J. Edu. & Sci., Vol. (24), No. (4) 2011

2-Phenylchroman-4-one as Synthone in Synthesis of New Five and Six Membered Rings Heterocyclic Compounds

Moneera Y. Raoof
Department of Chemistry
College of science
University of Mosul, Iraq

Shakir M. Saied
Department of Pharmacy
Institute of Technical Mosul
Foundation of Technical Education

Moayed S. AL. Gawady
Department of Chemistry / College of science
University of Mosul, Iraq

Received
29 / 06 / 2010

Accepted
06 / 10 / 2010

المستخلص:

حضرت مشتقات الكرومان– ٤–اون1(a -i) بوساطة تكاثف بجمان للفينول او معوضاته مع حامض السيناميك باستخدام متعدد حامض الفوسفريك . فوعلت هذه المشتقات مع الهيدرازين المائى بالتصعيد بالايثانول لانتاج مشتقات البايرازولين (٢). وبالاستفادة من تكاثف كليسن – شميدت لاصطناع ٣–اريليدين – ٢– فنيل معوضات الكرومين – ٤– اون 3(a -e) بتفاعل الكرومان– ٤– اون المناسب مع الالديهايدات الارروماتية وبوجود هيدروكسيد الصوديوم . حضرت البايروزينلات 4(a -c) من تفاعل الاريديلينات المناسبة مع الهيدرازين المائى بوجود البريدين. اخيرا تكاثف هذه الاريديلينات مع اليوريا اعطى بريميدين – ٢–اون ٥(a -d).

تم إثبات التراكيب الكيميائية للمركبات بوساطة خواصها الفيزيائية إضافة إلى أطيافها في منطقة الأشعة تحت الحمراء وفوق البنفسجية.

Keywords: Chroman-4-one, cinnamic acid, pyrazoline, pyrimidin-2-ones

Abstract:

Chroman-4-one derivatives 1(a-i) were prepared by Pechman condensation of phenol or its substitutions with cinnamic acid by using polyphosphoric acid. These derivatives were reacted with hydrazine hydrate in refluxing ethanol to yield pyrazoline derivatives (2). The utility of the Claisen-Schmidt condensation in the synthesis of -3-arylidene-substituted 2-phenyl chroman-4-one 3(a-e) by reaction of proper 4-chromanone (1) with aromatic aldehydes in presence of KOH. Pyrazolines 4(a-c) were synthesized by the reaction of proper arylidenes 2 with hydrazine hydrate in presence of pyridine. Finally, the condensation of arylidines with urea gave pyrimidin-2-ones 5(a-d).

The structures of these compounds were confirmed by their physical properties in addition to the IR and UV Spectra.

Introduction:

Chromans containing pyrazoline or pyrimidines were synthesized owing to their biological activities as anticoagulant, antibacterial, antielminthic, hypothermal and vasodilatory [1-3]. Recently an increasing attention has been focused on these ring system[4].

Also, a potential useful structure - activity relationship appeared to exist with pyrazolines nuclei[5-6], which were important nitrogen-containing heterocyclic compounds owing to their useful bioactivities such as invitro antiamoebic activity [7].

The reaction of carboxylic acid such as tiglic acid and crotonic acid with substituted phenols as Pechman like action using polyphosphoric acid was previously reported [8].

The chromanone moieties formed by this reaction was a good examples of α,β -unsaturated ketones (chalcones) and they were especially important starting materials or intermediates for the synthesis of naturally occurring flavonoids and various nitrogen-containing heterocyclic compounds [9].

While these compounds were reacted with hydrazine hydrate in hot pyridine to yield pyrazolines derivatives [10], they reacted with urea or thiourea to afforded pyrimidines derivatives[11].

It was hoped that a new class of 2-phenylchroman-4-one derivatives and of general formula 3-5 that contained combined elements of both chromanone and pyrazoline or pyrimidines derivatives might show enhanced biological properties.

As part of continuous program directed toward the synthesis of important heterocyclic compounds, oxygenous and nitrogenous five and six membered ring [11-12]. It was become of interest to investigate preparative routs to synthesis of 2-Phenylchroman-4-one 1(a-i) to use it as synthon in synthesis of the title compounds.

