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JIF = 1.500	SJIF (Morocco) = 2.031	

SOI: [1.1/TAS](#) DOI: [10.15863/TAS](#)

International Scientific Journal Theoretical & Applied Science

p-ISSN: 2308-4944 (print) e-ISSN: 2409-0085 (online)

Year: 2017 Issue: 07 Volume: 51

Published: 15.07.2017 <http://T-Science.org>

SECTION 9. Chemistry and chemical technology.

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REFORMATION OF 1-(N-1¹, 2¹-EPITIOPROPYL)-4-PHENYL-5-ACETYL-6-METHYL-1, 2,3,4-TETRAHYDROPYRIMIDINE-2 ONE WITH VARIOUS AMINES

Abstract: This article is dedicated to the investigation of nucleophilic substitution reactions of 3,4-dihydropyrimidine-2 (1H) ones with 1, 2-epoxy-3-chloropropane, including the synthesis of oxiranes unknown to literature in this way. It has been determined that the nucleophilic substitution reaction occurs due to the active hydrogen atoms in the third situation in pyrimidine ring. At the same time, it was revealed that thione-thiol tautomerism was characteristic of 3,4-dihydropyrimidine-2 (1H) thiones and the reaction goes in thiol form.

Key words: 1, 2-epoxy-3-chloropropane, oxirane, thione-thiol tautomerism, nucleophilic substitution reaction.

Language: English

Citation: Sujayev A, Najafova R, Hasanli S, Grigoryeva N (2017) REFORMATION OF 1-(N-1¹, 2¹-EPITIOPROPYL)-4-PHENYL-5-ACETYL-6-METHYL-1, 2,3,4-TETRAHYDROPYRIMIDINE-2 ONE WITH VARIOUS AMINES. ISJ Theoretical & Applied Science, 07 (51): 42-46.

Soi: <http://s-o-i.org/1.1/TAS-07-51-8> **Doi:**  <https://dx.doi.org/10.15863/TAS.2017.07.51.8>

INTRODUCTION

Aminothiols are bifunctional compounds and are widely used in the pharmacological studies since they have physiological feature in a wide spectrum [1]. On the other hand, they are used as radioprotector preventing radiation rays [2]. Medications such as tifen, aprofen are being successfully implemented at this time in medical clinic as derivatives of aminothiols [3]. It has been determined from systematic study in laboratory of Theoretical Bases of Synthesis and Action Mechanism of Additives of Institute of Chemistry of Additives that amino thiols and their metallic salts are the most effective antioxidants that prevent the oxidation of cumene [4-6].

EXPERIMENTAL

Synthesis of 4-phenyl-5-acetyl-6-methyl-1,2,3,4-tetrahydropyrimidine-4-one (I)

5.3 g (0.05 moles) benzaldehyde, 8 g (0.08 moles) acetylacetone, 3 g (0.05 moles) urea and 15 ml ethyl alcohol are located in three neck 50 ml flask equipped with the thermometer, dropping funnel and mixed quickly. 1 g trifluoroacetic acid is added on reaction mixture drop by drop and heated at 60-65 ° C for 4 hours. Then the reaction product is cooled. Sank white crystals are filtered and re-crystallized in hexane. 3.8 g combination was obtained (I).

Synthesis of 1-(N-1¹,2¹-epoxypropyl)-4-phenyl-5-acetyl-6-methyl-1,2,3,4-tetrahydropyrimidine-2 (II)



5.8 g (0.025 mol) 4-methyl-5-acetyl-6-methyl-1,2,3,4-tetrahydropyrimidine-2-one (II), 2.8 g (0.05 moles) potassium hydroxide and 20 ml isopropyl are positioned in 50 ml three neck flask equipped with thermometer, dropping funnel and mechanical mixer and rapidly mixed. The reaction mixture is heated as much as isopropyl alcohol boils. 2.3 g (0.025 moles) were added to 1,2-epoxy-3-chloropropane and the reaction mixture is mixed at the boiling temperature of isopropyl alcohol for 5 hours. Collapsed crystals are separated by filtration after cooling. Obtained crystals are recrystallized in hexane. 5 g new combination was obtained. (II).

