JETIR.ORG ISSN: 2349-5162 | ESTD Year : 2014 | Monthly Issue
JOURNAL OF EMERGING TECHNOLOGIES AND INNOVATIVE RESEARCH (JETIR)
An International Scholarly Open Access, Peer-reviewed, Refereed Journal

SYNTHESIS OF CHALCONES AND THEIR PHARMACOLOGICAL ACTIVITY

[*1]Gummalla.Mercy Beula, [2]Dr.Nallajerla. Sai Krishna, [3]Kolikipamula.Susmitha, [4]Mandhapati.Hima Bindhu, [5]Maddukuri.Bhavya Sri Sai Datta, [6]Kambhapu. Issac,[7] Kosuri. Murali Manikanta Swamy, [8]Edubilli.Kiran

[*1]Associate Professor, Pharmaceutical Chemistry, A.K.R.G College of pharmacy, Nallajerla, India
[2]Professor&Principal, Pharmacology A.K.R.G College of pharmacy, Nallajerla, India.

Abstract: Chalcones are a class of manufactured and naturally occurring chemicals that belong to the flavonoid family. This paper gives a thorough introduction of chalcones. Chalcones are crucial precursors in the production of flavonoids and are defined chemically by two aromatic rings joined by an α, β-unsaturated carbonyl system. Their chemical structure, synthesis, biological importance, and therapeutic uses are covered in the review. The Wittig reaction, Friedel-Crafts acylation, Claisen-Schmidt condensation, and condensation with β-chlorovinyl ketones are among the synthetic techniques outlined, along with the function of various condensing agents.

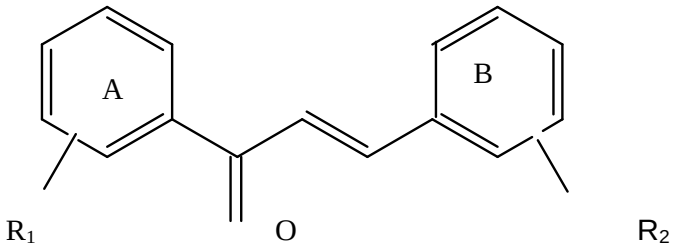
Chalcones have a wide range of pharmacological properties, including antibacterial, anti-inflammatory, antioxidant, anticancer, antimalarial, antiviral, antidepressant, and neuroprotective actions. Additionally, it highlights the structure–activity relationship (SAR), elucidating how various substituents—such as hydroxyl, methoxy, halogen, nitro, and amino groups—affect their biological characteristics. Chalcones' significance in medicinal chemistry, drug research, and industrial uses—such as artificial sweeteners, catalysts, stabilizers, and fluorescent agents—is also covered. Overall, the review shows that chalcones are promising bioactive compounds with substantial therapeutic potential and are still a crucial field of study for creating novel medications to treat a variety of illnesses.

key words: chalcones, flavonoid, benzaldehyde, Acetophenone, α, β-unsaturated carbonyl system, anti-bacterial,anti-fungal,anti-microbial, anti-inflammatory, anti-oxidant, anti-cancer, anti-malarial, anti-viral, anti-deprassant,anti-protozoal, neuroprotective, enzyme inhibition activity, antileishmaniasis activity.

INTRODUCTION

Chalcones are molecules that have aromatic substituents added at the system's terminal position (C=C-C=O). Therefore, the position of an Ar (A)-CO-CH=CH-Ar (B)-, where two aromatic rings A and B are connected by an aliphatic three-carbon chain, is what defines chalcones. The flavonoid family includes chalcones (1,3-diaryl-2-propen-1-ones). Chemically, they are open-chain flavonoids with a three-carbon α, β-unsaturated

carbonyl system connecting the two aromatic rings. The building blocks for the biosynthesis of flavones and anthocyanins are called chalcones. In a lab setting, acetophenone or substituted acetophenones with aromatic aldehydes can undergo Claisen-Schmidt condensation to produce chalcones and substituted chalcones.



chalcones

Chalcones are widely distributed in edible plants and are thought to be the progenitors of flavonoids and isoflavonoids. They have also been demonstrated to have a wide range of pharmacological actions. An overview of the pharmacological action of synthetic and naturally occurring chalcones is the aim of this paper. In addition to more recent studies of chalcones' antimicrobial action (antibacterial and antifungal), this review also discusses the compounds' antileishmanial, antimalarial, antiviral, and anti-inflammatory properties [1].

