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# 3-Formylchromones as diverse building blocks in heterocycles synthesis

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ABSTRACT

This review covers the chemical reactivity of 3-formylchromones towards condensation reactions with a variety of carbon and nitrogen nucleophiles. Some chromone derivatives linked a variety of heterocyclic systems were prepared from the direct condensation of 3-formylchromones with heterocyclic compounds containing active methylene groups. A diverse number of fused heterocyclic systems were prepared from the reaction of 3-formylchromones with some bifunctional nucleophiles, these reactions mainly proceed via condensation with the aldehydic function followed by nucleophilic attack at C-2 position of the chromone moiety.

## 1. Introduction

Chromone derivatives are widely known as an important class of biologically active compounds. The chemical reactivity of 3-substituted chromones is widely different depending on the nature of the functional group present at the position 3 and the reaction conditions. Among the 3-functionalized chromones, their 3-formyl derivatives are widely used in heterocyclic synthesis. 3-Formylchromones are also known as 4-oxo-4*H*-1-benzopyran-3-carboxaldehydes, 4-oxo-4*H*-chromene-3-carboxaldehydes and chromone-3-carboxaldehydes. Although many methods are known for the synthesis of 3-formylchromones, Vilsmeier-Haack reaction on substituted 2-hydroxyacetophenones is the most suitable among them [1-17]. In Vilsmeier-Haack reaction, the reaction takes place via double formylation of *o*-hydroxyacetophenones followed by cycloaddition with concomitant dehydration (Scheme 1). DMF-$POCl_3$ plays a dual role of a reagent as well as a solvent. A variety of substituted 3-formylchromones **1a-z** were prepared under traditional and microwave irradiation using Vilsmeier-Haack reagent and are reported herein.

## 2. Chemical reactivity of 3-formylchromones

3-Formylchromones, **1a-z**, are a versatile synthons for the synthesis of a variety of novel heterocyclic systems possessing diverse biological activities. From a synthetic view point, 3-formylchromones,**1a-z**, occupy an important position in the synthesis of various heterocyclic systems, due to the availability of three electron deficient sites, the aldehydes carbon, C-2 carbon, and the C-4 carbon of the carbonyl group. Also, 3-formylchromones are able to serve as a heterodiene as well as a dienophile or a Michael acceptor. Moreover, a variety of fused heterocycles were prepared directly from the reaction of compounds **1a-z** with some bifunctional nucleophiles. The present review aims to study the chemical reactivity of 3-formylchromones towards a variety of carbon and nitrogen nucleophiles under different reaction conditions.

### *2.1. Chemical reactivity of 3-formylchromones towards active methyl and methylene compounds*

#### *2.1.1. Condensation reactions with active methyl compounds*

Condensation reactions of 3-formylchromone **1a-c**, **h** with substituted acetophenone **2** in freshly distilled pyridine or glacial acetic acid containing perchloric acid afforded substituted 3-(3-oxo-3-arylprop-1-enyl)chromones, **3** (Scheme 2) [18-21].

4-Hydroxy-1-alkyl-3-[3-(4-oxo-4*H*-chromen-3-yl)]quinolin-2(1*H*)-ones (**5**) were smoothly obtained *via* a Knoevenagel condensation of 3-formylchromone (**1a**) with 3-acetyl-4-hydroxy-1-alkylquinolin-2(1*H*)-one (**4**) in ethanol containing piperidine as basic catalyst (Scheme 3) [22,23].

Interaction of equimolar amount of 3-formyl-6-chlorochromone (**1c**) with 4-acetyl-5,6-diphenylpyridazin-3(2*H*)-one (**6**) in sodium ethoxide afforded 4-[3-(6-chloro-4-oxochromen-3-yl)prop-2-enoyl]-5,6-diphenylpyridazin-3(2*H*)-one (**7**) in 87% yield. When this reaction was carried out in ethanol containing few drops of piperidine, 7-(6-chloro-4-oxochromen-3-yl)-3,4-diphenyl-6,7-dihydropyrano[2,3-*c*]-pyraidazin-5-one (**8**) was obtained in 55% yield, *via* intramolecular cycloaddition reaction in compound **7** (Scheme 4) [24].

