Preparation and identification of some new compounds chalcone and new derivatives of 1,3- oxazpine

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Abstract

Some novel heterocyclic derivatives such as Thazines, Oxazines, and oxazepine were synthesized from various Chalcones. The synthesized compounds have been characterized by Elemental analysis, FT- IR and 1H.NMR Spectroscopy . Thin Layer Chromatography were used to follow the chemical reaction, the Results proved correctiness of the chemical structures for the prepard derivatives .

Key words: *Chalcones, Thazines, Oxazines and oxazepine*

Introduction

Chalcones are prepared by condensing Aryl ketones with aromatic aldehydes in presence of Suitable condensing agents. They undergo a variety of chemical reactions and are found useful in synthesis of variety of heterocyclic compounds(1,2). Chalcones have been used as intermediate for the preparations of compounds having therapeutic value.

Literature review reveals that chalcone derivatives exhibit diverse pharmacological activities(3)such as potential cytotoxic agents, antimicrobial agents, antiviral, anti-inflammatory, anesthetics, mydriatics etc. Based on the above observation it is worthwhile to prepare newer compounds for their antimicrobial(4) and antiinflammatory activities(5) . The paramount importance of heterocycles in nature product chemistry and pharmacology constantly drive the search for new methods for the construction of heterocyclic .

Oxazepine ring is unsaturated seven- membered heterocycle . 1,3- oxazepine ring containing two hetero atoms are oxygen in position (1) and nitrogen in position (3) in eddition of five carbon atoms(6,7) . Oxazepine derivatives showed biological activities against different types of bacteria(8) , in edition of their uses as inhibitors of some enzymes action(9), some of oxazepine ring derivatives are used in another applied fields(10) .

Material

The necessary chemical materials were purchased from Merck and Fluka :ethanol absolute, 4- amino acetophenone ,urea ,thiourea , 4_ nitro benzaldehyde , methanol , salicyldehyde ,sodium Hydroxide , phthalic anhydride , N,N- (4- amino di methyl benzaldehyde), benzene and iodine **.**

Measurements

Melting points were determined in open capillary tubes and were found uncorrected. IR spectra were recorded on FT-IR spectrometer (Perkin Elmer) using KBr disc method. 1HNMR spectra were recorded on 1H -NMR (Br 1-(4-aminophenyl)-3-(4-nitrophenyl)prop-2-en-1-one 1-(4-aminophenyl)-3-(4-nitrophenyl)prop-2-en-1-one ucker AMX 400 MHz) spectrometer in DMSO . The compounds were analyzed for elemental analysis and the percentage of elements were found to be very near that of the calculated values. Thin layer chromatography (TLC) was performed on silica gel G for(TLC) and Spots were visualized by Iodine vapors. Physical data of the compounds are recorded in Table-1 and the spectral data are recorded in Table-2.

Preparation of chalcones (A,B) :

A:- 1-(4-aminophenyl)-3-(4-nitrophenyl)prop-2-en-1-one

B:- 1-(4-aminophenyl)-3-(2-hydroxyphenyl)prop-2-en-1-one

Equimolar quantities of salicyldehyde/ 4-Nitro benzaldehyde (0.01 mol) and 4- amino acetophenone (0.01 mol) were dissolved in minimum amount of alcohol. Sodium hydroxide solution 3ml(10%) was added slowly and the mixture stirred for 2hr until the entire mixture becomes very cloud then the mixture was poured slowly into 20 ml of water with constant stirring and kept in refrigerator for

24 hours. The precipitate obtained was filtered, washed and recrystallized from ethanol The completion of the reaction was monitored by TLC (methanol : Benzen) (1:4)

Preparation of Oxazine/Thiazine derivatives(A_1, B_1 / A_2,B_2) :

A1:- 4-(4-aminophenyl)-6-(4-nitrophenyl)-6*H*-1,3-oxazin-2-amine

B1:- 2-(2-amino-4-(4-aminophenyl)-6*H*-1,3-oxazin-6-yl)phenol

A2:- 4-(4-aminophenyl)-6-(4-nitrophenyl)-6*H*-1,3-thiazin-2-amine

B2:- 2-(2-amino-4-(4-aminophenyl)-6*H*-1,3-thiazin-6-yl)phenol

A mixture of Chalcone A,B (0.02mol), urea /thiourea (0.02 mol) were dissolved in ethanolic sodium hydroxide (30ml) was stirred about 3-4 hours with a magnetic stirrer. This was then poured into 20 ml of cold water with continuous stirring for an hour and then kept in refrigerator for 24 hours. The precipitate obtained was filtered, washed and recrystallized. The completion the reaction was monitored by TLC (methanol : Benzen) (1:4)

Preparation of Schiff bases derivatives(A3, B3):

A_3:- 1-(4-(4-(dimethylamino)benzalideneamino)phenyl)-3-(4-nitrophenyl)prop-2-en-1-one

B_3:- 1-(4-(4-(dimethylamino)benzylideneamino)phenyl)-3-(4-nitrophenyl)prop-2-en-1-one

