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A facile and efficient synthesis of new Heterocyclic Compounds derived from Bis-chalcones of 3-acetylcumarine

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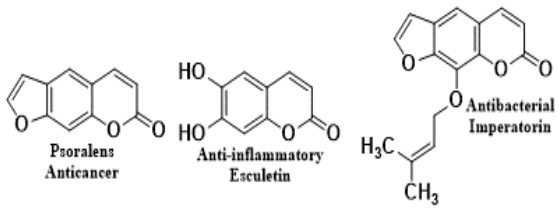
Abstract

The present work involves the new bis-chalcones of 3-acetylcoumarin are synthesized by reaction with (terephthaldehyde and isophthalaldehyde) followed by condensation of these chalcones with some compounds (hydroxylamine, aminophenol, phenylenediamine, hydrazine, semicarbazide, thiosemicarbazide, urea, thiourea and quanidine) as precursor to form Isoxazole, oxazepane, diazepine, pyrazoles and pyrimidine derivatives (1-3k) in basic medium using classical and ultrasonic technique. The comparison of the classical methods with ultrasonic methods was achieved. The structures of synthesized compounds were confirmed by FT-IR and 1H NMR spectroscopy

Keywords: Pyrazoles, Isoxazoles, Chalcones, 3-Acetylcoumarin, ultrasonic technique.

1. Introduction

Coumarin and its derivatives represent one of the most active classes of compounds possessing a wide spectrum of biological activity. A review article dealing with the varied physiological activities of coumarin derivatives have been published describing their anticoagulant properties [1], antimicrobial [2], analgesic [3], antibacterial [4], antifungal [5], anti-inflammatory [6], and antitumor activities [7]. Chalcones are considered as flavonoid compounds which have therapeutic effects in a range of biological activities as anti-cancer, anti-oxidant, and anti-inflammatory [8]. Pyrazole, isoxazole and pyrimidines are also interesting classes of heterocyclic compounds because of their application in pharmaceutical and biological fields including; antifungal [9], antiviral [10], anti-inflammatory [11], anticancer [12], analgesic [13], antibacterial [14], and antipyretic [15], In this presentation, a series of new five and six heterocyclic membered ring compounds, pyrazoles, isoxazoles and pyrimidine compounds were prepared from bis-chalcone derived from 3-acetylcoumarin and (terephthaldehyde and isophthalaldehyde), they reacted with ammonia derivatives. Green chemistry has been employed as a new approach in the field of organic chemistry that requires chemical synthesis that results in less waste, less energy, and more safety for workers and the environment [16-17]. Ultrasonic irradiation of liquids locally leads to rapid changes of pressure. When the liquid is locally subjected to depression, the pressure becomes lower than the vapor pressure of the sonicated liquid, thus generating a cavitation bubble composed of gas and vapors of liquid. Once formed, these cavitation bubbles absorb energy from the sound waves, grow and then collapse, locally resulting in the formation of shock waves, high speed jets or radicals.[18] The effect of the cavitation bubble collapse on a liquid is depending on the applied frequency [19].



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2. Experimental

Melting points were measured on Electrothermal Gallen Kamp melting points and were uncorrected. Infrared (FT.IR.) spectra was recorded as (KBr) disk using a Brucker FT.IR. spectrophotometer. 1HNMR spectra was recorded using Inova 500 MHz by using DMSO – d6 as solvent, and using TMS as internal standard in University of Khashan, Iran.

Preparation of 3-Acetyl Coumarin (1) [1]

A mixture of Salicylaldehyde (0.01 moles, 1.22gm) ethylacetoacetate (0.01moles, 1.30gm) dissolved in ethanol (15ml) and piperidine (0.732ml) was stirred at room temperature for 25 min. The mixture was filtered and the precipitated product was recrystallized from ethanol. to give a light-yellow precipitate, melting point (120-122°C) with a yield of 90% as fixed in table (1).

Preparation of 3,3`-(1,4-phenylene) bis(acryloyl)bisCoumarin) (2), and 3,3`-(1,3-phenylene) bis(acryloyl)bis Coumarin) (3) [20]

A mixture of 3-Acetyl Coumarin (0.002 moles, 0.367gm) dissolved in ethanol (25mL), (0.73ml) piperidine and (0.001 moles, 0.134gm) aldehyde (Terephthaldehyde, isophthalaldehyde). The reaction mixture refluxed for (6 hrs.), cooled and poured into crushed- ice water, the solid product was filtered then dried and recrystallized from hot methanol. Table (1) shows the physical properties of the compound.

Preparation of 3,3`-(1,4-phenylenebis(4,5-dihydroisoxazole-5,3-diyl))bis(2H-chromen-2-one) (2a) and 3,3`-(1,3-phenylenebis(4,5-dihydroisoxazole-5,3-diyl))bis(2H-chromen-2-one) (3a) [21]

To a mixture of the bis-chalcone (2,3) (0.001 moles, 0.474gm), dissolved in (10 mL) of DMF, and (0.002moles, 0.139gm) hydroxylamine hydrochloride dissolved in DMF (10 mL), 10mL of (10 % NaOH) were added dropwise. The reaction mixture was refluxed for (8 hrs.). the mixture was then poured into ice-cold water, the product filtrate and was recrystallized from (DMF/EtOH), Table (1) shows the physical properties of the compound.

Preparation of 3,3`-(1,4-phenylenebis(2,3-dihydrobenzo[b][1,4]oxazepine-2,4-diyl)bis Coumarin (2b) and 3,3`-(1,3-phenylenebis(2,3-dihydrobenzo[b][1,4]oxazepine-2,4-diyl)bis Coumarin (3b) [20]

A mixture of the bis-chalcone (2,3) (0.001 moles, 0.474gm) and (0.002moles, .0218 gm) 2-aminophenol dissolved in DMF (25 mL) and few drops of glacial acetic acid. The mixture was refluxed for (10 hrs.). The mixture was then poured into crushed-ice to give the solid product, filtered, recrystallized from (ethanol/water), Table (1) shows the physical properties of the compound.

Preparation of 3,3`-(1,4-phenylenebis(2,3-dihydrobenzo[b][1,4]diazepine-2,4-diyl)bis Coumarin (2c) and 3,3`-(1,3-phenylenebis(2,3-dihydrobenzo[b][1,4]diazepine-2,4-diyl)bis Coumarin (3c)[19]

A mixture of the bis-chalcone (2,3) (0.001 moles, 0.474gm) and (0.002moles, .0216 gm) ortho phenylenediamine dissolved in DMF (25 mL) and few drops of glacial acetic acid was added. the reaction mixture was refluxed for (10 hrs.). then poured into an ice-cold water, filtered and recrystallized from (ethanol/water), Table (1) shows the physical properties of the compound.

Preparation of 3,3`- (1,4-phenylenebis(4,5-dihydro-1H-pyrazole-5,3-diyl) bis Coumarin (2d) and 3,3`-(1,3-phenylenebis(4,5-dihydro-1H-pyrazole-5,3-diyl) bis Coumarin (3d) [22]

A mixture of the bis-chalcone (2,3) (0.001 moles, 0.474gm) in DMF (25mL), (0.004moles) hydrazine hydrate (80%). the reaction mixture was refluxed for (12 hrs.). Then cooled and poured into ice water, the solid product was filtered, dried and recrystallized from (DMF/EtOH), Table (1) shows the physical properties of the compound.