Treating 3-formylchromones **1a-c** with 5-acetylbarbituric acid (**9a**) and 5-acetylthiobarbituric acid (**9b**), in ethanol containing pyridine or water-Zn(L-proline)$_2$, gave the corresponding α,β-unsaturated ketones, **10a**,**b** (Scheme 5) [25].

Similarly, treating 3-formylchromones **1a**,**b** with 5-acetyl-1,3-dimethylbarbituric acid (**11**) under the same reaction conditions afforded 1-(1,3-dimethyl-2,4,6-pyrimidinetrione-5-yl)-3-(4-oxo-4*H*-chromen-3-yl)-2-propen-1-one (**12a**) and


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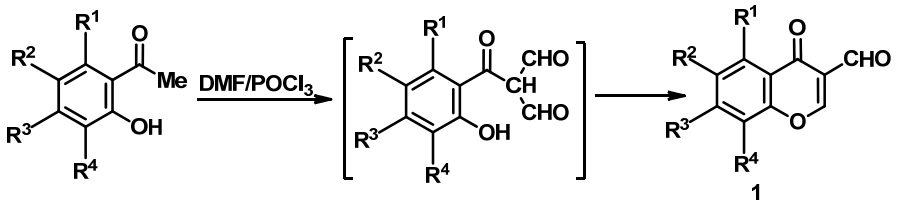
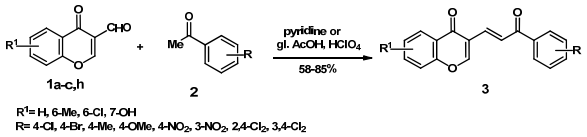


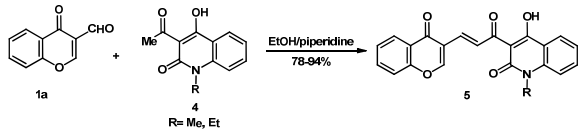

| 1 | R¹ | R² | R³ | R⁴ | Yield (%) | M.p.(°C) |
|---|---|---|---|---|---|---|
| a | H | H | H | H | 63 | 150-151 |
| b | H | Me | H | H | 65 | 174-175 |
| c | H | Cl | H | H | 72 | 166-168 |
| d | H | Br | H | H | 57 | 190-191 |
| e | H | F | H | H | 76 | 155-160 |
| f | H | OH | H | H | 55 | 210-212 |
| g | H | $NO_2$ | H | H | 82 | 253-254 |
| h | H | H | OH | H | 41 | 269 |
| i | H | H | OMe | H | 62 | 188-190 |
| j | H | OMe | H | H | 65 | 174-175 |
| k | H | H | H | allyl | 42 | 73-74 |
| l | H | Me | Me | H | 63 | 192-193 |
| m | Me | H | Me | H | 68 | 145-147 |
| n | H | Me | H | Me | 61 | 187-190 |
| o | H | Me | H | Cl | 69 | 170-171 |
| p | H | Me | Cl | H | 45 | 166-167 |
| q | H | Cl | H | Cl | 46 | 169-174 |
| r | H | Br | H | Br | 40 | 177-178 |
| s | H | Cl | H | $NO_2$ | 67 | 108 |
| t | H | Cl | H | Br | 65 | 155 |
| u | H | Me | H | $NO_2$ | 69 | 180 |
| v | H | Me | H | Br | 66 | 145 |
| w | H | $NO_2$ | H | Br | 63 | 81 |
| x | H | OH | H | H | 68 | 198 |
| y | H | H | OH | $NO_2$ | 64 | 162 |
| z | H | H | OH | Br | 74 | 210 |

**Scheme 1**

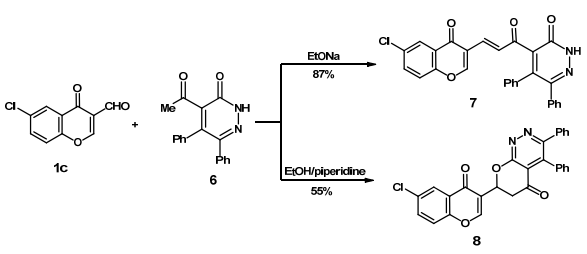
1-(1,3-dimethyl-2,4,6-pyrimidinetrione-5-yl)-3-(6-methyl-4-oxo-4*H*-chromen-3-yl)-2-propen-1-one (**12b**), respectively (Scheme 6) [26].