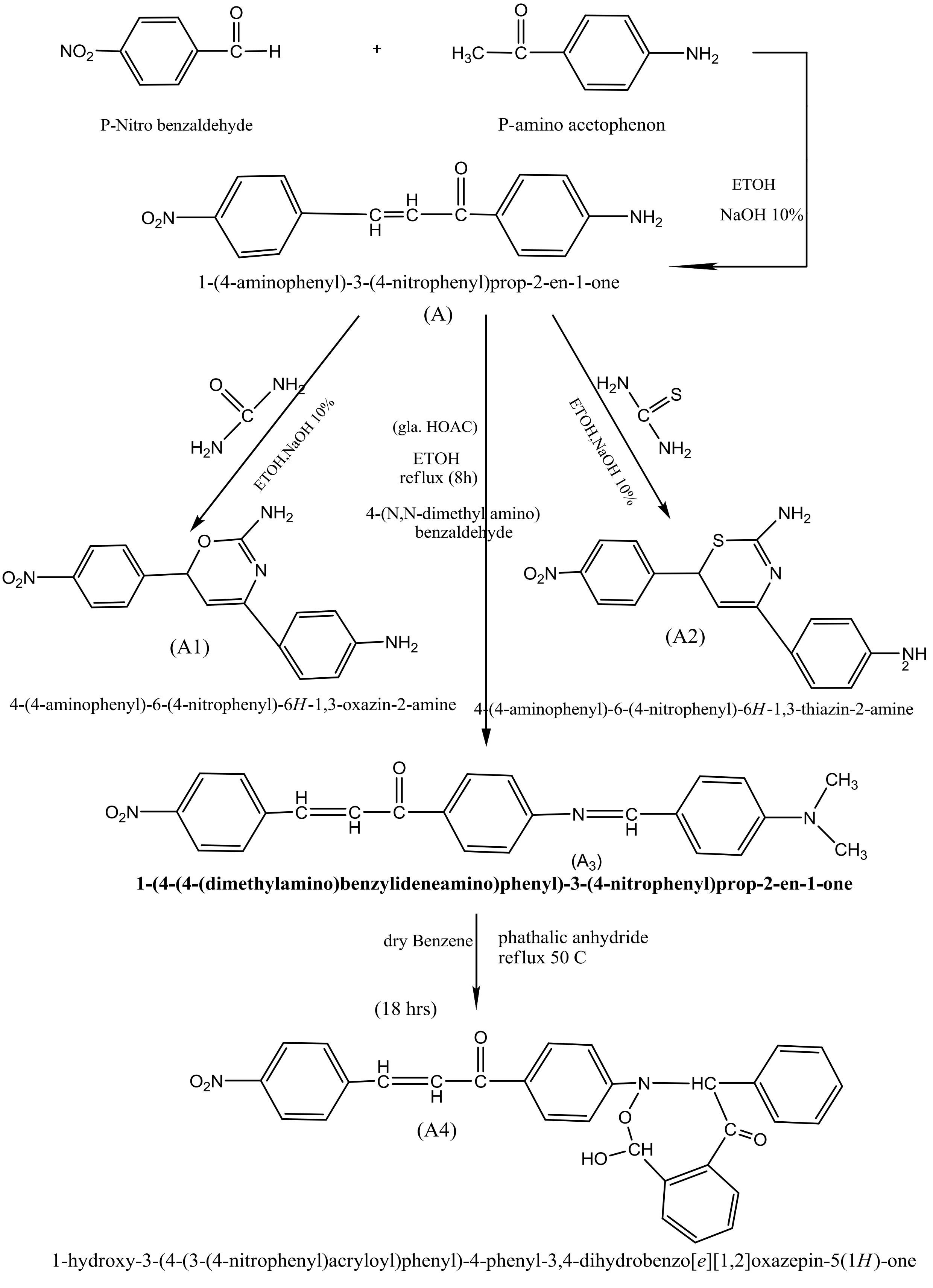
A mixture of Chalcone A,B (0.02 mole) was dissolved in (15 ml) of absolute ethanol containing a drop of glacial acetic , then equimolar amount (o.o2 mole) of N,N-(4- amino benzaldehyde) was dissolved in (15 ml) of absolute ethanol and added dropwise , The reaction mixture was refluxed with stirring on a water bath at (70 C^o) for 5hrs. Then the mixture was allowed to cool to room temperature , The precipitate obtained was filtered, washed and recrystallized. The completion the reaction was monitored by TLC (methanol : Benzen) (1:4)

Preparation of 1,3- oxazepine ring derivatives (A4, B4):

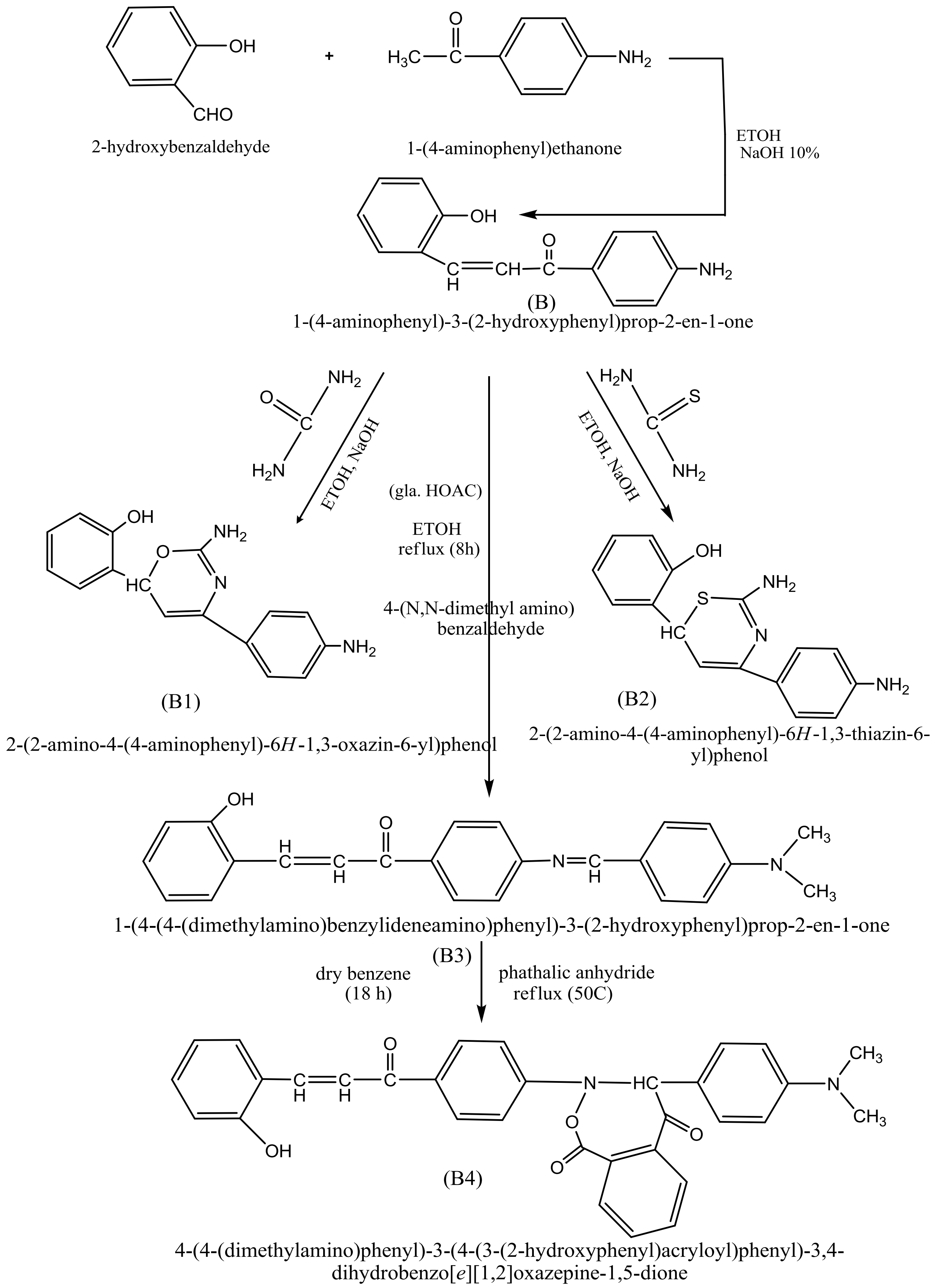
A_4:- 1-hydroxy-3-(4-(3-(4-nitrophenyl)acryloyl)phenyl)-4-phenyl-3,4-dihydrobenzo[*e*][1,2]oxazepin-5(1*H*)-one.

