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RESEARCH ARTICLE

Synthesis of Novel Heterocyclic Derivatives Containing Di aze

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ABSTRACT:
Chalcones are starting compounds in synthesis of heterocycles containing di nitrogen atoms which named (di aze) , an attempt to synthesis of chalcones from acetanilide with aromatic aldehydes such as P-N,N-dimethyl benzaldehyde and P-hydroxy benzaldehyde by Claisen- Schmidt condensation.The resulting chalcones after purification have been converted into substituted pyrazoline and pyrimidine by reaction with hydrazine hydrate,urea,thiourea and guanidine.All these compounds were characterized by Physical and spectral methods such as melting point, FT-IR,H-NMR and C.H.N analysis.

KEYWORDS: Chalcons,synthesis of pyrazoline,pyrimidine.

INTRODUCTION:
The synthesis of chalcone compounds incorporating with hetero cycles became great importance in medicinal chemistry[1,2] .The hetero atoms in there structure such as (S, N, O) explain variety applications in the biological engineering and in other field of their specific structures[3] . Chalcones are natural biocides and are well known intermediates in the synthesis of heterocyclic compounds exhibiting various biological activities. Chalcones and their derivatives posses some interesting biological properties such as antibacterial, antifungal, insecticidal, anesthetic, anti-inflammatory, analgesic etc [4-6]. Pyrazole is a class of compounds, which has many applications in different field [7]. In addition, Pyrazolines have played a curcial part in the development of theory in heterocyclic chemistry and also used extensively in organic synthesis. Among the methods employed in synthesis of pyrazolines, condensation of a variety of substituted chalcones with hydrazine and its derivatives is commonly used[8]. Pyrimidine derivatives occupy an important place in the present day therapeutics. They were reported to possess abroad spectrum of biological activities such as anticancer, antitubercular antimalarial properties[9]. The resulting chalcones after purification and characterization by physical and spectral methods have been successfully converted into substituted pyrimidines by reaction with guanidine hydrochloride [10-12].

EXPERIMENTAL:
Materials:
All the chemicals were supplied by BDH and Fluka – Chemical Company.

The melting point of compounds was determined by Electro thermal melting point apparatus.

Elemental analysis were carried out by micro analytical unit of 1180 C. H. N Elemental analyzer (Malaysia).

FT.IR spectra were recorded using (KBR pellets) 4000-400 cm^{-1}. on. FT.IR. tests cam. Shimadzu 8000 series.

The ^{1}H-NMR spectra were obtained in (DMSO) solvent using (Bruker, Ultra. Shield.3000 MKZ, Switzerland).

Synthesis of chalcones[13]:
To Acetanalyde (1.35gm, 0.01 mole) added aromatic aldehydes [P-N-dimethyl benzaldehyde (1.49gm, 0.01 mole) or P-Hydroxy benzaldehyde (1.22gm, 0.01 mole)] in Ethanol (25ml) and catalytic quantity of Sodium hydroxide (10%). The mixture was stirred for 6 hours at room temperature using magnetic stirrer The reaction was monitored by T.L.C and The solvent was evaporated and the precipitation was recrystallized from absolute EtOH to give Comp.(1): (1.8gm, 67.6%), Comp.(2): (1.6gm,66.9%). Scheme (1)

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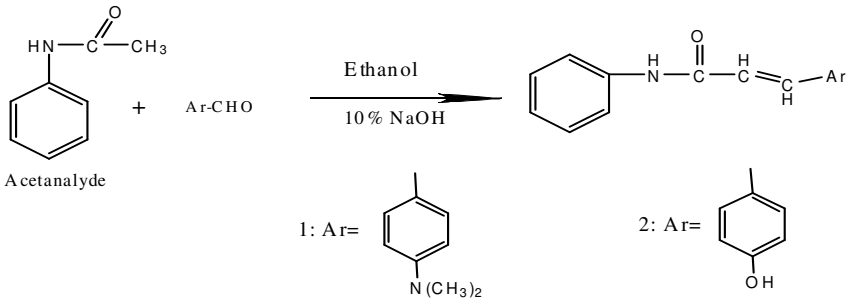
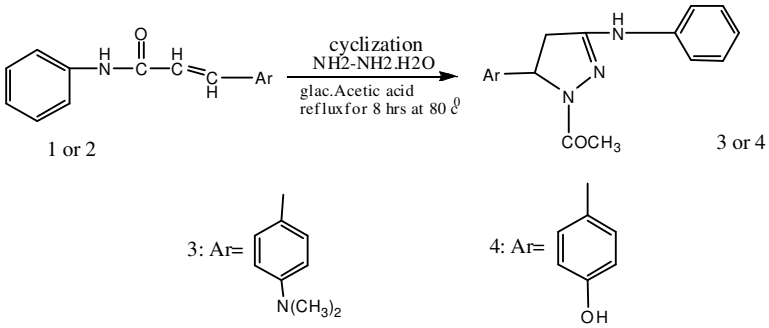


Scheme (1) preparation of Chalcones

Synthesis of pyrazolines [13]