Experimental:

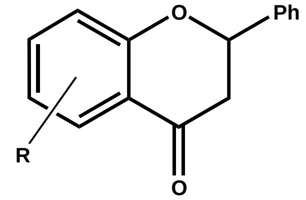
All melting points were determined on a Gallen Kamp and Electrothermal 1A9300 Digital-Series (1998) apparatus and were uncorrected. The IR – spectra (ν max cm^{-1} KBr Disc) were recorded on Perkin – Elmer 590B Spectrophotometer. UV-On Shimadzu UV-160 us in $CHCl_3$ as solvent

substituted 2-phenyl chroman-4-one 1(a-i): [8]

Polyphosphoric acid (40gm) was added to a mixture of proper phenol (25mmole) and cinnamic acid (3.7 gm, 25 mmole) at room temperature.The mixture was stirred and heated on a steam bath at 70-80 ^{O}C for 1-5 hrs. The mixture was poured into ice water. The solid which separated out was filtered off, washed with water, dried and recrystallized from the suitable solvent to give compounds 1(a-e).

Compounds 1(f-i) which gave a gummy products were extracted by benzene, washed with water, dried over $MgSO_4$. Evaporation under vacuum and the residual solids were recrystallized from the suitable solvent. Physical and spectral data were listed in Table (1).

Table (1) : Physical and spectral data of substituted 2-phenyl chroman-4-one 1(a-i)



Comp. No.1	R	M.P. ^{O}C	Yield %	Colour	Solvent of crystallization	IR, KBr (disc), Cm $^{-1}$	**Uv** λmax **(nm)** $CHCl_3$
						C=O	
a	H	158 60-	30	Orange	Aqueous ethanol	1645	322
b	7-NO_2	108 -10	30	Pale yellow	Aqueous methanol	1689	300
c	8-Br	110 12-	30	White	Aqueous methanol	1685	310
d	6-Br	106 -108	77	Pale yellow	Aqueous methanol	1635	316
e	6-CH_3O	60 -62	33	Yellow	Aqueous methanol	1635	286
f	6Cl	101- 02	93	White	Ethanol	1635	306
g	6,8)CH_3($_2$	62 -64	32	Yellow	Ethanol	1635	316
h	6,7)CH_3($_2$	65 -67	37	Yellow	Ethanol	1639	310
i	5,7)CH_3($_2$	68- 70	76	Yellow	Diethyl ether	1614	272

3-aryl-5-phenyl-2-pyrazolines 2(a-g): [8]

Equimolecular amounts of proper compound (1) (0.9mmole)in 15-20 ml ethanol and hydrazine hydrate was refluxed for 48hours .

The mixture was gradually poured into crushed ice.The solid was filtered washed with cold water, dried and crystallized from ethanol to afford the title compounds. Physical and spectral data were listed in Table (2).

Table (2) : Physical and spectral data of 3-aryl-5-phenyl-2-pyrazolines 2(a-g)

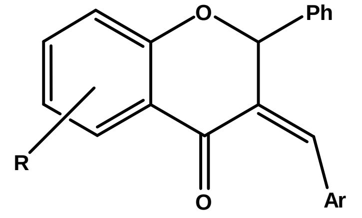
Comp. No.2	R	M.P. ^{O}C	Yield %	Colour	IR, KBr (disc), Cm $^{-1}$		**Uv** λmax **(nm)** $CHCl_3$
					C=N	NH	
a	H	82-4	44	Pale Yellow	1639	3318	286
b	7-NO_2	230*	43	Brown	1637	3236	262
c	8-Br	120*	44	White	1637	3411	282
d	6-Br	97-9	46	White	1620	3305	282
e	6-CH_3O	174-76	44	White	1620	3240	304
f	6,8$(CH_3)_2$	98-100	42	Brown	1637	3236	304
g	6,7$(CH_3)_2$	92-4	44	White	1637	3233	284

*Decomposed

3-Arylidene-substituted 2-phenyl chroman-4-one 3(a-e): [11]

To a mixture of (0-01mole) of the proper aldehyde and (0.01mole) of appropriate substituted 2-phenyl chroman-4-one 1, a solution of (0.33gm) of potassium hydroxide in 50 ml ethanol was added. The reaction mixture was stirred. The reaction mixture was stirred at room temperature for 3 hours, the precipitate productwas filtered, washed with ethanol, dried and crystallized from ethanol to give compounds 3(a-e). Physical and spectral data were listed in Table (3).

