IASJ المجلات الاكاديمية العراقية

Tikrit Journal of Pure Science

ISSN: 1813 – 1662 (Print) --- E-ISSN: 2415 – 1726 (Online)

Journal Homepage: http://tjps.tu.edu.iq/index.php/j

Synthesis, characterisation and biological activities of N-phenyl-ethan-1-one-2,4-dimethyl-1,3-butadiene-1,4-thiazin derivatives

Nabaz Abdulmajeed Mohammad Salih

Dept. of Chemistry, Faculty of Science, University of Soran, Soran, Kurdistan Region of Iraq

https://doi.org/0.25130/tjps.v28i1.1261

ARTICLE INFO.

Article history:

-Received: 15 / 9 / 2022

-Accepted: 23/ 10 / 2022

-Available online: 20 / 2 / 2023

Keywords: Claisen–Schmidt reaction, chalcones, and pyrimidines

Corresponding Author:

Name: Nabaz Abdulmajeed Mohammad

E-mail: nabazsalih82@gmail.com

Tel:

ABSTRACT

A facile synthesis of some new 1, 2- thiazine derivatives by the Claisen-Schmidt reaction-induced aldolic condensation of enolizable aromatic ketones with substituted benzaldehydes, and then they were treated with urea and thiourea to obtain the corresponding pyrimidine derivatives. IR, ^{1}H and ^{13}C-NMR spectroscopy were used to analyze all produced substances. The synthesized compounds (**5, 9-11** and **14-15**) were screened for their biological activity against two species of bacteria and fungi according to the gram stain, and all compounds indicated growth inhibition against *Escherichia coli*, *Staphylococcus aureus*, and fungi respectively with different inhibition zones starting from 11 to 26 mm. In all cases, the used two doses were (10 mg/ 1 ml in DMSO) and (20 mg/ 1ml DMSO).

1. Introduction

Synthesis of new heterocyclic compounds is still in demand, as microbes are becoming increasingly resistant to currently available antimicrobial medications. In general sultams **1** (figure 1) are cyclic esters of amino sulfonic acids .They present in crystalline forms whose melting point depends on substituent on the sultams ring. They are generally not soluble in water, but soluble in chloroform, trifluoroacetic acid and acetone. Some of them are soluble in hot alcohols especially methanol .The main type of compound with sulfur and nitrogen in a six-member ring is thiazines [1]. Chalcone is an alternative name for 1, 3-diphenylprop-2-en-1-one. The system consists of two aromatic rings, A and B, connected by an open chain three of carbon α,β-unsaturated carbonyl system compound **2** (figure 1). Kostanecki and Tambor are the ones that coined the term "chalcones." These substances are also referred to as benzylidene acetophenone or benzalacetophenone. [2]. Chalcones occur in nature as precursors of flavonoids; chalcones are organic chemicals that occur naturally in a wide range of plant parts such as leaves, buds, blossoms, heartwood, seeds, roots, and petals [3,4]. A large number of chalcones have been isolated, having various types of substituted groups on either ring A or ring B such as methoxy, methyl, isopentyl and hydroxyl groups [5] .They are also readily to manufactured in the laboratory and structural modifications to the chalcone template are easily achieved. The presence of chromophores and auxochromes in the chalcone structure gives these compounds their various colors. The red pigment Carthaming compound **3** (figure 1) was obtained from the flower of Carthamus tinctoria and was the first chemically synthesized chalcone [6].

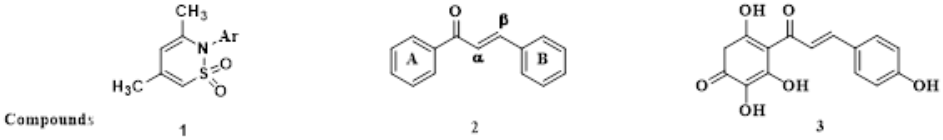
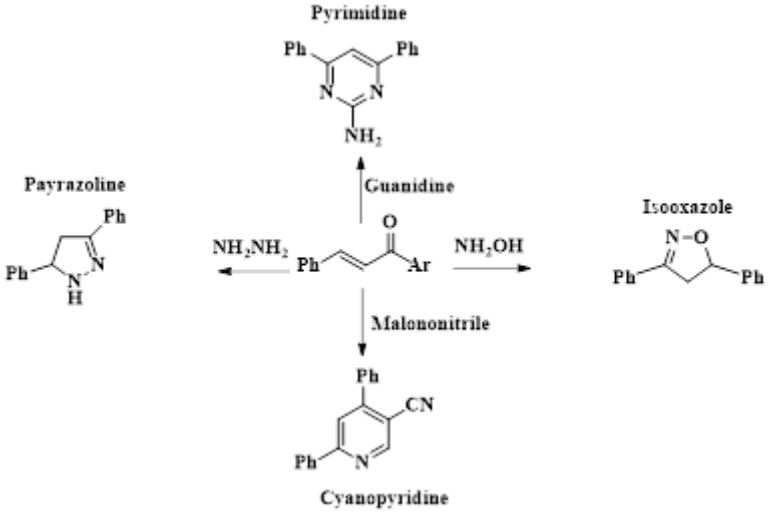


Fig. 1: an examples for 1,2- thiazine and chalcons

Furthermore, chalcones can react with a wide range of chemicals to generate a variety of heterocyclic ring systems, including five-membered rings (e.g. pyrazoles, pyrroles, oxazoles, isoxazoles, thiazoles) [7], six-membered (e.g. pyrimidines, triazines) [8], seven-membered (e.g. benzodiazepines, benzothiazepines) [9]. Chalcones are flexible reactive intermediates; therefore, the chemistry of chalcones has attracted the attention of the scientific community.



