



SYNTHESIS AND PROPERTIES OF SOME 4-(4-HYDROXY-PHENYL)-2-METHYL-6-THIOXO-1,5-DIHYDRO-PYRIMIDINE-3-CYCLIC THIOUREAS

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4-(4-hydroxy-phenyl)-2-methyl-6-thioxo-1,5-dihydro-pyridine-3-cyclic thioureas were synthesized on the basis of three-component condensation of ethyl ether of salicyl aldehyde and acetoacetic acid with thiourea. The simplest and most convenient way to synthesize cyclic thioureas is the single-stage three-component condensation of aldehydes, methylene active compounds and thiourea in an acidic environment. The synthesized compounds are crystalline substances. These compounds have the ability to exhibit antioxidant properties due to the presence of thiourea fragment.

Keywords: thiourea, acetylacetoacetic ether, ethyl alcohol

INTRODUCTION

Corresponding cyclic thioureas were synthesized in the presence of trifluoroacetic acid in the ethanol medium by the interaction of aldehydes, methylene active compounds and thioureas [1]. The simplest and most convenient way to synthesize cyclic thioureas is based on the single-stage three-component condensation of aldehydes, methylene active compounds and thiourea in an acidic environment [2]. An efficient method of synthesis of 4-(4-hydroxy-phenyl)-2-methyl-6-thioxo-1,5-dihydro-pyridine-3-cyclic thioureas based on three-component condensation of ethyl ether of salicyl aldehyde and acetoacetic ether with thiourea was developed and was found the optimal condition for increasing the yield [3]. These compounds have the ability to exhibit antioxidant properties due to the presence of thiourea fragment [4-6]. For this purpose, their antioxidant properties were studied in a model reaction. To evaluate the antioxidant activity of the compounds, cumene was used as a hydrocarbon in the model [7-9].

Heterocyclic compounds containing nitrogen heterocyclic heteroatom are very common in nature and play a special role in living organisms [10]. They have a high biological activity and contribute to the development of biological life by participating in alkaloids, vitamins, enzymes and nucleic acids [11-12]. Given that cyclic thioureas are compounds with a wide range of pharmacological activity, the development of an optimal method of synthesis of these compounds is always in the focus of researchers [13].

EXPERIMENTAL PART

Synthesis of (I) compound:

0.7612 g of thiourea, 1.07 ml of salicyl aldehyde, 5 ml of acetoacetate ether added to the three-neck flask which equipped with mechanical stirrer, thermometer and drop funnel. After the first mixture is obtained, 2 drops of CF_3COOH catalyst are added to the reaction medium and dynamically mixed. Then 33.5% water solution of ammonia added slowly to the reaction mixture. Mixed in 4 hours in 25°C temperature. Reaction process have observed with thin-layer chromatography. When the reaction completed the mixture persisted during 24 hours at room temperature and white crystals precipitated. Crystals filtrated and separated, then washed in dichloromethane and crystallized in ethyl alcohol. Obtained 3.8-5 g (I-IV) compounds.

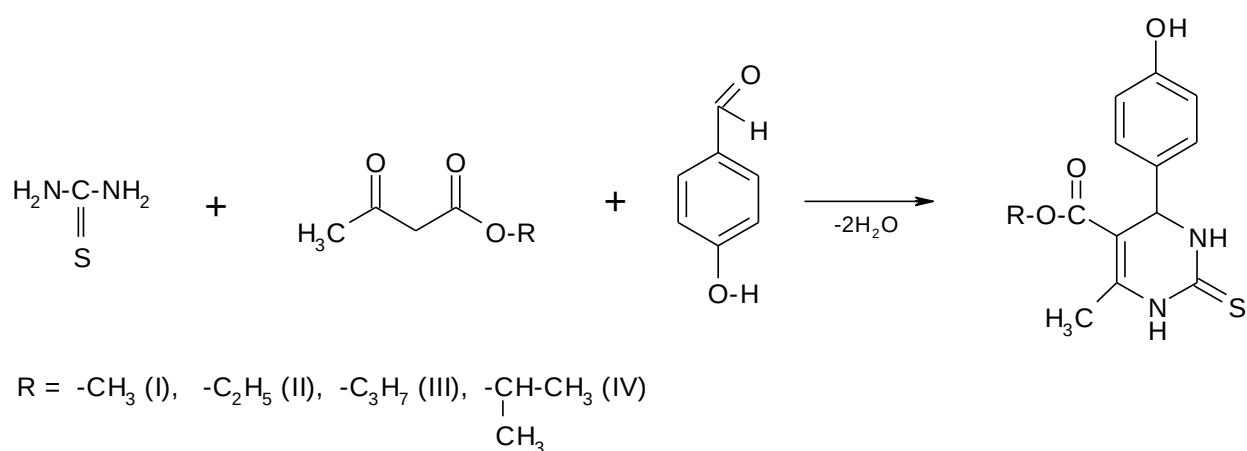
Other substances have also been synthesized according to this method.