Chalcones are an essential structural motif found in many physiologically active compounds, both natural and manufactured. Chalcones are being synthetically modified or isolated from natural sources in an effort to create more powerful and effective medications to cure a number of terrible illnesses, including cancer, diabetes, HIV, tuberculosis, malaria, and more. A substantial amount of research papers and review articles emphasizing the importance of chalcone derivatives have been collected in the literature over the last several years. The current advancements (2010–2014) on several pharmacological and therapeutic features of chalcones and their analogues are the main topic of this review paper. The current advancements (2010–2014) on different pharmacological and therapeutic features of chalcones and their analogues are the main topic of this review paper [2].

Amyloid-beta (Aβ) plaque deposition, tau hyperphosphorylation, oxidative stress, persistent neuroinflammation, and cognitive impairments are the hallmarks of Alzheimer's disease (AD), a progressive neurodegenerative illness. Currently, the majority of therapeutic approaches are symptomatic and do not change how the condition progresses. Because they can protect neurons and have anti-inflammatory and antioxidant properties, natural chalcones, which are precursors of flavonoids, are becoming popular multi-target drugs for neuroprotection [3].

3-acetyl-4-hydroxy coumarin and 3-formylchromone were refluxed in ethanol with a catalytic quantity of pyridine to create chalcone 3. 3 was treated with hydrazine and phenyl hydrazine to produce bipyrazoles 4a-b. The antibacterial activity of the compounds was examined [4].

It was rather interesting to manufacture the cytotoxic, anticancer polyhydroxy chalcones that were identified.

The poly-hydroxychalcones produced by the Claisen-Schmidt reaction of resacetophenone with o-, m-, and p-toluaI-dehydes, 2, 3-dimethoxybenzaldehyde, and vanillin in the presence of aqueous-alcoholic potassium hydroxide are documented in this paper using either the cold or hot condensation method described by Geissman and Clinton. 1 A certain amount of flavanone was found to accompany the equivalent chalcone in every example that was documented, with the exception of vanillin. After that, 4% aqueous-alcoholic sulfuric acid was used to cyclize the previously synthesized chalcones into flava-nones.

Compared to cold condensation, high temperature condensation of resacetophenone with isomeric tolu aldehydes is advantageous because it increases chalcone production and reduces resin formation. When the reaction is conducted at room temperature for 48 hours as opposed to seven days, more 2', 4'-dihydroxy-2, 3-dimethoxychalcone is recovered. Because of its higher solubility in alcohol, the longer reaction time increases the amount of a slowly crystallizable oil that forms alongside the chalcone and can be easily separated from it. It was discovered that the matching flavanone makes up the majority of this oil, which slowly solidifies with age. This result leads to the conclusion that the reaction does not terminate with the synthesis of chalcone when the reaction time is increased; instead, the latter partially undergoes progressive cyclization into flavanone. This conclusion aligns with what Shah and his colleagues reported. Russell and Todd3 previously obtained 2 2', 4, 4'-trihydroxy~ 3-methoxychalcone by condensing resacetophenone dibenzoate with vanillin benzoate in the presence of dry hydrogen chloride and saponifying the resulting 2', 4, 4'-tribenzoyloxy-3-methoxychalcone into the necessary chalcone. However, by condensing resacetophenone, we have been able to directly synthesize 2', 4, 4'-trihydroxy-3-methoxychalcone [5].

An explanation of these unsaturated ketones as antimicrobial agents follows a description of the cytotoxic, anticancer, chemo preventative, and mutagenic characteristics of many chalcones. A range of chalcones are examined for their antiviral, antiprotozoal, and insecticidal characteristics, as well as for their enzyme-inhibitory qualities and other activities [6].

Chalcones exhibit a variety of biological functions, including anti-microbial [7], anti-malarial [8], anti-depressant [9], anti-inflammatory [10], and anti-cancer [11]. Numerous investigations have demonstrated that chalcones are molecules of high chemical and pharmacological importance.