Preparation of 3,3` (1,4-phenylenebis(1-phenyl-4,5-dihydro-1H-pyrazole-5,3-diyl) bis Coumarin (2e) and 3,3`(1,3-phenylenebis(1-phenyl-4,5-dihydro-1H-pyrazole-5,3-diyl) bis Coumarin (3e) [23]

A mixture of the bis-chalcone (2,3) (0.001 moles, 0.474gm) in DMF (25mL), (0.002moles, 0.216gm) phenyl hydrazine hydrate. the reaction mixture was refluxed for (12 hrs.). Then cooled and poured into ice water, the solid product was filtered, dried and recrystallized from DMSO, Table (1) shows the physical properties of the compound.

Preparation of 3,3'-(1,4-phenylenebis(1-acetyl-4,5-dihydro-1H-pyrazole-5,3-diyl) bis Coumarin (2f) and 3,3'-(1,3-phenylenebis(1-acetyl-4,5-dihydro-1H-pyrazole-5,3-diyl) bis Coumarin (3f) [20]

A mixture of the bis-chalcone (2,3) (0.001 moles, 0.474gm) in glacial acetic acid (25mL), (0.004moles) hydrazine hydrate (80%). The reaction mixture was refluxed for (12 hrs.). The cooled and poured into ice water, the solid product was filtered then dried and recrystallized from DMSO, Table (1) shows the physical properties of the compound.

Preparation of 5,5`-(1,4-phenylene)bis(3-( Coumarin3-yl)-4,5-dihydro-1H-pyrazole-1-carboxamide) (2g) and 5,5`- (1,3-phenylene) bis (3-

(Coumarin3-yl)-4,5-dihydro-1H-pyrazole-1-carboxamide) (2g) [24]

A mixture of the bis-chalcone (2,3) (0.001 moles, 0.474gm) in (10 mL) DMF, and (0.002moles, 0.182gm) semicarbazide dissolved in DMF (10 mL), 10 mL of 10 % KOH were added drop wise. The contents were reflux temperature for 9 hrs. The reaction mixture was then poured into ice cold-water, to give the solid product, filtered then recrystallized from (ethanol/water), Table (1) shows the physical properties of the compound.

P**reparation of 5,5`-(1,4-phenylene) bis(coumarin-3-yl)-4,5-dihydro-1H-pyrazole-1-carbothioamide) (2h) and 5,5`-(1,3-phenylene) bis(coumarin-3-yl)-4,5-dihydro-1H-pyrazole-1-carbothioamide) (3h) [17]**

A mixture of the bis-chalcone (2,3) (0.001 moles, 0.474gm) in (10 mL) DMF, and (0.002moesl, 0.182gm) thiosemicarbazide dissolved in DMF (10 mL), 10 mL of (10 % KOH) were added dropwise. The contents were reflux temperature for 9 hrs. The reaction mixture was then poured into crushed- ice, to obtained the solid product, recrystallized from (ethanol/water), Table (1) shows the physical properties of the compound.

Preparation of 6,6`-(1,4-phenylene)bis(4-( Coumarin-3-yl)pyrimidin-2(1H)-one) (2i) and 6,6`-(1,3-phenylene)bis(4-(Coumarin-3-yl) pyrimidin-2(1H)-one) (3i) [25]

A mixture of the bis-chalcone (2,3) (0.001 moles, 0.474gm), and urea (0.0022 moles, 0.12gm) were dissolved in DMF (0.004mole) piperidine were refluxed for (12 hrs.), cool and poured into an ice-cold water, The formed product was recrystallized from (ethanol/water), Table (1) shows the physical properties of the compound.

Preparation of 3,3`-(1,4-phenylenebis(2-thioxo-1,2-dihydropyrimidine-6,4-diyl) bis Coumarin (2j) and 3,3`-(1,3-phenylenebis(2-thioxo-1,2 dihydropyrimidine-6,4-diyl)bisCoumarin (3j) [20]

A mixture of the bis-Chalcone (2,3) (0.001 moles, 0.474gm), and thiourea (0.002 moles, 0.152gm) were dissolved in DMF (0.004moles) piperidine were refluxed for (12 hrs.). Cooled then poured into ice-cold water, filtrated and recrystallized from (ethanol/water), Table (1) shows the physical properties of the compound.

Preparation of 3,3'-(1,4-phenylenebis(2-amino-5,6-dihydropyrimidine-6,4-diyl)) bis coumarin (2k) and 3,3'-(1,4-phenylenebis(2-amino-5,6-dihydropyrimidine-6,4-diyl))biscoumarin (2k) [18]

A mixture of the bis-Chalcone (2,3) (0.001 moles, 0.474gm), and guanidine nitrate (0.002 moles, 0.48gm) were dissolved in DMF (0.002moles) sodium ethoxide were added. then refluxed for (12 hrs.). Cooled then poured into ice-cold water, filtrated and recrystallized from ethanol, table (1) shows the physical properties of the compound

Greener methods (ultrasonic technique)

All the above-mentioned compounds were prepared using ultrasonic technique with zirconium chloride Lewis's acids are important and interesting catalysts in most organic transformations. Among different Lewis's acids, Zr (IV) species such as ZrCl4 and ZrOCl2·8H2O are allocated special attention because of their low toxicity, availability and handling, moisture stability, and low cost in comparison to some of their corresponding compounds. During recent decades, Lewis's acids have been used to promote different types of organic reactions because they naturally possess mild acidity properties and, as such, can catalyze reactions selectively. This means that in the presence of various functional groups, they can operate on a specific group to produce the objective product. In this review we have focused on the reactions which have been progressed in the presence of ZrCl4 and ZrOCl2·8H2O. The study has been ordered based on the number of the reaction components and their solvent media. octahydrate as a catalyst at (50-60°C) and yields were given at the times indicated in Table (1) [26] [27].

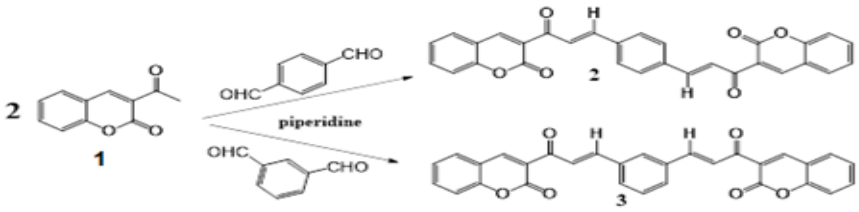
Table (1) shows the physical properties of synthesized compounds

Compound No.	M.P. (°C)	Color	Ultrasonic (min.)	Classic method yield%	Ultrasonic yield%
2	280-282	Brown	30	70	75
2a	290-292	Yellow	50	55	57
2b	Dec. 320<	Orange	60	62	65
2c	Dec. 322>	Orange	60	66	70
2d	248-250	Red	65	72	70
2e	252-255	Deep red	65	70	70

2f	257-260	Yellow	60	50	55
2g	322-324	Green	50	70	75
2h	317-319	Deep green	50	65	65
2i	265-268	Deep yellow	65	79	80
2j	266-270	Yellow	65	74	75
2k	295-297	Deep brown	65	60	55
3	240-242	Brown	35	70	75
3a	250-252	Yellow	50	50	55
3b	280-282	Deep orange	60	65	65
3c	300-302	Orange	60	65	65
3d	255-257	Light orange	65	68	72
3e	235-237	White	65	75	70
3f	225-227	Brown	60	70	75
3g	287-289	Deep orange	55	70	72
3h	292-293	Green	55	66	69
3i	259-262	Yellow	65	65	66
3j	273-275	Orange	65	71	73
3k	277-280	Brown	65	55	60

3- Results and Discussion

The Key of this work is the bis-chalcone intermediate was obtained by Clasian –Schmidt condensation of corresponding 3-Acetylcoumarin (1) with aldehyde (terephthaldehyde and isophthalaldehyde). in basic condition by addition of piperidine, the structural formula of this compound (2,3) was established by physical and spectral data of FT.IR. which show two position of carbonyl groups at (1690 Cm^{-1} and at 1720 cm^{-1}), and the ^{1}HNMR, shows an identical FT-IR of bis-chalcone as discussed before and show in the chart (1), as shown in scheme 1.



