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A review: Synthesis of azachalcone and its biological activity

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Abstract

The heterogeneous chemical potential of azachalcone has six-membered motifs containing nitrogen in the ring, leading to active research in their synthetic methodologies. This paper summarizes various methods via aldol reaction, Claisen-Schmidt condensation, molecular hybridization, environmentally trendy microwave-assisted method etc. to acquire azachalcones and their derivatives along with biological activities.

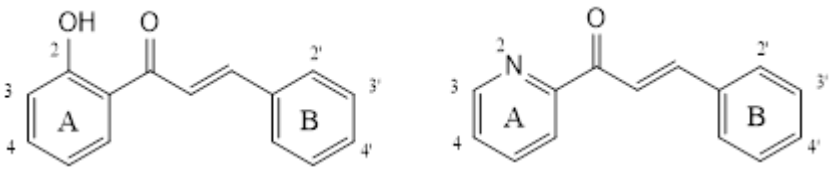
Keywords: Azachalcones; Condensation; Biological activities; Aldol reaction

1. Introduction

Chalcones are a class of naturally occurring compounds with various biological activities.[1] They are known as the precursors of all flavonoid–type natural products in biosynthesis.[2] Among the various biological activities of chalcones are their insecticidal, antimicrobial, antichinoviral and antipicorniviral, and bacteriostatic properties.[3] Azachalcones (the derivatives of chalcones with an annular nitrogen atom in the phenyl ring). Have also been reported to have wide variety of biological activities such as antibacterial, anti-tubercular, and anti-inflammatory potential[3].

Heterocycles are abundant in nature and significant to life because their structural subunits exist in many natural products such as vitamins, hormones, and antibiotics. etc[4] they have attracted considerable attention in the design of biologically active molecules.[5] Azachalcones are not naturally occurring compounds.[6] The most common strategy for the synthesis of chalcones is Claisen-Schmidt condensation.[7-8] A practical method for the synthesis of such compounds is of great interest in synthetic organic chemistry.

Azachalcone is another class of the chalcone family in which the carbons of either rings A or B or both were replaced with a nitrogen atom. Because of their structural similarity, azachalcones were synthesized with the same strategy as chalcones, in which the substituted acetophenone was replaced with 2-acetyl pyridine.[9-10]



Chalcone Azachalcone

Structure of chalcone and azachalcone

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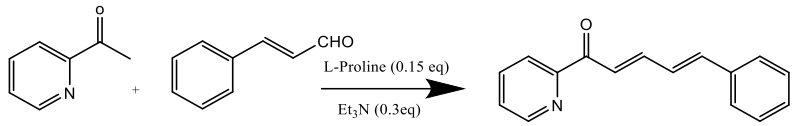
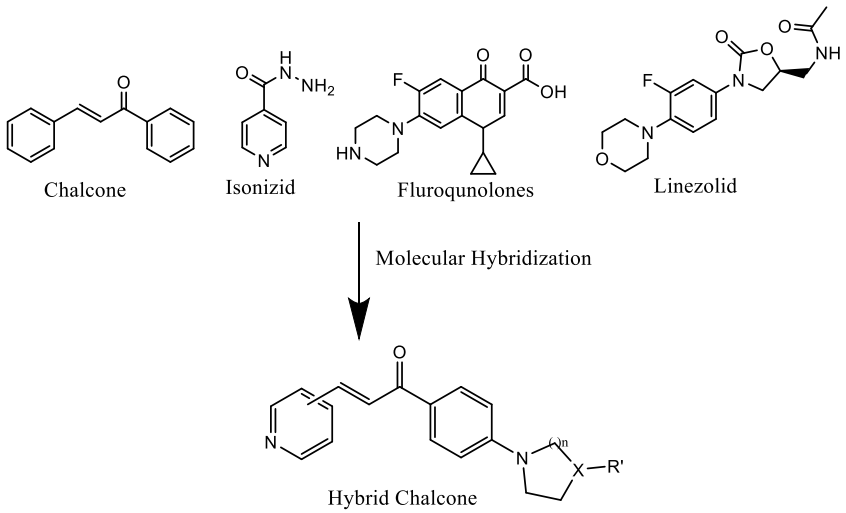
1.1. Synthesis of Azachalcone Derivatives

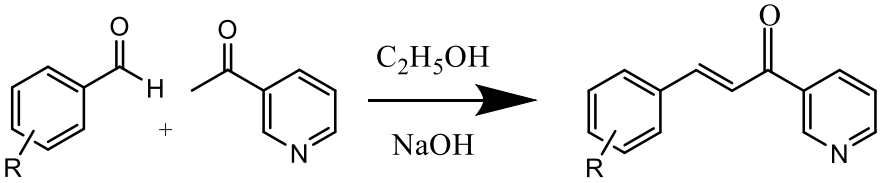
Nur Rohman[11] focuses on crafting azachalcone derivatives from 2-acetylpyridine and aromatic aldehydes using l-proline/Et3N as a catalyst. Refinements encompass catalyst dosage, solvents, temperature, and post-reaction treatments and show significant antioxidant potency with inhibition.



