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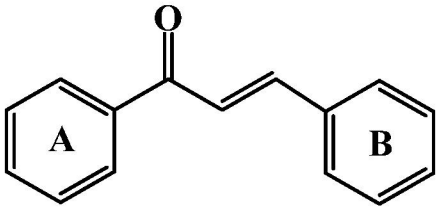
CHALCONES-SYNTHONS IN SYNTHESIZING BIOLOGICALLY ACTIVE MATTERS

Abstract. The review paper summarizes and systematizes the literature data of recent years, as well as the results of the authors' research in the field of functionally substituted chalcones. The most common natural chalcones, methods of production, reactivity and biological properties of synthetic chalcones are given.

Keywords: substituted aromatic aldehyde, chalcone, pyrazoline, flavonone, cytokine, NF-κB transcription factor.

Important representatives of organic compounds having a preparative value are α, β-unsaturated carbonyl compounds, among which benzylideneacetophenones (chalcones) occupy a notable place. Since the discovery in 1896 of chalcones [1], the interest in the chemistry of its substituted and heterocyclic analogs has not faded. The name "chalkone" was proposed by the Polish chemist Stanislav Kostanecki. It comes from the Greek word *"chalcos"(χαλκός)* that means "copper".

Chalcones 1,3-diphenyl-2-propen-1-ons (1) belong to the compounds in which two aromatic nuclei are bound by three carbon atoms of the α, β-unsaturated carbonyl system [2]. Chalcones can have *cis*- and *trans*-forms, but the *trans*-form is thermodynamically more stable.



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1. Widespread natural chalcones

Chalcones are quite widespread in nature: they are found in flowers, fruits, seeds, and wood. They are closely related to a number of substances that belong to the class of flavonoids: flavones, flavonones, flavonols. Most of the representatives of the chalcones are found in all plant organs in the form of aglycones and glycosides and differ in the number of substituents in the A ring. So, for example, butein chalcone that is often found in the family of comatose chalcones, is in the form of *Coreopsis giganiea* 4-glycoside; chalconoraine is in the form of 2-glycoside isosalipurposide in *Salix purpyrea* [3, 4]. By now more than 200 different aglicones of the chalconic nature are known. Quite often dihydrochalcones are found in plants, in which the three-carbon fragment has a reduced double bond. They are known exclusively in glycosidized form, as well as methoxy- and pyrano-derivatives. So, some species of apple

tree contain glycoside phloridzin (2'-glucoside, 4', 2', 4,6-tetraoxidyhydrochalcone) that causes intensive release of glucose from the body in a person (phluoridinine diabetes), siboldin (3-hydroxyfloretin-4'-glucoside), azepogenin in the form of azobothin 2'-glycoside [4]. It is believed that chalcones are precursors of various groups of flavonoid compounds in biosynthesis.

Many bright colors of the plant world of our planet in spring, summer and autumn are caused by compounds of one flavonoid class, i.e. chalcones. They are called "antichloropigments", they are yellow pigments of flowers that turn orange in pairs of ammonia. In particular, discoloration of the contained chalcones of the preparative forms is used in the field of pharmaceuticals, for example as a color-changing oral care component that can be phenyl-3-methoxy-4-hydroxystyryl ketone and 3-(4'-hydroxy-3'-methoxy)1-phenylprop-2-en-1-on [5]. Chalcones are relatively often found in one family: *Compositae*, especially in *Coreopsis* and *Dahlia.* They are also found in some *Leguminosae (Butia, Cylicodiscus, Glycyrhiza, Plathymenia, Ulex)* and in *Dihymocarpus (Gesneriaceae).* Table 1 lists some chalcones and their derivatives isolated from natural raw materials.

