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New Opportunities in the Synthesis of Monastrol

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ABSTRACT

The synthesis of eutectic mixtures based on 3- (carboxymethyl) -1-vinyl-1H-imidazole-3-ium (chloride, bromide, hexofluorophosphate) and thiourea in various ratios (from 2: 1 to 1: 3) was realized, the aggregate state and established catalytic activity for the synthesis of Monastrol, which showed a wide range of pharmacological activity. Recently, interest in the significance of dihydropyrimidines has attracted great interest. Dihydropyrimidines occupy a key place in various biological processes of various body structures that carry vital information. The most effective method currently used for the synthesis of dihydropyrimidines remains the well-studied multicomponent Biginelli reaction. The Biginelli reaction, which is commonly used for the direct preparation of Monastrol and its derivatives, has many advantages over traditional synthetic methods.

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Introduction

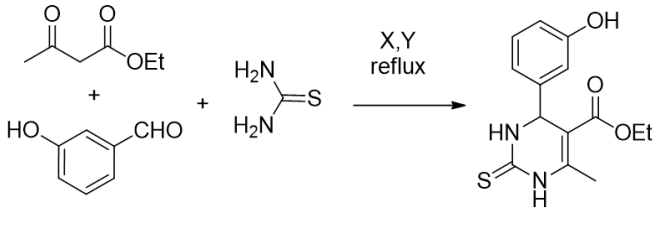
The growing number of publications and patents on various compounds of this series of this topic only confirm this interest [1]. One of the earliest examples of the use of dihydropyrimidines was as an agent to protect wool from moths [2,3]. In addition, the importance of these compounds in the presence of a heterocyclic system with multifunctional key points having different pharmacological efficacy, which is a goal for study in the future. This direction may be interesting for the pharmaceutical industry [4-6].

Materials and Methods

Three-component and one-pot synthesis under Biginelli reaction conditions makes it possible to obtain monastrol based on the result of the interaction of acetoacetic ester, thiourea, and 3-hydroxybenzaldehyde in the presence of various eutectic catalysts and various solvents and without them [7-9]. From the point of view of environmentally friendly conditions, they have the advantage of many reagents collected in one vessel, which avoids waste from multi-stage purification and the formation of residues [10].

Discussion and Results

A derivative of 3,4-dihydropyrimidine-2(1H)-thiones is the compound ethyl 4-(3-hydroxyphenyl)-6-methyl-2-sulfanylidene-3,4-dihydro-1H-pyrimidine-5-carboxylate, with the trivial name Monastrol 1 showed biological activity in various directions. Monastrol is a polyfunctional compound. The presence of functional groups in the molecule allows various chemical modifications. The biological role of Monastrol has led to significant interest in its synthesis and is a 3-component one-pot synthesis based on the interaction of acetoacetic ester, thiourea and 3-hydroxybenzaldehyde, which avoids waste from multi-stage purification and the formation of residues. The synthesis is catalyzed by inorganic acids, ionic liquids, eutectic solvents, or under microwave irradiation (Scheme 1) [11-13].



X – catalizator

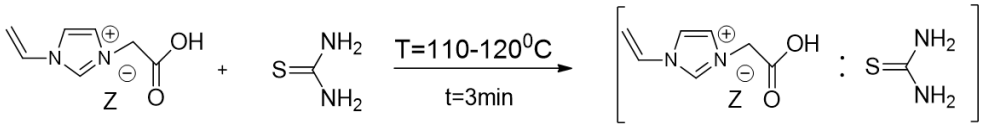
1 -monastrol

Y – solvent

Scheme 1: Obtaining Monastrol 1 under Biginelli Reaction

Along with side products, yields of dihydropyrimidines in highly protic or acidic media give low results due to the sensitivity of aldehydes to acid in the case of the classic Biginelli reaction [12]. Therefore, the search for more efficient catalysts is very relevant to this day. From the point of view of "green chemistry", it is of interest to obtain ionic liquids containing various active groups, such as cyanoethyl, carboxyl, etc., and on their basis to obtain eutectic mixtures with thiourea and to study their catalytic properties in synthesis using the most waste-free and eco-friendly process. monastrol [13-15]. No less important is the fact that ionic liquids and eutectic mixtures in themselves represent substances with the inclusion of biologically active structures. Presented salts

5 are fused with an equimolar amount of thiourea at 103-1050C. Received eutectic mixtures 2,3,4. The compounds are a whitish solid mass with Tm=105-1100C [16-21]. For this purpose, the following were obtained: 3-vinyl-imidazolyl acetic acid hexofluorophosphate: thiourea 2, 3-vinyl-imidazolyl acetic acid bromide: thiourea 3, 3-vinyl-imidazolyl acetic acid chloride: thiourea 4 according to the following scheme 2:



5: Z- counterion: a - hexafluorophosphate
в - bromide
c – chloride

eutectic mixture 2, 3, 4

Scheme 2: Obtaining Eutectic Mixtures

2 - 3-vinyl-imidazolyl acetic acid hexofluorophosphate: thiourea, Z=**a**;

3 - 3-vinyl-imidazolyl acetic acid bromide: thiourea, Z=**в**;

4 - 3-vinyl-imidazolyl acetic acid chlorid: thiourea, Z=**c**.

In developing the approach to eutectic mixtures based on salt **5**, our attention was drawn to thiourea, which has a melting point of 180-182^{0}C and is used as a reagent in the synthesis of Monastrol 1. thiourea, the melting point of the obtained substances is much lower than that of the starting materials. The structure of the compound is confirmed by elemental analysis, IR and NMR spectral data.

As a result of **2,3,4** as catalysts, a yellowish-gray crystalline substance was obtained as a result, the physicochemical constants of which, including Tm = 182-1840C, indicated the formation of monastrol, the yield of which was 40%. The maximum yield of the product was 79%.

Conclusions

In the synthesis of Monastrol, the goal is to select reagents and test various catalysts that are environmentally friendly, least toxic and financially attractive in order to maximize product yield, reduce reaction time, selectivity and minimize reagent surpluses, formation of by-products, high temperatures, environmental pollution. environment, waste and costs. Catalysis plays a fundamental role in Biginelli synthesis, especially in developing strategies to approach eco-friendly catalytic conditions for further use in the renewable chemical industry.

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