B_4:- 4-(4-(dimethylamino)phenyl)-3-(4-(3-(2-hydroxyphenyl)acryloyl)phenyl)-3,4-dihydrobenzo[*e*][1,2]oxazepine-1,5-dione

A mixture of imine derivatives(A3,B3) 0.001 mole with equimolar amount (0.001 mole) of one of phthalic anhydride in (20 ml) of dry benzene , was refluxed on a water bath at(50 C^o) for 5hrs , Then the mixture was allowed to cool to room temperature , The precipitate obtained was filtered, washed and recrystallized. The completion the reaction was monitored by TLC (methanol : Benzen) (1:4)



Scheme.1: Synthetic path way for preparation of A,A_1, A_2,A_3, A_4 compounds



Scheme. 2: Synthetic path way for preparation of B,B$_1$, B$_2$, B$_3$, B$_4$ compounds

Results and discussion

p- nitrobenzaldehyde was mixed with p- aminoacetophenone in ethanol absolute and sodium hydroxide (10 %) to produce compound A . The structure of the synthesized compound (A) : yield 59% , m.p: 220-222 C^o , the FT-IR spectrum of (A) compound υ(cm^{-1}) showed bands at :

1635 (C= O,ketone), 1589 (C=C, alkene), 1560 (C=C , aromatic), 3483 (_ NH2) , 1502 (_ NO2, bending) ,1340 (_ NO2, streching), The elemental analysis calculated (%) for $C_{15}H_{12}N_2O_3$ (268) : C, 67.16 ; H, 4.47 ; N, 10.44 ; Found : C, 67.05 ; H, 4.33 ; N, 10.21 ; the H^1- NMR spectrum of compound A : (2.68-2.36) δ (d,2H,CH=CH) ; 3.04 δ (S,2H,NH2) ; (7.82-7.10) δ (d,4H,Ar-H) .

Compound (A) was reacted with Urea and Thiourea via cyclization to produce six- membered ring derivatives (A1), (A2) respectively . The structure of the synthesized compound (A1) : yield 68% , m.p. : 208-210 C^o , the FT-IR spectrum of (A1) compound υ(cm^{-1}) showed bands at : 1562 (C=C, aromatic) , 1650 (C= N,endo cyclic) , 3487 (_ NH2) group , 1504 (_ NO2, bending) , 1350 (_ NO2, streching) and disappearance of band of (C=O , ketone) which appeared in 1635 cm^{-1} and the band of (C=C , alkene) which appeared in 1560 cm^{-1} in compound (A) spectrum , The elemental analysis calculated (%) for $C_{16}H_{13}N_4O_3$(309) ; C,62.13 ; H, 4.20 ; N, 18.12 ; Found : C, 62.02 ; H, 4.07 ; N, 18.01 .

The structure of the synthesized compound (A2) : % 60 yield , m.p. : 194- 196 C^o ; the FT-IR spectrum of (A2) compound υ(cm^{-1}) showed bands at : 1610 (C=C, aromatic) , 1645 (C=N, endo cyclic) , 3487 (_ NH2 , group) , 1504 (_NO2, bending) , 1317(_NO2,stretching) and dissappearnace of band of (C=O, ketone) which appeared in 1635 cm^{-1} and the band of (C=C,alkene) which appeared in 1589 cm^{-1} in compound (A) spectrum . ; the H^1- NMR spectrum of compound A2 : (3.33 - 3.24) δ (S,4H,NH2) ; 5.96 δ (S,1H,thiazin ring) ; (6.81-6.34) δ (d,4H,Ar- H)

Compound (A) was refluxed with 4-(N,N- dimethylaminobenzaldehyde) to produce dreviative (A3) , The structure of the synthesized compound (A3) : % 47 yield , m.p. : 138- 140 C^o , the FT-IR spectrum of (A3) compound υ(cm^{-1}) showed bands at : 1660(C=O,ketone), 1600 (C=C, alkene) , 1590 (C=C, aromatic), 1670 (C=N, imine) , 1548(_NO2, bending), 1371(_NO2, stretching) , The elemental analysis calculated (%) for $C_{24}H_{21}N_3O_3$ (469) : C,61.40; H, 4.47; N, 8.95 , Found : C, 61.15 ; H, 4.20 ; N, 8.74

Compound (A3) was refluxed with phthalic anhydride to produce seven- membered ring dreviative (A4) : The structure of the synthesized compound (A4) :% 54 yield ; m.p.:334- 336 C^o The FT-IR spectrum of (A4) compound υ(cm^{-1}) showed bands at : 1690 (C=O, ketone) , 1654 (C=C, alkene) , 1600 (C=C, aromatic) , 1533 (_NO2 , bending) , 1373 (_NO2 , stretching) and disappearance band of (C=N, imine) in compound (A3) spectrum which appeared in 1670 cm^{-1} 2-hydroxy benzaldehyde was mixed with p- amino acetophenone in ethanol absolute and sodium hydroxide (10%) to produce compound (B) The structure of the synthesized compound : yield 62% , m.p. : 211-213 C^{o} , The FT-IR spectrum of (B) compound $\upsilon(cm^{-1})$ showed bands at : 1675(C=O, ketone), 1654 (C=C, alkene) , 1600 (C=C, aromatic), 3334 (O_ H, phenol) , 3396 (_ NH_2 , group) , The elemental analysis calculated (%) for $C_{15}H_{13}NO$ (223) : C,80.71 ; H, 5.82; N, 6.27 ; Found : C, 80.23 ; H , 5.45 ; N , 6.10.

Compound (B) was reacted with Urea and Thiourea via cyclization to produce six- membered ring derivatives (B1), (B2) respectively . The structure of the synthesized compound (B1) :