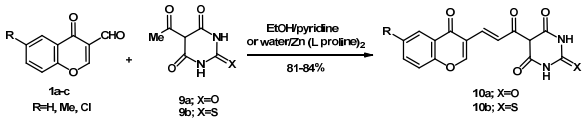

**Scheme 2**



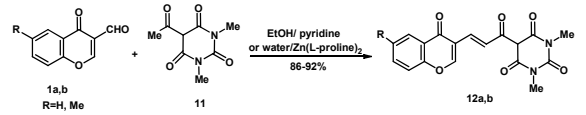

**Scheme 3**




**Scheme 4**

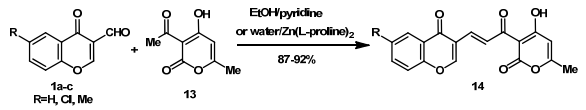



**Scheme 5**



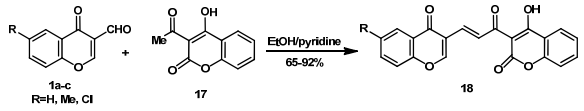

**Scheme 6**

Condensation of 3-formylchromones **1a-c** with dehydroacetic acid (**13**) in ethanol containing pyridine or water-Zn(L-proline)$_2$ gave α,β-unsaturated ketones **14** in high yields (87-92%) (Scheme 7) [26].



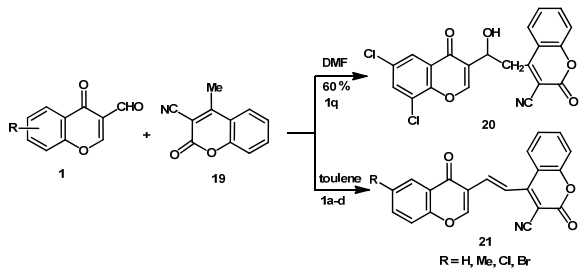

**Scheme 7**

Refluxing 3-formylchromones **1a-c** with 3-acetyl-4-hydroxycoumarin (**17**) in ethanol containing pyridine as a basic catalyst gave 1-(4-hydroxychromen-2-one-3-yl)-3-(chromen-4-one-3-yl)-2-propen-1-ones (**18**) in 65-92% yields (Scheme8) [26,27].



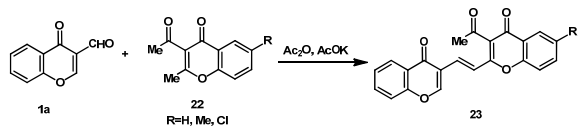

**Scheme 8**

Reaction of 6,8-dichloro-3-formylchromone (**1q**) with 4-methyl-2-oxo-2*H*-chromone-3-carbonitrile (**19**) gave the addition product **20** as recently reported by El-Shaaer [28]. While Melikyan *et al*. [29] isolate the condensation products **21** on the reaction of **1a-d** with compound **19** in refluxing toluene (Scheme 9).



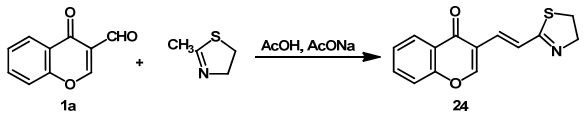

**Scheme 9**

Condensation of 3-formylchromone (**1a**) with 2-methyl-3-acetylchromones **22** in acetic anhydride-potassium acetate led to *bis*-chromonylethylene **23** (Scheme 10). This reaction occurred only at 2-methyl group [30].



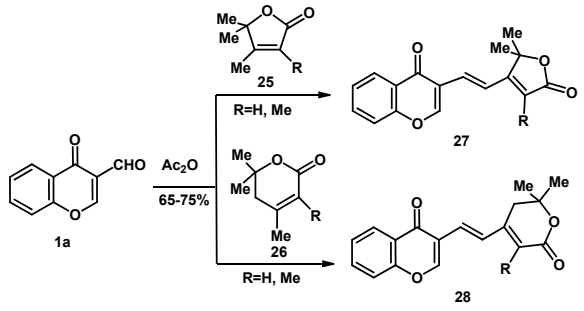

**Scheme 10**

2-(4-Oxo-4*H*-chromen-3-yl)vinylthiazoline (**24**) was synthesized by condensation of 3-formylchromone **1a** with 2-methylthiazoline in glacial acetic acid containing sodium acetate (Scheme 11) [31].



