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Synthesis and Chemical Characterization of Some Novel Azachalcones compounds and Evaluation of their Biological Activity

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Abstract : A series of novel Azachalcone compounds were prepared by the reaction of 3-acetyl pyridine with different aromatic aldehyd . Azachalcone was reacted with thiourea to give good yields of thiazines , all the new compounds were characterized by I.R , U.V and TLC. Also the Biological Activities of these compounds against anti bacteril and anti fungal were evaluated . some of these compounds gave good activity

Key words : Synthesis , Characterization ,Azachalcones , Biological Activity

Introduction :

Chalcones are a class of naturally occurring compounds with various biological activites (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 bacterio static properties (3) . Azachalcones (the derivatives of chalcones with an annular nitrogen atom in the phenyl ring)
Have also been reported to have awide variety of biological activities such as anti bacterial , anti tuberculostatic , and anti-inflammatory potential (3).

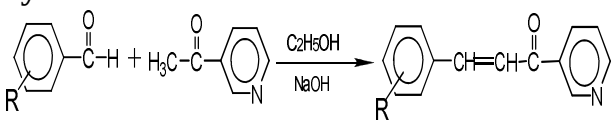
Hetrocycles are abundant in nature and are of great significance to life because their structural subunits exist in many natural products such as vitamins , hormones , antibiotics . etc. (4) they have attacted considerabe attention in the design of biologically active molecules (5) . Apractical method for the synthesis of such compound is of great interest in synthetic organic chemistry . Among the hetrocycles ,1,3-thiazines are a class of compoundes with biological activity such as antimicrobial (6), antitumor (7) , antioxidant (8) . calcium channel modulators (9) . In view of these observation and continuation of our work on biologically active hetrocycles(10) ,and there increasing importance in farmaceutical and biological field . it was conceder of interest to synthesize some new chemical entities incorporation the two active pharmacophores in a singl molecular fram work and to evaluate their biological activity. In this regard , azachalcone would be suited for preparing thiazines (scheme 1)

Experimental

Material and Methods

Melting point of the synthesized compounds were determined by open capillary and are un corrected. The purity of the compounds was checked using precoated TLC plates (MERCK , 60F) using chloroform : methanol (8:2) solvent system . The developed chromatographic plates
were visualized under U.V at 254 nm. I.R spectra were recorder using KBr on shimadzu FTIR model 8400 spectrophotometer .Physical data of the compounds are recorder in Tab.(1) and the the spectral data are recorder in Tab.(2).

Synthesis of azachalcons

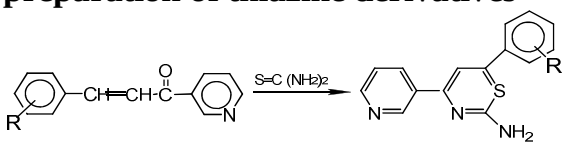


where R is
R= m-NO2 , p-OH , m-Br , m-OCH3 , p-N(CH3)2

Equimolar quantities of m-nitro-benzaldehyd , p-hydroxy benzaldehyd , m-chloro benzaldehyd , Anisaldehyd , N,N-dimethyl benzaldehyd (0.01 mol) and 3-acetyl pyridine (0.1 mol) were dissolved in minmmum amount of alcohol .sudium hydroxide solution (0.02 mol) was added slowly and the mixture stirred for 2hr until the entire mixture becomes very cloud . then the mixture was poured slowly into 400 ml of water with constant stirring and kept in

refrigcrator for 24 hours . The precipitat obtained was filtered . washed and recrystallized from ethanol . the completion of the reaction was monitored by TLC (11) .

preparation of thiazine derivatives



where R is

R= m-NO2 , p-OH , m-Br , m-OCH3 , p-N(CH3)2

Amixture of azachalcons (1-5) (0.02 mol) , thiourea (0.02 mol) were dissolved in ethanol , sodium hydroxid (10 ml) was stirrer about 2-3 hours with a magnetic stirrer . this was then poured in to 400 ml of cold water with continuous stirring for an hours and then kept in refrigerator for 24 hours . the precipitat obtained was filtered . washed and recrystallized. the completion of the reaction was monitored by TLC (11) .