Scheme 1: The reaction of chalcone with different reagents

Chalcones **2** [10] and thiazine **1** [11] have a strong synthon framework, allowing for the design of a wide range of new heterocycles with favourable pharmacological properties. Chemistry of both of them has always been the most emphasized field of study among scientists. Chalcones represent an important class of natural compounds with a variety of biological activities such as, antioxidant [12], cytotoxic activity [13], antitubercular [14], antiulcerative [15], antimalarial [16], antiviral [17] chalcone derivatives as effective against SARS-CoV-2 agent [18], antihyperglycemic [19], anti-cancer [20], antibacterial [21], anti-inflammatory [22], antiplatelet [23]. Antimicrobial action is attributed to the presence of reactive chalcone, which varies depending on the kind and position of substituent on the aromatic rings.

2. Materials and methods

The substances and solvents used in this study as well as the characterization were as follows:

Mesityl oxide was prepared in our lab, diethyl ether from (Scharlau), ethyl acetate from (Licrosolv), ethanol from (Hongwell) and aldehyde derivatives from a commercial lab in china. All substances and solvents were used without purification. The purification of the products was done by recrystallization in ethanol, as well as the progress of reactions was monitored by thin layer chromatography (TLC) (silica gel on aluminium plates), Ethyl acetate with toluene (1:9) as an eluent, the result was observed by UV light.^{1}H and ^{13}C-NMR spectrum was observed by 400 and 100 MHz (Ascend) respectively in Kurd Central Research Facilities (KCRF) in Iran. IRAffinity-1S spectrometer was Shimadzu, and all spectra have been done at the University of Mosul, Education College for Girls, melting points were taken in the College of Pharmacy, Hawler Medical University by Stuart Scientific melting point apparatus (SMP3).

General procedure A

A mixture of compound 5 (0.001 mole, 1 equivalent weight) and benzaldehyde derivatives (0.001 mole, 1 equivalent weight) was used to make the chalcone. Ethanol (15 mL) was added to the mixture, to which dropwise additions of NaOH solution (1.3 equivalents) were added. The reaction mixture was stirred under these conditions for one hour before boiling it at 50 ^{o}C under reflux for another two hours. The reaction mixture was put into (25 ml) of ice water after acidic work-up, and the precipitated solid was filtered out and mostly recrystallized with ethanol. [24-26].

General procedure B

Chalcone (0.001 mol) and urea or thiourea (0.001 mol) was dissolved in absolute alcohol (15 ml). The reaction mixture was refluxed and the reaction was monitored by TLC. The reaction mixture was poured into (25 ml) of ice-cold water and kept for some time. The crude solid was filtered off and gave relatively pure compounds as colored solids [27].

4,6-dimethyl-1,2-oxathiine 2,2-dioxide (4)

(88 ml) of acetic anhydride (0.8 mol) were charged into a two-necked round bottomed flask, which was subsequently cooled to 0 to -1 °C. Then, drop by drop, sulfuric acid (24 ml, 0.2 mol) was added, keeping the temperature of the developing viscous mixture below 0°C. Mesityl oxide (44 ml, 0.4 mol) was added dropwise and stirred at 0 °C. The reaction mixture was kept in the freezer for (48 hours) before being kept at room temperature for one week; the reaction mixture turned brownish dark, then it poured on ice cube. After filtration, the crude product was

recovered and purified by crystallization in methanol to obtain a 70% yield, m.p/68-68.5 0°C [28].

1-(4-(3,5-dimethyl-1,1-dioxido-2H-1,2-thiazin-2-yl)phenyl)ethan-1-one (5) [29]

A mixture of oxathine (4 gm, 0.025 mol) and 4-aminoacetophenone (3.37 gm, 0.025 mol) in a beaker (100 ml) was heated for (1.5 hr) at 135 °C to 140 °C. Then the reaction mixture cooled down at room temperature, and the crude product was purified by recrystallization in ethanol to give the product **5** as a red-maroon, solid, yield (69%), m.p./35-38 °C. **^{1}H-NMR** (400 MHz, DMSO-d^{6}) δ ppm: 7.7 (2H, d, *J* = 7.7 Hz, Ar- disubstituted), 6.7 (2H, d, *J* = 6.7 Hz, Ar-disubstituted), 6.6 (1H, s, thiazine), 5.8 (1H, s, thiazine), 2.6 (3H, s, MeO), 2.4 (3H, s, Me, thiazine), 1.93 (3H, Me, thiazine); **^{13}C-NMR** (100 MHz, DMSO-d^{6}) δ ppm: 194, 156, 153, 146, 130, 129, 113, 112, 105, 25, 20, 19; IR (cm^{-1}): 1651 (C=O) str., 1155, 1266 (SO_2) str. assym. and symm., 914 (S-N) str.