Synthesis of 1-(N-1', 2' epitiopropyl)-4-phenyl-5-acetyl-6-methyl-1,2,3,4-tetrahydropyrimidine-2 one (III)

1-(N-1', 2' epitiopropyl)-4-phenyl-5-acetyl-6-methyl-1,2,3,4-tetrahydropyrimidine-2 one (III) and 0.8 g (0.01 moles) thiocarbamide and 20 ml isopropyl are positioned in alcohol within 50 ml three neck flask equipped with thermometer, dropping funnel and mechanical mixer and rapidly mixed. 5 drops of thick sulphuric acid are added to the reaction mixture. The temperature of the reaction mixture is increased up to 40-50 °C and mixed for 2 hours. The reaction mixture is cooled and white crystals are separated by filtration. Obtained crystals are recrystallized in hexane. 1.9 (III) g new combination was obtained.

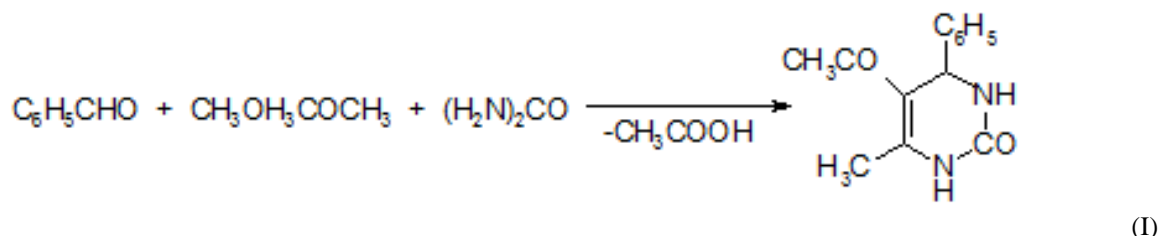
Synthesis of 1-(N-1' phenylamino-2'-mercaptopropyl)-4-phenyl-5-acetyl-6-methyl-1,2,3,4-tetrahydropyrimidine-2 one (IV-VII)

2.98 g (0.01 moles) (III) solution and 20 ml ethyl alcohol are positioned inside 50 ml three neck flask equipped with thermometer, dropping funnel and mechanical mixer and rapidly mixed. 2 g (0.02 moles) aniline is added on reaction mixture drop by drop. Then it is heated at 65-75 °C for 3 hours. The reaction product is cooled. Once solvent and aniline residues are distilled in vacuum, residue is recrystallized in hexane. 2.57 g (V) combination was obtained.

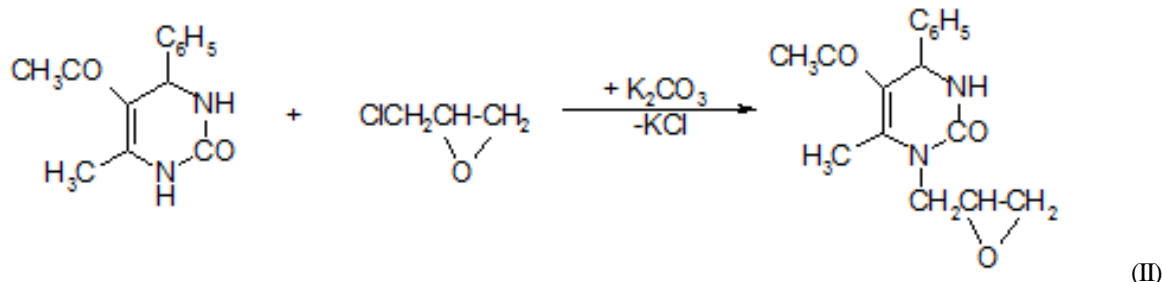
Other compounds have been synthesized in a similar manner.