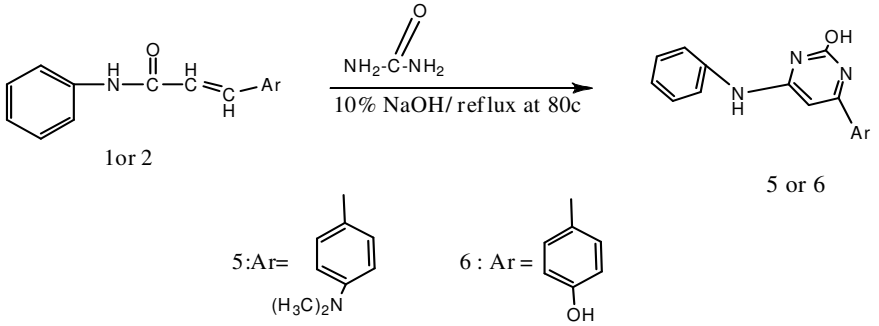
To the two different Chalcones[(*E*)-3-(4-(dimethylamino)phenyl)-N-phenylacrylamide , (*E*)-3-(4-hydroxy phenyl)-N-phenyl acrylamide] (0.01 moles)in absolute ethanol (25ml) added glacial acetic acid(2 ml) and hydrazine hydrate 99% (0.01mole). Refluxed with stirring at 80 C^{o} for 8 hours The reaction was monitored by T.L.C and The solvent was evaporated and the precipitation was recrystallized from absolute EtOH to give comp.(3) (1.9gm , 59%), and(4) (1.6gm, 54%). Scheme (2).



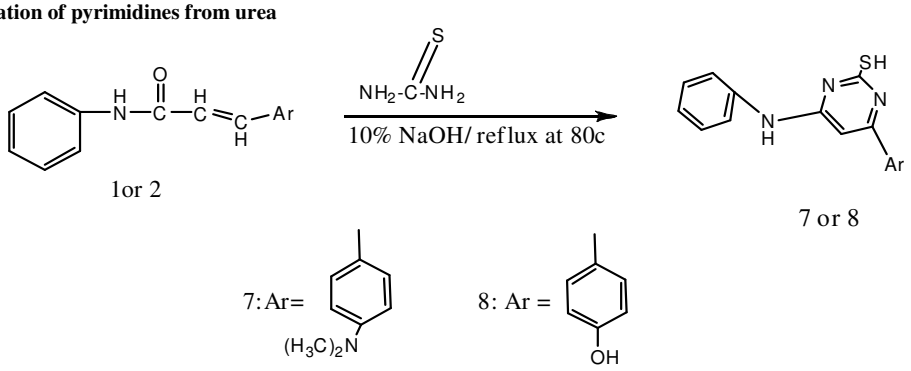
Scheme (2) preparation of pyrazolines

Synthesis of pyriminines[14] from Chalcones

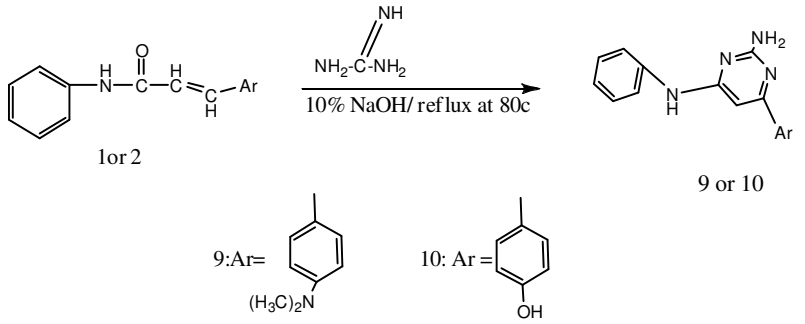
A mixture of chalcones (1 or 2) (0.01 mole), urea or thiourea or guanedin (0.01mole) in absolute ethanol (25ml) and 10% NaOH (2ml) were refluxed with stirring for 8h. The reaction was monitored by T.L.C and The solvent was evaporated and the precipitation was recrystallized from absolute EtOH to give compounds (5-10).



Scheme(3) preparation of pyrimidines from urea



Scheme (4) preparation of pyrimidines from thio urea



Scheme(5) preparation of pyrimidines from guanidine

RESULTTS AND DISCUSSION:

All synthesized derivatives [1-10] have been characterized by their melting points and spectroscopic methods such as (FT-IR , H-NMR)spectra and C.H.N analysis. The FT-IR[15] spectrum of comp.(1) showed strong band at (3294 cm^{-1}) attributed to (N-H) stretching, (1670 cm^{-1}) due to (C=O) amide, (1600cm^{-1})(C=C) alkene, (1560 cm^{-1}) (C=C) aromatic and bands in (3194, 3082)cm^{-1} due to (C-H aromatic, C-H alkene) respectively in addition to band of (C-H aliphatic) assigned at (2912 cm^{-1}). comp.(2) showed weak bands at (3292,3400 cm^{-1}) attributed to(N-H) and (OH) stretching respectively, (1676cm^{-1}) due to(C=O) amide, (1600cm^{-1}) (C=C)alkene,(1502 cm^{-1}) (C=C)aromatic Anal. Calcd/ found for comp.(2)C, 75.313/ 75.121 ; H, 5.439 / 5.268 ; N,5.857 / 5.593. in pyrazoline derivatives comp.(3 and 4) showed appearance bands of (N-H) in both compounds at (3292,3294cm^{-1}), bands of (C=O) amide at (1650,1664cm^{-1}), (C=C) aromatic (1600, 1597)cm^{-1}, (C=N) endo cyclic at (1520,1512)cm^{-1}respectively in addition to band at (3483)cm^{-1} due to (O-H) in comp.(4) and sharp peak attributed to[$N(CH_3)$]bending in comp. (3) at(1166 cm^{-1}). In pyrimidine derivatives from chalcones with urea comp.(5 and 6) showed appearance bands of (O-H) in both compounds at about (3400 , 3458)cm^{-1},broad band of (N-H) due to tutomerism between (O-H) and (C=N) in pyimidine cycle at (3296 cm^{-1}), band of (C=N)endo cyclic shifted to frequency about(1675, 1665)cm^{-1}in these compounds respectively due to the tutomerism which showed previously, (C=C) aromatic (1610, 1600)cm^{-1} in addition to sharp peak at (1166)cm^{-1} due to[$N(CH_3)$]bending in comp. (5).