Results and discussion .

The azachalcons was synthesized by claisen condensation of 3-acetyl pyridine with aromatic aldehyd in ethanol as solvent in the presence of aqueous NaOH at room temperature .

(mech. (1) searches) the reaction time as well as the yield varies dependin on the corresponding reaction the crude product was contaminated with some starting materials which could easily by removed by extraction ether . the azachalcons reaction with thiourea in the presence of alcoholic NaOH to get the corresponding thiazin.

(mech. (2) searches) the compounds have low solubilbty in most common solvents.

They were purified in small quantities by crystallizing the solid productes in appropriate amounts of ethyl alcohol/ benzene . The physical characterization

Tab. (1) . The structures of the synthesized compounds were confirmed by I.R , U.V spectral data are presented in Tab.(2) and further screened for their antibacterial , antifungal .

Antimicrobial activity

All the newly synthesized compounds were screened for antimicrobial activity against both gram positive S.aurous and gram negative E.Coli bacteria and antifungal activity against C.albicans and A.flavus according to cup plate method (13) at a concentration of 0.005 mole / ml . streptomycin Gresofulvin were used as standard for comparison of antibacterial and antifungal activity (14) . solvent dimethyl formamide (DMF) was used as control . the result of screening are given in table 3 and 4 from the results. It is evident that most of the compounds are very weakly and few are moderately active against staphylococcus and Escherishia coli but compounds 7,9,6 possess very good activity against fungi aspergillus flavus and compound 8,6,10 showed moderate activity all bacteria and fungi tested

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Table NO. 1: Physico chemical data of synthesized compound (1 - 10)

Compound NO.	Molecular formula	M.PC°	R_f value	% Yield
1	$C_{14}H_{10}O_3N_2$	140	0.53	60
2	$C_{14}H_{11}O_2N$	108	0.65	50
3	$C_{14}H_{10}ONBr$	115	0.72	48
4	$C_{15}H_{13}O_2N$	123	0.62	52
5	$C_{16}H_{16}ON_2$	131	0.57	73
6	$C_{15}H_{16}O_2N_4S$	129	0.76	80
7	$C_{15}H_{17}ON_3S$	110	0.82	78
8	$C_{15}H_{16}N_3S$	116	0.75	56
9	$C_{16}H_{17}ON_3S$	97	0.58	66
10	$C_{17}H_{19}N_4S$	105	0.71	46

Table NO. 2 Spectral data of the compounds (1 - 10)

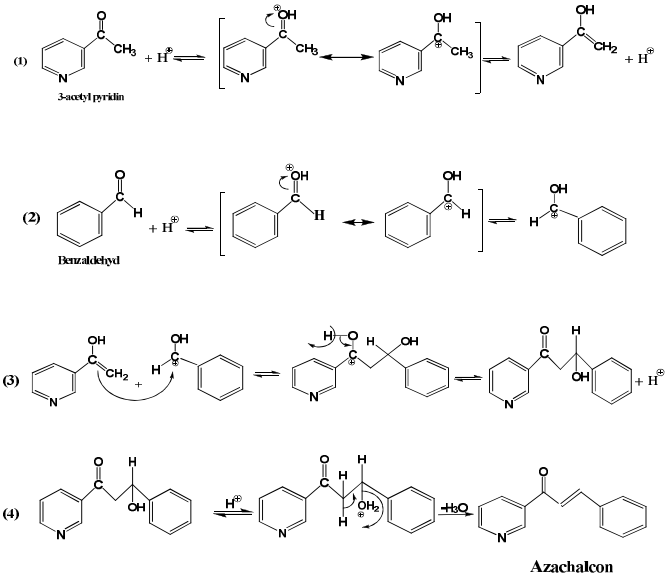
NO.	I.R. (KBr) , ν (cm^{-1})						U.V.
	C = O	C = C	C = N	NH_2	C-S-C,St	Others ν	λ_{max} (nm)
1	1726	1640	1480	——	——	C-NO_2 (1374)	315
2	1730	1648	1510	——	——	C-OH (3330)	301
3	1688	1652	1536	——	——	C-Br (863)	320
4	1690	1650	1526	——	——	$COCH_3$ (1170)	350
5	1721	1621	1492	——	——		346
6	——	1620	1500	3398	2360		290
7	——	1600	1513	3398	2355		293
8	——	1616	1520	3396	2300		280
9	——	1642	1493	3392	2410		303
10	——	1623	1516	3399	2523		335