Table (3) : Physical and spectral data of 3-Arylidene-substituted 2-phenyl chroman-4-one 3(a-e)



Comp. No.3	R	Ar	M.P. ^{O}C	Yield %	IR, KBr (disc), Cm $^{-1}$		**Uv** λmax **(nm)** $CHCl_3$
					C=C	C=O	
a	7-NO_2	C_6H_5-	111-13	60	1624	1680	290
b	8-Br	C_6H_5-	118-20	66	1619	1680	288
c	6-Br	C_6H_5-	120-21	50	1603	1680	288
d	6,7$(CH_3)_2$	2-Cl-C_6H_4-	186-88	62	1624	1678	300
e	5,7$(CH_3)_2$	2-Cl-C_6H_4-	180 (decomposed)	44	1614	1666	299

3-Aryl-4-phenyl-substituted chromano[4,3-c]pyrazole 4(a-c): [11]

A mixture of proper 3-arylidene-substituted 2-phenyl chroman-4-one 3(a-e) (0.01 mole) in 25 ml ethanol, hydrazine hydrate(0.06 mole) and pyridine (4ml)was refluxed for 6 hours, cooled, concentrated under vacuum, then poured into water and acidified with acetic acid. The residue was filtered off, washed with water and crystallized from methanol to afford compounds 4(a-j). Physical and spectral data were listed in Table (4).

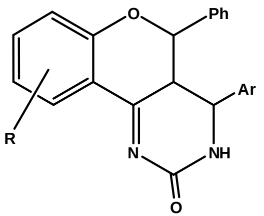
Table (4): Physical and spectral data of 3-Aryl-4-phenyl-substituted chromano[4,3-c]pyrazole 4(a-c)

Comp. No.3	R	Ar	M.P. ^{O}C	Yield %	IR, KBr (disc), Cm $^{-1}$		**Uv** λmax **(nm)** $CHCl_3$
					C=N	NH	
a	6Cl	2-ClC_6H_4-	130 (decomposed)	30	1630	3330	260
b	6,7$(CH_3)_2$	2-ClC_6H_4-	119-21	45	1633	3418	345
c	5,7$(CH_3)_2$	2-ClC_6H_4-	126-30	33	1630	3234	270

4-(2-Chlorophenyl)-5-phenyl-3,4,4a,5-substituted chromano[4,3-d]pyrimidin-2-one 5(a-d): [11]

A mixture of proper 3-arylidene-substituted 2-phenyl chroman-4-one 3 (0.01 mole) in 100 ml ethanol and urea (0.6 gm, 0.01 mole) was refluxed for 24 hours, cooled, concentrated under vacuum, then poured into water and acidified with acetic acid. The precipitated product was filtered, dried and crystallized from ethanol to afford compounds 5(a-d). Physical and spectral data were listed in Table (5).

Table (5) :Physical and spectral data of 4-(substitutedphenyl)-5-phenyl-3,4,4a,5-substituted chromano[4,3-d]pyrimidin-2-one 5(a-d)