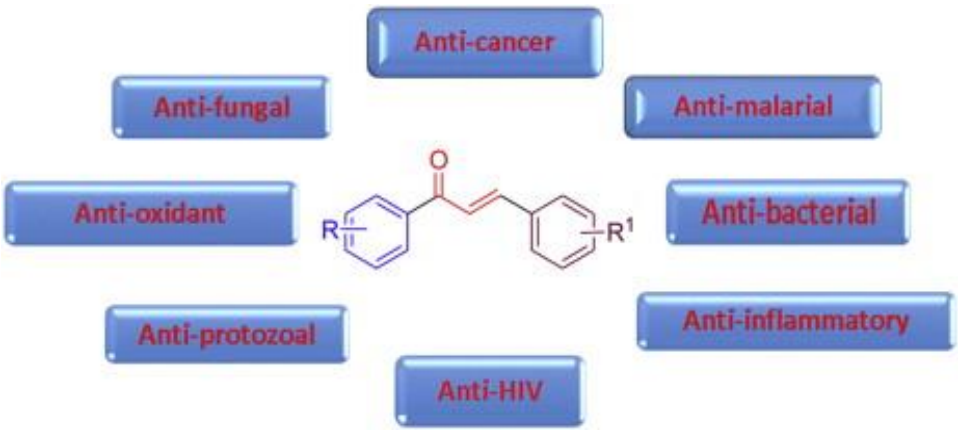
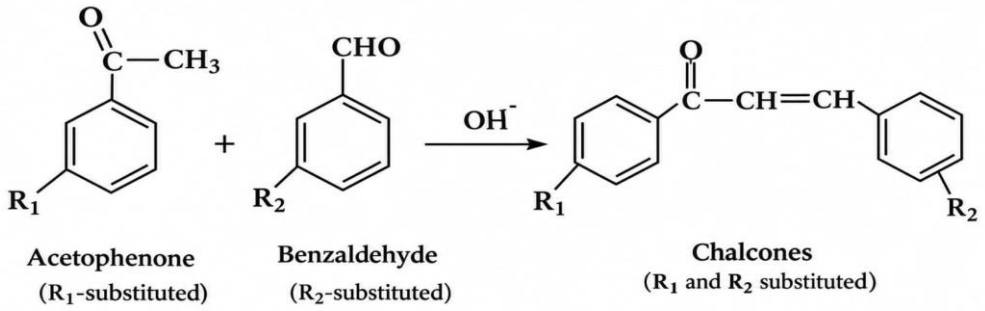


Figure1: acting on diseases

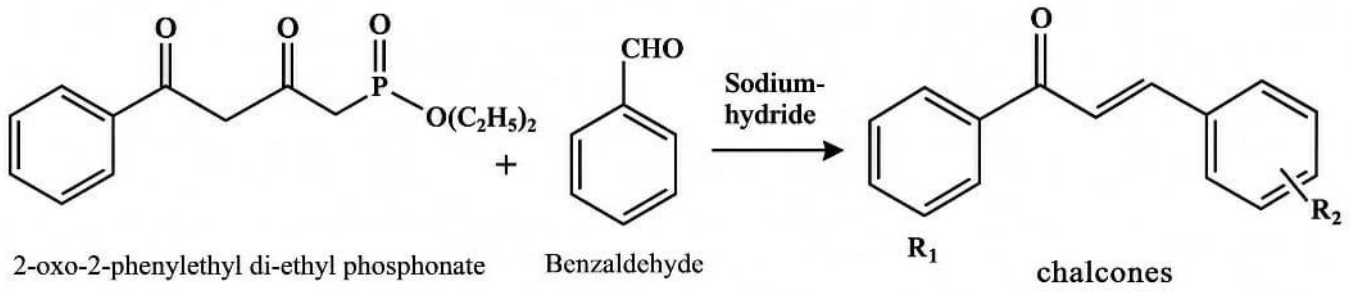
General methods for synthesis of chalcones

Chalcones can be synthesized using a variety of techniques. The Claisen-Schmidt condensation of equimolar amounts of a substituted acetophenone with aromatic aldehyde in the presence of an aqueous alkali is the most practical technique. The concentration of alkali employed in the Claisen-Schmidt reaction typically falls between 10 and 60%. The reaction takes place for six to eight hours at room temperature. The Cannizaro reaction [12] also occurs in these circumstances, which lowers the yield of the intended product.