(E)-1-(4-(3,5-dimethyl-1,1-dioxido-2H-1,2-thiazin-2-yl)phenyl)-3-phenylprop-2-en-1-one (9)

General procedure **A** compound **5** (0.8 g, 0.003 mol, 1.0 eq.) was dissolved in EtOH (15 ml) benzaldehyde **6** (0.318 gm, 0.003 mol, 1 eq.), NaOH (0.156 gm, 0.004 mol, 1.3 eq.) in H_2O (4 ml), gave the product **9** as a dark brown-black solid, yield (84%), m.p./119-122 °C. **^{1}H-NMR** (400 MHz, DMSO-d^{6}) δ ppm: 8.04 (1H, HC=CH), 6.8-7.9 (12H, Ar and alkene), 2.39 (3H, s, Me, thiazine), 1.44 (3H, Me, thiazine); **^{13}C-NMR** (100 MHz, DMSO-d^{6}) δ ppm: 190, 147, 145, 144, 140, 136, 132, 128, 127.9, 127.5, 127, 121, 119, 116, 109, 21, 20; IR (cm^{-1}): 1597 (C=O) str., 1153, 1267 (SO_2) str. assym. and symm., 1033 (S-N) str..

(E)-1-(4-(3,5-dimethyl-1,1-dioxido-2H-1,2-thiazin-2-yl)phenyl)-3-(*p*-tolyl)prop-2-en-1-one (10)

General procedure **A** compound **5** (0.277 g, 0.001 mol, 1.0 eq.) was dissolved in EtOH (15 ml) 4-methylbenzaldehyde **7** (0.12 gm, 0.001 mol, 1 eq.), NaOH (0.052 gm, 0.0013 mol, 1.3 eq.) in H_2O (4 ml), gave the product **10** as a yellow-greenish, yield (0.3 g, 0.0008 mole, 79%), m.p./83-86 °C. **^{1}H-NMR** (400 MHz, DMSO-d^{6}) δ ppm: 8 (1H, HC=CH), 6.5-7.9 (11H, Ar and alkene), 2.43 (3H, s, Me, thiazine), 2.38 (3H, s, ph-Me), 1.45 (3H, s, Me, thiazine); **^{13}C-NMR** (100 MHz, DMSO-d^{6}) δ ppm: 185, 153, 153.4, 141, 140, 132, 130.9, 130, 129, 128, 126.9, 126, 121.1, 113, 112.9, 26, 25, 20; IR (cm^{-1}): 1593 (C=O) str., 1172, 1278 (SO_2) str. assym. and symm., 831 (S-N) str..

(E)-3-(3,4-dimethoxyphenyl)-1-(4-(3,5-dimethyl-1,1-dioxido-2H-1,2-thiazin-2-yl)phenyl) prop-2-en-1-one (11)

General procedure **A** compound **5** (0.277 g, 0.001 mol, 1.0 eq.) was dissolved in EtOH (15 ml) and 3,4-dimethoxybenzaldehyde **8** (0.166 gm, 0.001 mol, 1 eq.), NaOH (0.052 gm, 0.0013 mol, 1.3 eq.) in H_2O (4 ml), gave the product **11** as a brown-maroon, yield (75%), m.p./125-128 °C. 1H-NMR (400 MHz, DMSO-d^{6}) δ ppm: 6.3-8.2 (11H, Ar and alkene), 3.7 (3H, s, MeO), 3.6 (3H, s, MeO), 2.4 (3H, s, Me, thiazine), 1.43 (3H, s, Me, thiazine); **^{13}C-NMR** (100 MHz, DMSO-d^{6}) δ ppm: 196, 151, 149, 148, 144, 135, 130.3, 130, 129.4, 127, 123, 119, 118, 114, 112, 111,9, 111, 55.4, 55, 26.5, 20; IR (cm^{-1}): 1595 (C=O) str., 1139, 1259 (SO_2) str. assym. and symm., 1022 (S-N) str..

2-(4-(2-hydroxy-6-phenylpyrimidin-4-yl)phenyl)-3,5-dimethyl-2H-1,2-thiazine1,1-dioxide (14)

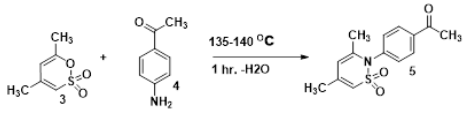
General procedure **B** compound **9** (0.365 g, 0.001 mol, 1.0 eq.) was dissolved in EtOH (20 ml) compound **12** (0.06 gm, 0.001 mol, 1 eq.), giving the product 14 as a brown - grey, yield (0.29 g, 0.0007 mol, 72%), m.p./105-110 °C. **^{1}H-NMR** (400 MHz, DMSO-d^{6}) δ ppm: 8.04 (2H, br.d, ph-2H), 7.76 (2H, d, *J* = 6.7 Hz, Ar-disubstituted), 6.71 (2H, d, *J* = 7.7, Ar-disubstituted), 6.91-7.62 (6H, thiazine-2H, pyrimidine-1H and ph-3H), 4.7 (1H, br.s, NH), 2.43 (3H, s, thiazine-Me), 1.45 (3H, thiazine-Me); **^{13}C-NMR** (100 MHz, DMSO-d^{6}) δ ppm: 160, 157, 153, 140, 139, 132, 131, 130, 129.5, 128.4, 128.2, 127.2, 115.5, 112.9, 112.4, 102.3, 26, 25; IR (cm^{-1}): 3462 (NH) str., 1674 (C=N) str., 1593 (C=O) str., 1151, 1334 (SO_2) str. assym. and symm., 1035 (S-N) str..