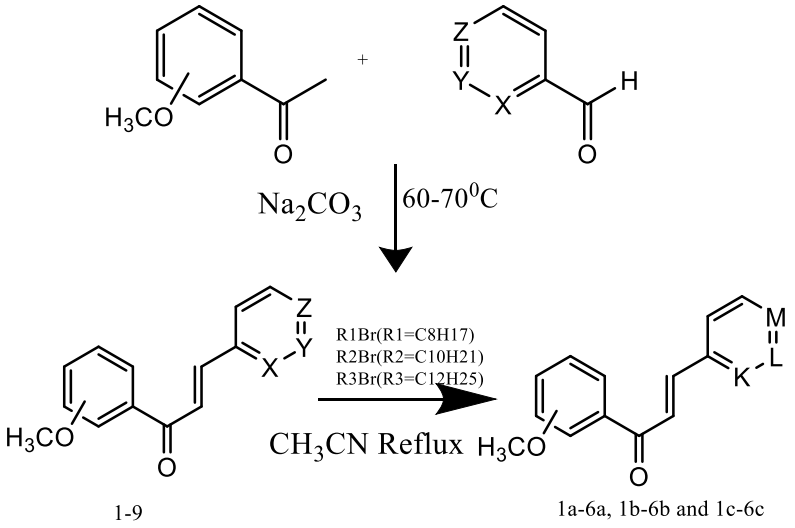
Jefferson R reported[12] twenty-four heterocyclic amine-azachalcones compounds through molecular hybridization of chalcone scaffold and fragments of isoniazid, fluoroquinolones, and linezolid with antituberculosis potential



Mohammed Abed Kadhim[13] synthesized novel Azachalcone compounds that were prepared by the reaction of 3- 3-acetyl pyridine with different aromatic aldehyde.



Canan Albay[14] The convenient approach for the synthesis of o-, m-, and p-methoxy (E)-2-, -3-, and 4-azachalcones (1-9) involves the Claisen-Schmidt condensation of methoxy-substituted aryl methyl ketones with pyridine carboxaldehyde with 3 equivalents of Na 2 CO3 solution (EtOH, 95%), which yields the trans isomer of the corresponding α,β-unsaturated (J = 15.4/16.8 Hz, respectively) compounds (1-9)

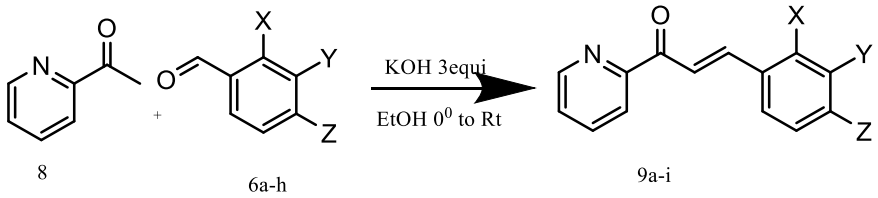


Asu Usta[15] Two new azachalcones prepared by both claisen- Schmidt condensation and simple environmentally trendy microwave-assisted method. Ten new N-alkyl substituted azachalconium bromide were prepared from compounds 1 and 2 with corresponding alkyl halides the antimicrobial activity of all the compounds were tested against *Enterococcus faecalis, Yersinia pseudotuberculosis, Pseudomonas aeruginosa, Escherichia coli and Staphylococcus aureus* microorganism.