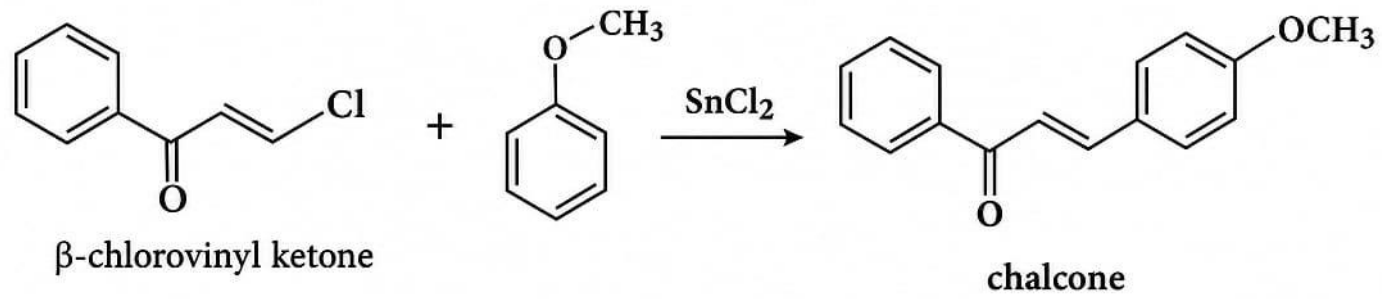
Witting Reaction:

Chalcone is produced by the Witting reaction between benzaldehyde and phosphonate carbanion [13], which is formed from diethyl phenyl acylphosphonate and sodium hydride.



From Phenolic ether with chlorovinyl ketone:

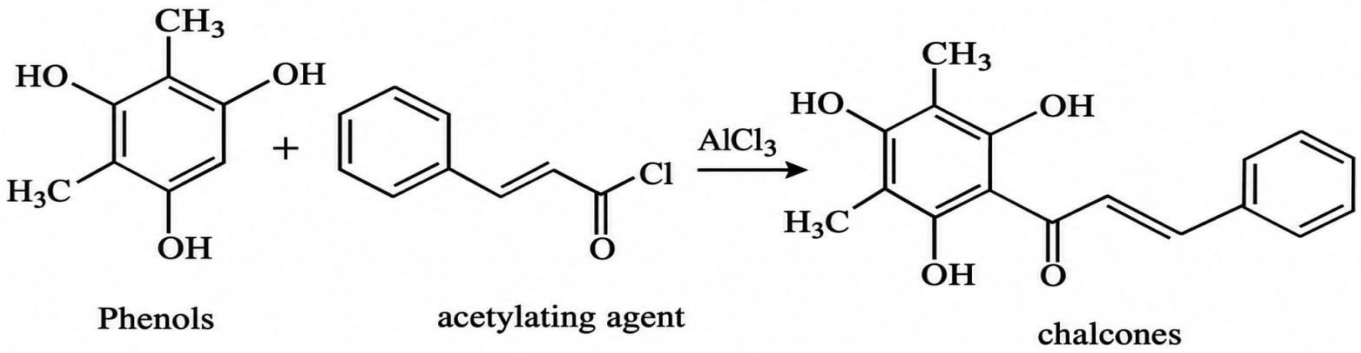
Condensing substituted β-chlorovinyl ketone with phenolic ether in the presence of stannic chloride has also been shown to produce a substituted chalcone in a quite excellent yield [14].



β-chlorovinyl ketone chalcone

Friedel-CraftsAcylation:

In addition to the Claisen-Schmidt process, direct Friedel-Crafts acylation of a phenol can be used to create substituted chalcones. In this method, the acylating agent supplies the B-ring carbons and the three-carbon bridge to form the C6-C3-C6 unit, while the phenol becomes the A-ring.



Phenols acetylating agent chalcones

VARIOUS CONDENSING AGENTS USED IN SYNTHESIS OF CHALCONES

1. Alkali The most popular condensing agent for chalcone synthesis has been alkali. It is utilized as an aqueous solution with the appropriate concentrations of 30%, 40%, 50%, and 70%.

2.The hydrochloric acid:

In a few chalcone syntheses from aromatic ketones, dry hydrochloric gas was employed as a condensing agent in an appropriate solvent, such as ethyl acetate, at 0 oC. Additionally, a dry hydrochloric acid gas methanolic solution at 0 oC was utilized.