In pyrimidine derivatives from chalcones with thiourea comp.(7 and 8) showed appearance band of (N-H) in both compounds at about (3292 , 3284)cm^{-1} band of (C=N)end ocyclic shifted to frequency about(1664,1678)cm^{-1}in these compounds respectively, (C=C)aromatic(1604, 1600)cm^{-1} band of marcapto (S-H) at(2688 , 2698cm^{-1}) respectively .in addition to band at(2980cm^{-1})due to (C-H)aliphatic in comp.(7) and band at(3383)cm^{-1}due to stretching of (O-H)in comp.(8). Anal. Calcd/ found for comp.(8):C, 65.085 / 65.002; H, 4.406 / 4.324; N, 14.237 / 14.093.

Pyrimidine derivatives from chalcones with Guanidine comp.(9 and 10) showed appearance two bands of (NH2) in both compounds at about (3294 , 3296)cm^{-1}, single band of (N-H) in both compounds at about (3196 , 3192)cm^{-1}, band of (C=N)endo cyclic shifted to frequency about (1675)cm^{-1}in these compounds, (C=C) aromatic (1600, 1597) cm^{-1}, in addition to band at(3080cm^{1})due to (C-H)aliphatic in comp.(9) and appearance band of (O-H) interaction with band of(NH2)from (3300)cm^{-1} to (3450)cm^{-1} in comp.(10). . Anal Calcd/ found for comp. (10): C,69.064 / 68.918; H, 5.036/ 4.956 ; N, 20.144 / 20.016^{1}HNMR(3000 MKZ, DMSO) δppm:

Comp.(1) ; 10.0 ,(s , 1H, -NH-C=O) , 6.85- 7.60(m, 9H, aromatic) , 3.4(s,6H, $N(CH_3)_2$) , 2.5 (d, 2H, CH=CH=C=O) .

Comp.(3) : 9.5 (s ,1H, -NH-) , 2.1(s , 3H, CH_3-C=O), 6.7-7.5(m , 9H , aromatic) , 3.4,3.5 , (d , 2H , t ,1H) pyrazoline cycle, 3.6 (s, 6H, $N(CH_3)_2$

Comp.(5): 11.2(s , 1H , OH) , 8.95(s , 1H , -NH-) , 6.8-7.6(m , 9H, Phenyl , 1H, pyrimidine, 3.6(s , 6H , $N(CH_3)_2$).

Comp.(7): 12.3 (s , 1H , SH aromatic) , 9.10(s , 1H , -NH-) , 6.80- 7.70(m , 9H, Phenyl , 1H, pyrimidine,3.5(s,6H , $N(CH_3)_2$).

Comp.(9) : 9.10(s , 2H , - NH_2) , 8.85 (s , 1H, -NH-) , 6.9-7.8(m , 9H , Phenyl , 1H, pyrimidine , 3.5(s , 6H, $N(CH_3)_2$).

Table(1) Names of prepared compound

Comp.	Name
1	(*E*)-3-(4-(dimethylamino)phenyl)-N-phenylacrylamide
2	(*E*)-3-(4-hydroxy phenyl)-N-phenyl acrylamide:
3	1-(5-(4-dimethylamino)phenyl)-3-phenyl-4,5-dihydro-1H-pyrazol-1-yl)ethanone
4	1-(5-(-(4-hydroxyphenyl)phenyl)-3-phenyl-4,5-dihydro-1H-pyrazol-1-yl)ethanone
5	[4-(4-(dimethylamino)phenyl)-6-(phenylamino)pyrimidin-2-ol]
6	[4-(4-hydroxyphenyl)-6-(phenylamino)pyrimidin-2-ol]:
7	[4-(4-dimethylamino)phenyl)-6-(phenylamino)pyrimidine-2-thiol]
8	[4-(2-mercapto-6-(phenylamino)pyrimidin-4-yl)phenol]
9	[6-(4-(dimethylamino)phenyl)-N^4-phenylpyrimidine-2,4-diamine]
10	[4-(2-amino-6-(phenylamino)pyrimidin-4-yl)phenol]

Table(2) physical properties from prepared compound

Comp.	M.f	M.Wt	Rf	m.p C□	Yield %,gm	Colour
1	C17 H18 N2 O	266	0.8	300□	67.6 , 1.8	Yellow
2	C15H13N O2	239	0.71	108-110	66.9, 1.6	Light gray
3	C19 H22 N4O	322	0.68	300□	59, 1.9	Brown
4	C17H17N3 O2	295	0.8	159-161	54, 1.6	Earthy color
5	C 18H 18N4 O	306	0.9	105-107	55.5, 1.7	Yellow
6	C 16H13 N3 O2	279	0.65	300□	57.3, 1.6	Earthy color
7	C 18H18 N 4S	322	0.8	150-152	43.5, 1.4	Orange
8	C 16 H 13N3 OS	295	0.43	103-105	51, 1.5	Orange
9	C 18 H 19N5	305	0.94	110-112	69, 2.1	Yellow
10	C 16 H 14N4O	278	0.63	120-122	62.3, 1.9	Brown