Scheme(1): The synthetic route of compound (2,3)

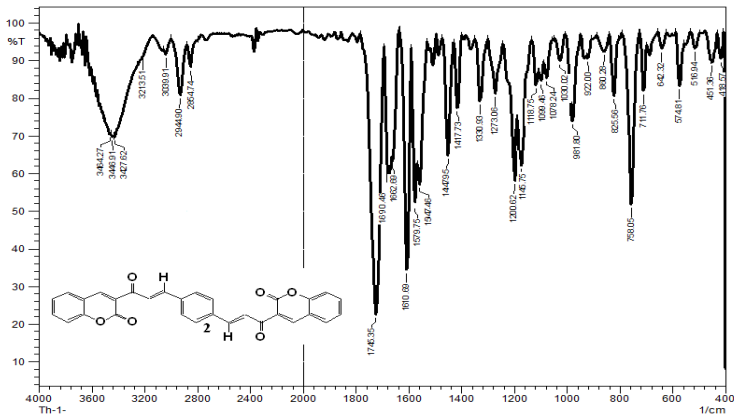


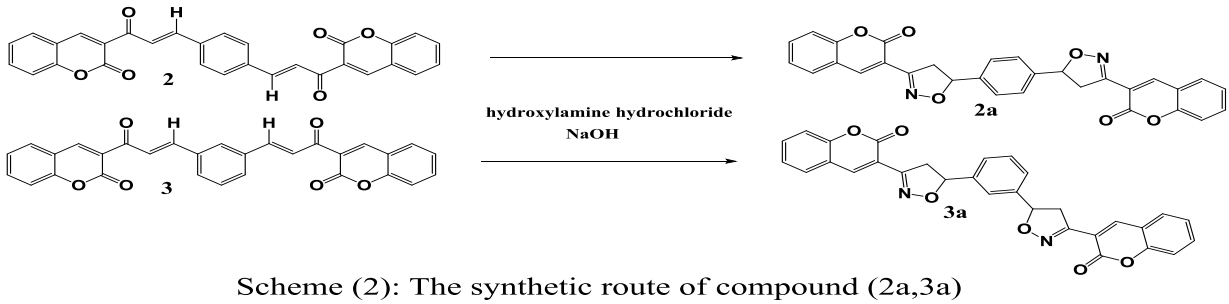
Figure (1) FT-IR spectrum of bis–Chalcone compound (2)

The reaction of bis–chalcone (2,3) with two equivalent moles of hydroxylamine hydrochloride and under basic condition gave oxazole compound (2a,3a) respectively, the scheme 2 showed these reactions.

The reaction of bis-chalcone compound (2,3) with o-amino phenol and o-phenylene diamine respectively which indicated in the scheme 3.

The reaction of bis-chalcone (2,3) with hydrazine hydrate and phenyl hydrazine respectively gave (2d,3d, 2e, 3e) compounds which indicated in the scheme 4.

The reaction of bis-chalcone (2,3) with hydrazine hydrate in the presence glacial acetic acid respectively gave (2f, 3f) compounds which indicated in the scheme 5.



Scheme (2): The synthetic route of compound (2a,3a)

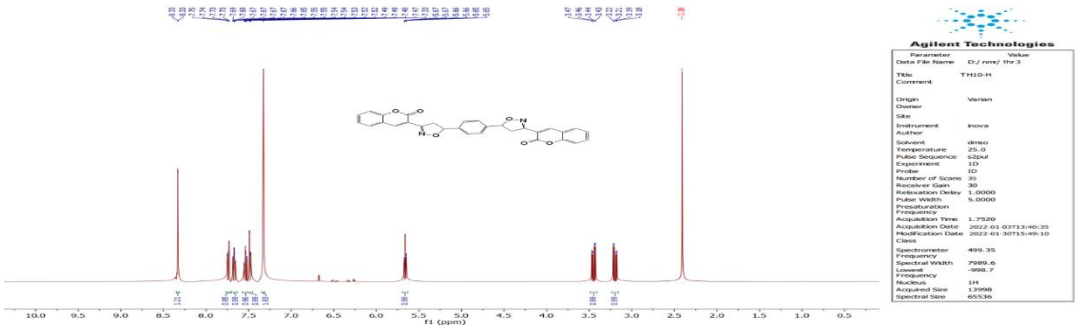
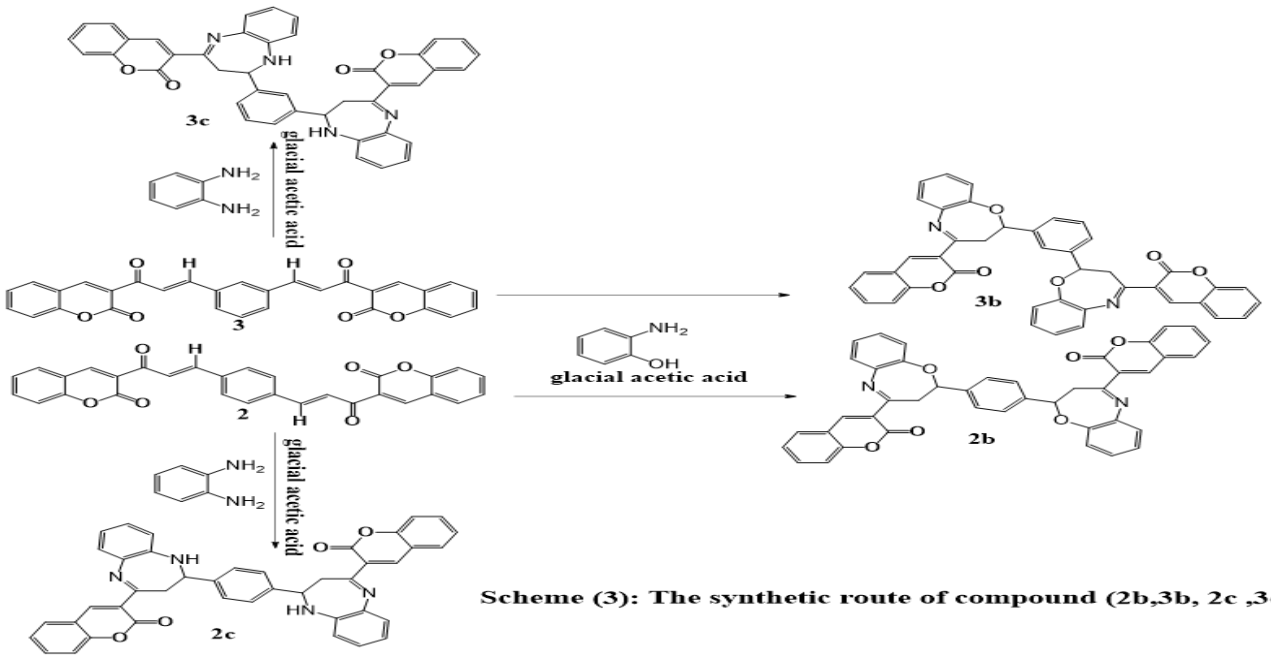
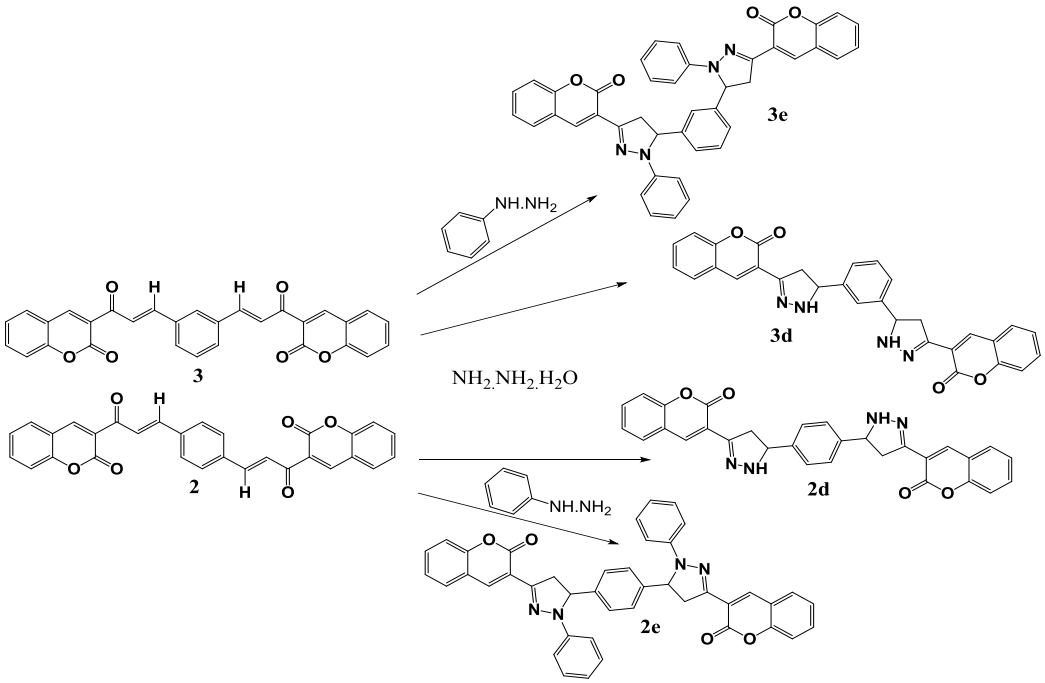