2-(4-(2-mercapto-6-phenylpyrimidin-4-yl)phenyl)-3,5-dimethyl-2H-1,2-thiazine-1,1-dioxide (15)

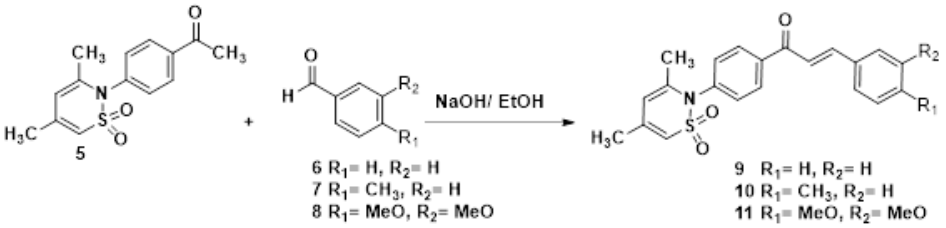
General procedure **B** compound **9** (0.365 g, 0.001 mol, 1.0 eq.) was dissolved in EtOH (20 ml) compound **13** (0.07 gm, 0.001 mol, 1 eq.), giving the product **15** as a grey-black, yield (0.3 g, 0.0007 mol, 71%), m.p./109-112 °C. **^{1}H-NMR** (400 MHz, DMSO-d^{6}) δ ppm: 8.04 (2H, br.d, ph-2H), 7.75 (2H, d, *J* = 6.7 Hz, Ar-disubstituted), 7.11-7.59 (6H, Ar-H), 6.9 (1H, br.s,NH), 6.7 (2H, d, *J* = 7.7, Ar-disubstituted), 2.43 (3H, s, thiazine-Me), 1.44 (3H, thiazine-Me); **^{13}C-NMR** (100 MHz, DMSO-d^{6}) δ ppm: 194, 183, 171, 152, 132, 130, 129.7, 129.5, 129.3, 128.6, 128.7, 128.5, 127, 126, 113, 112, 26, 25; IR (cm^{-1}): 3323 (NH) str., 1595 (C=N) str., 1174, 1153 (SO_2) str. assym. and symm., 1087 (S-N) str., 1070 (C=S) str.,

3. Results and discussion:

This work started with the synthesis of the new 1,2-thiazine, in addition to synthesis different chalcones were envisaged using the Claisen Schmidt reaction. Chalcones are important as key intermediates for the synthesis of biologically active heterocycles. The aldolic condensation of equimolar amounts of benzaldehyde derivatives and enolizable aromatic ketones play the role of the nucleophile in ethanol using NaOH solution as the catalyst. Dehydration of the hydroxyketone to form a stable conjugated unsaturated carbonyl compound occurs spontaneously. By applying these reaction conditions, good yields were obtained in scheme 3.

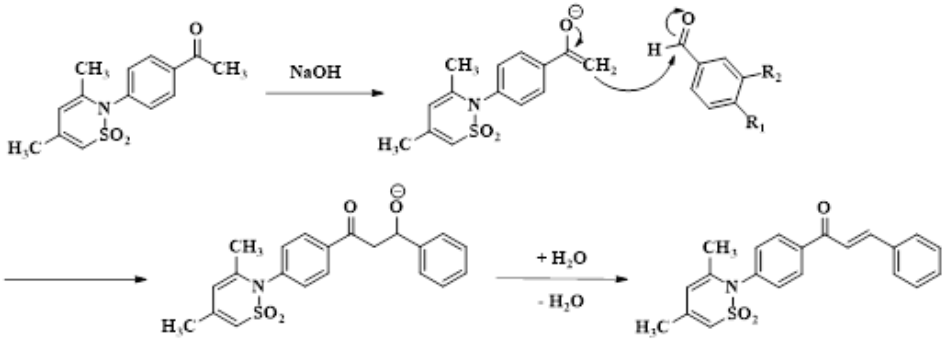


Scheme 2: Synthesis of N-phenyl-ethan-1-one-2,4-dimethyl-1,3-butadiene-1, 4-thiazin