Table 1- Chalconesandtheirderivativesisolatedfromnaturalsources

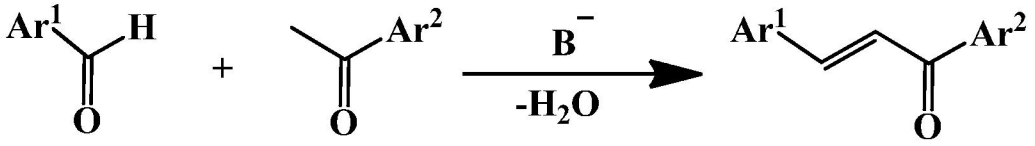
No	Chalcones and their derivatives	Natural sources	Reference
1	2'-hydroxy-2,4,6-trimethoxychalcone	*Andrographis lincate (Acanthaceae)*	[6]
2	2', 4'-dihydroxy-4-methoxydihydroalchalcone (davidigenin)	*Artemisia dracuiiculus L. (Asteraceae)*	[7]
3	2 ', 4', 4-trihydroxy-3 '- [6-hydroxy-3,7-dimethyl-2 (E) -7-octadienyl] chalcone	*Artocarpus nobilis*	[8; 9]
4	2 ', 4', 6 ', 4-tetrahydroxychalcone (isosalipurpol);	*Arabidopsis thaliana (Angiosperm)*	[10; 11; 12; 13]
5	2 & apos;, 4 & apos;, 4-trihydroxychalcone (iso-liquitytigenin)	*Asarum canadense (Aristolochiaceae)*	[14]
6	chalcononanerenine 2'-O-β-D-glucoside-4'-O-β-gentobiose; 2 ', 4'-di-O-β-D-glucoside	*Boesenbergia pandurata (Robx.)*	[15]
7	2', 6'-dihydroxy-4'-methoxychalcone;	*Brassica alba (Cruciferae)*	[16]
8	2'-hydroxy-4,4'6'-trimethoxychalcone	*Caesalpinia pulcherrima L.*	[17]
9	4-hydroxy-2 ', 4'-dimethoxy dihydroqualone; isocyclitis	*Crinum bulbispermum bulbs.*	[18]
10	4,4'-bis-a-0-glucosyl-4,2 ', 4'-trihydroxy-6, -methoxychalcon (aglycone)	*Derodendron phlomidis (Vcrbenaceae)*	[19]
11	3'- (3 "-methyl-3" -hydroxybutyl) -2', 4,4'-trihydroxy-6'-methoxychalcone; 4'-O-glucuronyl-2,4-dihydroxy-6'-methoxy-3'-prenylalkalkone; 1 - [(2 ', 4'-dihydroxy-3'-isoprenyl-6'-methoxy) - phenyl] - [3- (4-hydroxyphenyl)] - 2,3-epoxypropan-1-one; 4-acetoxy-2 ', 4'-dihydroxin-6'-methoxy-3'-prenylalkalcon; 1 - [(2', 4'-dihydroxy-3'-isoprenyl-6'-methoxy) -phenyl] - [3- (4-hydroxyphenyl)] - 2,3-epoxypropan-1-one; 4-acetoxy-2', 4'-dihydroxin-6'-methoxy-3'-prenylalchalcone	*Humulus lupulus L. (Cannabaceae)*	[20; 21]
12	4', 6', 4-trihydroxy-5-methoxychalcone; 4 ', 6'-dihydroxy-4, 5-dimethoxychalcone	*Iryanthcra polyneura (Myristicaceae)*	[22]
13	2', 4', 6'-trihydroxy-4-methoxydihydrochalcone;	*Iryanthcra virola (Myristicaceae)*	[22]
14	2'-megoxy-4 ', 6', 4-trihydroxidehydrochalcone;	*Iryanthera sagotiana (Myristicaceae)*	[22]
15	2', 4-dimethoxy-4', b'-dihydroxydihydrochalcone;	*Marchantia paleaceae*	[10]
16	2'-glucoside-4 ', 6'-dihydroxy-4-methoxy-dihydro-chalcone; 4 ', 6', 4-trihydroxy-5-methoxydihydro-chalcone; 2', 4, 5-trimethoxy-4', 6'-dihydroxydi-hydrohalcon; 4 ', 4-dimethoxy-6'-α-dihydroxydi-hydrochalcone	*Medicago sativa L.*	[10; 12]
17	Bi-2 ', 4', 6'-trihydroxy-4-methoxydehydrochalcone	*Mellettia ferruginea (Fabaceae)*	[23]
18	2', 4', 6', 4-tetrahydroxychalcone (naringenin)	*Vitis vinifera (Angiosperm)*	[12; 24]

2. Methods of obtaining synthetic chalcones

Synthetic chalcones are of considerable interest for chemists and pharmacists, which is due to several factors: the comparative simplicity of the chemical structure that allows synthesizing on their base a large

variety of molecules with high pharmacological activity, as well as the possibility of using them as valuable synthetic intermediates, for example, in the synthesis of various heterocyclic compounds. It should be noted that α, β-unsaturated ketone groups are probably responsible for most of the observed biological properties of chalcones, since these groups are present in all biologically active molecules, and their removal is associated with losing activity [25]. Many authors attribute the presence of this fragment to the different biological activity of the substituted chalcones: anti-inflammatory [26], antitubercular [27], antioxidant, antiviral, antimicrobial, antifungal and many other activities [28, 29]. Substituted chalcones are promising antitumor preparations [30, 31]. They also attract attention as preparations that have selective activity against dermatophytes [32]. Substituted chalcones are of interest as components for solar cells [33], ion-selective electrodes, molecular devices and photofunctional materials [34-38].

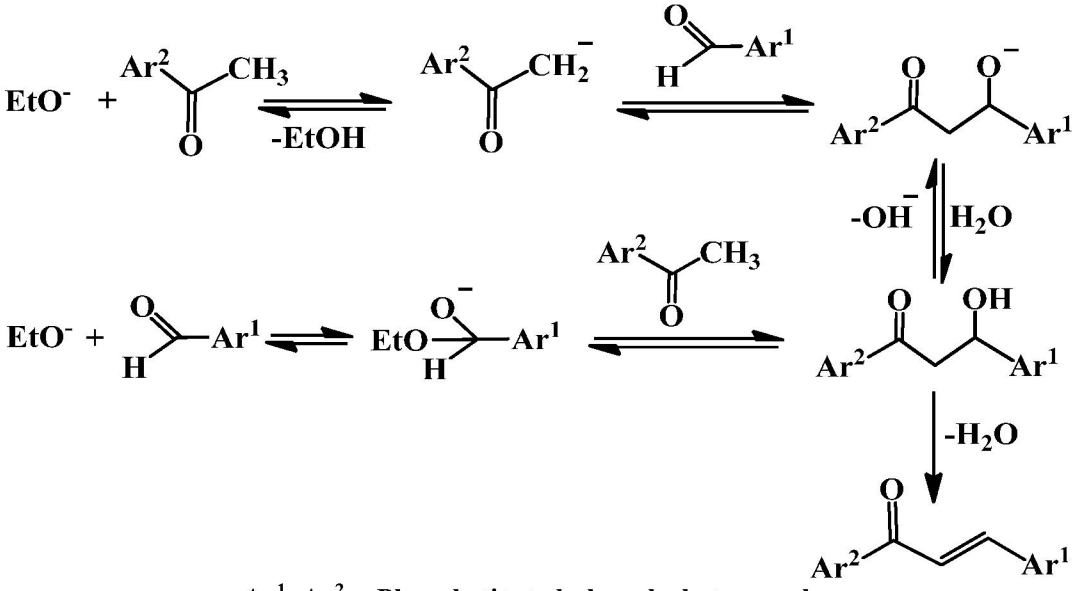
The most significant method of synthesizing chalcones is known [39] the croton condensation involving formyl- and acetyl-containing compounds. According to the Claisen-Schmidt reaction, from 32 substituted acetophenones and 40 aromatic benzaldehydes there were obtained 1280 substituted chalcones by combinatorial synthesis methods. The use of these chalcones in 9 condensation and cyclization reactions led to producing 74,000 five- and six-membered cyclic compounds [40].