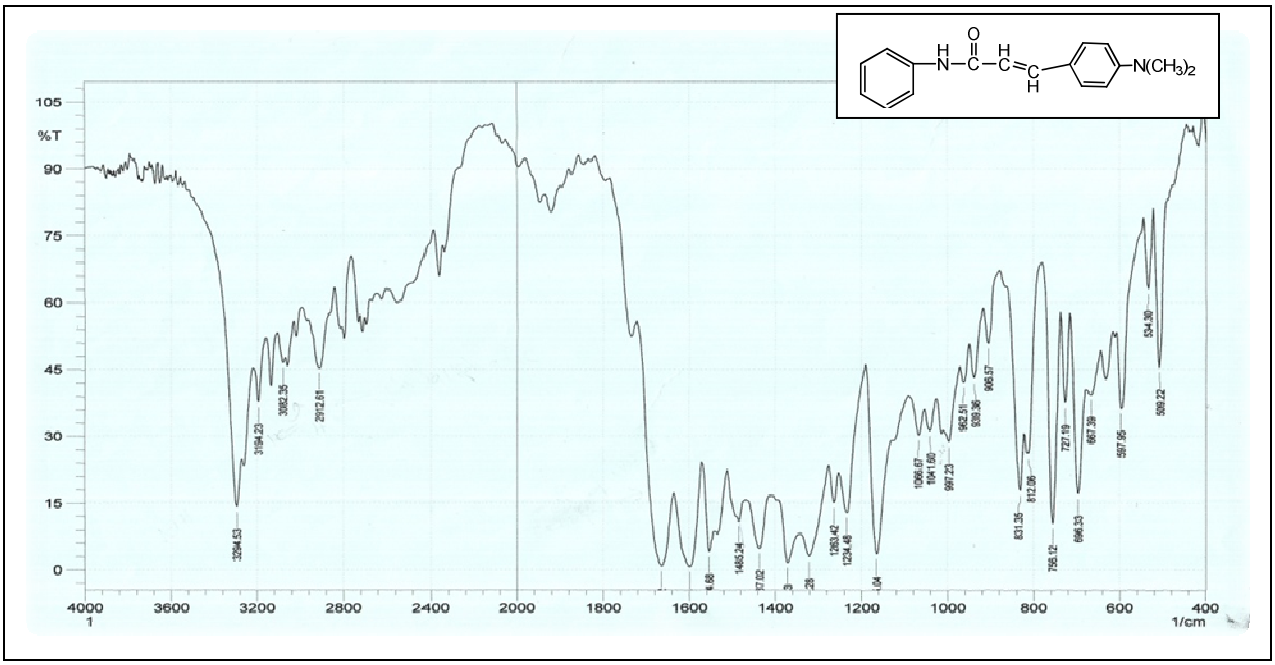


Figure (1) FT-IR spectrum of comp.(1)

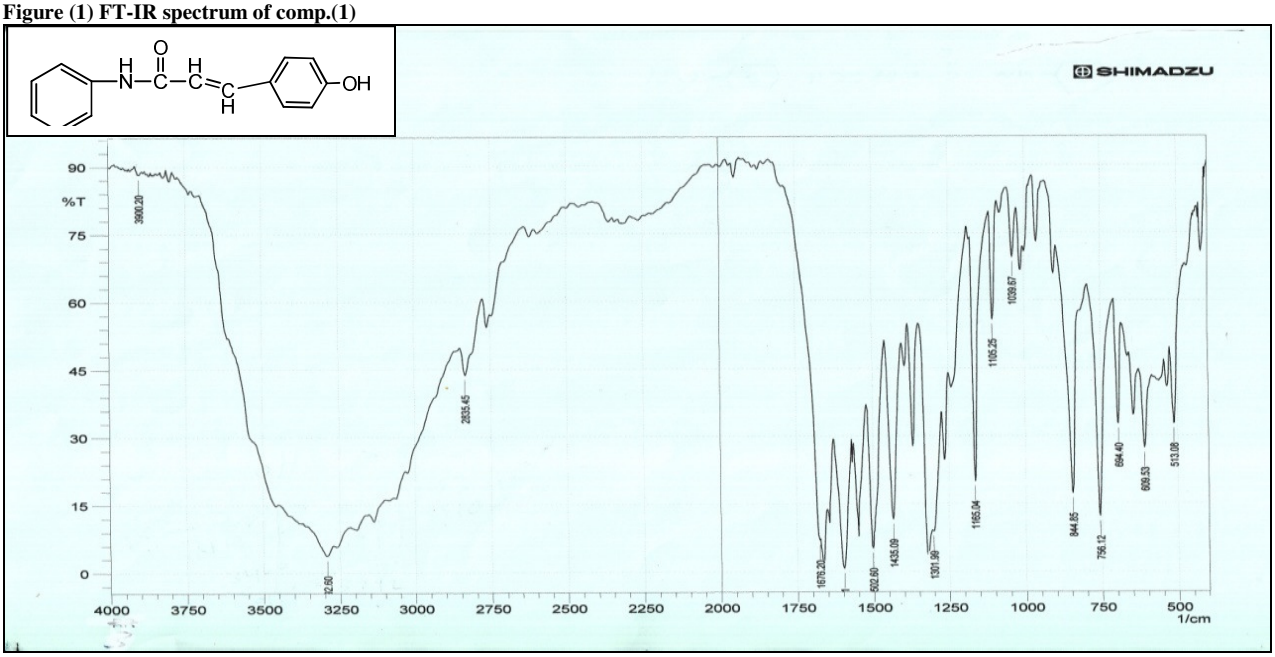


Figure (2) FT-IR spectrum of comp.(2)