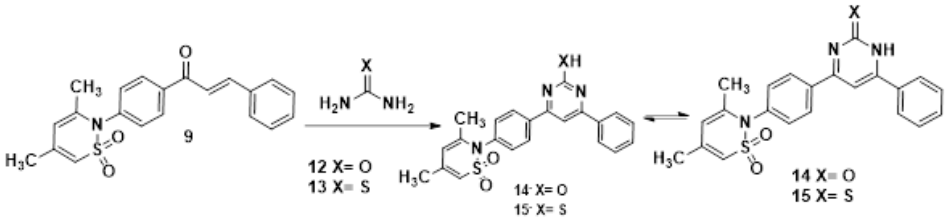


Scheme 3: Synthesis of bioactive molecules

Initially, the feasibility of the reaction between aldehyde and ketone was investigated, and it was discovered that in the presence of electron donating groups, aldehyde reactivity decreased. IR, ^{1}H, and ^{13}C-NMR spectrum data were used to confirm the molecular structures of the produced compounds. Infrared spectra showed the existence of a carbonyl group conjugated with the olefinic carbon–carbon bond, with the carbonyl peak occurring at a lower wave number than a usual carbonyl peak (1593–1597 cm^{-1}). ^{1}H-NMR spectra show alkene signal at (δ 8 ppm) as well as ^{13}C-NMR spectra show peak to conjugated carbonyl at (δ190-194 ppm).



Scheme 4: a plausible mechanism for chalcone synthesis



Scheme 5: Synthesis pyrimidines derivatives

A different procedure was used to make the other derivatives, because of the interesting biological activity of various substituted pyrimidines, this class has received a lot of attention. The reactions of chalcone with urea, and thiourea, yielded pyrimidine derivatives. IR, ^{1}H and ^{13}C-NMR spectrum were used to characterize compounds (14-15), and all of the data are completely consistent with the proposed structure. For instance, the pyrimidinyl moiety in the ^{1}H -NMR spectrum displayed the most significant signal for NH at (4.5–6.9 ppm), and many other signals were seen at the predicted chemical shift. However, it was noticed that there were some strange impurities that could be attributed to the technical errors of the device operator, which clearly led to the contamination of the outputs. The thione carbon peak in the ^{13}C-NMR spectrum was detected at 194 ppm. IR spectra revealed the absorption band in the range of 3462-3323 cm^{-1} for -NH and 1655-1674 cm^{-1} for aromatic C=N stretching.

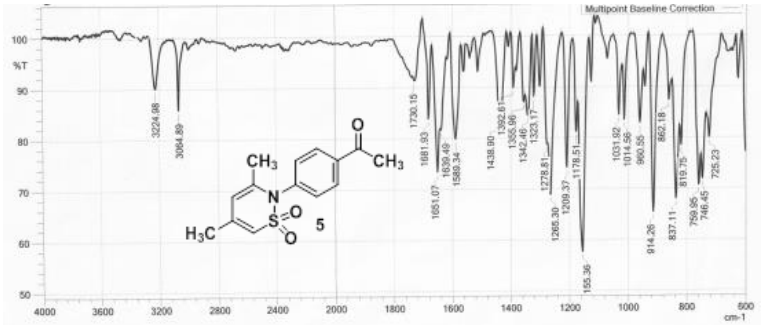


Fig. 1: FT-IR for 1-(4-(3,5-dimethyl-1,1-dioxido-2H-1,2-thiazin-2-yl)phenyl)ethan-1-one (5)

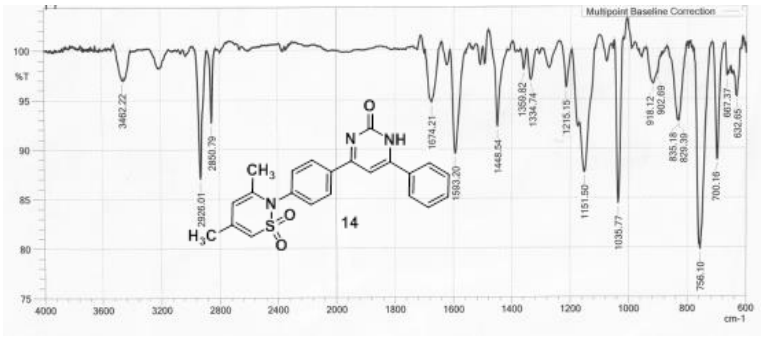


Fig. 2: 4-(4-(3,5-dimethyl-1,1-dioxido-2H-1,2-thiazin-2-yl)phenyl)-6-phenylpyrimidin-2(1H)-one (14)

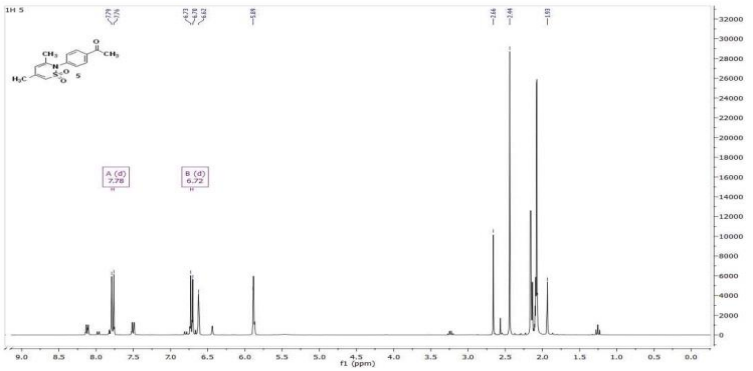


Fig. 3: ^{1}H-NMR for 1-(4-(3,5-dimethyl-1,1-dioxido-2H-1,2-thiazin-2-yl)phenyl)ethan-1-one (5).