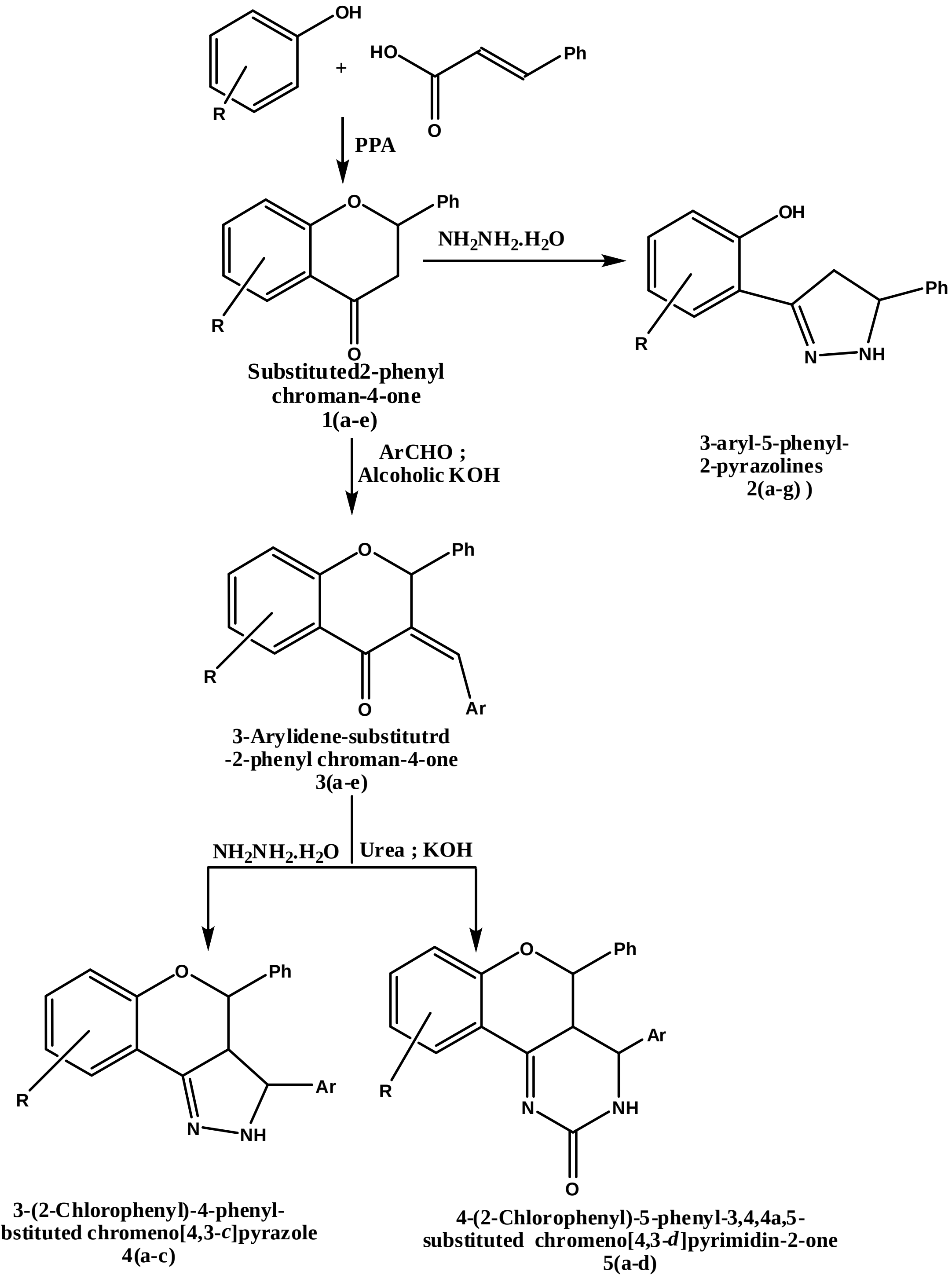


Comp. No.3	R	Ar	M.P. ^{O}C	Yield %	IR, KBr (disc), Cm $^{-1}$		**UV** λmax **(nm)** $CHCl_3$
					NH	C=O	
A	6-Br	C_6H_3	280*	25	3234	1671	278
B	6Cl	2Cl-C_6H_3	260*	36	3234	1701	304
C	5,7$(CH_3)_2$	2Cl-C_6H_3	158-60	22	3234	1566	304
D	6,7$(CH_3)_2$	2Cl-C_6H_3	140*	20	3334	1680	304

*Decomposed

Results and discussion:

A convenient synthesis of all new target compounds were accomplished by the route outlined in Scheme(1).



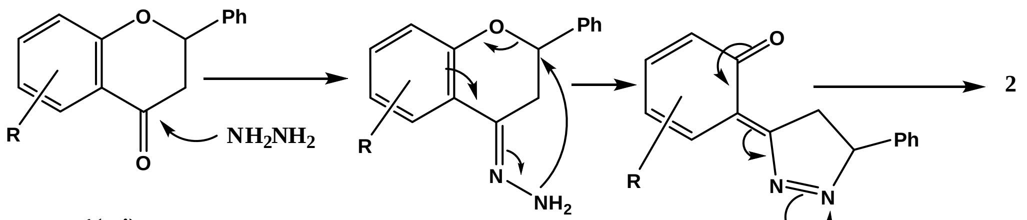
Scheme (1)
For R and Ar see Tables (1 - 5)

4-Chromanone derivatives 1(a-i) served as key intermediates for the synthesis of the target heterocyclic compounds (2-5) [8-11].

These new compounds were prepared by Pechman condensation of phenol or its substitutions with cinnamic acid by using polyphosphoric acid[9].