RESULTS AND DISCUSSION

New organic compounds containing sulfur and nitrogen atoms were synthesized for the first time and new methods of obtaining heterocyclic compounds were studied. According to the literature, such compounds have antimicrobial, bactericidal, inhibitory and other properties. For this reason, it is assumed that the synthesized and intended for synthesis compounds will be of practical importance in lubricants and lubricating oils, lubricating and cooling fluids used as multifunctional additives, as metal corrosion inhibitors, as compounds with pharmacological activity.

In view of the above, for the first time a method for the synthesis of cyclic thioureas in the presence of trifluoroacetic acid was developed. Studies have shown that in the presence of trifluoroacetic acid in the ethanol environment synthesized cyclic thioureas with a yield of 60-75% from the interaction of aldehydes, methylene active compounds and thioureas. The synthesized compounds are crystalline substances.

The synthesis was carried out according to the following scheme:



As can be seen from the mechanism, the enol form of acetoacetic ether is involved in the reaction. Keto-enol tautomerism is observed as a result of increased C-H acidity due to the fact that the methylene group, which is in the α -position relative to the carbonyl group in acetoacetic ether, is associated with the electron acceptor carboxy group. When acetoacetic ether is converted to the enol form, the energy gain obtained by the formation of intramolecular hydrogen bonds and the formation of a double bond system facilitates enolization and stabilizes the enol form. The physical-chemical properties obtain compounds (I-IV) shown in table.

The purity of the synthesized compounds is indicated with the method of thin-layer chromatography. Eluent is the mixture of isopropyl alcohol and hexane (3:1 ratio). The presence of the blot has explained with iodine smoke.

IR spectrums have painted in Specord – 75 spectrometer with suspension prepared in Vaseline oil. NMR ¹H and ¹³C spectrums are extracted in Bruker (300 Mhs) apparatus.

NMR ¹H spectrum of 4- (4-hydroxy-phenyl) -2-methyl-6-thioxo-1,5-dihydro-pyrimidine-3-cyclic thiourea (I) shown in Figure 1.

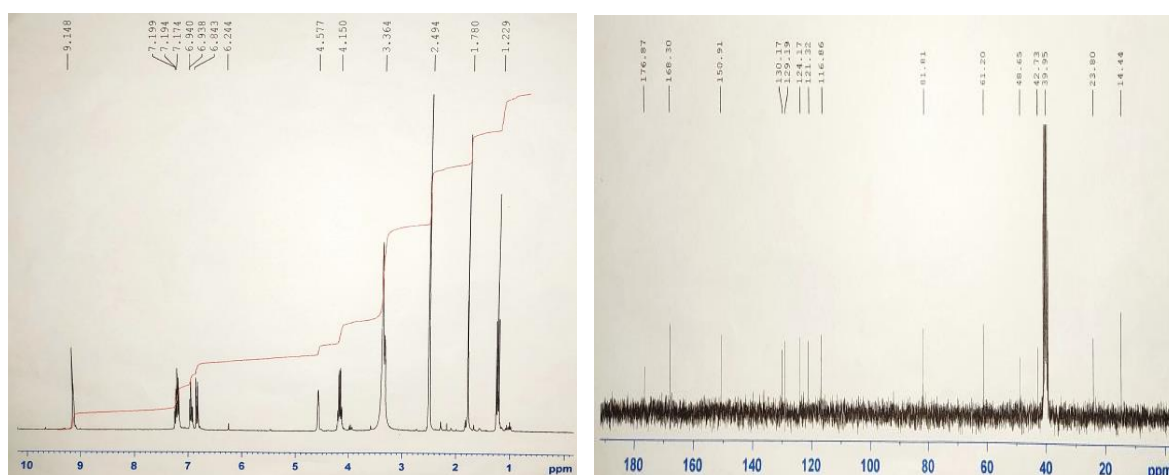
In the IR spectrum of the synthesized compound (I), the valence oscillations of the NH bond are observed in the band 3370-3040 cm⁻¹. The valence oscillations of the C = O bond in the acetyl group correspond to the absorption band 1635-1630 cm⁻¹.