RESULTS AND DISCUSSION

Studies on determining the contact between the synthesis of aminothiols and their antioxidant properties have been continued and in the current article, 1-(N-1', 2' epitiopropyl)-4-phenyl-5-acetyl-6-methyl-1,2,3,4-tetrahydropyrimidine-2-one has been synthesized and 1,2-aminopropantiols have been synthesized and characterized from its interaction with its various amines. To this end, 4-phenyl-5-acetyl-6-methyl-1,2,3,4-tetrahydropyrimidine-2-one (I) has been received from three component condensation of benzaldehyde, acetylacetone and carbamide with trifluoroacetic acid:



1-(N-1', 2'-epitiopropyl)-4-phenyl-5-acetyl-6-methyl-1,2,3,4-tetrahydropyrimidine-2-one (II) is



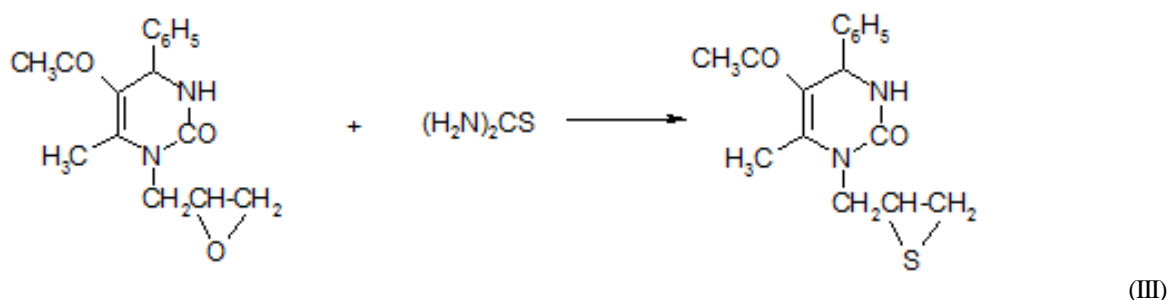
When synthesized oxirane (II) is thio epoxidized with the presence of catalytic sulphuric acid, it becomes 1-(N-1',

obtained when (I) combination is affected by 1,2-epoxy-3-chloropropane with potassium carbonate:

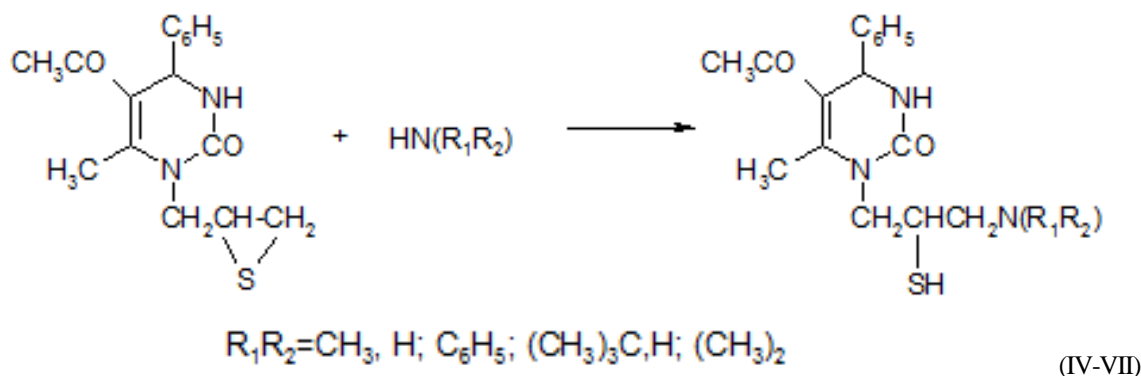
2' epitiopropyl) 4-phenyl-5-acetyl-6-methyl-1,2,3,4-tetrahydro pyrimidine-2-one (III):

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When thiirane (II) is heated at 70-75°C with various amines in ethyl alcohol environment for 3 hours, matching 1,2-amino thiols have been synthesized and characterized:



The nucleophilic compound reaction course of the thiirane with various amines has been regulated with thin layer chromatography method.

The structure of the synthesized compounds has been approved with IR and ^1H , ^{13}C NMR spectroscopy. Its cleanliness was set by the thin layer chromatography.