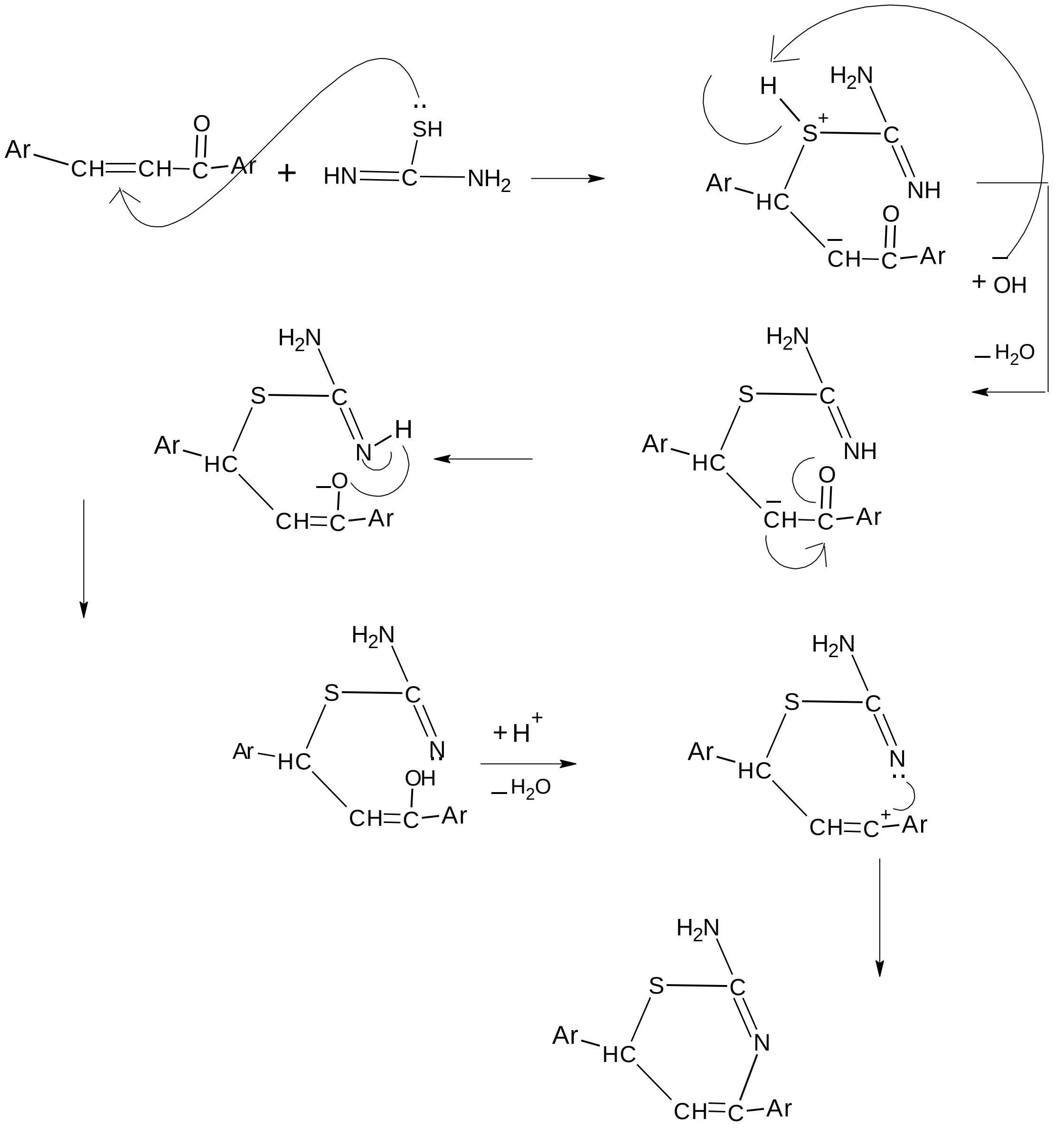
Yield 55% , m.p. : 244-246 C^{o} , The FT-IR spectrum of (B1) compound $\upsilon(cm^{-1})$ showed bands at: 1600 (C=C, aromatic) , 3336 (O_ H, phenol) , 1653 (C=N, endo cyclic) , 3396 (_ NH_2, group) , and disappearance of band of (C=O, ketone) which appeared in 1675 cm^{-1} and the band of (C=C, alkene) which appeared in 1663 cm^{-1} in compound (B) spectrum .

The structure of the synthesized compound (B2) : % 45 yield , m.p. : 228-230 C^{o}, The FT-IR spectrum of (B2) compound $\upsilon(cm^{-1})$ showed bands at : 1590 (C=C, aromatic) , 3334 (O_ H, phenol) , 1641(C=N, endo cyclic) , 3396 (_ NH_2, group) and disappearance of band of (C=O , ketone) which appeared in 1675 cm^{-1} and the band of (C=C, alkene) which appeared in 1663 cm^{-} in compound (B) spectrum . The elemental analysis calculated (%) for $C_{16}H_{14}N_3OS$ (366) : C, 52.45 ; H , 6.01 ; N , 11.47 ; S , 8.74 ; Found : C , 52.13 ; H , 5.85 ; N , 11.15 ; S , 8.23

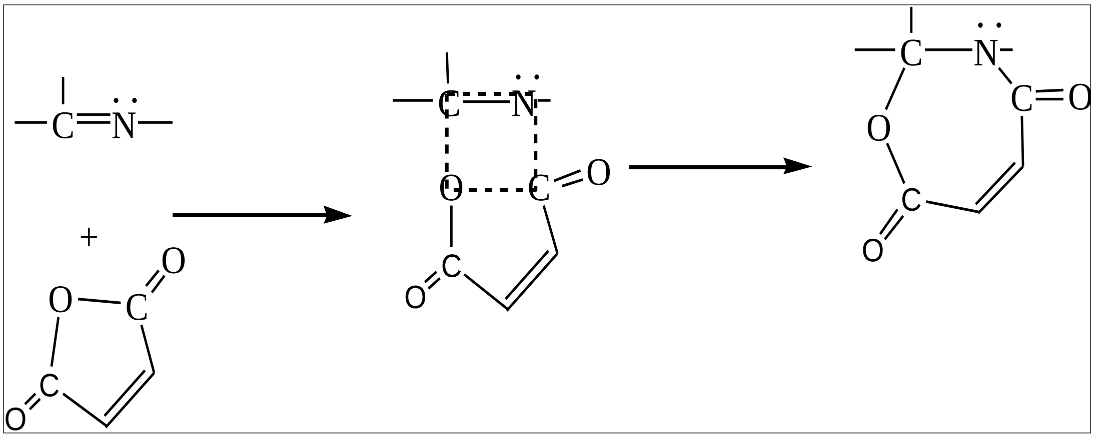
Compound (B) was refluxed with 4-(N,N- dimethylaminobenzaldehyde) to produce dreviative (B3) , The structure of the synthesized compound : % 72 yield ; m.p. : 255-257 C^{o} , The FT-IR spectrum of (B3) compound $\upsilon(cm^{-1})$ showed bands at : 1676 (C=O, ketone) , 1600 (C=C , alkene) , 1552 (C=C , aromatic) , 1653 (C=N , imine) , 3334 (O_ H , phenol) ; the H^1- NMR spectrum of compound B3: (2.38-2.17) δ (d,2H,CH=CH); 3.21 δ (S,6H,$(CH_3)_2$) ; (7.82-6.34) δ (d,4H,Ar-H) ; 8.81 δ (S,1H,imine) ; 11.97 δ (S,1H,OH) .

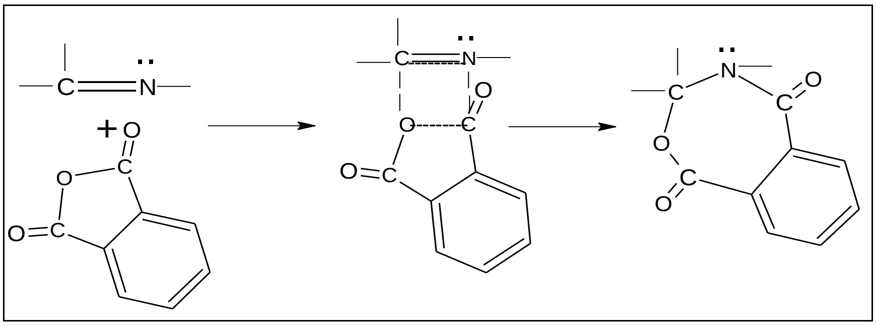
Compound (B3) was refluxed with phathalic anhydride to produce seven- membered ring dreviative (B4) , The structure of the synthesized compound : % 66 yield , m.p. : 212-214 C^{o} , The FT-IR spectrum of (B4) compound $\upsilon(cm^{-1})$ showed bands at : 1690 (C=O , ketone) , 1685 (C=C , alkene) , 1585 (C=C , aromatic) , 3435 (O_ H , phenol) and disappearance peak of (C=N, imine) in compound (B3) spectrum which appeared in 1653 cm^{-1} , The elemental analysis calculated (%) for $C_{33}H_{27}N_2O_5$ (531) : C, 74.57 ; H, 5.08 ; N , 5.27 ; Found : C , 74.35 ; H , 4.78 ; N , 5.02