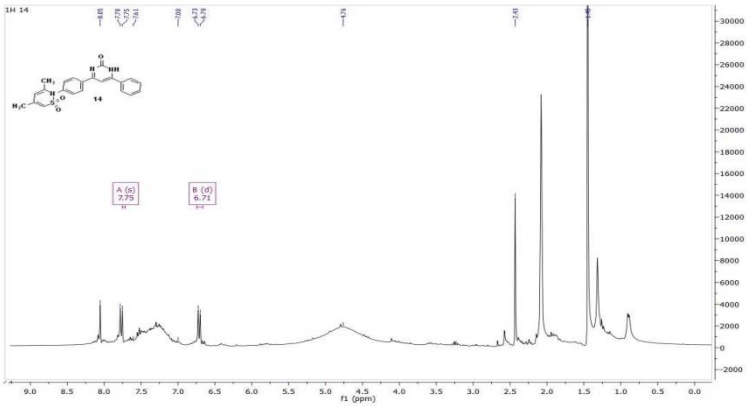


Fig. 4: 4-(4-(3,5-dimethyl-1,1-dioxido-2H-1,2-thiazin-2-yl)phenyl)-6-phenylpyrimidin-2(1H)-one (14).

Table 1: IR spectra for synthesized compounds in (cm^{-1})

Compounds	(NH) str.	(C=N) str.	(C=O) str.	(SO_2) str. assym. and symm.		(S-N) str.	(C=S) str.
5			1651	1155	1266	914	
9			1597	1153	1267	1033	
10			1593	1172	1278	831	
11			1595	1139	1259	1022	
14	3462	1674	1593	1151	1334	1035	
15	3323	1595		1174	1153	1087	1070

Table 2: physical state for synthesized compounds

Compounds	M.P. in ^{o}C	Color
5	35-38	red-maroon
9	119-122	dark brown-black
10	83-86	yellow-greenish
11	125-128	brown-maroon
14	105-110	brown - grey
15	109-112	grey-black

4. Biological activity

The synthesized compounds (**5, 9-11** and **14-15**) were screened for their antibacterial activity against two species of bacteria and fungi according to the gram stain, and all compounds indicated growth inhibition against *Escherichia coli*, *Staphylococcus aureus* and fungi respectively with different inhibition zones starting from 11 to 26 mm. In all cases the used two doses were (10 mg/ ml in 1ml DMSO) and (20 mg/ml in 1ml of DMSO).

Table 3: Biological activity of synthesized compounds

Compounds	Microorganism	(10 mg/ ml in 1ml DMSO) in mm	(20 mg/ml in 1ml DMSO) in mm
5	*Escherichia coli*	19	21
	Staphylococcus aureus	23	25
	Fungi	22	26
9	*Escherichia coli*	13	14
	Staphylococcus aureus	16	18
	Fungi	11	17
10	*Escherichia coli*	13	17
	Staphylococcus aureus	17	18
	Fungi	12	13
11	*Escherichia coli*	16	18
	Staphylococcus aureus	19	21
	Fungi	16	18
14	*Escherichia coli*	12	13
	Staphylococcus aureus	17	19
	Fungi	12	16
15	*Escherichia coli*	14	17
	Staphylococcus aureus	16	18
	Fungi	18	20

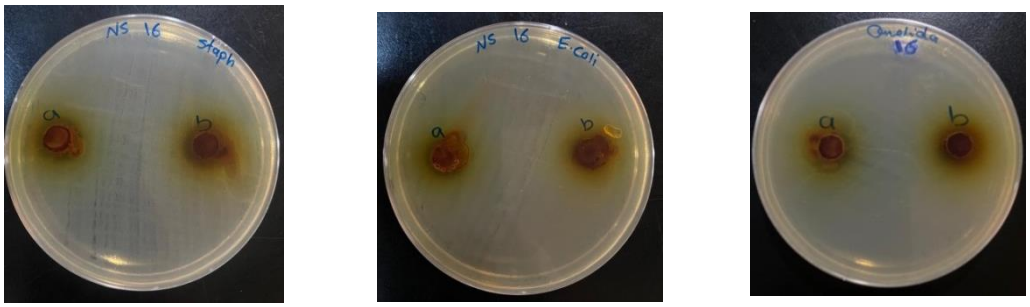


Fig. 5: Biological activities of compound 11.

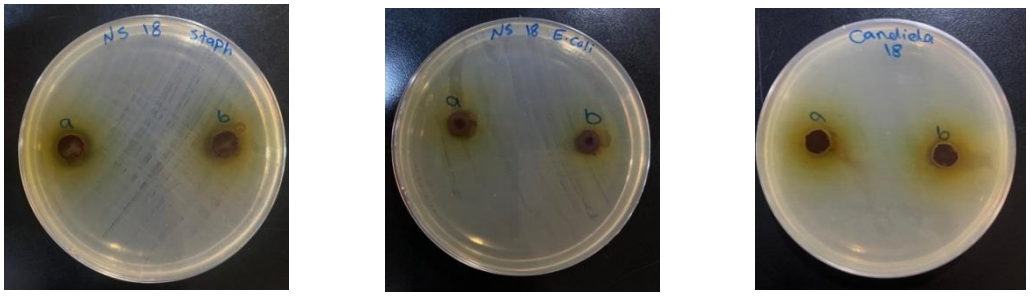


Fig. 6: Biological activities of compound 14.