Figure (2) 1H NMR spectrum of compound (2a)



Scheme (3): The synthetic route of compound (2b,3b, 2c ,3c)



Scheme (4): The synthetic route of compound (2d,3d, 2e ,3e)

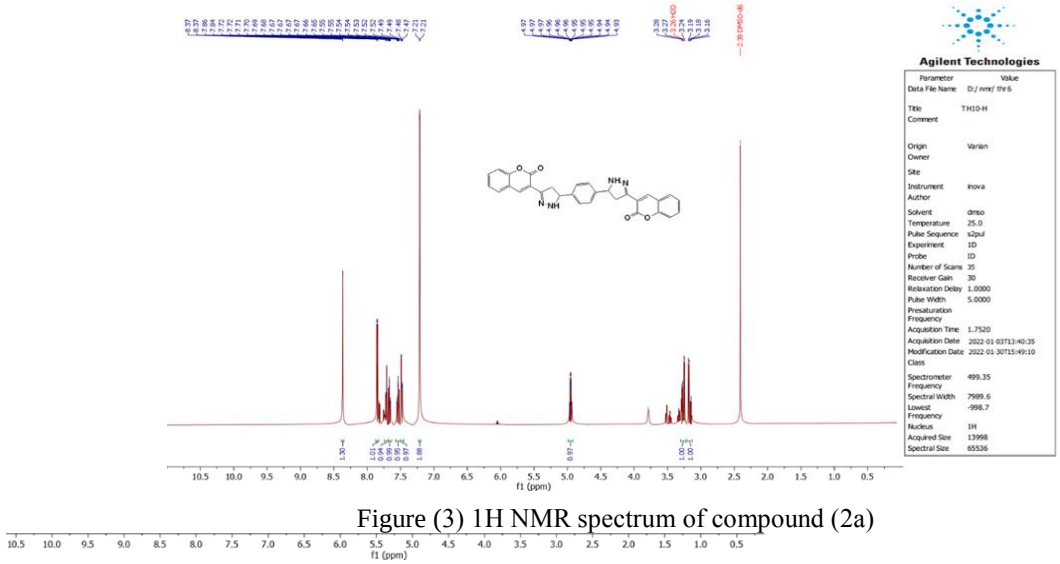
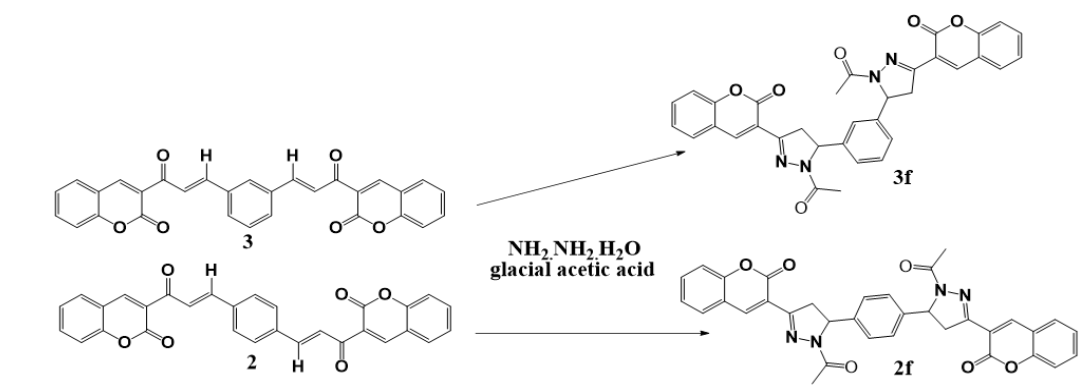
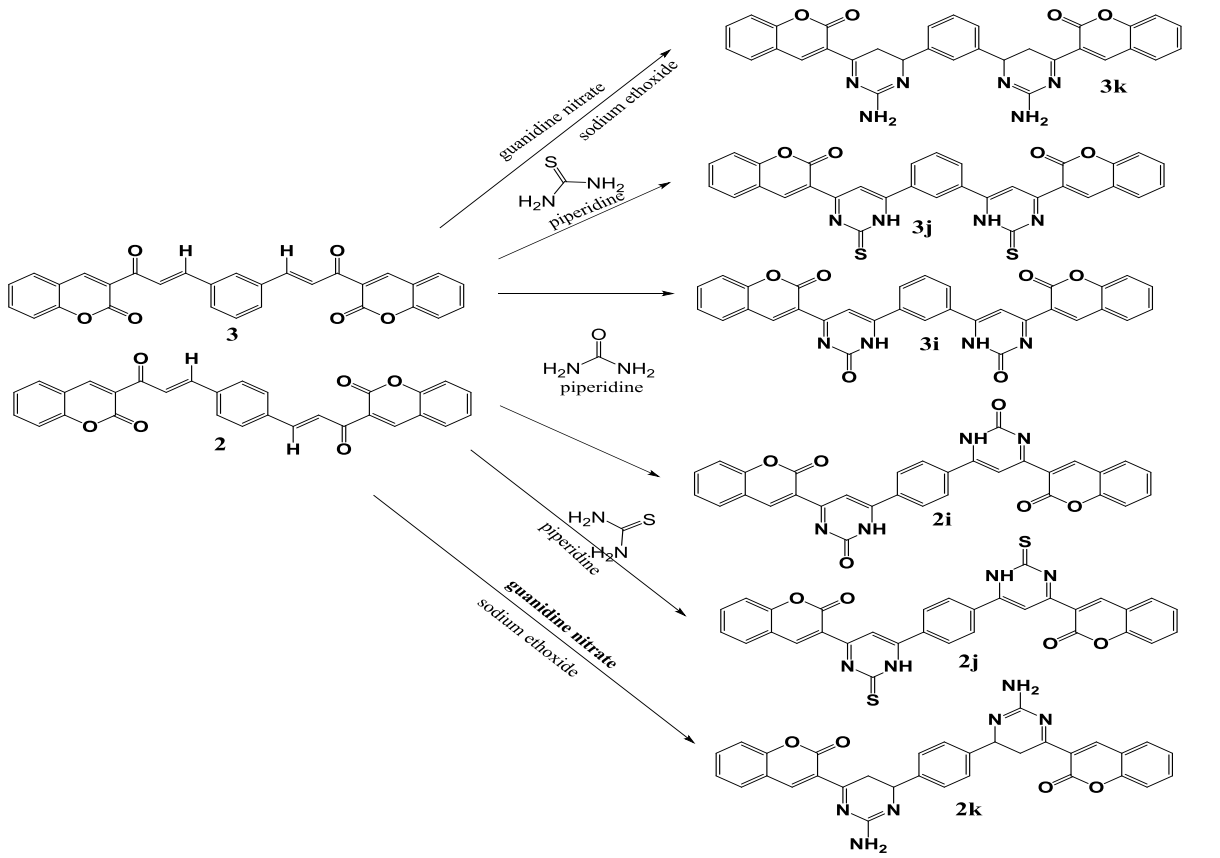