3.Additional Condensing Agents:

Raval and Shah synthesized chalcones using phosphorous oxychloride as a condensing agent. Szell and Sipos used anhydrous $AlCl_3$3 to condense 2-hydroxy-5-nitro-acetophenone with benzaldehyde. In the presence of anhydrous aluminium chloride, Kuroda, Matsukuma, and Nakasmura condensed acetophenone produced from anisole and other polymethoxy benzenes with certain methoxy aldehydes to produce chalcone.

Other condensing agents that have been employed in the manufacture of chalcones include:

(1) amino acid;

(2) borax aqueous solution;

(3) perchloric acid;

(4) piperidine;

(5) boron trifluoride;

(6) alkali metal alkoxide; and

(7)magnesiumtert-butoxide.

(8) The compound organocadmium

STRUCTURAL ACTIVITY RELATIONSHIP:

The kind and location of substituents on the aromatic rings have a major impact on chalcones' biological activity. • Hydroxyl (-OH) groups boost anti-inflammatory and antioxidant properties.

• Lipophilicity and anticancer activity are enhanced by methoxy (-OCH_3) groups.

• Halogens (Cl, F, Br) frequently boost anti-inflammatory and antibacterial activities.

• Nitro (-NO_2) groups may strengthen anticancer and antibacterial properties.

• Amino (-NH_2) groups can enhance an enzyme.

IMPORTANCE OF CHALCONES

(1) They are c loosely related to aziridines, flavones, aurones, and tetralones.
(2) Chalcones and their derivatives are used as scintillators, organic brightening agents, polymerization catalysts, artificial sweeteners, and stabilizers against heat, UV light, visible light, and aging.
(3) A synthetic sweetener that is 2200 times sweeter than glucose is 3,2',4',6'-tetrahydroxy-4-propoxy-dihydrochalcone-4-β'-neohesperdoside.
(4) Because they have a keto-ethylenic group, they react with a variety of substances, such as (a)phenyl hydrazine and (b) 2-amino thiophenol.

(5) The structure of natural compounds such as hemlock tannin, cyanomaclurin, ploretin, eriodictyol and homoeriodictyol, naringenin, etc., has been discovered to be clarified by chalcones.