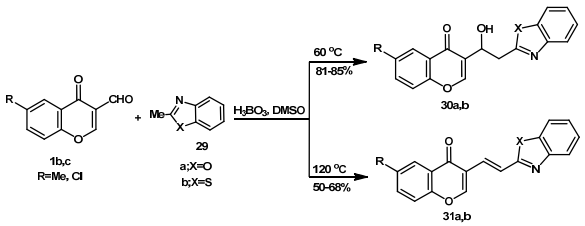

**Scheme 11**

Condensation of 3-formylchromone (**1a**) with 4,5,5-trimethyl-2,5-dihydrofuran-2-ones **25** and 4,6,6-trimethyl-5,6-dihydropyran-2-ones **26** in acetic anhydride yielded the condensation products **27** and **28**, respectively (Scheme 12) [29].



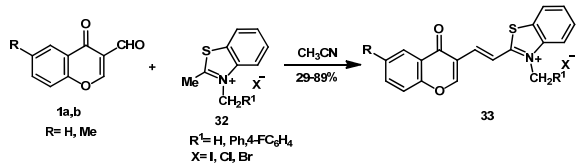

**Scheme 12**

3-Formylchromones **1b**,**c** reacted with 2-methylbenzimidazole **29a** and 2-methylbenzothiazole **29b** in dry DMSO and boric acid to give the addition products **30a**,**b** when the reactiontook place at 60 °C, but when the reaction took place at 120 °C afforded the condensation products **31a**,**b** (Scheme 13) [32].



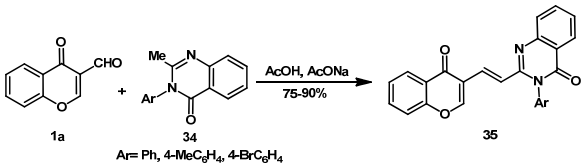

**Scheme 13**

Condensation of aldehydes **1a**,**b** with 2-methylbenzothiazolium halides **32** in boiling acetonitrile gave chromenylbenzothiazolium derivatives **33** (Scheme 14) [33].




**Scheme 14**

Treatment of 3-formylchromone **1a** with 3-aryl-2-methyl-4(3*H*)-quinazolinones (**34**) in glacial acetic acid containing fused sodium acetate led to the condensed product **35** (Scheme 15) [33].

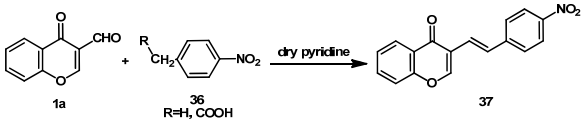



**Scheme 15**

As a result of the above reactions, a variety of chromone derivatives bearing various heterocyclic systems were obtained from the condensation of 3-formylchromones with some active methyl compounds either under acidic or basic conditions.

### *2.1.2. Condensation reactions with acyclic active methylene compounds*

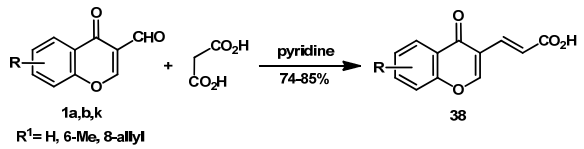
3-Styrylchromone **37**, which is associated with important biological activities, was obtained by the condensation of 4-nitrotoluene or 4-nitrophenylacetic acid **36** with 3-formyl-chromone **1a** in dry pyridine (Scheme 16) [34,35].




**Scheme 16**

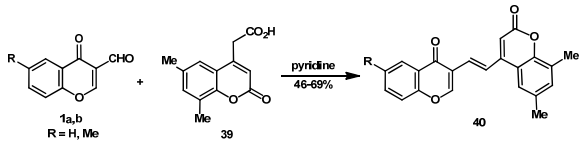
Synthesis of *trans*β-(chromon-3-yl)acrylic acids **38** were made by simple Knoevenagel condensation of 3-formyl-

chromones **1a**,**b**,**k** with malonic acid in dry pyridine under reflux (Scheme 17) [17,36-38].