In the NMR ¹H spectrum of pyrimidine, the ethoxymethyl group in the pyrimidine ring is in the strongest field -1.35 m.h. the signal of the three hydrogens in the methyl group is observed in singlet form. The signal of the three protons in the methyl group in the acetyl group is 2.35 m.h. it becomes clear.

Table

The physical-chemical properties obtain compounds (I-IV)

№	Yield, %	M _p , °C	Brutto formula	Elemental analysis, %			
				Found			
				Calculated			
				C	H	N	S
I	70	195	C ₁₃ H ₁₄ SN ₂ O ₃	67.67 67.80	6.25 6.12	12.06 12.16	8.96 9.01
II	55	208	C ₁₄ H ₁₆ SN ₂ O ₃	66.84 67.12	6.62 6.34	9.67 9.78	9.12 9.87
III	65	230	C ₁₅ H ₁₈ SN ₂ O ₃	63.40 63.55	5.85 6.00	9.13 9.26	8.38 8.60
IV	60	234	C ₁₆ H ₁₈ SN ₂ O ₃	61.21 61.41	6.47 6.67	12.54 12.64	8.24 8.16


Fig.1 NMR 1H spectrum of 4- (4-hydroxy-phenyl) -2-methyl-6-thioxo-1,5-dihydro-pyrimidine-3-cyclic thiourea (I)

The signal of the only proton in the text proton is 4.85 m.h. is being observed. The non-equivalent protons in the two phenyl groups located in positions 3 and 6 in the molecule are 6.8-7.1 and 7.4 m.h. areas are clarified in the form of multiplets. In the weakest area 9.35 m.h. singlet corresponds to the only proton located in the NH fragment.

Due to the fact that the synthesized compounds contain a fragment of thiourea, it has the ability to exhibit antioxidant properties. To evaluate the antioxidant activity of the compounds, cumene was used as a hydrocarbon in the model.

The model reaction used an oxidation reaction in a chlorobenzene solution at 60°C with the help of an α , α -azobisisobutyronitrile (AIBN) insulator. In all the experiments studied, the concentration of ADB was stable and equal to $2 \cdot 10^{-2}$ mol / l. To assess the antioxidant properties of the synthesized compounds, the kinetics of their reactions with cumylperoxide radicals and cumylhydroperoxide were studied.

Antioxidant properties of the studied compounds were studied in the range of $5 \cdot 10^{-5}$ mol / l to $5 \cdot 10^{-5}$ mol / l. Studies have shown that the synthesized compounds inhibit the oxidation of cumene by insulators and it was found that they break down cumylhydroperoxide into catalytic molecular products (Fig .2).

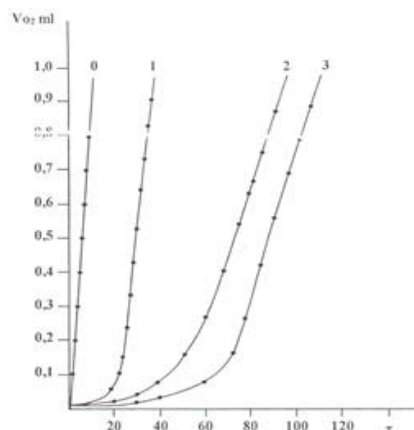


Fig.2. Kinetic curves of initiated oxidation of kumol in the presence of synthesized compounds (I-III). Volume of VO₂-oxygen (ml), τ time (min), 60 °C; [AIBN] = $2 \cdot 10^{-2}$ mol / l, [InH] = $5 \cdot 10^{-4}$ mol / l

The compounds under study (I-IV) belong to the class of compounds with a combined effect, interacting with couperoxide radicals, breaking the oxidation chain and breaking down the hydrochloric peroxide formed during the reaction into catalytic molecular products (Figure 3).