Characteristic stripes observed in 1245, 1030 and 825 cm^{-1} of IR spectrum of synthesized oxirane characterize asymmetric, symmetric and pulsation waves in oxirane ring. When oxirane is epoxidized stripes of oxirane are not observed. However, the stripe that characterizes valence waves of C-S communication in three membered thiirane ring in 665 cm^{-1} is clear. Valence dance stripe in NH communication in IR spectrum of 1,2-aminopropanthiols obtained from nucleophilic break of thiirane compounds is detected at 3345-3445 cm^{-1} area 2540 cm^{-1} stripe is compatible with the valence dances of SH communication.

Signal of two protons in CH_2O group in the oxirane (II) fragment is observed as doublet at 2.40-2.45 and 2.70-2.75 ppm, signal of single proton in CH-O group as multiplet at 2.80-3.45 ppm. While

examining ^1H NMR spectrum of thiirane (I) compound, we see that the signal of two protons in CH_2S group is observed as two doublets at 2.15-2.25 and 2.35-2.45 ppm compared to CH_2O group. Proton in CHS group is observed as multiplet at 3.10-3.20 ppm.

Signal of three protons in methyl group in pyrimidine fragment in synthesized compounds' molecule has been detected at 1.2-1.4 ppm, while signal of three protons in acetyl group at 2.5 ppm as singlet. Proton of single signal in methine group connected to aromatic ring is detected as singlet at 4.8 ppm, signal of asymmetrical protons in aromatic ring connected to pyrimidine fragment as multiplet. Signal in NH group is observed at the weakest area-9.45 ppm.

Signals that characterize the density of carbon atoms in ^{13}C NMR spectrum are detected at 25,29,47,53,86,117,123,127,132,142,151,180,208 ppm.

Physical and chemical constants and output of the synthesized compounds are listed in the table below.

Table 1

Physical and chemical constants and output of the synthesized compounds

№	Yield, %	T _m , °C	Brutto formul	Find/Calculated, %			
				C	H	N	S
I	65	260	C ₁₃ H ₁₄ N ₂ O ₂	67.67 67.80	6.25 6.12	12.06 12.16	-
II	70	220	C ₁₆ H ₁₈ N ₂ O ₃	66.84 67.12	6.62 6.34	9.67 9.78	-
III	65	208	C ₁₆ H ₁₈ N ₂ O ₂ S	63.40 63.55	5.85 6.00	9.13 9.26	10.48 10.60
IV	60	210	C ₁₇ H ₂₀ N ₃ O ₂ S	61.21 61.41	6.47 6.67	12.54 12.64	9.59 9.65
V	65	198	C ₂₂ H ₂₄ N ₃ O ₂ S	66.79 66.98	6.36 6.17	10.53 10.65	8.07 8.17
VI	55	220	C ₂₀ H ₂₈ N ₃ O ₂ S	64.01 64.14	7.41 7.54	11.19 11.22	8.47 8.56
VII	50	260	C ₁₈ H ₂₅ N ₃ O ₂ S	61.94 62.22	6.97 7.25	11.97 12.09	9.18 9.23

¹H, ¹³C NMR spectra were taken at Bruker-300 MHz spectrometer, while IR spectra were taken in the petrolatum oil at Specord-75 R device. Its cleanliness was checked by thin layer chromatography. Alcohol and hexane mixture (1: 3) as eluent was used.

CONSLSION

Reactivity of 3,4-dihydropyrimidine-2 (1H) ones with 1,2-epoxy-3-chloropropane in nucleophilic substitution reaction has been studied. It has been determined that the nucleophilic substitution reaction occurs due to the active hydrogen atom in the third situation in pyrimidine ring.

It was detected that the nucleophilic substitution reaction direction of 3,4-dihydropyrimidine-2 (1H)

thiones with 1,2-epoxy-3-chloropropane had been different. It was determined that thione-thiol tautomerism was characteristic of 3,4-dihydropyrimidine-2 (1H) thiones and the reaction goes in thiol form.

Oxyranes unknown in new literature have been synthesized from interaction of 1,2-epoxy-3-chloropropane with 3,4-dihydropyrimidine-2 (1H) - ones (thiones).

Acknowledgments

This synthesis reactions was supported by the Science Development Foundation under the President of the Republic of Azerbaijan - Grant №EIF/GAM-3-2014-6(21)-24/08/4-M-17, 21.12.2015.

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