Figure (3) 1H NMR spectrum of compound (2a)



Scheme (5): The synthetic route of compound (2f,3f)



Scheme (7): The synthetic route of compound (2i,3i,2j,3j,2k,3k)

The reaction of bis–chalcone (2,3) with two equivalent moles of thiosemicarbazide and semicarbazide and under basic condition gave amido and thioamido respectively gave (2g,3g, 2h ,3h) compounds which indicated in the scheme 6.

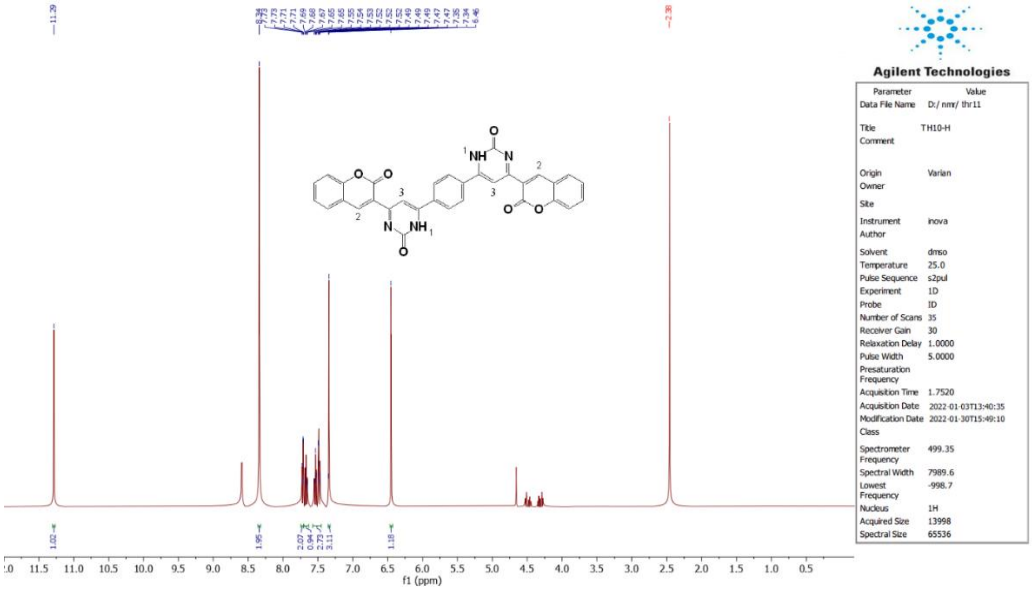


Figure (4) 1H NMR spectrum of compound (2j)