Ar^1, Ar^2 = Ph, substituted phenyls, heterocycles

When studying the Claisen-Schmidt reaction using the UV spectroscopy method, it was found that the interaction of substituted benzaldehydes with acetophenone is described by the second-order velocity equation. In this connection the authors of [41] proposed two reaction mechanisms. The first one is through removing acetophenone by the proton base from the methyl group (mechanism I), the second one is through attacking the ethylate anion on the carbon of the carbonyl group of the aldehyde (mechanism II). Using the thermodynamic parameters in the discussion of each stage of the proposed mechanisms, the authors concluded that the mechanism II should be more profitable [41]:

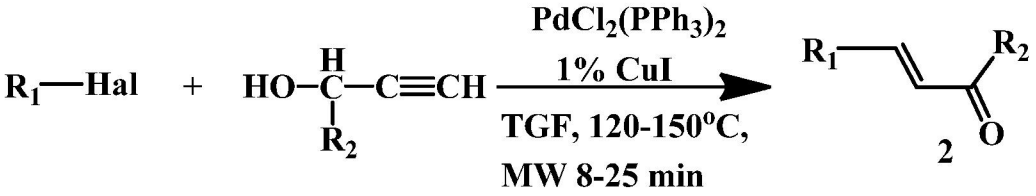
MechanismI



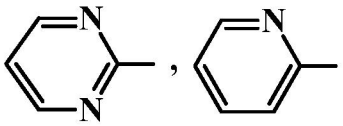
Ar^1, Ar^2 = Ph, substituted phenyls, heterocycles

But in some cases, with the use of substituted chalcones, this method is accompanied by side oxidation-reduction processes leading to reducing the yield of the desired product. In literature a large number of methods for synthesizing chalcones using homogeneous and heterogeneous catalysis techniques have been described [42, 43], among which the catalysis with activated barium hydroxide [44], hydrochloric acid formed in situ by interaction of $SOCl_2$ in absolute EtOH [45], BF_3-Et_2O [46], potassium hydroxide deposited on KF-Al_2O_3 in combination with ultrasonic irradiation, ionic liquids [47, 48]. There are known works using microwave irradiation, using metal oxides, I_2-Al_2O_3 without using solvents, which reduced the reaction time from 3 hours to 80 seconds [49, 50]. These conditions allow getting rid of unwanted reaction products [51], increasing the yield and shortening the reaction time to several minutes.

In addition to the Claisen-Schmidt reaction, alternative waysof synthesizing substituted chalcones are described in literature, which make it possible to obtain them with high yields under mild conditions. In some cases the methods allow avoiding undesirable redox processes or obtaining compounds not available in the classical Claisen-Schmidt reaction. However, in this case, as a rule, expensive reagents are required, the use of microwave or ultrasound exposure and inert atmosphere. Thus, for synthesizing chalcones 2, there was used the Sonogashira coupling reaction under microwave conditions between the aryl halide and substituted propargyl alcohol, which allowed producing the target products with high yields in a short time [26]. It was shown that the reaction proceeded only in the presence of an electron-withdrawing group as a substituent in the aromatic nucleus R_1.

