mechanism. Purification of compound MEE-2 was carried out using preparative thin-layer chromatography (TLC) on Al_2O_3 in the system ($HCOOH:CH_3COCH_3:CHCl_3$ = 0.5:5.0:0.5).

Derivatives of N,N’-hexamethylene bis-[(m-cresol)-carbamate] are the most valuable raw materials for the further synthesis of various biologically active compounds used in technology and agriculture, and also have a high reaction center of the N-H group for carrying out the reaction nucleophilic and electrophilic substitutions. We have developed an effective method for the implementation of N,N’-dichlorinated m-cresol-carbamate derivatives with calcium hypochlorite on wet alumina:



To prove the structure of the N,N'-dichloro-substituted product, elemental analysis was carried out using silver salts ($AgNO_3$ solution).

During N-dinitrosation, retention reacts with nitrogen atoms directly associated with the polyethylene –(CH2)– chain. As a result of the reaction of N,N'-dinitrosation, N,N'-hexamethylene bis-[(m-cresol)-carbamate] with $NaNO_2$ (in excess) in 98% HCOOH at a temperature of 0-5°C, N,N'-dinitrososated N,N'-hexamethylene bis-[(m-cresol)-carbamate] with a yield of 89.7% N,N'-dinitrosed occurs via the electrophilic substitution (S_E) mechanism:



The attacking agent is the nitrozone ion – NO. Since nitrous acid, which is the most common nitrosating agent, does not exist in free form, sodium nitrite and a strong acid (HCOOH) are used to carry out the process; the resulting nitrous acid, by adding a proton, generates an ion - NO:

$$HNO_2 + H^+ \longleftrightarrow H_2\overset{\oplus}{N}O_2 \longleftrightarrow \overset{\oplus}{N}O + H_2O$$

$$NaNO_2 + HCOOH\ (conc.) \longleftrightarrow H_2\overset{\oplus}{N}O_2 \longleftrightarrow \overset{\oplus}{N}O + HCOONa + H_2O$$

N,N'-dinitrosation is carried out while cooling the reaction mixture. Increasing the temperature is undesirable since it reduces the yield of the target product and sometimes affects the direction of the reaction.

Conclusion. Thus, in this research work, a waste-free, energy-saving, highly efficient and low-toxic method for the synthesis and production of bis-carbamate compounds MEE-2 and its derivatives with high yield has been developed. It is necessary to continue research into these results of studying physicochemical properties and find promising directions for their application.

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