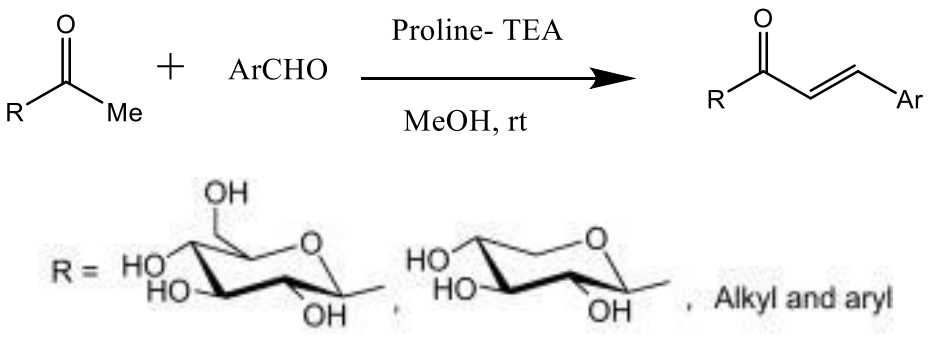
ze zang[16] Michael addition reaction of chalone and azachalcone with ethyl acetoacetate has been successfully performed in the presence of the catalytic amount of (k_2CO_3 10 mole %) and under the high-speed vibrational milling condition the reaction takes place at ambient temperature without any solvent and full completion can be achieved in a very short time (22-40 min) in the most cases conventional side reaction were avoided.

Eleni Hadjikyprianou[17] reported thirteen (13) azachalcone dienophiles with various substituents (1a–m, Scheme S1, Supporting Information) were synthesized via aldol reaction of the corresponding aromatic aldehydes with an enolate generated from 2-acetylpyridine under basic conditions, followed by in situ dehydration.

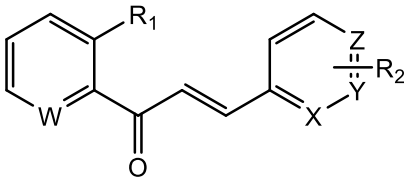
Tzenge-Lien Shih[18] A series of B-ring, halo-substituted chalcones and azachalcones were synthesized to evaluate and compare their anti-inflammatory activity.



A novel and efficient direct aldol condensation from various ketones and a wide range of aldehydes was catalyzed by L-proline–TEA (triethylamine) in MeOH at room temperature, affording the corresponding (*E*)-α,β-unsaturated ketones[19].



A potent inhibitor of polyphenol oxidase and their structure-activity relationships are described. Azachalcone derivatives were synthesized and tested for their tyrosinase inhibitory activity. Their inhibitory activities on mushroom tyrosinase using L-DOPA as a substrate were investigated[20].



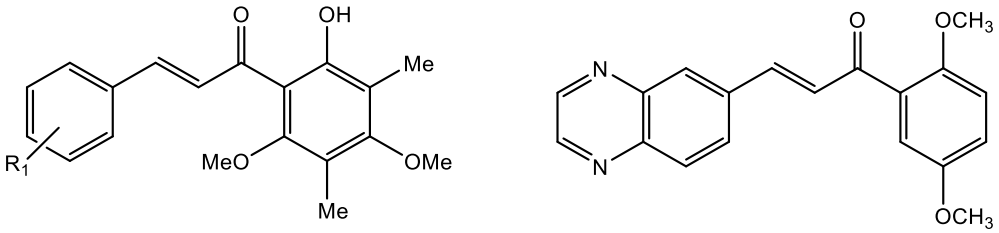
New N-substituted derivatives of 3-azachalcone of potential antimicrobial activity.[21] Synthesis and antimicrobial properties of N-substituted derivatives of (E)-4-azachalcones.[22]

1.2. Biological Activity of Azachalcone

Chalcones (1,3-diphenyl-2-propen-1-ones) are key precursors in the synthesis of a large array of biologically important heterocycles (azachalcones). 23,24 Thus, the synthesis of azachalcones has generated vast interest among organic and medicinal chemists. Chalcones and their heterocyclic analogs (azachalcones) display a wide range of biological activities, such as anticancer, 25 antimitotic, 26 anti-inflammatory, 27 antituberculosis, 28 antimalarial, 29,30 antileishmanial, 31,32 nitric oxide regulation modulatory, 33 cardiovascular, 34 cell differentiation inducing 35 and antihyperglycemic, 36 activities.

Nur Rohman[11] focuses on crafting azachalcone shows significant antioxidant potency with inhibition. Heterocyclic amine-azachalcones compounds through molecular hybridization with antituberculosis potential[12]. azachalcones prepared by both claisen- Schmidt condensation with antimicrobial activity,[15] anti-inflammatory activity,[18]

Studies have shown that azachalcones possess anti-bacterial, anti-inflammatory, and anti-cancer properties.[37–40] Recent reports[41] aimed at chalcones as compounds with a wide range of biological activities such as anticancer, cancer-preventative effects, anti-inflammatory, antibacterial, antidiabetic, antioxidant, antimicrobial, antiviral, antimalarial, and neuroprotective effects. Many studies showed other structural combinations, aiming for new antitubercular agents, as seen in chalcones [42,43] by the use of creative and intuitive molecular hybridization approach.