Suggestion Mechanism of Six – membared



Suggestion Mechanism of Seven - membared





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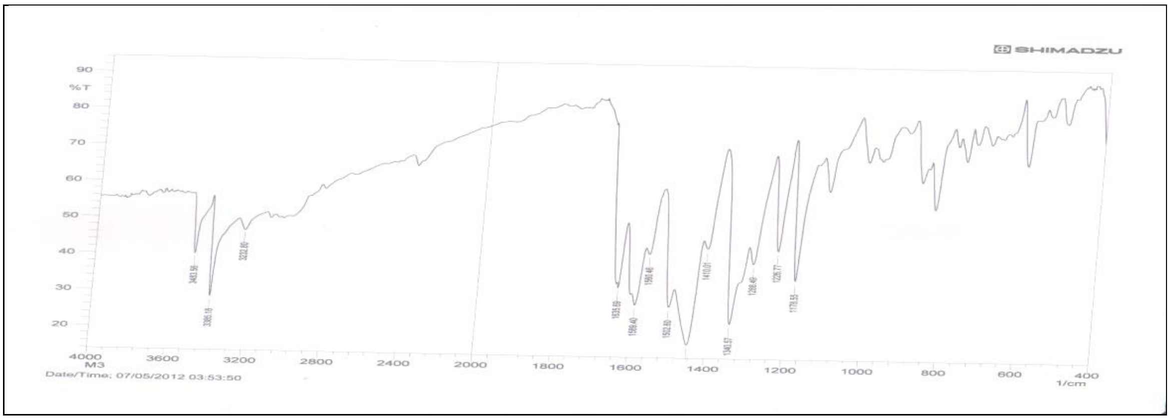
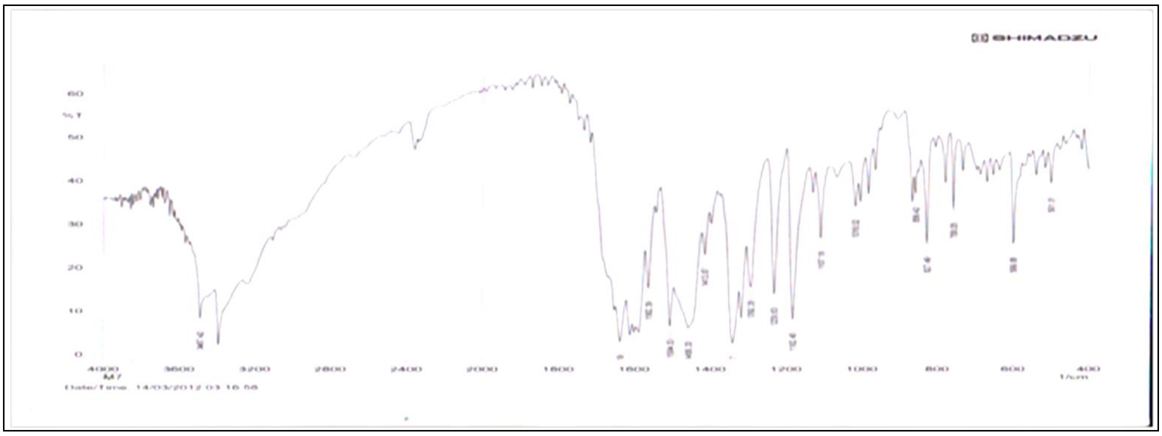
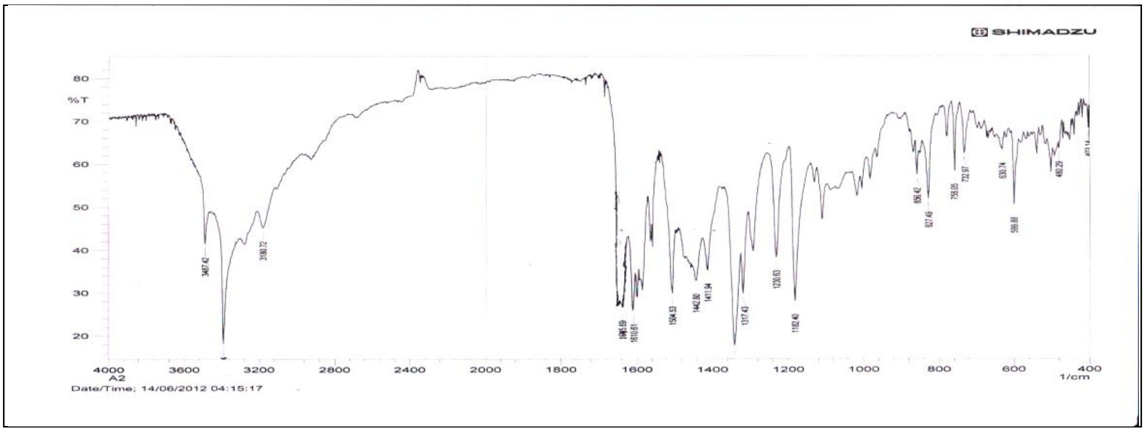


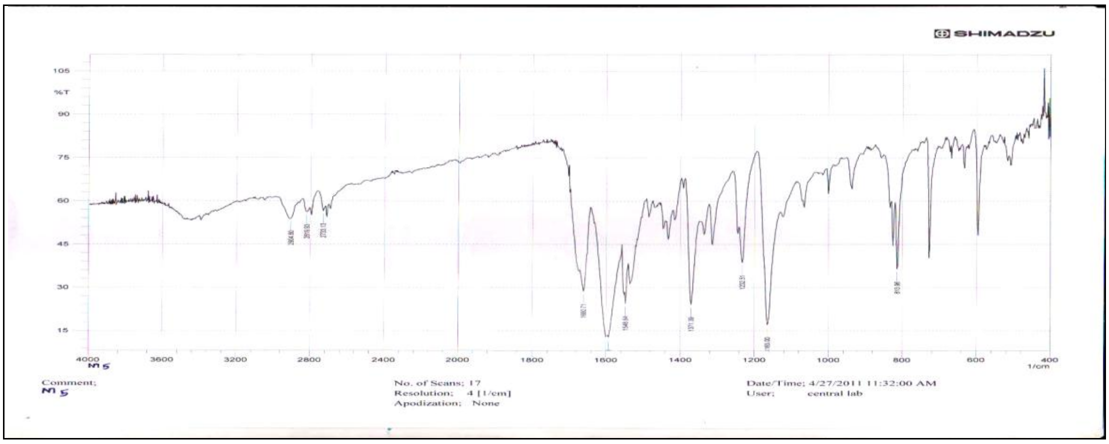
Fig(1): FT-IR Spectra for the compound A(1-(4-aminophenyl)-3-(4-nitrophenyl)prop-2-en-1-one)



