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OPTICALLY ACTIVE 2-AMINE-4-ARYL-7,7-DYMETHYL-5-OXO-5,6,7,8-TETRAHYDRO-4H-CHROMENE-3-CARBONITRILES SYNTHESIZED WITH THE PARTICIPATION OF KHIRAL ORGANIC CATALYSTYS AND STUDY OF ANTIMICROBAL PROPERTIES

***Abstract**: Optically active 2-amine-4-aryl-7,7-dimethyl-5-oxo-5,6,7 8-tetrahydro-4H-chromen-3-carbonitriles were synthesized from multi-component condensation of aromatic aldehydes with malonnitryl and methylenactive compound of 5,5-dimethylcyclohexane-1,3-dion in the presence of chiral organic catalysts and their antimicrobial properties were studied.*

***Key words**: Asymmetric synthesis, optically active 4H-chromens, chiral organic catalysts, antimicrobial properties.*

***Language**: English*

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Introduction

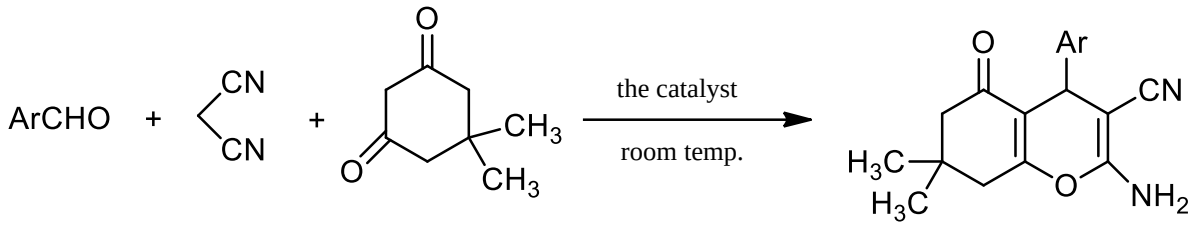
Multicomponent domino reactions are a useful field in the field of organic synthesis that meets the requirements of green chemistry [1-5]. 4H-chromens (benzo-γ-pyranes) synthesized by this method are a class of heterocyclic compounds that are very important for a biological and pharmacological areas [6-9]. The role of functional 4H-chromens derivatives is increasing in medicine [10], agrochemistry, cosmetics and pigment industry [11]. 4H-pyran drugs are used in the treatment of many diseases such as hypertension, asthma and ischemia [12]. Given the successfull use of these drugs in medicine, the synthesis of optical isomers is one of the most important issues on the basis of enantioselective synthesis. The anti-epileptic, antidiabetic and anticholinic properties of some 4H-chromens synthesized by us have been investigated [13].

Continuing our research, it was important to investigate the antimicrobial properties of some synthesized 2-amine-4-aryl-7,7-dimethyl-5-oxo-5,6,7,8-tetrahydro-4H-chromene-3-carbonitriles.

For this purpose, we first synthesized some 2-amine-4-aryl-7,7-dimethyl-5-oxo-5,6,7,8-tetrahydro-4H-chromen-3-carbonitriles on the basis of three-component condensation in the presence of chiral organic catalysts.

Aromatic aldehydes, 5,5-dimethylcyclohexane-1,3-dion and malonnitrile were used as the aim of study, and more easily and cheaply obtained optically active α-amino acids were used as catalysts, and the reaction was carried out at room temperature.

The scheme of the reaction is as follows:



Ar= C_6H_5 (I), 2-ClC_6H_4 (II), 2-C_4H_3O (III), 4-$CH_3OC_6H_4$ (IV).

Catalyst = L-glutamine, L-cysteine, L-arginine

The course of the reaction was followed by thin-layer chromatography (sorbphil).

The antimicrobial properties of the synthesized compounds I-IV were studied at the Department of Microbiology and Immunology of the Azerbaijan Medical University.