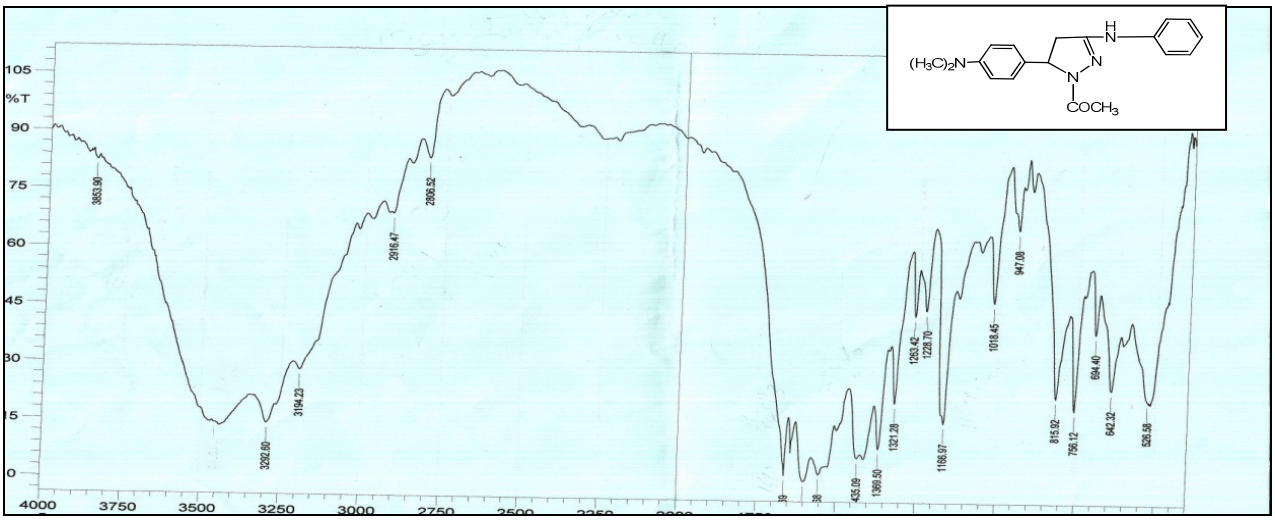


Figure (3) FT-IR spectrum of comp.(3)

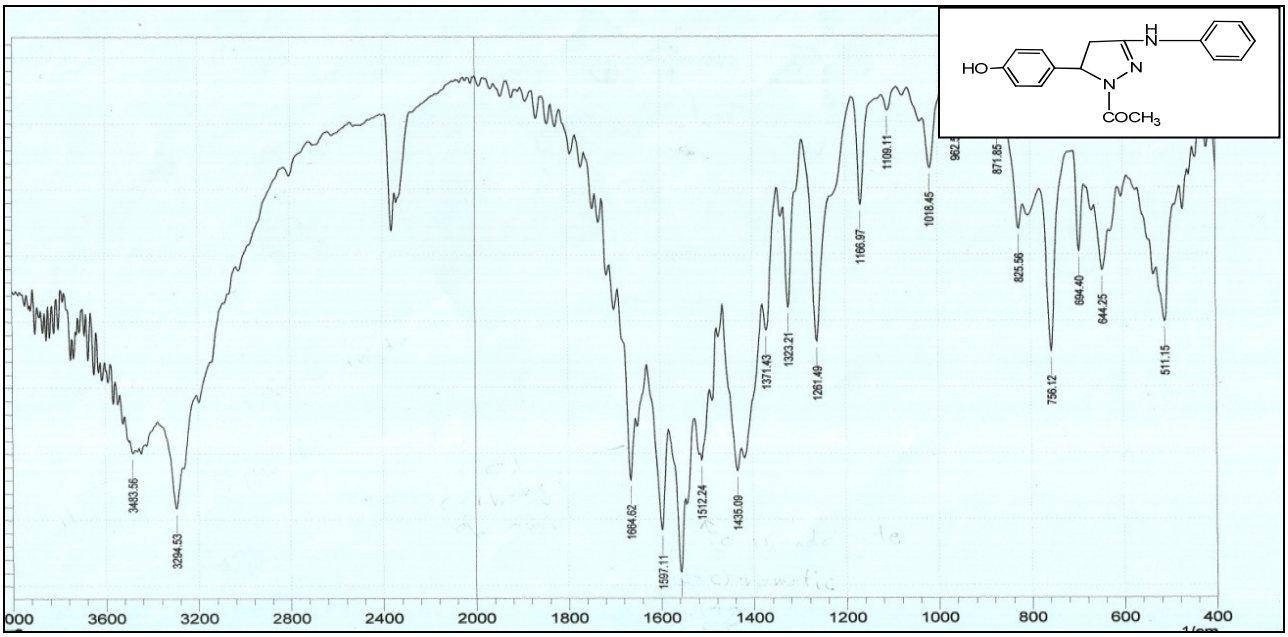


Figure (4) FT-IR spectrum of comp.(4)

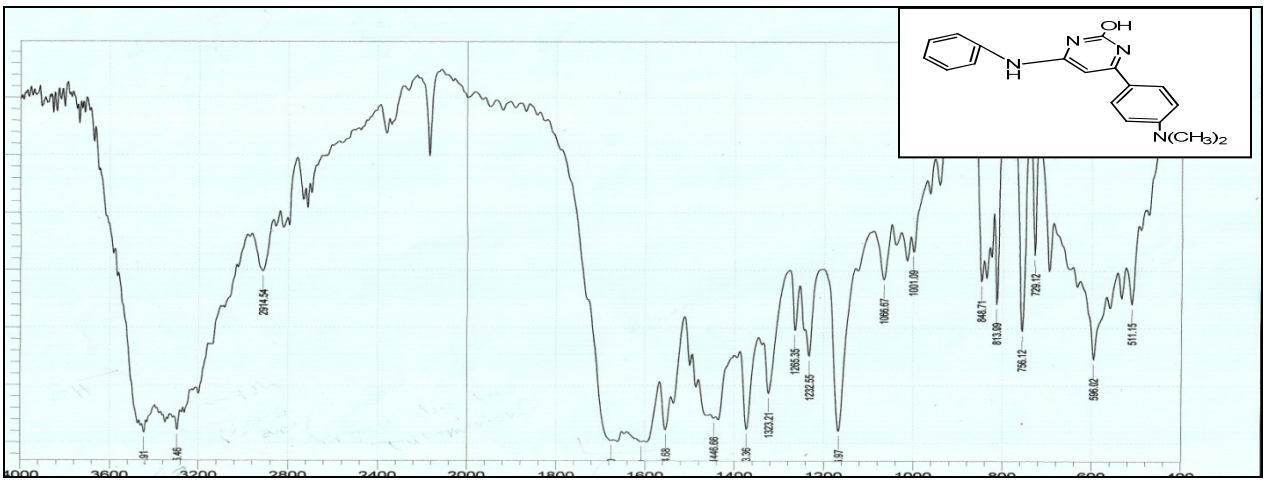


Figure (5) FT-IR spectrum of comp.(5)