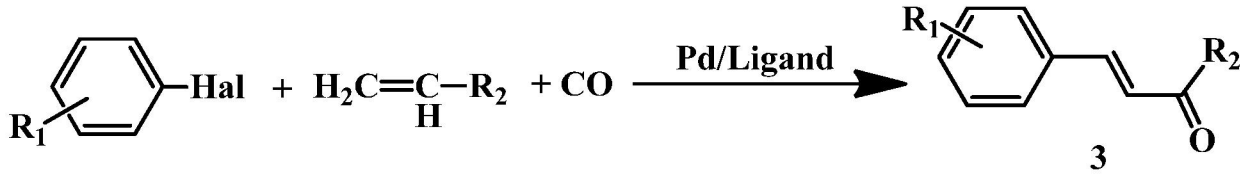


R_1 = Ph, 4-CN-Ph, 4-EtO_2C-Ph, 3-NH_2Ph,



R_2 = Ph, 2-tienyl, 3-tienyl, C_3H_8,

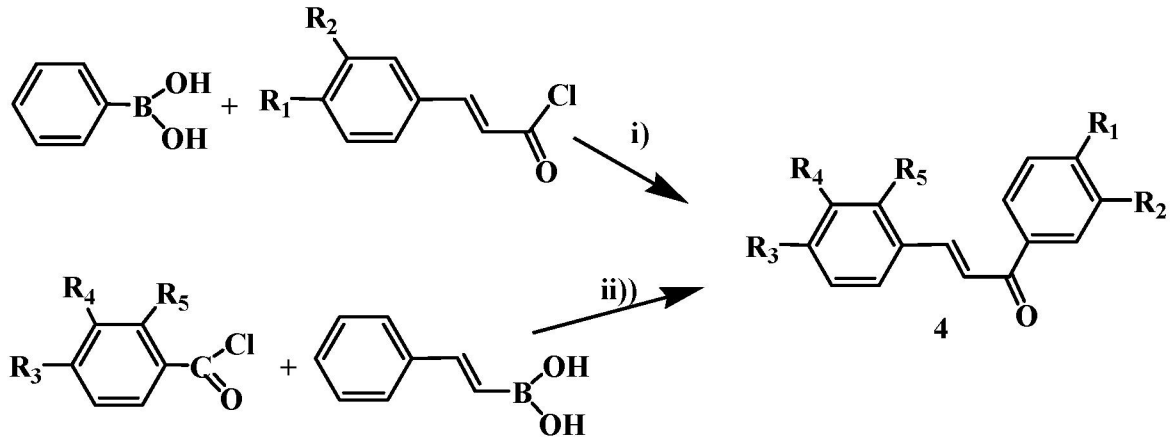
In [52] there are presented the data of the Heck coupling-carbonylation reaction involving aryl halide and styrene or substituted vinyl in the presence of carbon monoxide using a palladium catalyst leading to formation of chalcones 3. It is shown that the yields of the product 3 make 41-90%, depending on using the ligand and a substituent in the aromatic ring of the chalcone.



R_1 = H, 4-CH_3, 2-t-Bu, 2-CH_3, 4-CF_3, 4-Br, 4-Cl, 4-CO_2Me, 4-OCH_3, 3,4-O-CH_2-CH_2-O, 4-OEt

R_2 = Ph, 4-t-BuPh, 3-CH_3Ph, 4-CH_3OPh, 4-ClPh, 4-FPh, -C(O)-O-nBu, -O-nBu

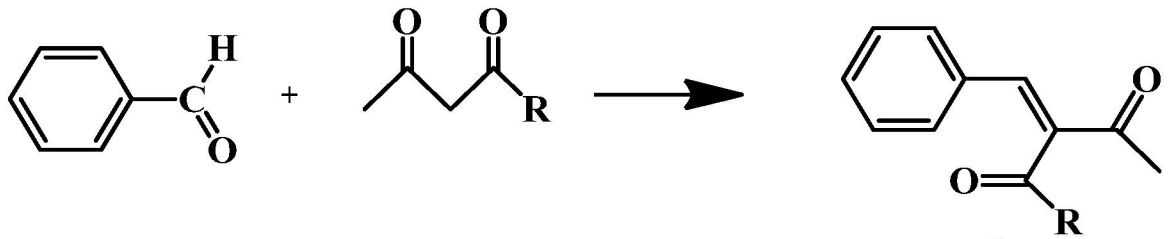
The authors of Ref. [53] obtained chalcones 4 under mild conditions using several variants of the Suzuki reaction: the first one using cinnamoyl chloride and phenylboronic acid, and the other with benzoyl chloride and phenyl vinyl boric acid. Both reactions led to the desired product 4.



R_1 = H, OCH_3; R_2 = H, NO_2, OCH_3;
R_3 = H, OCH_3; R_4 = H, CF_3, NO_2, OCH_3; R_5 = H, CF_3

i): $(PPh_3)_4Pd(o)$, Cs_2CO_3, toluol. Yield 40-50%
ii)): $(PPh_3)_4Pd(o)$, Cs_2CO_3, toluol.Yield 70-95%

Chalcones can also be obtained by the Knoevenagel condensing, i.e. interaction of aldehydes or ketones with compounds having an active methylene component, for example, acetoacetic ether under conditions of the basic catalysis [39]. This reaction with interaction of benzaldehyde with AAE leads to the formation of chalcone 5.



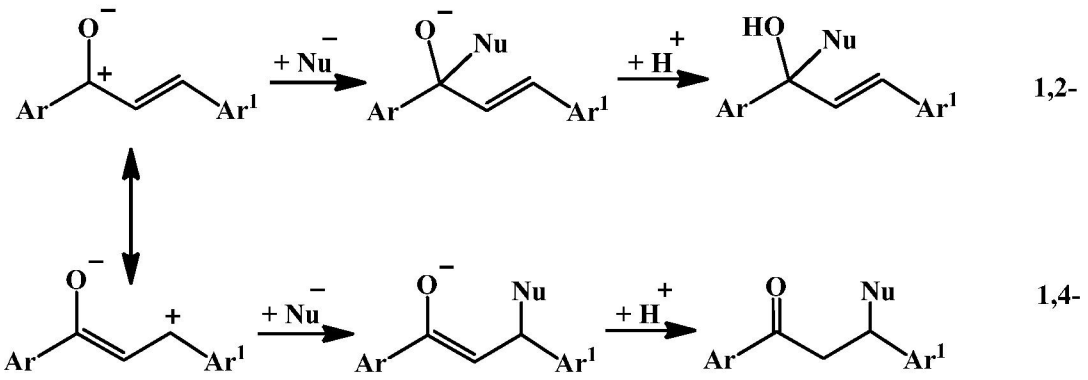
R = OAlk, Alk

Despite a large amount of literature dealing with optimization of methods for synthesizing chalcones, a lot of authors use an exclusively traditional method of synthesis, i.e. Claisen-Schmidt condensation (mixing under basic conditions in ethanol within 3-48 hours) [31, 34-37, 54].