The antimicrobial effects of these substances have been compared with the widely used alcohol, furacillin and nitrofungin. As a test culture, golden staphylococci (St. aureus) were obtained from Gram-positive microorganisms, intestinal spores (E. coli) from Gram-negative microorganisms , blue-green purulent spores (Ps. aeruginoza) from pigment-forming organisms and Candida (Cand. albicans) from fungi. Meat-peptone agar was used to grow bacteria and Saburo nutrient medium was used to grow mushrooms.

The seedlings were kept in a thermostat at 37 ° C for 24 hours for bacteria and 48 hours at 28 ° C for fungi. Thus, the antimicrobial properties of 2-amine-4-phenyl-7,7-dimethyl-5-oxo- 5,6,7,8- tetrahydro-4H- chromene-3- carbonitrile and 2-amine-4-(2-chlorophenyl)-7,7-dimethyl-5-oxo-5,6,7,8-tetrahydro-4H-chromene-3- carbonitrile were investigated by serial dilution method. For this purpose, dilution of a 1% solution of each substance in ethyl alcohol in sterile distilled water was performed as follows: 1: 100, 1: 200, 1: 400, 1: 800 (1, 2, 3, 4).

Table 1. Antımıcrob effects of new synthesed substances

Test cultures	Exposure time (minutes)	Analyzed substances							
		I				II			
		1	2	3	4	1	2	3	4
St. aureus	10	-	-	-	+	-	-	+	+
	20	-	-	-	+	-	-	+	+
	40	-	-	-	+	-	-	-	+
	60	-	-	-	+	-	-	-	+
Ps. aeruginoza	10	-	-	-	+	-	-	+	+
	20	-	-	-	+	-	-	+	+
	40	-	-	-	+	-	-	+	+
	60	-	-	-	+	-	-	+	+
E.coli	10	-	-	-	+	-	-	+	+
	20	-	-	-	+	-	-	+	+
	40	-	-	-	+	-	-	+	+
	60	-	-	-	+	-	-	+	+
Cand. albicans	10	-	-	+	+	-	-	+	+
	20	-	-	-	+	-	-	+	+
	40	-	-	-	+	-	-	-	+
	60	-	-	-	-	-	-	-	+

Note: "+" indicates full completion
"-" indicates no ending

According to the experiments, 2-amine-4-phenyl-7,7-dimethyl-5-oxo-5,6,7,8-tetrahydro-4H-chromene-3-carbon-nitrile (I) and 2-amine-4- (2-chlorophenyl) -7,7-dimethyl-5-oxo-5,6,7,8-tetrahydro-4H-chromene-3-carbonitrile (II) were considered the more active antimicrobials. As can be

seen from the table, these substances are antimicrobial. Even the effects on Candida albicans are quite different, especially when they are destroyed in a ratio of 1: 200 in 10 minutes, diluting 1: 400 destroys them in 40 minutes, and 1: 400 substance I kills Canidida in 20 minutes.

All experiments were performed in the same way as the controls (ethyl alcohol, furacillin, nitrofungin).

Table 2. Antımıcrob effect of control substances

Test cultures	Exposure time (minutes)	Control items											
		Furasilin				Ethyl alcohol				Nitrofungin			
		1	2	3	4	1	2	3	4	1	2	3	4
St. aureus	10	-	+	+	+	-	+	+	+				
	20	-	+	+	+	-	+	+	+				
	40	-	+	+	+	-	+	+	+				
	60	-	+	+	+	-	+	+	+				
Ps. aeruginoza	10	+	+	+	+	+	+	+	+				
	20	+	+	+	+	-	+	+	+				
	40	+	+	+	+	-	+	+	+				
	60	-	+	+	+	-	+	+	+				
E.coli	10	-	+	+	+	+	+	+	+				
	20	-	+	+	+	-	+	+	+				
	40	-	-	+	+	-	+	+	+				
	60	-	-	-	+	-	+	+	+				
Cand. albicans	10	+	+	+	+	+	+	+	+	+	+	+	+
	20	+	+	+	+	+	+	+	+	+	+	+	+
	40	+	+	+	+	-	+	+	+	-	+	+	+
	60	+	+	+	+	-	+	+	+	-	+	+	+

Based on these experiments, substances I and II can be considered as active antimicrobial substances.

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