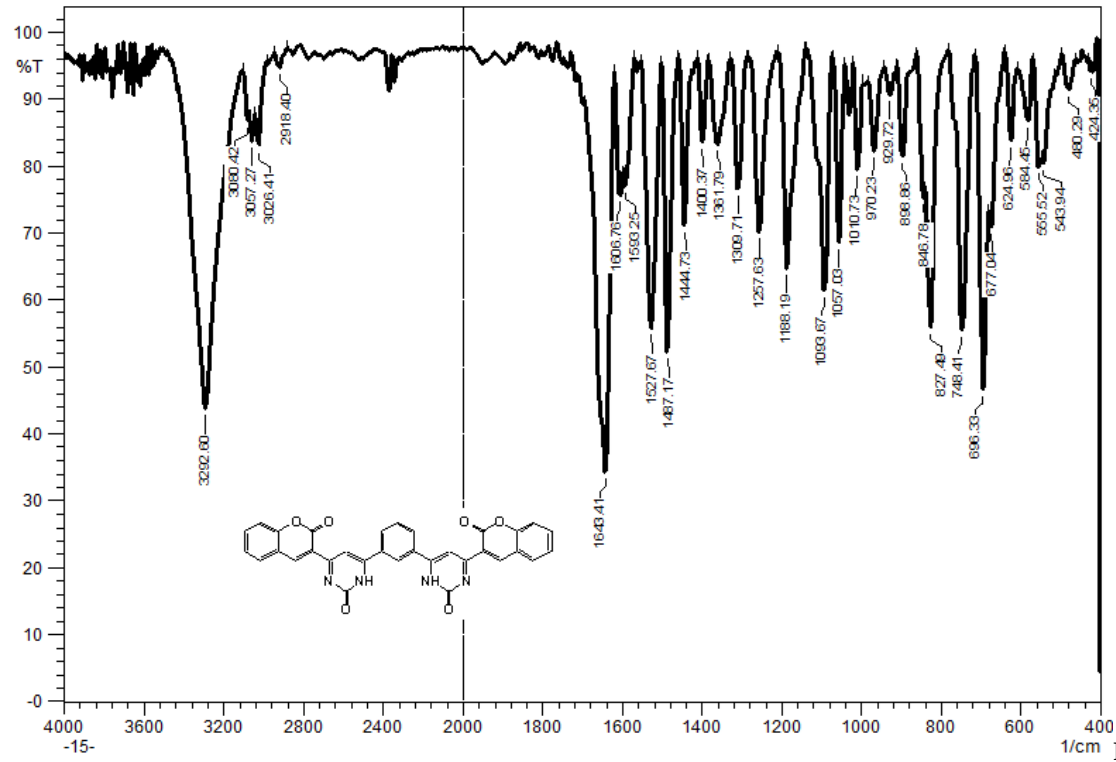


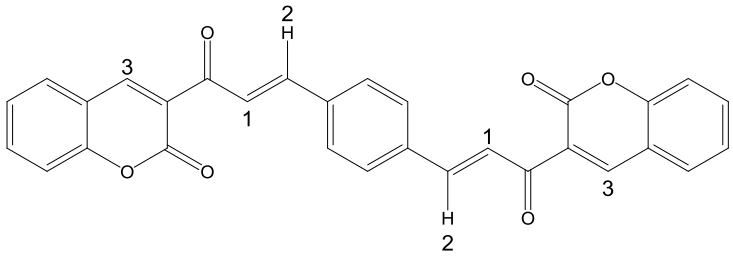
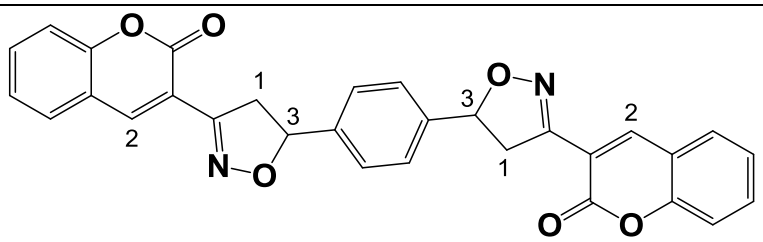
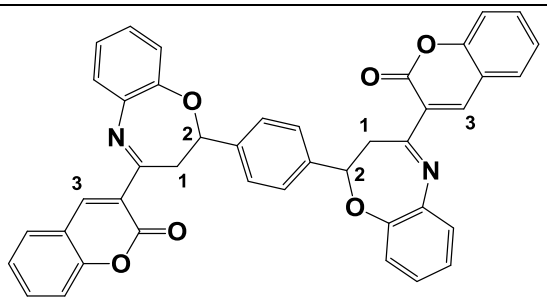
Figure (5) FT-IR spectrum of bis–Chalcone compound (3i)

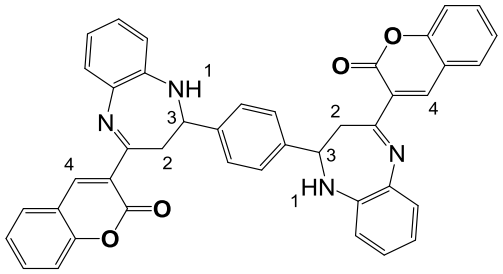
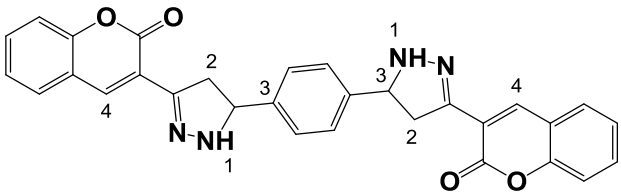
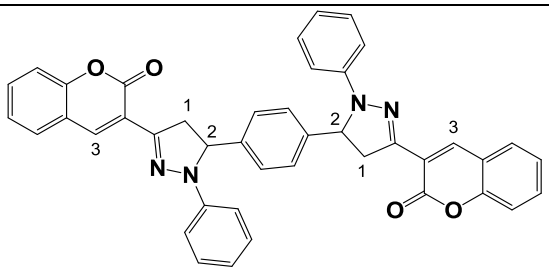
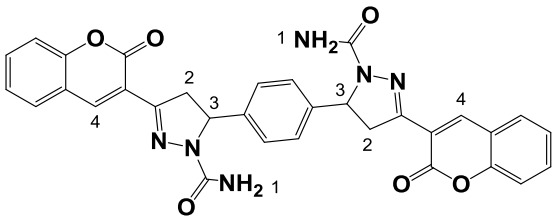
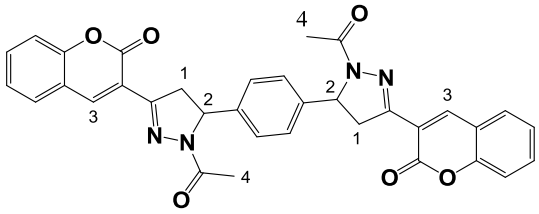
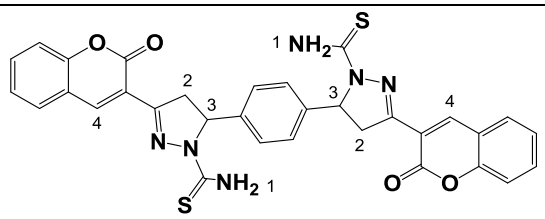
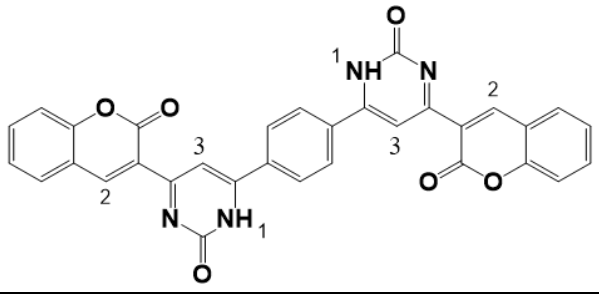
Table (2) shows the I.R. spectrum of synthesized compounds