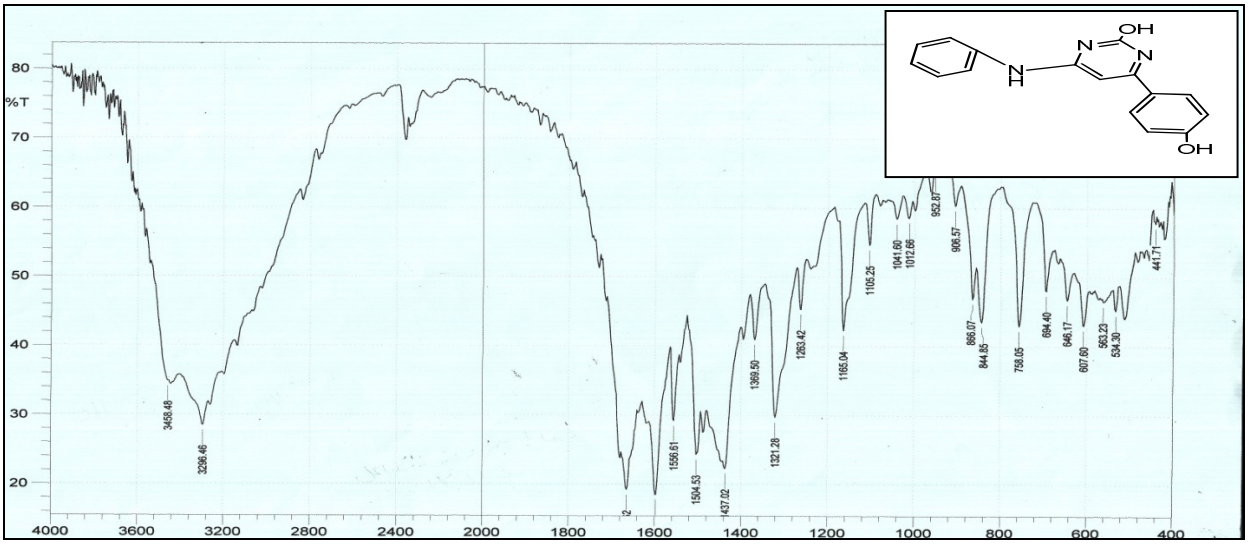


Figure (6) FT-IR spectrum of comp.(6)

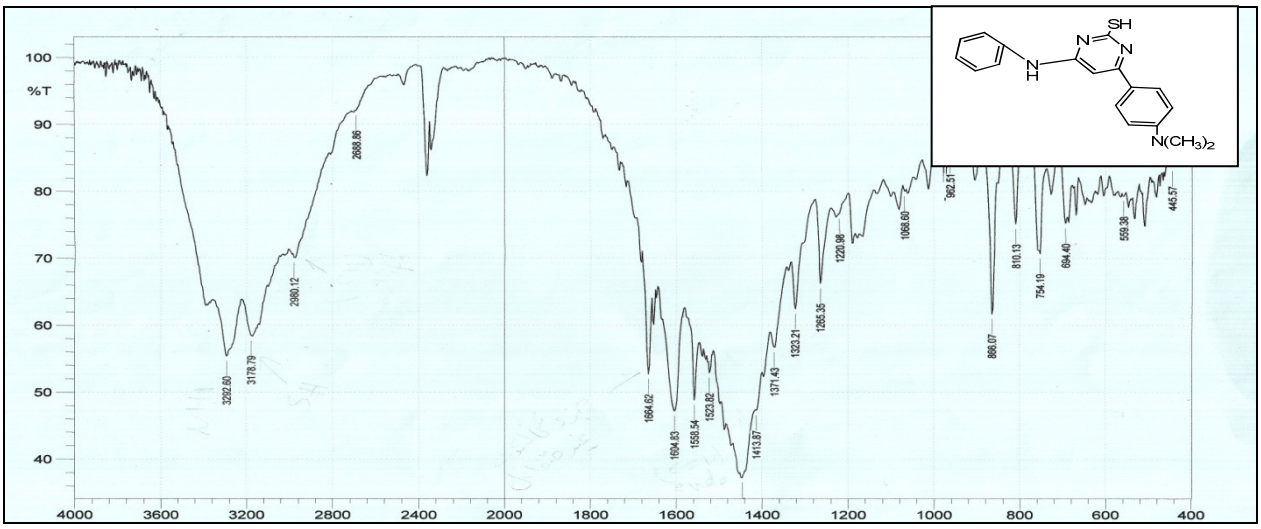


Figure (7) FT-IR spectrum of comp.(7)