5. Conclusions

In the present work, firstly 1,2- thiazine was synthesized then we designed and synthesized in good to excellent yield chalcone derivatives using Claisen-Schmidt reactions; in the presence of electron donating groups, aldehyde reactivity decrease. Then some chalcones submitted to intramolecular cyclization to get pyrimidine derivatives. All compounds indicated growth inhibition against *Escherichia coli*, *Staphylococcus aureus*, and fungi.

6. References

[1] Voichita, M. (2012). *Memory of Chirality : Synthesis of enantiopure sultams derived from α - amino acids*. PhD thesis, Università degli studi di milano, Italy: pp 144. (Attached as PDF)

[2] Mohamad, A. S. etal. (2010). Antinociceptive activity of a synthetic chalcone, flavokawin B on chemical and thermal models of nociception in mice. *European Journal of Pharmacology*, *647* (1–3): 103–109.

[3] Mithun, R. Johra, K.; Abdul Aziz, B.; Randa, M.; Emmanuel, I.; Tripti, S.; Shubham, J. and Atul, R. (2021). Chalcone scaffolds, bioprecursors of flavonoids: Chemistry, bioactivities, and pharmacokinetics. *Molecules*, *26* (23): 1–21.

[4] Serkan, K.; Ibrahim, D. ; Dogukan, M.; Mehmet, N. A. ;Hakan, Ü. & Şevki, A. (2021). New cytotoxic chalcone derivatives from Astragalus ponticus Pall. *Natural Product Research*, 36 (18).