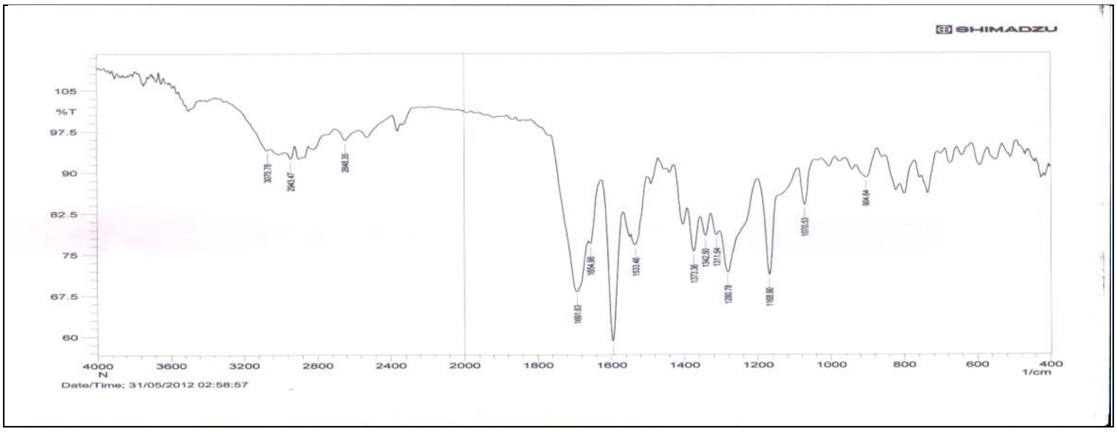
Fig(2): FT-IR Spectra for the compound A1(4-(4-aminophenyl)-6-(4-nitrophenyl)-6*H*-1,3-oxazin-2-amine)



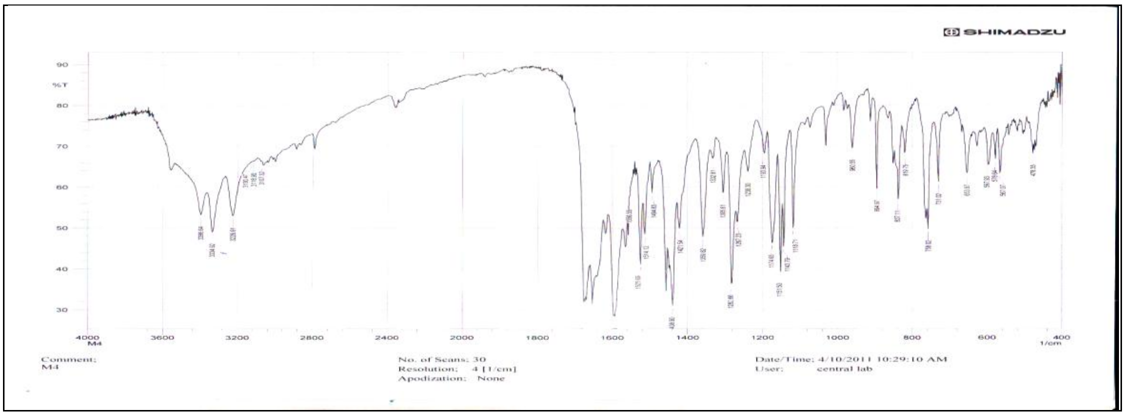
Fig(3): FT-IR Spectra for the compound A2(4-(4-aminophenyl)-6-(4-nitrophenyl)-6*H*-1,3-thiazin-2-amine)



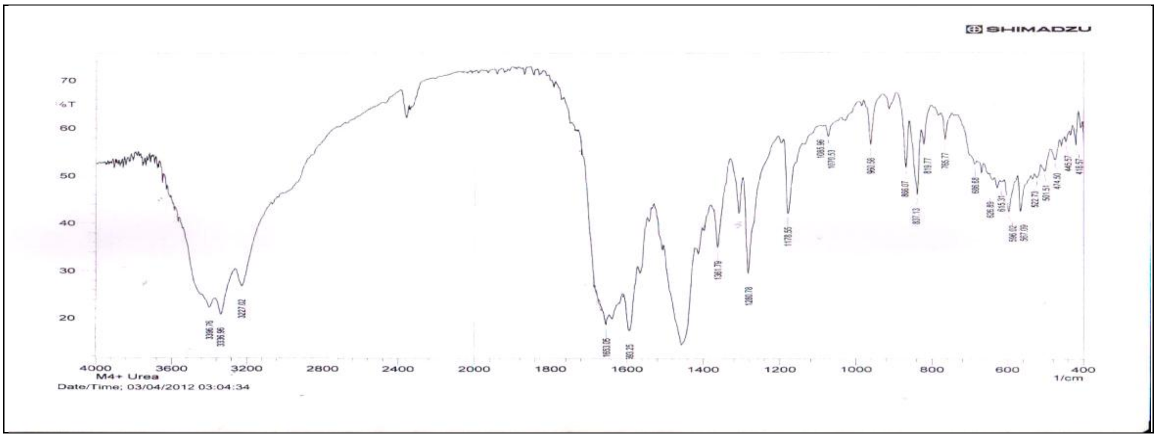
Fig(4): FT-IR Spectra for the compound A3(4-(4-aminophenyl)-6-(4-nitrophenyl)-6*H*-1,3-thiazin-2-amine)



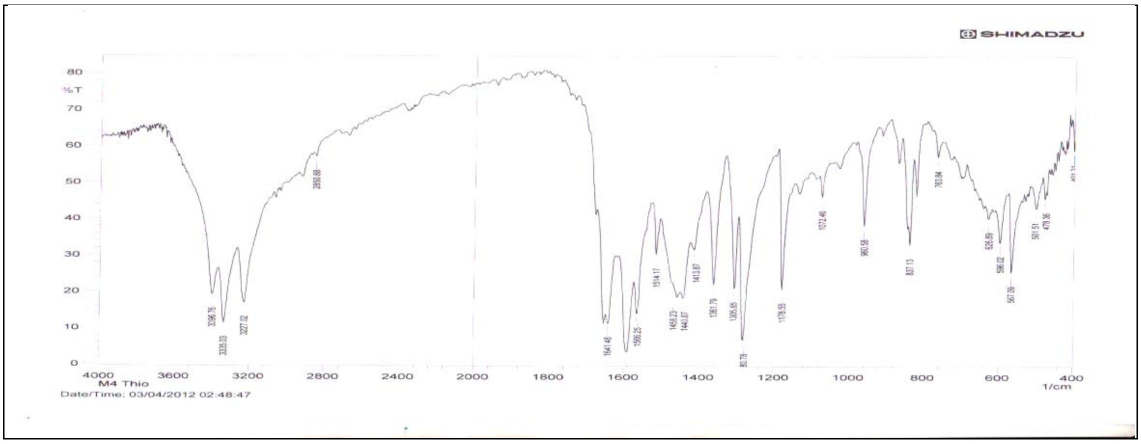
Fig(5): FT-IR Spectra for the compound A4(1-hydroxy-3-(4-(3-(4-nitrophenyl)acryloyl)phenyl)-4-phenyl-3,4-dihydrobenzo[*e*][1,2]oxazepin-5(1*H*)-one)