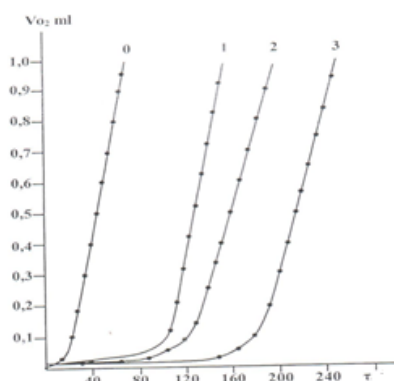


Fig.3. Kinetic curves of kumol oxidation in the presence of synthesized compounds (I-III). Volume of VO₂ oxygen (ml), τ -time (min), 110°C, [InH] = 5·10⁻⁵ mol / l

In order to study the ability of 4- (4-hydroxy-phenyl) -2-methyl-6-thioxo-1,5-dihydro-pyrimidine-3-cyclic thioureas to decompose cumylhydroperoxide (I-III), we studied the reaction of KHP with chlorbenzene at 110°C. KHP is thermally stable at this temperature. The inhibitor studied was found to break down cumylhydroperoxide (Figure 4).

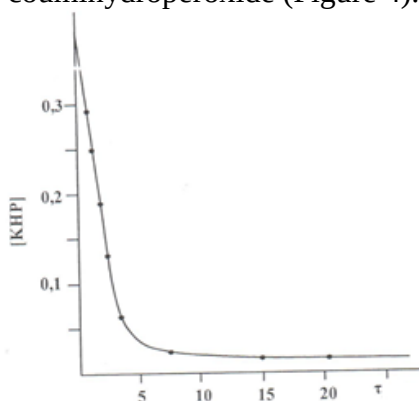


Fig.4. Kinetic curve of decomposition of cumylhydroperoxide in the presence of the synthesized compound (I). [KHP] = 0.38 mol / l, [InH] = $1 \cdot 10^{-4}$ mol / l



CONCLUSION

The antioxidant properties of the obtained compounds were studied in model reactions. Studies have shown that 4- (4-hydroxy-phenyl) -2-methyl-6-thioxo-1,5-dihydro-pyrimidine-3-cyclic thioureas also catalytically break down the cumyl peroxide formed during the oxidation process into reaction products.

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4-(4-HİDROKSİ-FENİL)-2-METİL-6-TİOKSO-1,5-DİHİDRO-İRİMİDİN-3-TSİKLIK TİOKARBAMİDLƏRİN SİNTEZİ VƏ XASSƏLƏRİ

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Tiokarbamidlə salisil aldehidinin və asetosirkə turşusunun etil efirinin üçkomponentli kondensləşməsi əsasında 4-(4-hidroksi-fenil)-2-metil-6-tiokso-1,5-dihidro-pirimidin-3-tiokarbamid sintez olunmuşdur. Tsiklik tiokarbamidlərin ən sadə və əlverişli yolla sintezi aldehidlərin, metilenaktiv birləşmələrin və tiokarbamidin turş mühitdə birmərhələli üçkomponentli kondensləşməsidir. Sintez olunan birləşmələr kristal maddələrdir. Bu birləşmələrin tərkibinə tiokarbamid fragmenti daxil olduğuna görə antioksidant xassə göstərmək qabiliyyətinə malikdir.

Açar sözlər: tiokarbamid, asetilasetosirkə efiri, etil spirti



СИНТЕЗ И СВОЙСТВА 4- (4-ГИДРОКСИ-ФЕНИЛ) -2-МЕТИЛ-6-ТИОКСО-1,5-ДИГИДРО-ПИРИМИДИН-3-ЦИКЛИЧЕСКИХ ТИОКАРБАМИДОВ

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4-(4-гидроксифенил)-2-метил-6-тиоксо-1,5-дигидропиримидин-3-тиомочевина синтезирована на основе трехкомпонентной конденсации тиомочевины с салициловым альдегидом и ацетилацетилэтиловым эфиром. Самый простой и удобный способ синтеза циклических тиомочевин - это одностадийная трехкомпонентная конденсация альдегидов, метиленовых активных соединений и тиомочевины в кислой среде. Синтезированные соединения представляют собой кристаллические вещества. Эти соединения обладают способностью проявлять антиоксидантные свойства из-за присутствия фрагмента тиомочевины.

Ключевые слова: *тиомочевина, ацетилацетоуксусный эфир, этиловый спирт*