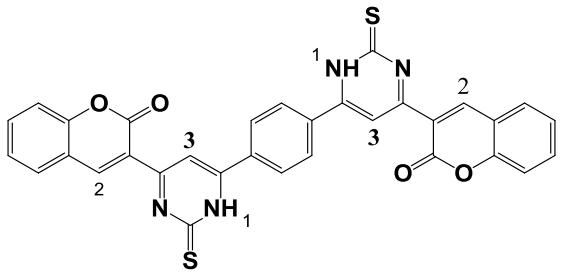
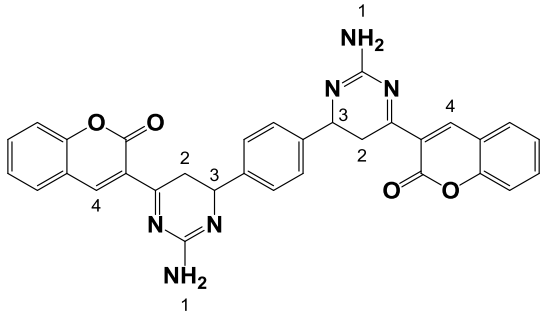
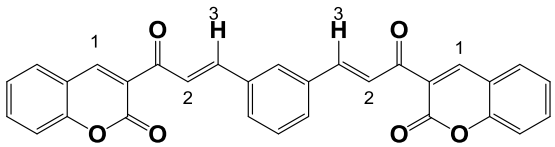
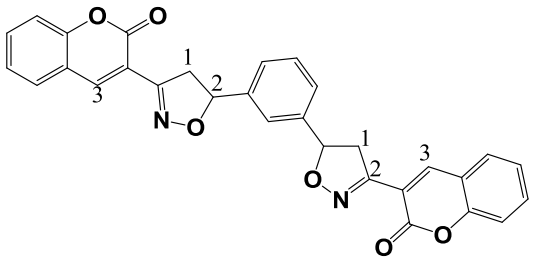
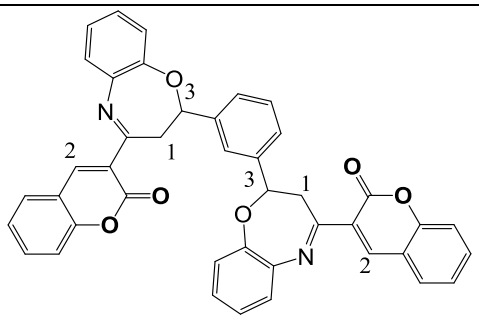
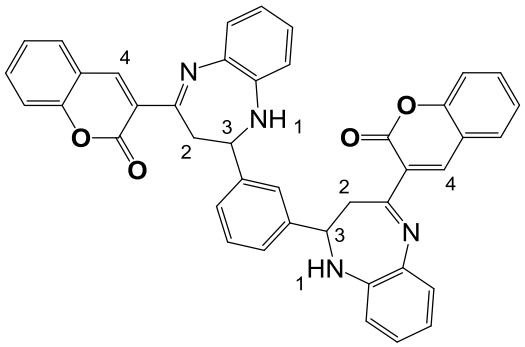
Comp. No.	IR υ(cm-1), KBr							
	N-H	C-H (Ar.)	C-H (Aliph.) Sym. Asym	C=O Cyclic Ester	C=O	C=N	C=C C…C (Ar.)	C-O-C Ether Sym. Asym
1	-----	3040	2944 2864	1745	1690	-----	1547 1448	1200 1145
2	-----	3043	2941 2825	1725	1680	-----	1501 1413	1190 1140
2a	-----	3032	2962 2810	1748	-----	1643	1565 1479	1263 1180
2b	-----	3054	2915 2840	1750	-----	1680	1550 1415	1200 1185
2c	3350	3070	2914 2825	1726	-----	1640	1500 1450	1171 1160
2d	3370	3078	2919 2900	1723	-----	1620	1498 1415	1200 1150
2e	------	3060	2940 2878	1740	-----	1600	1500 1410	1215 1197
2f	-----	3059	2930 2810	1725	-----	1620	1520 1425	1210 1178
2g	3250 3410	3040	2922 2869	1730	-----	1630	1510 1440	1210 1168
2h	3240 3450	3090	2915 2845	1720	-----	1625	1510 1430	1190 1164
2i	3400	3095	2940 2890	1750	1650	1590	1530 1425	1180 1140
2j	3410	3080	2910 2820	1710	1660	1599	1520 1450	1220 1192

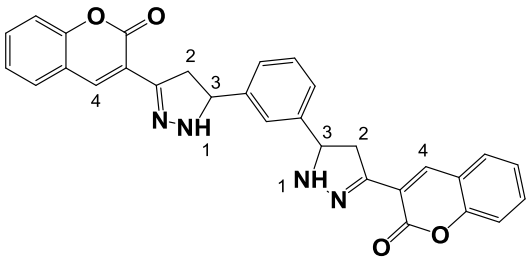
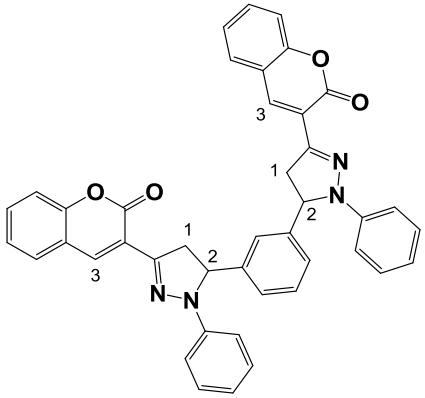
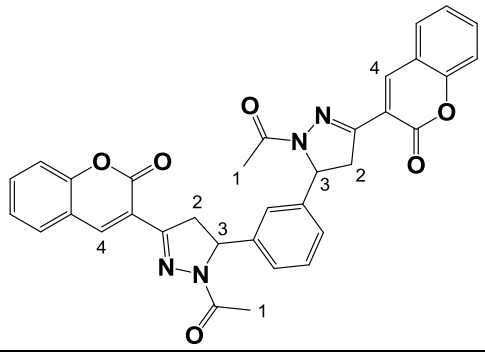
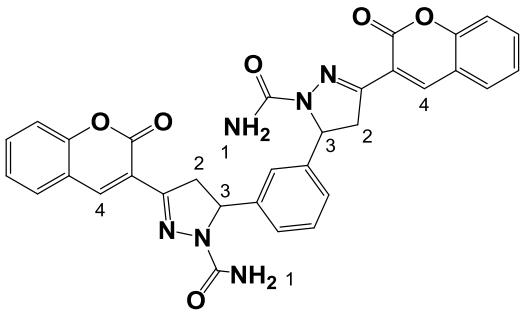
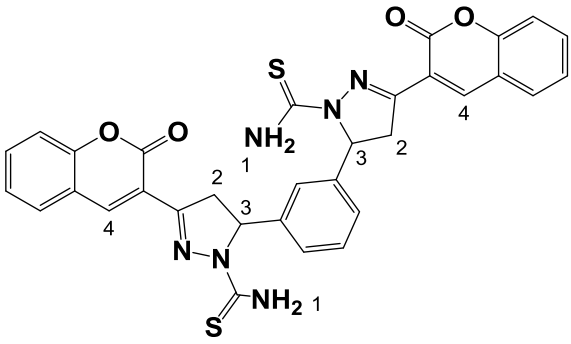
2k	3200 3420	3085	2920 2835	1740	------	1620	1500 1420	1210 1190
3	-----	3055	2940 2847	1720	1685	-----	1555 1414	1195 1175
3a	-----	3070	2976 2863	1750	-----	1650	1560 1450	1240 1200
3b	-----	3051	2921 2859	1746	-----	1680	1552 1417	1200 1147
3c	3356	3064	2912 2850	1723	-----	1640	1523 1452	1175 1169
3d	3379	3057	2938 2874	1742	-----	1594	1496 1453	1219 1180
3e	-----	3057	2932 2810	1726	-----	1616	1518 1419	1208 1197
3f	3452	3038	2922 2820	1736	1709	1635	1515 1443	1216 1190
3g	3244 3452	3087	2917 2835	1718	1700	1627	1514 1434	1185 1150
3h	3395 3430	3094	2945 2849	1754	-----	1594	1536 1428	1187 1125
3i	3292	3057	3026 2918	1643	1606	1593	1440 1400	1257 1118
3j	3461	3085	2920 2830	1740	------	1620	1500 1420	1210 1156
3k	3244 3452	3081	2918 2819	1738	------	1616	1496 1413	1205 1154