3. Reactivity of chalcones

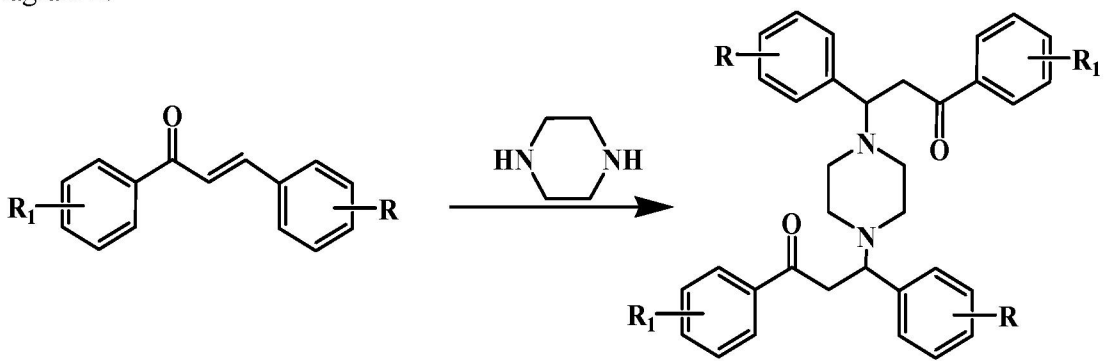
Chalcones possess high reactivity. This is connected with the presence in their molecule of two electrophilic centers:a carbonyl group and aβ-carbon atom of the conjugated double bond [1]. Chalcones can react as ambiguous electrophiles as a result of delocalization of the electron density in the conjugate system C = C-C = O. When interacting with the chalcone, the nucleophile attacks either the carbon atom of the carbonyl group (1,2-addition) or the β-carbon atom (1,4-addition); the mechanism of the reactions is shown in Diagram 1. The nature of these two electrophilic centers in chalcones is different, which is reflected in the high regioselectivity of reactions with mono- and binucleophiles.

Diagram 1



The interaction of chalcones with piperazine usually leads to the formation of Michael bis-aza-adducts. These reactions performed under various conditions, have been repeatedly described in literature as an example of forming a carbon-nitrogen bond [55-57]. Thus, chalcones, both unsubstituted and substituted, react with anhydrous piperazine in toluene giving the corresponding Michael bis-aza-adducts [55]. Similarly there takes place a reaction in the mixture of cyclohexane ether (1:2) in the presence of calcined potassium carbonate [56]. Under ultrasonic irradiation chalcones interact with piperazine in water, also forming Michael bis-aza-adduct with a high yield [57].

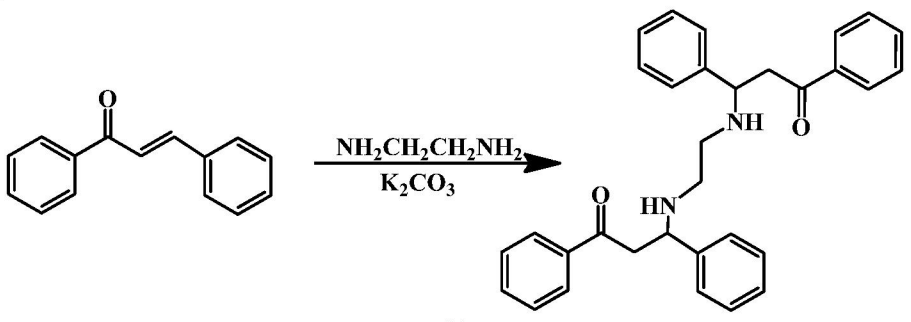
Diagram 2.



R_1=R=H; R_1=H, R=3-NO_2; R_1=H, R=2-Cl; R_1=4-Cl, R=H; R_1=H, R=4-Cl; R_1=R=4-Cl; R_1=4-Br, R=H; R_1=H, R=4-Me; R_1=4-Me, R=H; R_1=H, R=4-OMe; R_1=R=4-Me; R_1=4-Me, R=4-OMe; $C_6H_5CH_3$.

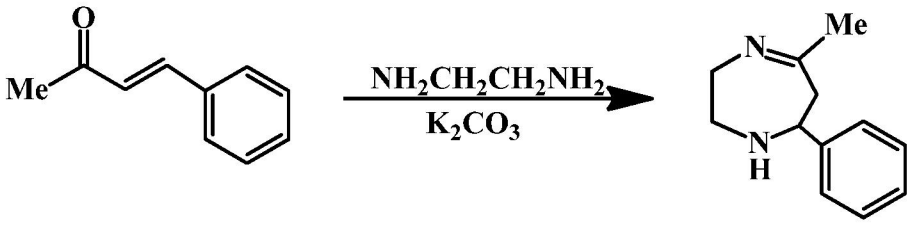
The reactions of chalcones with ethylenediamine can proceed with forming Michael bis-aza-adducts [56] or diazepines [58, 59]. Thus, the interaction of unsubstituted chalcones with ethylenediamine in low-polar solvents occurs along the path of attaching to the β-atom of carbon and leads to Michael bis-aza-adduct [56].