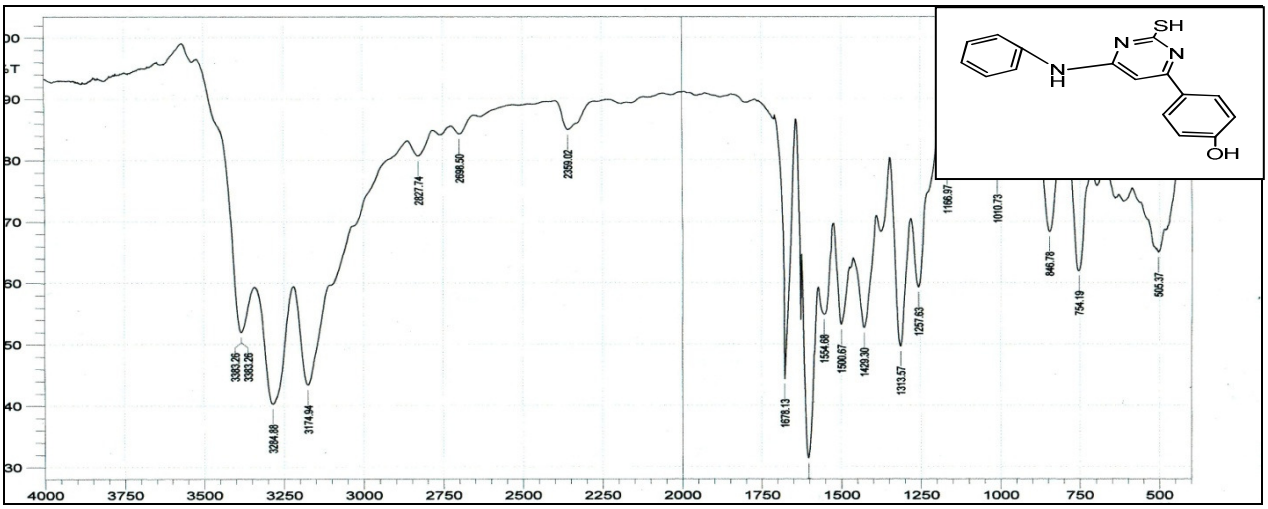


Figure (8) FT-IR spectrum of comp.(8)

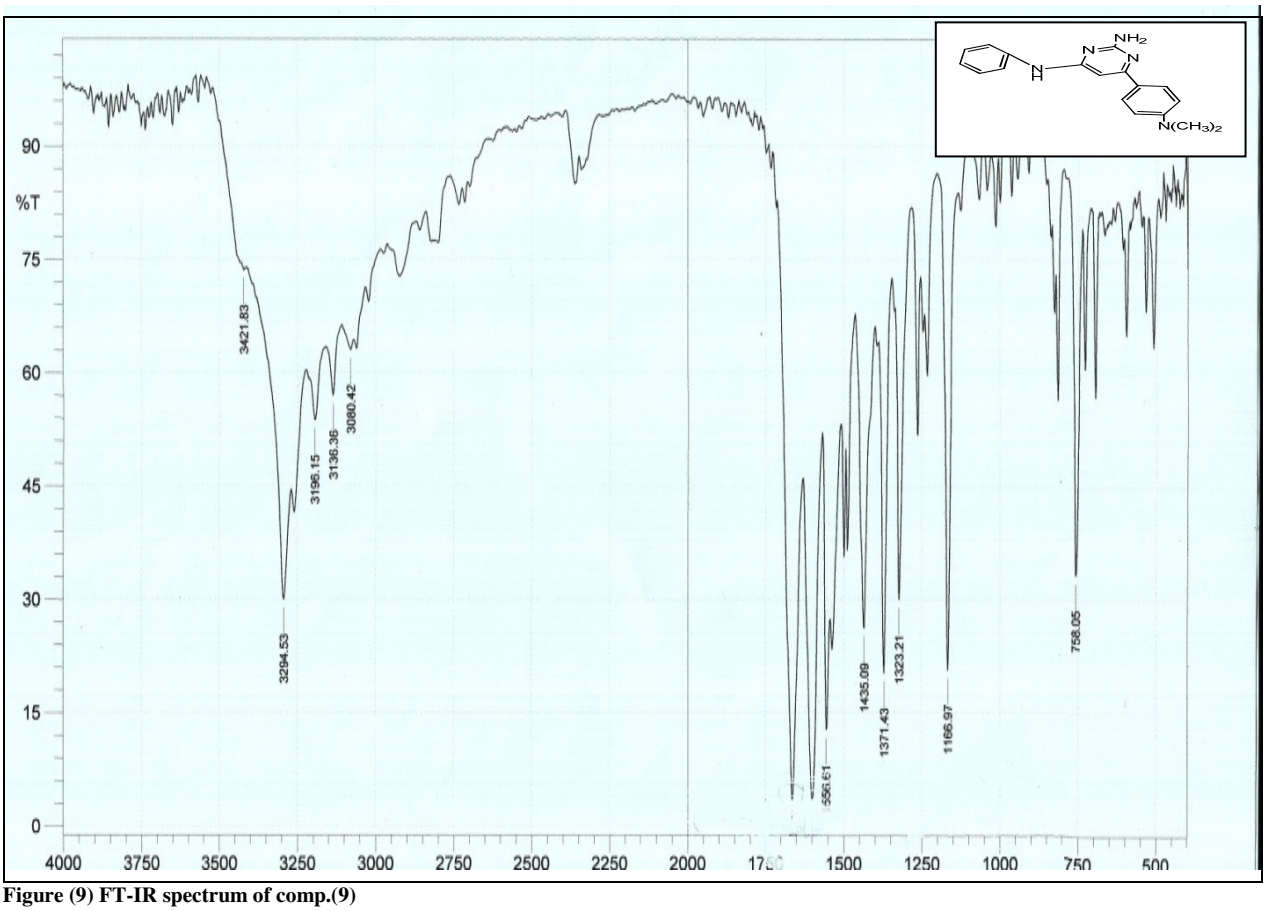


Figure (9) FT-IR spectrum of comp.(9)