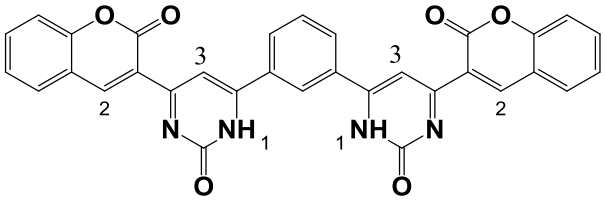
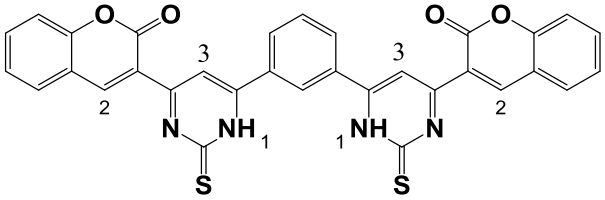
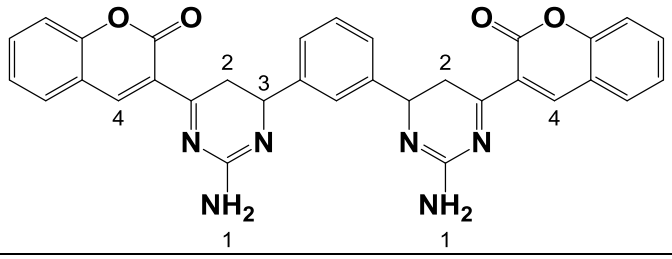
Table (3) shows the 1HNMR Spectrum of synthesized Compounds

Comp. No.	Structure	^{1}HNMR, DMSO-d6, δ (ppm)
2		7.3 (2H, d-d, H1) 7.6 (2H, d-d, H2) 6.55 (2H, s, H3) 7.4-7.7 (8H, m, Ar-H) 7.80-7.82 (4H, d, Benzylic Ring)
2a		3.2-3.4 (4H, d, H1) 7.30 (2H, s, H2) 7.42 (4H, s, Benzylic ring) 7.4-7.7 (8H, m, Ar-H) 5.6 (2H, d, H3)
2b		3.00-3.09(4H, d-d, H1) 5.80(2H, t, H2) 6.5(1H, s, H3) 7.31(4H, s, Benzylic ring) 6.9-7.67 (16H, m, Ar-H)

Comp. No.	Structure	^{1}HNMR, DMSO-d6, δ (ppm)
2c		5.94(4H, d, 1H) 2.87-2.93(4H, d, H2) 5.28(1H, t, H3) 7.17(4H, s, Benzylic ring) 7.09-7.73 (16H, m, Ar-H4) 6.49(2H, s, H3)
2d		7.85(2H, d, H1) 3.17-3.26(4H, d-d, H2) 4.95(2H, t, H3) 8.37(2H, s, H4) 7.21(4H, s, Benzylic ring) 7.49-7.72 (8H, m, Ar-H)
2e		2.46-2.56 (4H, d-d, H1) 5.17 (2H, t, H2) 6.49(2H, s, H3) 6.97-7.23(12H, m, Benzylic ring) 7.48-7.73 (8H, m, Ar-H)
2f		6.55 (4H, s, H1) 2.47-2.56 (4H, d-d, H2) 5.43 (2H, t, H3) 7.30 (2H, s, H4) 8.25(4H, s, Benzylic ring) 7.48-7.73 (8H, m, Ar-H)
2g		2.49-2.6 (4H, d, H1) 5.49 (2H, t, H2) 7.25 (2H, s, H3) 2.37(6H, s, H4) 8.25(4H, s, Benzylic ring) 7.48-7.73 (8H, m, Ar-H)
2h		7.89 (4H, s, H1) 2.53-2.53.64 (4H, d-d, H2) 5.89 (1H, t, H3) 6.5 (2H, s, H4) 7.25 (4H, s, benzylic ring) 7.48-7.73 (8H, m, Ar-H)
2i		11.29 (2H, s, H1) 6.44 (2H, s, H2) 7.34(2H, s, H3) 8.34 (4H, s, benzylic ring) 7.48-7.72 (8H, m, Ar-H)

Comp. No.	Structure	^{1}HNMR, DMSO-d6, δ (ppm)
2j		12.85(2H, s, H1) 6.44(2H, s, H2) 7.34(2H, s, H3) 8.31(2H, s, benzylic ring) 7.48-7.72 (8H, m, Ar-H)
2k		7.09(4H, s, H1) 2.90-3.06(4H. m, H2) 5.28(2H, t, H3) 6.55(2H, s, H4) 7.33(2H, s, benzylic ring) 7.48-7.77 (8H, m, Ar-H)
3		6.6(2, s, H1) 7.35(2H, d, H2) 7.62(2H, d, H2) 7.38-7.93(4H, m, benzylic ring) 7.48-7.71(8H, m, Ar-H)
3a		3.25-3.5 (4H, d, H1) 5.73 (2H, t, H2) 7.01 (2H, s, H3) 7.35-7.41 (4H, m, Benzylic ring) 7.48-7.74 (8H, m, Ar-H)
3b		3.04-3.13(4H, d-d, H1) 5.73(2H, t, H3) 6.39(2H, s, H2) 7.30-7.49(4H, m, Benzylic ring) 6.95-7.43 (16H, m, Ar-H)
3c		4.17(4H, d, 1H) 2.91-2.98(4H, d, H2) 5.25(1H, t, H3) 6.40(1H, s, H4) 7.27(4H, s, Benzylic ring) 7.08-7.73 (16H, m, Ar-H)

Comp. No.	Structure	^{1}HNMR, DMSO-d6, δ (ppm)
3d		8.16(2H, d, H1) 3.22-3.34(4H, d-d, H2) 4.92(2H, t, H3) 6.44(1H, s, H4) 7.31-736(4H, m, Benzylic ring) 7.48-7.71 (8H, m, Ar-H)
3e		2.47-2.58 (4H, d-d, H1) 5.11 (2H, t, H2) 6.35(2H, s, H3) 6.99-7.36(12H, m, Benzylic ring) 7.48-7.73 (8H, m, Ar-H)
3f		2.37 (6H, s, H1) 2.50-2.61 (4H, d-d, H2) 5.43 (2H, t, H3) 6.34 (2H, s, H4) 7.35(4H, s, Benzylic ring) 7.48-7.73 (8H, m, Ar-H)
3g		6.55 (4H, s, H1) 2.49-2.59 (4H, d-d, H2) 5.45 (2H, t, H3) 6.39 (2H, s, H4) 7.33-7.36(4H, m, Benzylic ring) 7.48-7.73 (8H, m, Ar-H)
3h		7.89 (4H, s, H1) 2.54-2.65 (4H, d-d, H2) 5.87 (1H, t, H3) 6.38 (2H, s, H4) 7.35 (4H, s, benzylic ring) 7.48-7.73 (8H, m, Ar-H)

Comp. No.	Structure	^{1}HNMR, DMSO-d6, δ (ppm)
3i		11.26 (2H, s, H1) 6.5 (2H, s, H2) 7.40(2H, s, H3) 7.50-8.95 (4H, s, m benzylic ring) 7.48-7.72 (8H, m, Ar-H)
3j		12.77(2H, s, H1) 6.65(2H, s, H2) 7.50-8.89(2H, s, benzylic ring) 7.48-7.72 (8H, m, Ar-H)
3k		7.09(4H, s, H1) 2.90-3.06(4H. m, H2) 5.15(2H, t, H3) 8.43(2H, s, H4) 7.55(2H, s, benzylic ring) 7.48-7.778H, m, Ar-H)

3- Conclusions

A series of reactions for bis-chlcone which prepared from reaction of two moles 3-acetylcoumarin with one mole terephthaldehyde and isophthalaldehyde were achieved with different chemical reagent to synthesize Isoxazole, oxazepane, diazepine, pyrazoles and pyrimidine derivatives. The results obtained from this investigation indicated that the strategy adapted for the synthesis of the designed derivatives was successful.

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