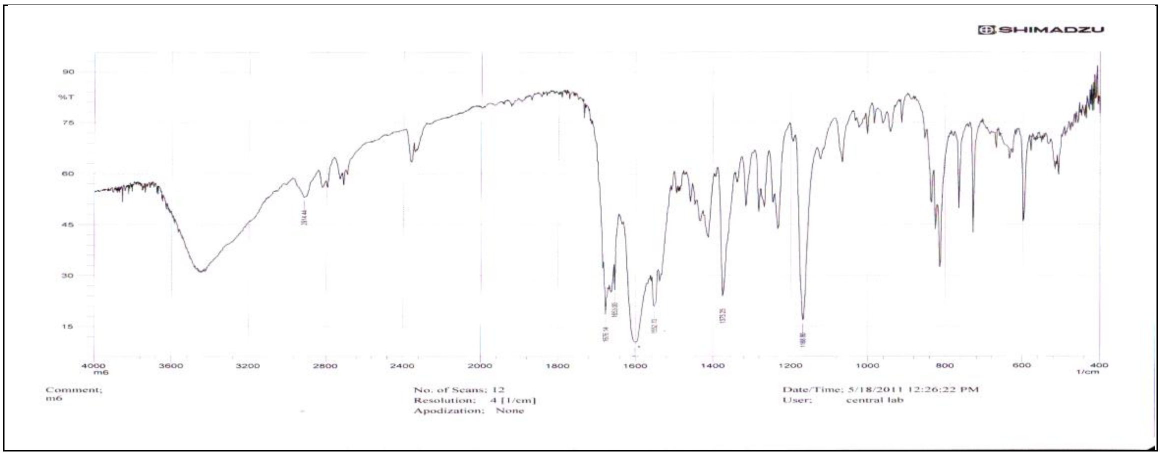
Fig(6): FT-IR Spectra for the compound B(1-(4-aminophenyl)-3-(2-hydroxyphenyl)prop-2-en-1-one)



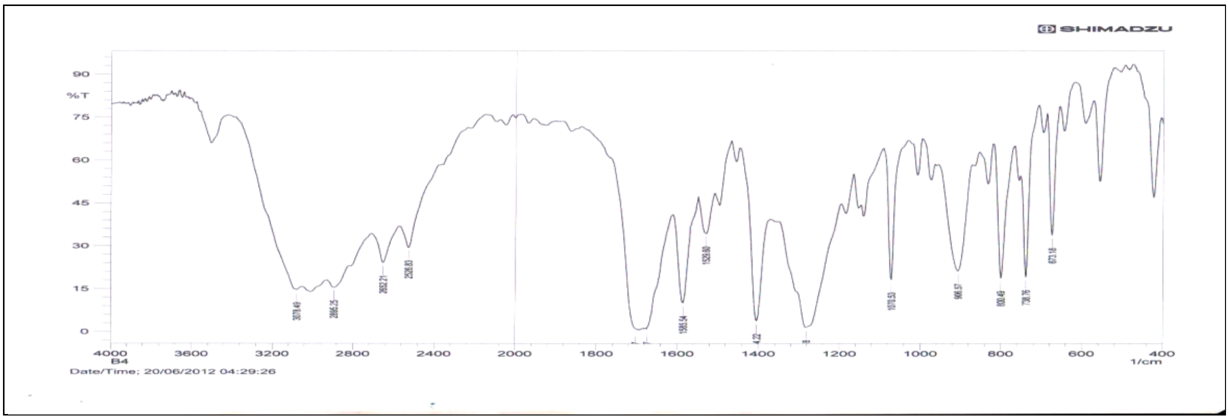
Fig(7): FT-IR Spectra for the compound B1(2-(2-amino-4-(4-aminophenyl)-6*H*-1,3-oxazin-6-yl)phenol)



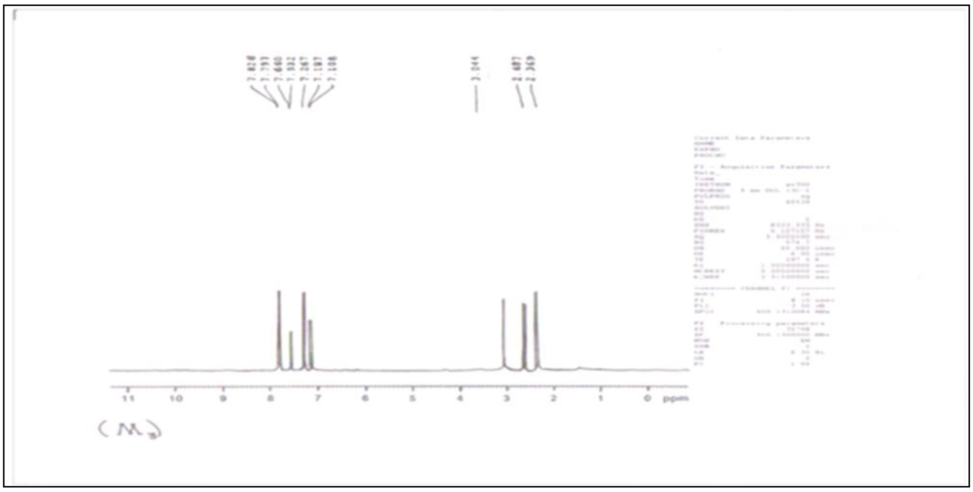
Fig(8): FT-IR Spectra for the compound B2(2-(2-amino-4-(4-aminophenyl)-6*H*-1,3-thiazin-6-yl)phenol)



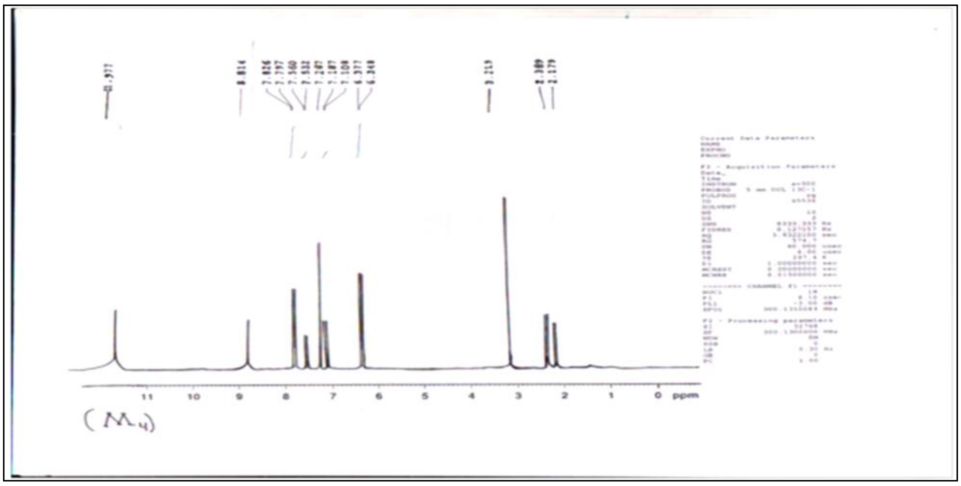
Fig(9): FT-IR Spectra for the compound B3(1-(4-(4-(dimethylamino)benzylideneamino)phenyl)-3-(4-nitrophenyl)prop-2-en-1-one)