Structure of new antitubercular agents

2. Conclusion

Author should provide an appropriate conclusion to the article. Write a conclusion as a single para. Conclusion should be concise, informative and can be started with summarizing the outcome of the study in 1-2 sentences and end with one line stating: how this study will benefit the society and the way forward

References

[1] J.B. (1988) . "The flavonoids, Advances in Research", chapman & Hall, Newyork Ny, 329-388,

[2] Jannie P J Marais , Daneel Ferreira and etal Stereoselective synthesis of monomeric flavonoids, phytochemistry, (2005), 66,2145-2176.

[3] Z.N., E.w. and B.k. II Farmaca, (2001), 56,325- 329

[4] J.u.,.R.S. (2006). J.org. chem.71, 135.

[5] M. K., T.I., a.M, and etal (2003), J. Am. chem. soc. 125, 1700.

[6] Li, C.W.; Shen, T.H.; Shih, T.-L. (2017) Reinvestigation of synthesis of halo-substituted 3-phenyl-1-(2-pyridyl)-2-propen-1-ones (azachalcones). A tandem reaction for the formation of penta-substituted cyclohexanols. Tetrahedron, 73, 4644–4652. [CrossRef]

[7] Fang, D.; Cheng, J.; Fei, Z.; and etal (2008), Synthesis of chalcones via Claisen-Schmidt condensation reaction catalyzed by acyclic acidic ionic liquids. Catal. Commun., 9, 1924–1927.

[8] Qian, H. and Liu, D (2011) Synthesis of chalcones via Claisen-Schmidt reaction catalyzed by sulfonic acid-functional ionic liquids. Ind. Eng. Chem. Res., 50, 1146–1149. [CrossRef]

[9] Otto, S.; Bertoncin, F, and etal (1996) J.B.F.N. Lewis acid catalysis of a Diels-Alder reaction in water. J. Am. Chem. Soc., 118, 702–7707. [CrossRef]

[10] Lu, Y.; Zhou, Y. and etal, (2016). N, N'-dioxide/nickel (II)-catalyzed asymmetric Diels-Alder reaction of cyclopentadiene with 2,3-dioxopyrrolidines and 2-alkenoyl pyridines. Chem. Commun., 52, 8255–8258. [CrossRef] [PubMed]

[11] Nur Rohmana , Bayu Ardiansaha, and etal (2023) Preparation of azachalcone derivatives via l-proline/ Et3N-catalyzed aldol condensation and study of their antioxidant potential., MethodsX 11 102427.

[12] Jefferson R. S. Oliveira, Cristiane Y. K. Shiguemoto, and etal (2020) Design, Synthesis and Antitubercular Activity of Novel Isoniazid-Cyclic-Amine-Azachalcones Hybrids., J. Braz. Chem. Soc., Vol. 31, No. 6, 1284-1295,.

[13] Mohammed Abed Kadhim, (2010) Synthesis and Chemical Characterization of Some Novel Azachalcones compounds and Evaluation of their Biological Activity, Journal of University of Anbar for Pure Science (JUAPS),(4), (3):39-42.

[14] Canan ALBAY, Nuran KAHR˙ IMAN, and etal (2011), Synthesis and antimicrobial activity of methoxy azachalcones and N-alkyl substituted methoxy azachalconium bromides., Turk J Chem 35, 441 – 454.

[15] Asu Usta, Elif Öztürk , and etal (2014) Microwave-assisted preparation of azachalcones and their N-alkyl derivatives with antimicrobial activities., Formerly Natural Product Letters., Volume 28, - Issue 7.

[16] ze zang, ya-wei Dong, and etal (Feb2024) Mechanochemical Michael reaction of chalcone and azachalcone with ethyl acetoacetate catalyzed by k2CO3 using solvent free condition., chemistry letter volume 33, issue 2, page 168-169.

[17] Eleni Hadjikyprianou, Sotiris Petrides, and etal (2023) Catalysis of a Diels–Alder Reaction between Azachalcones and Cyclopentadiene by a Recyclable Copper(II)-PEIP Metal-Organic Framework., Materials, 16, 5298.

[18] Tzenge-Lien Shih, Ming-Hwa Liu and etal (2018), Halo-Substituted Chalcones and Azachalcones Inhibited Lipopolysaccharited-Stimulated Pro-Inflammatory Responses through the TLR4-Mediated Pathway., Molecules, 23, 597.

[19] feng Wang, Meng Lei, and etal (June 2009), A novel and efficient direct aldol condensation from ketones and aromatic aldehydes catalyzed by proline–TEA through a new pathway., Tetrahedron, Volume 65, Issue 25, 20, Pages 4826-4833.