A special attention has been given as a part of efforts to develop practical synthesis of compounds 1(f-i) duo to their gummy products by using benzene to extract them.

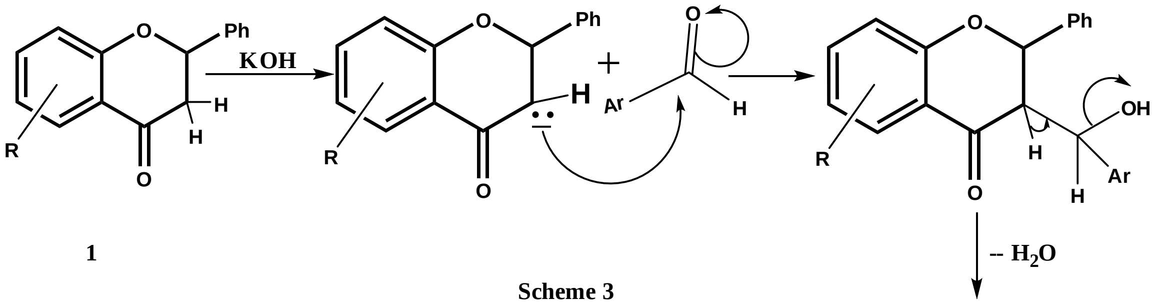
4-Chromanone moiety reacted with hydrazine hydrate in refluxing ethanol to yield pyrazoline derivatives[11]. Consequently; the structures of these compounds were clearly established by IR and UV spectral features. The absence of carbonyl absorption bands at 1700cm^{-1}confirmed the reaction of these groups with hydrazine hydrate by the suggested mechanism, Scheme 2 [11].



1(a-i)

Scheme (2)

In the course of the synthetic studies on chromanone derivatives, this work demonstrated the utility of the Claisen-Schmidt condensation in the synthesis of these new Z-(3-arylidene-2-phenylsubstituted chroman-4-ones 3(a-e). These compounds were prepared by condensation of proper 4-chromanone 1 with corresponding aromatic aldehydes in presence of KOH, Scheme 3[11].



1

Scheme 3

3

Inspection of models indicated that these compounds may adopted the strainless (Sofa) conformation in which all the atoms of heterocyclic ring, except C2 were coplanar[13-14], and performed the chair conformation[13]. Fig(1) showed the model of compound 3a which was selected as a representative for this serious as drawn by Chem3D with solvent accessible surface: translucent surface type and atom colors map property.

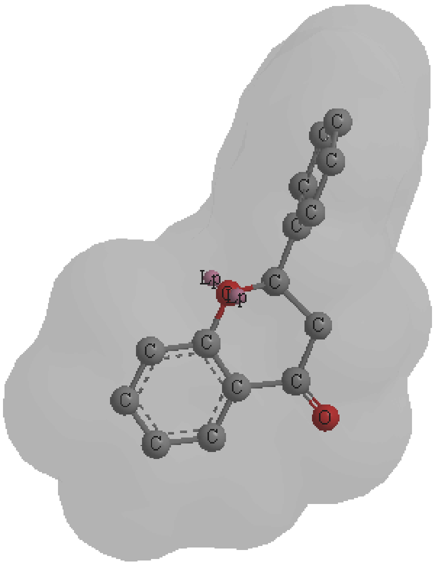
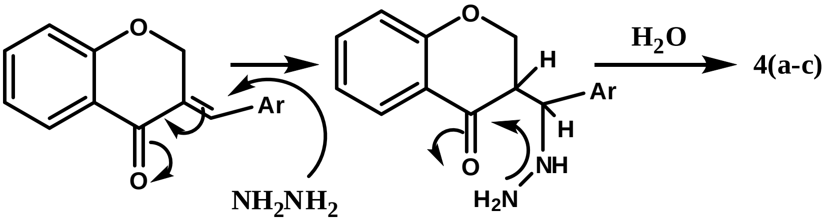


Fig. (1)
Model of 3(a) as drawn by Chem3D with solvent accessible surface : translucent surface type and atom colors map property

The IR frequencies of these compounds showed the presence of conjugated carbonyl carbon at (168-1666m^{-1}) with the exocyclic double bonds (1624-1600cm^{-1}), Table 3.

The decrease in frequency was due to the decrease of the force constant result from conjugation[11]. Finally the UV absorption between 284-305 nm(Table 3) showing the relationship of these structures to that of related chalcons[11].