Diagram 3



However, the formation of Michael bis-aza-adducts is not the only way of the reaction proceeding. In [58] the reaction of chalcone with ethylenediamine there was obtained tetrahydrodiazepine with the 59% yield.

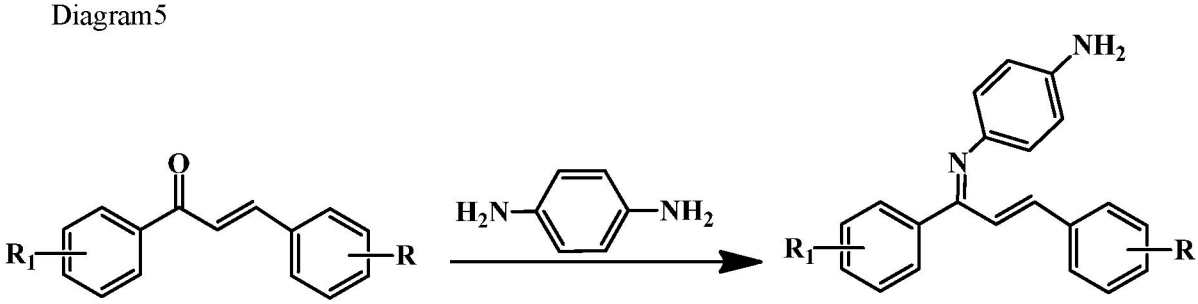
Diagram 4



The mechanism of this reaction is not described in literature, but it can be assumed that it proceeds in two stages: at first there is formed the Michael aza adduct, then there takes place its cyclization by attacking the second amino-group on the carbon atom of the carbonyl group.

The interaction of chalcons with n-phenylenediamine leads to the formation of Schiff bases that can then be used in synthesizing flavones. Synthesizing flavones and their derivatives attracts considerable attention due to their high antioxidant [60-63], anxiolytic [64], antitumor [65] and anti-inflammatory [66, 67] activity. In [68] the synthesis of iminoflavones is reported by the oxidative cyclization of chalconeimines. One of the stages of this synthesis is interaction of chalcons with substituted anilines, in particular, n-phenylenediamine, and forming the corresponding imine with a high yield. The Schiff bases that possess antibacterial activity were also obtained in [69] by the reaction of chalcones with n-phenylenediamine in water-alcohol alkali.

Diagram5

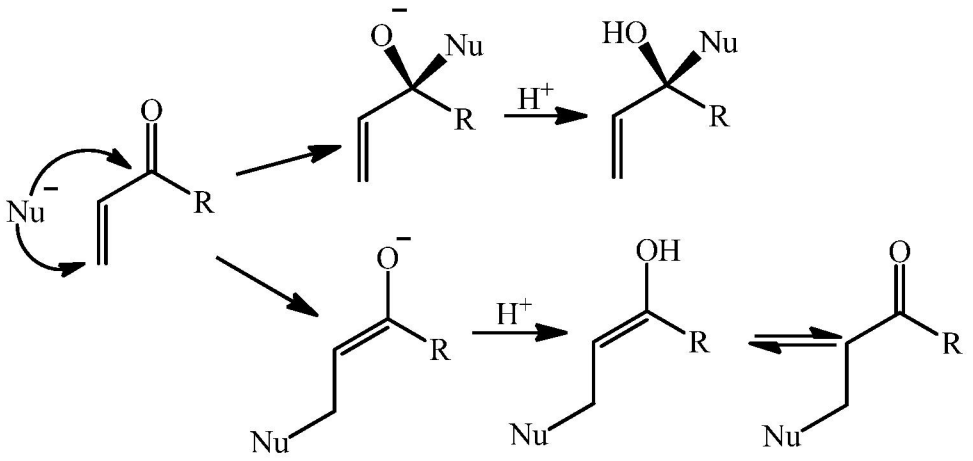


R_1=2-OH, 5-Br, R=4-OMe.
R_1=R=H, R_1=H, R=4-OMe; R_1=2-OH, R=4-NMe_2; R_1=H, R=4-NMe_2; R_1=2-OH, 5-Cl, R=4-OMe; R_1=2-OH, 5-Cl, R=H; R_1=2-OH, 5-Cl, R=4-NMe_2; R_1=2-OH, 5-Me, R=4-NMe_2.

It is known that α,β-unsaturated carbonyl compounds make it possible to synthesize practically any three-, four-, five-, six-, seven-membered carbo- and heterocycles with various substituents [1]. Therefore, chalcones are extremely popular as key intermediates in combinatorial chemistry [70]. The presence of two electrophilic centers in chalcones upon interaction with binucleophiles leads to the formation of heterocycles including annelated ones [1].

Among numerous reactions in which chalcones can participate, the interaction with binucleophilic reagents that leads to a variety of carbo- and heterocyclic compounds, in particular to substituted cyclohexanones and pyrimidines that also possess a wide spectrum of biological activity, is of particular interest.

The interaction of α,β-unsaturated carbonyl compounds (aldehydes, ketones (chalcones), acids, ethers) with nucleophiles leads to the formation of a new C-C or C-N bond. A new bond is formed between the donor and the second or fourth carbon atom of the acceptor. The first type of reaction is a simple addition via the carbonyl group, in the second case when the nucleophile is attached, the electron pair moves from the donor carbon to the acceptor oxygen.