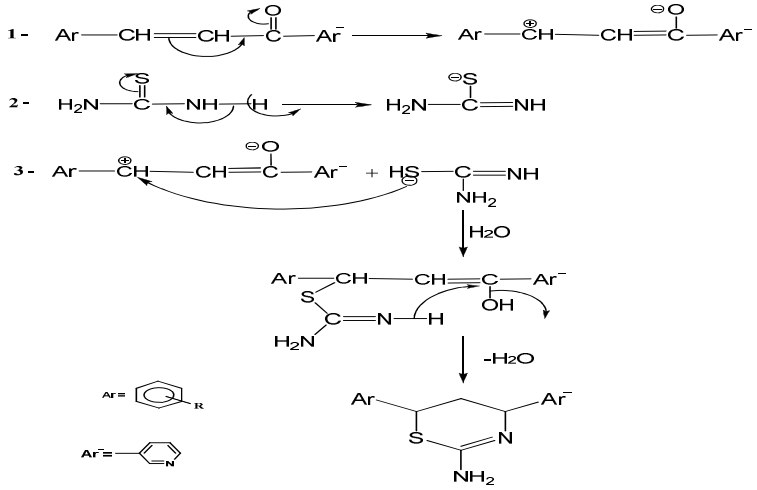
Table NO. 3 Antibacterial activity

Compounds NO.	Mean zone of inhibition (in mm)			
	Staphylococcu aureus		Escherichia Coli	
	50 Mg	100 Mg	50 Mg	100 Mg
1	13	12	10	15
2	9	12	8	10
3	12	13	14	8
4	10	10	9	11
5	8	10	11	9
6	13	13	12	15
7	8	10	23	18
8	9	——	8	6
9	14	16	18	16
10	13	——	10	8
Procaine penicillin	——	——	10	13
Strepto-mycin	20	18	——	13

Table NO. 4 Antifungal activity

Compounds NO.	Mean zone of inhibition (in mm)			
	Candida albicans		Asperagillus flavus	
	50 Mg	100 Mg	50 Mg	100 Mg
1	16	15	13	10
2	12	10	14	13
3	9	13	10	10
4	18	14	12	18
5	20	18	20	16
6	16	16	20	21
7	18	16	13	20
8	13	18	23	21
9	14	16	21	20
10	17	15	19	23
Griseofulvin	23	23	22	20





Thiazine derivatives

تحضير ودراسة الخواص الكيميائية لبعض مركبات ازاجالكون الجديدة وتقدير نشاطها الحيوي

محمد عبد كاظم

الخلاصة حضرت سلسلة من مركبات ازاجالكون الجديدة بواسطة تفاعل ٣-اسيتايل بيريدين مع الديهيدات اروماتية مختلفة وتم مفاعله مركب الازاجالكون الناتج مع الثايوبوريا حيث أعطى ناتج جيد من الثايازين . تم تشخيص كل المركبات الجديدة بواسطة أطياف R.I و V.U وتقنية كروماتوكرافيا الطبقات الرقيقة (TLC) وكذلك تم تقدير نشاطها الحيوي تجاه بعض البكتريا والفطريات حيث أعطى بعض هذه المركبات نشاطا جيدا