[20] Sini Karanayil Radhakrishnan, Ronald Gibrial Shimmon, and etal (March 2015) Azachalcones: A new class of potent polyphenol oxidase inhibitors, Bioorganic & Medicinal Chemistry Letters · 25, 1753-1756.

[21] M Szajda and B Kedzia, (1991) New N-substituted derivatives of 3-azachalcone of potential antimicrobial activity, Pharmazie; 46(10):745-6.

[22] Z Nowakowska , E Wyrzykiewicz, and etal (2001), Synthesis and antimicrobial properties of N-substituted derivatives of (E)-4-azachalcones., J of Farmaco;56(4):325-9.

[23] Dhar, D. N. (Ed.) (1981) The Chemistry of Chalcones and Related Compounds, Wiley, New York, p. 214.

[24] Agrawal, P. K. and Bansal, M. C. (1989), In Carbon-13 NMR of Flavonoids; Elsevier, New York, , pp. 365-431.

[25] Bois, F.; Beney, C and etal (1998)J. Med. Chem., 41, 4161-4164.

[26] Ducki, S.; Forrest, R. and etal (1998), Bioorg. Med. Chem. Lett., 8, 1051-1056.

[27] Hsieh, H. K.; Tsao, L. T, and etal (2000), J. Pharm. Pharmacol., 52, 163-171.

[28] Lin, L. M.; Zhou, Y.; and etal (2002), Bioorgan. Med. Chem., 10, 2795-2802.

[29] Dominguez, J. N.; Charris, J. E.; and etal (2001), J. Eur. J. Med. Chem., 36, 555-560.

[30] Ram, V. J.; Saxena, A. S.; and etal (2000), Bioorg. Med. Chem. Lett., 10, 2159-2161.

[31] Zhai, L.; Chen, M.; Blom, J.; and etal (1999), J. Antimicrob. Chemoth., 43, 793-803.

[32] Torres-Santos, E. C.; Rodrigues, J. M. and etal (1999), Antimicrob. Agents Ch., 43, 1776-1778.

[33] Herencia, F.; Ferrandiz, M. L.; and etal. (2001), M. J. Free Radical Bio. Med., 30, 43-50.

[34] Furman, C.; Lebeau, J.; and etal (2001), J. Biochem. Mol. Toxicol., 15, 270-278.

[35] Park, E. J.; Park, R.; and etal (1998), J. Planta Med., 64, 464-466.

[36] Satyanarayana, M.; Tiwari, P.; and etal (2004), Bioorgan. Med. Chem.,12, 883-889

[37] Gill, N.S.; Kaur, A.; and etal (2012), Synthetic studies of novel azaflavanone derivatives and its biological activities. Curr. Res. Chem., 4, 88–98. [CrossRef]

[38] Dias, T.A.; Duarte, C.L.; and etal (2013), Superior anticancer activity of halogenated chalcones and flavonols over the natural flavonol quercetin. Eur. J. Med. Chem., 65, 500–510. [CrossRef] [PubMed]

[39] Kupcewicz, B.; Jarzecki, A.A.; and etal (2014), Cytotoxic activity of substituted chalcones in terms of molecular electronic properties. Bioorg. Med. Chem. Lett., 24, 4260–4265. [CrossRef] [PubMed]

[40] Batagin-Neto, A. and Lavarda, F.C. (2014), The correlation between electronic structure and antimalarial activity of alkoxylated and hydroxylated chalcones. Med. Chem. Res., 23, 580–586. [CrossRef]

[41] Zhuang, C.; Zhang, W.; and etal. (2017), Chem. Rev., 117, 7762.

[42] Anandan, R.; Jadav, S. S.; and etal. (2018), Med. Chem. Res., 27, 1690.

[43] Muradás, T. C.; Abbadi, B. L.; Villela, A. D.; Macchi, F. S.; Bergo, P. F.; Freitas, T. F.; Sperotto, N. D. M.; Timmers, L. F. S. M.; Souza, O. N.; Picada, J. N.; Facchini, J.; Silva, J. B.; Albuquerque, N. C. P.; Habenschus, M. D.; Carrão, D. B.; Rocha, B. A.; Barbosa Jr., F.; Oliveira, A. R. M.; Mascarello, A.; Neuenfeldf, P.; Nunes, R. J.; Morbidoni, H. R.; Campos, M. M.; Basso, L. A.; Rodrigues-Junior, V. S.; PLoS One 2018, 13, e0202568.