[5] Wenjing, L.; Min, H.; Yongjun, L.; Zhiyun, P. and Guangcheng, W. (2022). A review on synthetic chalcone derivatives as tubulin polymerisation inhibitors. *Journal of Enzyme Inhibition and Medicinal Chemistry*, *37* (1): 9–38.
[6] Junichi, S.; Hiromichi, K.; Kenichi, N.; Kazuo, M.; Masaaki, N.; Katsuhiro, K.; Yoshinori, A. and Kohei, K. (2016). Cloning and functional analysis of three chalcone synthases from the flowers of safflowers Carthamus tinctorius. *Natural Product Communications*, *11* (6): 787–790.
[7] Gosavi, S. A.; Nandal, D. H. and Pawar, S. S. (2019). Synthesis and biological evaluation of some novel mannich bases of isoxazoline derivatives as possible antimicrobial agents. *Asian Journal of Chemistry*, *31* (12): 2821–2826.
[8] Kanagarajan, V.; Thanusu, J. and Gopalakrishnan, M. (2010). Synthesis and in vitro microbiological evaluation of an array of biolabile 2-morpholino-N-(4,6-diarylpyrimidin-2-yl)acetamides. *European Journal of Medicinal Chemistry*, *45* (4): 1583–1589.
[9] Aastha, P.; Priyanka, R.; Navneet, K.; Pratima, S. and Kishore D. (2013). An Efficient Synthesis and Applications of Chalcones in Organic Synthesis. *International Journal of Chemical and Pharmaceutical Sciences*, *4* (3): 19.
[10] Duha, D.; Bijender, S.; Surinder, K. M.; Vinod, K. and Ramesh, K. (2020). Simple and solvent free practical procedure for chalcones: An expeditious, mild and greener approach. *Current Research in Green and Sustainable Chemistry*, *3* (October): 100041.
[11] Syed, L. B. and AbdulNaeem. (2016). Bioactive thiazine and benzothiazine derivatives: Green synthesis methods and their medicinal importance. *Molecules*, *21* (8):
[12] Mohd, R. A.; Girija, S.; Nasreen, B.; Ravichandra, S. and Raghavendra, M.(2011). Synthesis and cytotoxic, anti oxidant activites of new chalcone derivatives. *Rasayan Journal of Chemistry*, *4* (2): 289–294.
[13] Go, M.; Wu, X. and Liu, X. (2005). Chalcones: An Update on Cytotoxic and Chemoprotective Properties. *Current Medicinal Chemistry*, *12* (4), 483–499.
[14] Sylvie, D.; Richard, F.; John, A. H.; Alex, K.; Nicholas, J. L.; Alan, T. M. and David, R. (1998). Potent antimitotic and cell growth inhibitory properties of substituted chalcones. *Bioorganic and Medicinal Chemistry Letters*, *8* (9): 1051–1056.
[15] Sweety, S.; Kumar, K.; Nepali, S.; Sapra, O. P.; Suri, K. L.; Dhar, G. S.; Sarma and Saxena. A. K. (2010). Synthesis and biological evaluation of chalcones having heterosubstituent(s). *Indian Journal of Pharmaceutical Sciences*, *72* (6): 801–806.
[16] Alain, V. (2006). New syntheses and potential antimalarial activities of new "retinoid-like chalcones. *European Journal of Medicinal Chemistry*, *41* (1): 142–146.
[17] Malhotra, B.; Malhotra, B.; Onyilagha, C. J.; Bohm, B. A.; Towers, G. H. N.; James, D.; Harborne, J. B. and French, C. J. (1996). Inhibition of tomato ringspot virus by flavonoids. *Phytochemistry*, *43* (6): 1271–1276.
[18] Nizami, D.; Fatih, P.; Derya, A. ; Abdullah, A.; Emrah, A.; Funda, C.; Erhan, T.; Baris, A.; Serdar, B.;Oztekin, A. (2021). New chalcone derivatives as effective against SARS-CoV-2 agent. *Int J Clin Pract*, 75(12): e14846.
[19] Satyanarayana, M. etal (2004). Synthesis and antihyperglycemic activity of chalcone based aryloxypropanolamines. *Bioorganic and Medicinal Chemistry*, *12* (5): 883–889.
[20] Marek, T. K.; Wojciech, K.; Michal, S.; Andrzej, S.; Roland, W.; Ewa, A. and Zofia, Z. (2007). Synthesis of isomeric, oxathiolone fused chalcones, and comparison of their activity toward various microorganisms and human cancer cells line. *Chemical and Pharmaceutical Bulletin*, *55* (5): 817–820.
[21] Opletalová, V. (2000). Chalcones and their heterocyclic analogs as potential therapeutic agents in bacterial diseases. *Ceska a Slovenska farmacie*, *49* (6): 278–284.
[22] Sung, H. L. Geom, S. S.; Ji, Y. K.; Xing, Y. J.; Hee-Doo, K.; Dong, H. S. (2006). Heme oxygenase 1 mediates anti-inflammatory effects of 2′,4′, 6′-tris(methoxymethoxy) chalcone. *European Journal of Pharmacology*, *532* (1–2): 178–186.
[23] Jayapal, M. R.; Prasad, K. S. and Sreedhar, N. Y. (2010). Synthesis and characterization of 2,4-dihydroxy substituted chalcones using aldol condensation by $SOCl_2$/EtOH. *J. Chem. Pharm. Res*, *2* (3): 127–132.
[24] Paula, B. (2006). Synthesis of chalcone analogues with increased antileishmanial activity. *Bioorganic and Medicinal Chemistry*, *14* (5): 1538–1545.
[25] Yun, F.; Dan, L.; Huanan, Z.; Xiaoli, R.; Baoan, S.; Deyu, H. and Xiuhai, G. (2020). New chalcone derivatives: synthesis, antiviral activity and mechanism of action. *The Royal Society of Chemistry*, 10, 24483–24490.
[26] Nadia A. A. Elkanzi,* Hajer Hrichi, Ruba A. Alolayan, Wassila Derafa, Fatin M. Zahou, and Rania B. Bakr. (2022). Synthesis of Chalcones Derivatives and Their Biological Activities: A Review. *American Chemical Society*, 7, 27769−27786.
[27] Panda, S. and Chowdary, P. V. R. (2008). Synthesis of novel indolyl-pyrimidine antiinflammatory, antioxidant and antibacterial agents. *Indian Journal of Pharmaceutical Sciences*, *70* (2): 208–215.
[28] Roberts, D. W. and Williams, D. L. (1987). Sulton Chemistry. *Tetrahedron*, *43*(6): 1027-1062.
[29] Rostam, R. B. (1997). Synthesis of some new dereivatives of the brominated 1,2-thiazines using ultrasound technique . M.Sc. thesis, Salahaddin University, Erbil, Iraq: pp 132.

تحضير و تشخيص و دراسة الفعالية البيولوجية لمشتقات *N*-phenyl-ethan-1-one-2,4-dimethyl-1,3-butadiene-1,4-thiazin

نبز عبدالمجيد محمد صالح

قسم الكيمياء ، كلية العلوم ، جامعة سوران ، سوران ، إقليم كردستان العراق

الملخص

يقدم البحث طريقة سهولة لتحضير بعض المشتقات الجديدة لـ 1,2-thiazine بواسطة تكاثف الألدول الناتج عن تفاعل كليزن – شمدت للكيتونات الأروماتية القابلة للتحويل مع البنزالديهايدات المعوضة، ثم تمت مفاعلتها مع اليوريا والثيوريا للحصول على مشتقات بيريميدين المقابلة. تم استخدام التحليل الطيفي للأشعة تحت الحمراء و ^{13}C-NMR ,^{1}H لتشخيص جميع المركبات الناتجة. أشارت حزم الـ ^{1}H-NMR و بوضوح إلى وجود المركبات المطلوبة .تم فحص المركبات المحضرة (5,9,10,11,14,15) لمعرفة نشاطها البيولوجي ضد نوعين من البكتيريا والفطريات وفقًا لصبغة جرام، و كانت التراكيز المستخدمة في جميع الفحوصات (10 mg/ 1 ml in DMSO) و(20 mg/ 1ml DMSO) ، أظهرت جميع المركبات فعالية في تثبيط نمو الإشريكية القولونية والمكورات العنقودية الذهبية والفطريات على التوالي مع نطاقات تثبيط مختلفة تبدأ من 11 – 26 ملم.