The factors determining this process directionare charge interacting and orbital matching that are closely related to the concepts of hardness and softness of acids and bases. The interaction of a hard acid with hard bases is determined by the interaction of charges, while the reaction of a soft acid with a soft base proceeds under orbital control [71]. The relative reactivity of carbanions in the reactions of 1,2- and 1,4-addition has been considered from the standpoint of perturbation theory of molecular orbitals. Within the framework of this theory, taking into account the electronic structure of the fragment, the maximum positive effective charge on carbonyl carbon, the maximum localization of HOMO is at the β-carbon atom. The addition on the carbonyl group goes under the charge control, and 1,4-addition under the orbital control. As a consequence, all other conditions being equal, the process of nucleophile addition via the carbonyl group is favored by the charge localization at the nucleophilic center, the lowering of the HOMO energy. On the contrary, increasing the degree of the charge delocalization, increasing the HOMO level of the nucleophile promotes the flow of orbitally controlled 1,4-addition [1].

The balance between the two directions of reactions is so sensitive to various actions (solvent, catalyst, temperature) that relatively small changes are sufficient to make one of the processes dominant.

Therefore, both the advantage and the disadvantage of this reaction is the different reactivity of the nucleophilic centers, since the conditions depend not only on the structure of the reaction products, but also on their yield and purity. The development of approaches to the production of various products depending on the reaction conditions has attracted the attention of synthetics in recent years. Such processes are called "selective switch reactions". They have become widespread recently, especially for synthesizing biologically active compounds. The "switching" methods, in addition to the above-mentioned ones (solvent, catalyst, temperature), can be microwave or ultrasonic effects [72, 73].

4. Biological activity of chalcone derivatives

Compounds with the chalconic fragment show different types of biological activity. For example, they show significant activity against a variety of tumors and have chemoprotective properties. This can be attributed to their antioxidant activity [74-77]. Other important properties of chalcones are the ability to inhibit bacterial growth [78], as well as manifestation of antifungal and antiviral activity [79]. In addition, they have the ability to strengthen capillaries and can be used as anti-inflammatory agents [80]. In addition to these types of activity, they possess antimalarial [81-85], anti-cancer [86-88], larvicide [89], immunomodulating [90], antihyperglycaemic, antituberculous [91], antiprotozoal and antimitotic activity [92] and can be used as antibacterial [93, 94] and antifungal [95, 96] preparations. The inhibitory effect on enzymes, especially on the alpha-amylase of mammals [97], cyclooxygenase (COG) [98], monoamine oxidase (MAO) [99], leukotriene B [100], tyrosinase [101], aldose reductase [102], etc.

High biological activity manifested by the chalcones, promoted the development of studying the interaction of these compounds with various biological targets. There are numerous experimental data of the chalcone functions in plants, which make it possible to assert that many chalcones play an active physiological role in the plant organism. They can be relatively easily oxidized or reduced and their oxidation-reduction potential indicates that they take part in the metabolism. Some compounds of the

chalcone structure perform a protective function [95], the functions of respiratory catalysts and are involved in oxidation-reduction processes during respiration of plant cells.

The compounds with electron-donor substituents, for example, methoxy-, hydroxyl groups, show the greatest antimicrobial activity [103]. Chalcones containing one or two chlorine or fluorine atoms exhibit high antifungal and antimicrobial activity. Among the chalcones containing the oxathiolone fragment [104] there have been found compounds showing cytotoxicity against human cancer cells, as well as against *Micrococcus luteus, Staphylococcus aureus, Micobacterium tuberculosis* H Rv.

Interesting properties of chalcones also include initiation of apoptosis of cancer cells [105], inhibition of their mitochondrial respiration. The authors of [106] noted that chalcones with a smaller number of hydroxyl groups in rings A and B are more effective in this respect compared to chalcones containing more hydroxyl groups. This difference in activity is explained by the acidity of the phenolic OH groups. One of the widely known mechanisms according to which chalcones show cytotoxic activity is the interaction of chalcones in the mitosis phase. N.H. Nam with co-authors [106] studied the activity of the derivatives of 2', 5'-dihydroxychalcones and found that most chalcones exhibit cytotoxic activity against various lines of tumor cells.

Dehydroxyderivatives of chalcones show antioxidant activity that depends on the compound structure [107]. The mechanism of antioxidant activity of chalcones is discussed in [108]. When a chalcone molecule interacts with a radical, a phenoxide radical is formed with the *ortho-* and *para*-dihydroxylated systems of the benzene ring are systems with delocalized electrons, therefore the phenoxide radicals formed in them are readily converted into stable seven-quinone radicals that are further converted into quinones. *Meta*-dihydroxylated benzene ring system is less effective for electron delocalization, as a result of which phenoxide radicals are unable to enter further transformations. It has been established that chalcones with *ortho-* (i.e. 2', 3'- and 3', 4'-) and *para-* (i.e. 2', 5'-) substituents exhibit a very high antioxidant activity (80-90 % in comparison with the control at the concentration of 50 μM), which is comparable with the activity of ascorbic acid and α-tocopherol. On the other hand, chalcones with *meta-* (i.e. 2', 4'- and 3', 5'-) substituents show rather sharp decrease in activity (25% vs. control) at the concentration of 200 μM (IC_{50} >200 μM). These data show that the position of the two hydroxyl groups in the B nucleus is an important structural factor of their antiradical activity, while *para*-substituted compounds show a higher activity than the *ortho*-substituted ones. The variation of the substituents in the *para*-position in the A ring does not strongly affect the antiradical activity.This indicates that the electronic effects of the *para*-substituent of the benzene ring do not affect the antiradical activity.