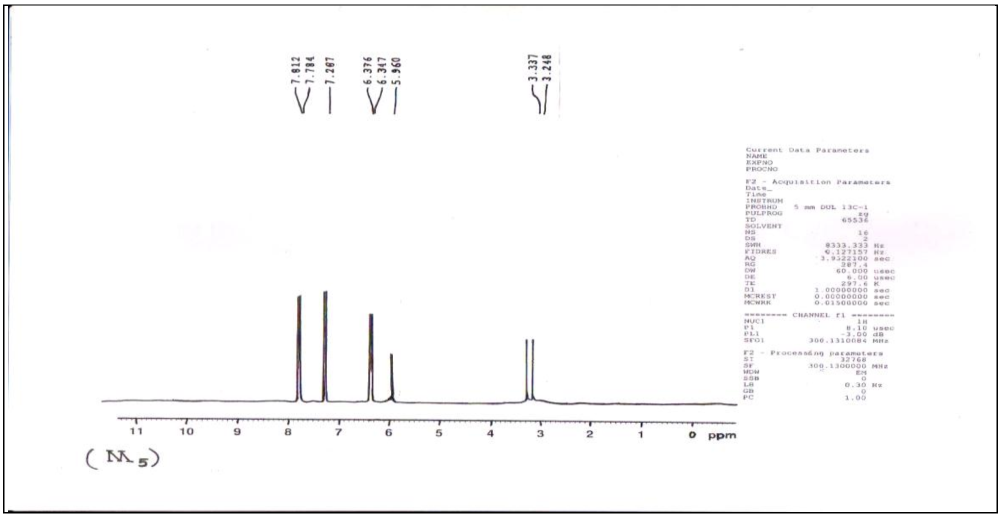
Fig(10): FT-IR Spectra for the compound B4(4-(4-(dimethylamino)phenyl)-3-(4-(3-(2-hydroxyphenyl)acryloyl)phenyl)-3,4-dihydrobenzo[*e*][1,2]oxazepine-1,5-dione)



Fig(11): H-NMR Spectra for the compound A((1-(4-aminophenyl)-3-(4-nitrophenyl)prop-2-en-1-one)



Fig(12): H-NMR Spectra for the compound A2(4-(4-aminophenyl)-6-(4-nitrophenyl)-6*H*-1,3-thiazin-2-amine)



Fig(13): H-NMR Spectra for the compound B3(1-(4-(4-(dimethylamino)benzylideneamino)phenyl)-3-(4-nitrophenyl)prop-2-en-1-one)

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Table (1) : physical and analytical data of compounds

N0. N_0.	M.F	M.W gm/ M	Yield %	m.p: C°	Rf (4:1) Ben : meth	Colour
A	$C_{15}H_{12}N2O3$	268	59	220 – 222	0.81	Dark orange
A1	$C_{16}H_{13}N_4O3$	309	68	208 – 210	0.63	Dark orange
A2	$C_{16}H_{13}N_4SO_2$	325	60	194 – 196	0.56	Light orange
A3	$C_{24}H_{21}N3O3$	469	47	138 – 140	0.67	Light orange
A4	$C_{32}H_{26}N_3O6$	548	54	334 – 336	0.84	Light orange
B	$C_{15}H_{13}NO$	223	62	211 – 213	0.75	Dark grey
B1	$C_{16}H_{14}N_3O2$	350	55	244 – 246	0.47	Dark grey
B2	$C_{16}H_{14}N_3O S$	366	45	228 – 230	0.60	Dark grey
B3	$C_{24}H_{22}N2O2$	370	72	255 – 257	0.52	Light grey
B4	$C_{33}H_{27}N2O5$	531	66	312 – 314	0.83	Light grey

Table (2) : the FT- IR spectral data of the prepared compounds (υ cm^{-1})

N0.	Ketone υ C=O	Alkene υ C=C	Aromatic υ C=C	Imine υ C=N	Phenol O – H	Cyclic υ C=N	Amine - NH_2	-- NO2	-- NO2
A	1635	1589	1560	___	___	____	3483	1502	1340
A1	____	____	1562	____	____	1650	3487	1504	1350
A2	___	___	1610	____	____	1645	3487	1504	1317
A3	1660	1600	1590	1670	____	____	____	1548	1371
A4	1690	1654	1600	____	___	___	___	1533	1373
B	1675	1668	1600	___	3334	___	3396	___	___
B1	___	___	1600	___	3336	1653	3396	___	___
B2	___	___	1590		3335	1641	3396	___	___
B3	1676	1600	1552	1653	3334	___	___	___	___
B4	1690	1685	1585	____	3435	____	___	___	___

Table (3) : Elemental analysis of compounds (A,A1,A3,B,B2,B4)

N_0.	M.F		% C	% H	% N	% S
A	$C_{15}H_{12}N2O3$	Calculi.	67.16	4.47	10.44	___
		Found	67.05	4.33	10.21	____
A_1	$C_{16}H_{13}N_4O3$		62.13	4.20	18.12	___
			62.02	4.07	18.01	___
A_3	$C_{24}H_{21}N3O3$		61.40	4.47	8.95	___
			61.15	4.20	8.74	-----
B	$C_{15}H_{13}NO$		80.71	5.82	6.27	___
			80.23	5.45	6.10	____
B_2	$C_{16}H_{14}N_3O S$		52.45	6.01	11.47	8.74
			52.13	5.85	11.15	8.23
B_4	$C_{33}H_{27}N2O5$		74.57	5.08	5.27	___
			74.35	4.78	5.02	___

تحضير وتشخيص مركبات الجالكون وبعض مشتقات ٣,١-الاوكسازبين الجديدة

نادية صادق مجيد

قسم الكيمياء/ كلية التربية للبنات / جامعة الكوفة

الخلاصة

يتضمن هذا البحث تخليق مشتقات جديدة لمركبات حلقية غير متجانسة مثل الثايازين والأوكسازين والأوكسازبين من مركبات الجالكون المتنوعة ، تم متابعة سير التفاعلات الكيميائية بواسطة تقنية كروماتوغرافيا الطبقة الرقيقة وتشخيص المركبات المحضرة بتقنية الأشعة تحت الحمراء والتحليل الدقيق للعناصر والرنين النووي المغناطيسي وقد أثبتت النتائج صحة التراكيب الكيميائية للمركبات المحضرة .