Pyrazolines 4(a-c) were synthesized by the reaction of proper arylidenes (2) with hydrazine hydrate in presence of pyridine by nucleophilic addition on β –carbon (1,4-Michael addition). The driving force for the pyrazoline ring formation was the water elimination[11]. Scheme 4.



Scheme 4

The spectra of these compounds were came in agreement with pyrazoline moiety.

The UV absorptions were in the range 260-345nm,while the IR spectrum showed the disappearing of carbonyl band and another bands at(1630-1633) of C=N str, and (3418-3234) for NH str were appeared.

Finally, the condensation of these arylidines with urea gave pyrimidin-2-ones 5(a-d) by the same mechanism of Michael addition.

The IR spectra of these compounds reflect a broad band in the region 1680cm^{-1} for C=O and 3334-3234 cm^{-1} for NH vibrations, Table 5.

The UV absorptions were in the range 278-304 nm resemble to those published for similar compounds[11].

References :

1) Okumura, K.; Ashino, K. and Okuda, T., ”Synthesis and antibacterial activity of some new fused chromenes" Yakugaku Zasshi 81, 1482, (1962) Chem. Abstr. 1962, 56, 7938.

2) El-saghier, A. M. M.; Al-afaleq, E. I.; Mouli, R. B. and Reddy, Y. D.; ”Synthetic Reactions of Coumarin-3-(4-aminosulfonyl-Carboanlide Derivatives with Active Methylene Compounds ” Ind. J. Chem. 2B, 176. (1983)

3) Khodairy, A. ”Synthesis of Some New Heterocyclic Compounds from Benzopyrano [2,3-c] Pyrazol-3-one Derevatives” Synthetic Communications Vol. 31, Issue 17PP 2697 – 2712, (2001).

4) Ahmed, M. M. El-Saghier; Mahbouba, B. N.; Bahlul Kh. R.; Nabil A. S.; and Khaled M. “Synthesis and antibacterial activity of some new fused chromenes” ARKIVOC (xvi) 83-91 (2007).

5) Lévai, A.; Katalin, E. K. and Jekő, J.” Synthesis of tricyclic fused pyrazolines by the reaction of 3-arylidenechromanones and 3-arylidene-1-thiochromanones with hydrazine” ARKIVOC (viii) 26-39 (2007).

6) Ramalingam, K.; Thyvelikakath, G. X.; Berlin, K. D.; Chesnut, R. W.; Brown, R. A.; Durham, N. N.; Ealick, S. E.; Van der Helm, D. J. Med. Chem., 20, 847 (1977).

7) Singh, S., Bharti, N. and Mohapatra, P. ”Chemistry and Biology of Synthetic and Naturally Occurring Antiamoebic Agents“, Chem. Rev., 109 (5), pp 1900–1947(2009).

8) Ayoub, M. T.; Al-Hamdany, R. and Al-Bayati, R. I. ”Synthesis of some substituted 3-aryl-5, 5-dimethyl-2-pyrazolines *Journal of the Iraqi Chemical Societ*y, 10(2), 131-40. ISSN: 0379-8321; (1985).

9) Dhar, D. N. “The Chemistry of Chalcones and Related Compounds’; Wiley-Interscience: NewYork (1981).

10) Lévai, A. ”Synthesis of exocyclic α,β -unsaturated ketones” ARKIVOC (vii) 15-33; (2004).

11) Saied, S. M. "Synthetic studies of important heterocyclic compounds"; (2000), PhD Thesis, Department of Chemistry, College of science; University of Mosul, Iraq(2000).

12) Shandala, M. Y. Ayoub, M. T. and Noori, M. S. "Synthesis of 5-substituted 1,3,4-oxadiazoline-2-thiones and related compounds derived from diphenyl acetic acid (part ii). J. Raf. Sci, Chemistry Special Issue,1.(2002)

13) Keane, D. D.; Marathe, K. G.; Teague, P. C.; Sullivan, W. I. O.; Philbin, E. M. and Simons, R. M. ”Configuration and conformation of 3-arylideneflavanones” J. Org. Chem., 35 (7), pp 2286–2290 (1970).

14) Potgieter, E. D., “Conformational Analysis of Oligomeric Profisetidins"; PhD Thesis, Department of Chemistry, Faculty of Natural and Agricultural Sciences, University of the Free State Bloemfontein, South Africa (2007).