5.PHARMACOLOGICAL ACTIVITIES

1.anti-bactirial

2.anti-fungal

3.anti-microbial

4.anti-inflammatory

5.anti-oxidant

6.anti-cancer

7.anti-malarial

8.anti-viral

9.anti-deprassant

10.anti-protozoal

11.neuroprotective

12.enzyme inhibition activity

13.anti-leishmaniasis activity

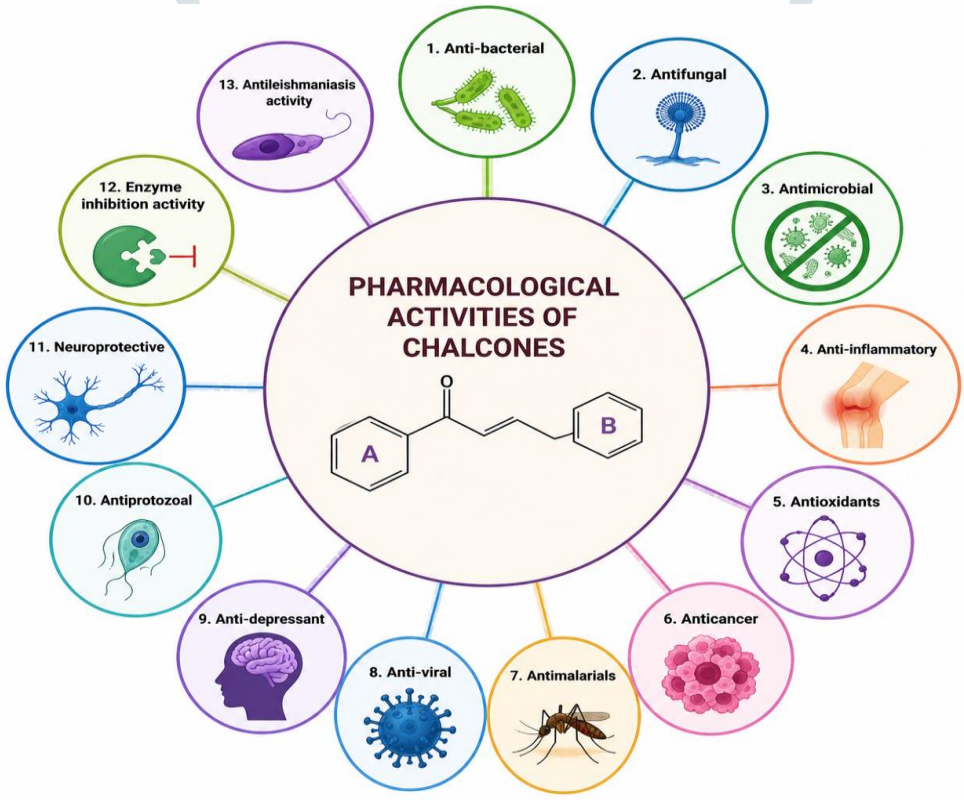


Figure2: chalcones pharmacological activity

CONCLUSION

Chalcones are an important class of flavonoid precursors that have garnered a lot of interest because of their straightforward chemical structure, ease of synthesis, and variety of pharmacological characteristics [15, 16]. A variety of chalcone derivatives with enhanced biological activity can be prepared using a variety of synthetic techniques, most notably the Claisen-Schmidt condensation [16,19]. Chalcones have been shown to have promise antibacterial, anti-inflammatory, antioxidant, antiviral, depressive, anticancer, antimalarial,

and neuroprotective properties [15–18,20]. Structure–activity relationship (SAR) investigations are crucial for the development of more potent medicinal medicines since the type and location of substituents on these compounds' aromatic rings have a significant impact on their biological activity [16, 17]. Chalcones have industrial uses as sweeteners, stabilizers, catalysts, and fluorescent agents in addition to their therapeutic significance [19]. All things considered, chalcones are useful lead compounds in contemporary drug discovery, and greater investigation into their synthesis, biological assessment, and therapeutic uses may help create safer and more potent therapies for a range of illnesses [15–20].

REFERENCES

1.Nowakowska, Z. (2007). A review of anti-infective and anti-inflammatory chalcones. *European Journal of Medicinal Chemistry*, 42(2), 125–137.

2. Singh, P., Anand, A., & Kumar, V. (2014). Recent developments in biological activities of chalcones: A mini review. *European Journal of Medicinal Chemistry*, 85, 758–777.

3.Yadav, V. R., Prasad, S., Sung, B., & Aggarwal, B. B. (2011). The role of chalcones in suppression of inflammatory pathways. *BioFactors*, 37(2), 103–112.

4. Siddiqui Z.N., Asad M.and Praveen S.;Med. Chem. Res.; 2008 (17) 318.

5.Dhar D.N. and Lal J.B.; J. Org.Chem., 1958 (23) 1159.

6. Dimmock JR, Elias DW, Beazely MA, Kandepu NM. Bioactivities of chalcones. *Current Medicinal Chemistry*. 1999;6(12):1125–1149.

7.Siddiqui Z.N., Asad M.and Praveen S.; Med. Chem. Res.; 2008 (17) 318.

8. Lim S., Kim H.and Lee D. Bull. Korean Chem.Soc., 2007 (28) 2495.

9. Prasad Y.R., Kumar P.R.and Ramesh B.Int. J.Chem. Sci.,2007 (5) 542.

10 ChiaradiaL. D. SantosR. VitorC.E, VieiraA.A, LealP.C, NunesR.J, CalixtoJ.B.and Yunesa R.A.; Bioorg MedChem,2008 (15) 658.

11. ModzelewskaA., PettitC., AchantaG., DavidsonN.E., HuangP.and KhanaS.R.; Bioorg MedChem, 2006 (14) 3491.

12. Dhar D.N. and Lal J.B.;J. Org.Chem., 1958 (23) 1159.

13. Bravo P., Tricozzi C.and Cezza A.; Gazz.Chim. Letters.,1975 105-109.

14. IkedaY, TakanoN, MatsushitaH, ShirakiY.,KoideT ,NagashimaR. Fujimura Y.Shindo M., Suzuki S., Iwasaki T. and Arzneim.-Forsch. 1979 (29) 511-520.

15. Ikeda, Y., Takano, N., Matsushita, H., Shiraki, Y., Koide, T., Nagashima, R., Fujimura, Y., Shindo, M., Suzuki, S., & Iwasaki, T. (1979). Arzneimittel-Forschung, 29, 511–520.