The potential antioxidant activity of some hydroxychalcones was evaluated owing to their ability to inhibit 1,1-diphenyl-2-picrylhydrazyl radicals and free hydroxyl radicals [108]. For naringenin and phloretin, antiproliferative activity against the breast cancer cell line (MCF-7) has not been detected. But other chalcones (including 2'-hydroxychalcon) have shown antiproliferative activity at high concentrations (10.50 μM), and at low concentrations (0.01-1 μM) they accelerated the cell growth.

For manifesting anti-inflammatory activity of chalcones α,β-unsaturated carbonyl functional group is responsible. H.L. Yadav and co-workers [109] synthesized a series of five derivatives of chalcones and investigated their anti-inflammatory activity in rats that modeled carrageenan hind paw edema. The chalconic derivatives in the dose of 25 mg/kg fedorally, significantly inhibited the development of edema. The results of studying the anti-inflammatory activity of chalcones are also given in Ref. [50]. Activated macrophages play the key role in anti-inflammatory responses and releasing a variety of mediators, including nitric oxide (NO) that is a potential vasodilator that facilitates leukocytes migration and edema forming, as well as leukocyte activity and cytokine formation. The chalcones with substituents that increase the electron density of the Bring, for example, MeO-, BuO-, Me N-groups, do not show significant activity in inhibiting the NO production process [110].

S.J. Won et al. [111] showed that 2', 4-dihydroxychalcone, 2'-hydroxy-2-thienylchalcone, 2'-hydroxy-3-thienylchalkone and 2', 5'-dihydroxyindol-3-yl-chalcone are potential anti-inflammatory agents.

Hyperglycemic activity of chalcones was studied in [112]. Non-insulin-dependent diabetes (Type II diabetes) is a chronic metabolic disease characterized by insulin resistance, hyperglycemia and hyperinsulinemia. From *Broussonetia papyrifera* there have been isolated substituted chalcones that selectively inhibit enzymes of protein tyrosine phosphatase (PTP1B) and aldose reductase. Their

antioxidant properties allow considering them as hyperglycemic agents, because oxidative stress also plays an important role in diabetics. 3,4-dimethoxy derivatives show a significant anti-hyperglycemic effect, while monomethoxy derivatives show reduced activity.

Chlorine-containing chalcones show significant antiplasmodial activity, and chalcones with triazole, pyrrole and benzotriazole rings possess antiparasitic activity. It has beens found that the chlorine-derived chalcones with the morpholino ring possess the lowest activity. Compounds containing a triazole ring and chlorine have the greatest antiplasmodial activity, confirming the fact that small lipophilic groups containing one or more nitrogen atoms can increase antimalarial activity *in vitro*.

In vitro studies of the antiplasmoidal activity of substituted [(4-Cl, 4-MeO, 3,4,5-$(MeO)_3$] have shown that small and medium-sized lipophilic groups containing nitrogen atoms or amine in the acetophenone fragment are potential antimalarial agents. Such compounds can provide additional hydrogen bonding to the histidine residue present in the active site of the cysteine proteinase enzyme.Antileishmanial activity[113, 114]ischaracteristic of chalcones with a more hydrophilic character, that is, for HO-derivatives of chalcones, as well as for chalcones with naphthalene and pyridine fragments in the A nucleus. The inhibiting activity of tyrosinase of a number of chalcones with respect to melanin formation reactions and their antioxidant potentials has been studied [115] .The position of OH groups in aromatic A and B nuclei is very important, since hydroxylation over the B ring leads to a much higher ability to inhibit tyrasinase than hydroxylation over the A ring.

5. Conclusion

Valuable pharmacological properties of natural chalcones possessing a wide spectrum of biological action allow predicting and expanding the possibilities of developing new approaches to solving the problem of increasing biological activity of this class. By changing the structure of the chalcone molecules it is possible to increase the absolute indices of their activity in biological tests. Chalcones asα,β-unsaturated ketones are of interest as starting materials for the production of unavailable derivatives of other classes of compounds, which is due to the presence of two electrophilic centers: the carbon atom of the carbonyl group and theβ-carbon atom.

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ХАЛКОНДАР–БИОЛОГИЯЛЫҚ БЕЛСЕНДІ ЗАТТАР СИНТЕЗІНДЕГІ СИНТОНДАР

Аннотация:бұл шолу мақаласында соңғы жылдардағы әдеби мәліметтер, сондай-ақ функционалды орынбасқан халкондароблысындағы авторлардың зерттеулер нәтижелері жинақталып, жүйеленген. Кең таралған табиғи халкондар, синтетикалық халкондардың алу әдістері, реакциялық қабілеті мен биологиялық қасиеттері келтірілге.

Түйін сөздер: орынбасқан ароматты альдегид, халкон, пиразолин, флавонон, цитокин, транскрипционды фактор NF-κB

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ХАЛКОНЫ - СИНТОНЫ В СИНТЕЗЕ БИОЛОГИЧЕСКИ АКТИВНЫХ ВЕЩЕСТВ

Аннотация: в обзорной статье обобщены и систематизированы литературные данные последних годов, а также результаты исследований авторов в области функционально замещенных халконов. Приведены наиболее распространённые природные халконы, методы получения, реакционная способность и биологические свойства синтетических халконов.

Ключевые слова: замещенный ароматический альдегид, халкон, пиразолин, флавонон, цитокин, транскрипционный фактор NF-κB.