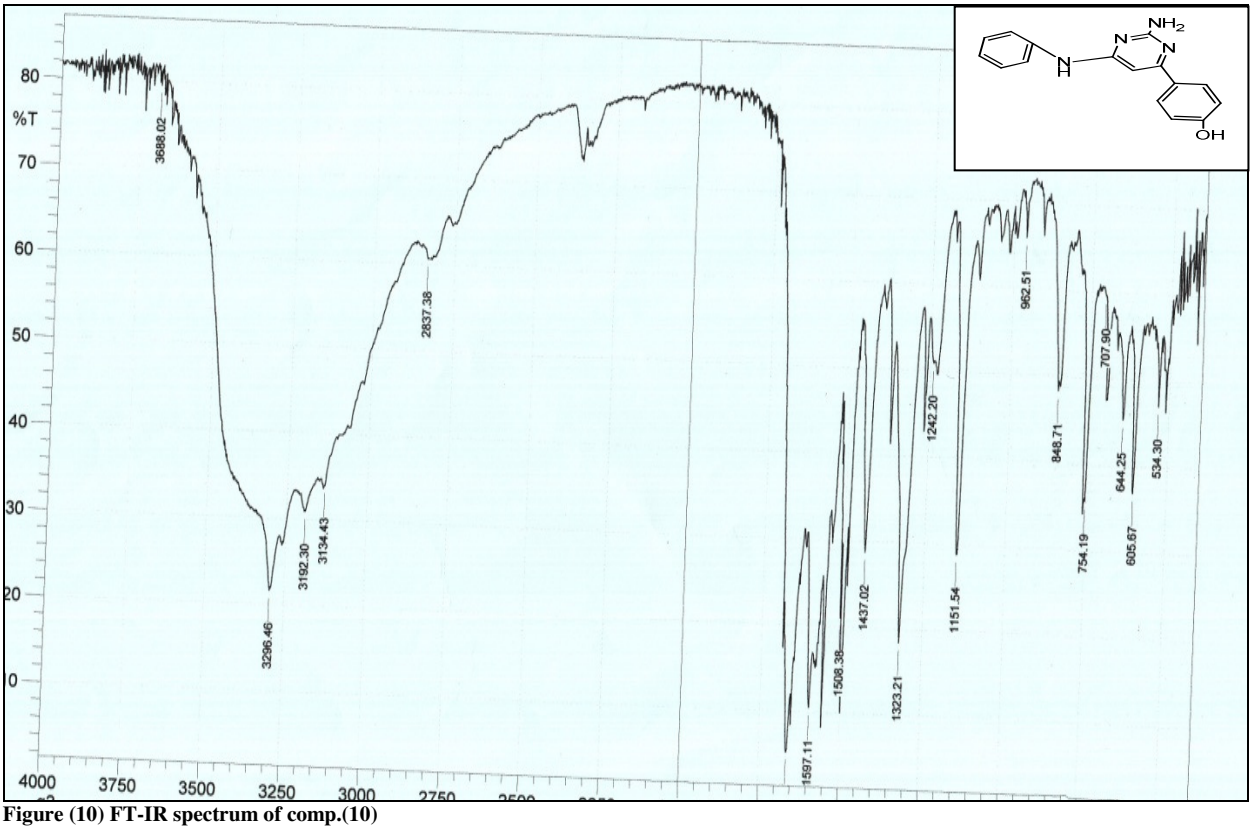
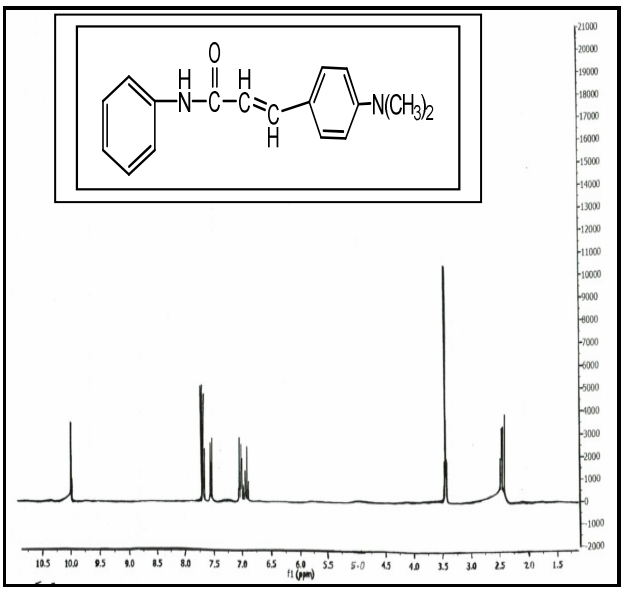


Figure (10) FT-IR spectrum of comp.(10)



Figure(11) H-NMR spectrum of comp.(1)

Figure(12) H-NMR spectrum of comp.(3)

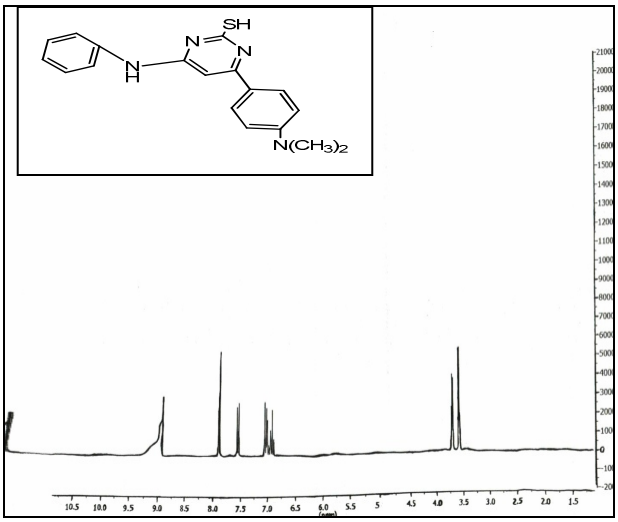


Figure (14) H-NMR spectrum of comp.(7)

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