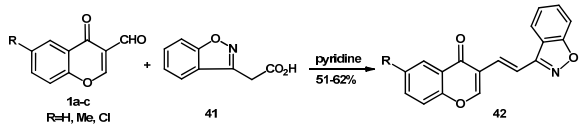

**Scheme 17**

6,8-Dimethylcoumarin-4-acetic acid (**39**) gave 3-styryl-chromones **40** when reacted with 3-formyl-chromones **1a**,**b** in boiling pyridine, *via* condensation followed by decarboxylation under the reaction conditions (Scheme 18) [39].



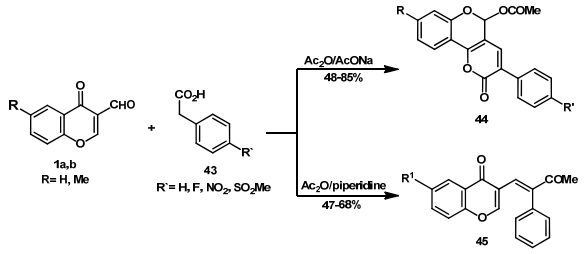

**Scheme 18**

In the same manner, 3-formylchromones **1a-c** reacted with benzo[*d*]isoxazol-3-ylacetic acid (**41**) in dry pyridine under reflux to give 3-(2-benzo[*d*]isoxazol-3-ylvinyl)-chromon-4-ones **42** in51-62% yields (Scheme 19) [40].



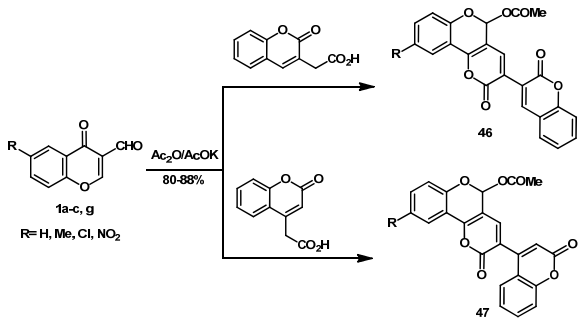

**Scheme 19**

Heating equimolar quantities of 3-formylchromones **1a**,**b** and phenylacetic acids **43** in acetic anhydride containing catalytic amounts of sodium acetate or potassium carbonate gave methyl 2-oxo-2*H*,5*H*-pyrano[3,2-*c*]chromen-5-yl acetates **44** in 48-85% yields (Scheme 20), [41-43] while Shingare *et al*. [44] reported the formation of compounds **45** in 47-68% yields in acetic anhydride containing piperidine as a catalyst, the spectral data showed the presence of acetyl instead of the carboxy group, which could be explained by decarboxylation followed by acetylation in *situ* (Scheme 20).



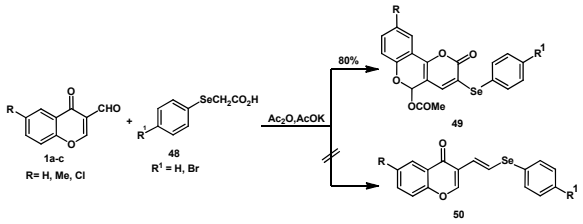

**Scheme 20**

Condensation of 3-formylchromones **1a-c**,**g** with 3- or 4-coumarinylacetic acids in acetic anhydride in the presence of potassium acetate either by heating at 90-100 °C or by microwave irradiation produced compounds **46** and **47**, respectively (Scheme 21) [41].



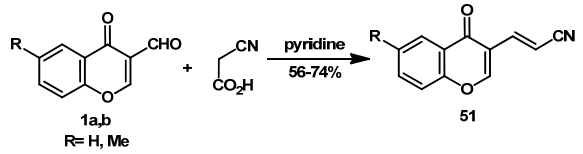

**Scheme 21**

Reactions of 3-formylchromones **1a-c** with 4-substituted phenylselenylacetic acids **48** in acetic anhydride containing potassium acetate yielded 3-(phenylselenyl)-2-oxo-2*H*,5*H*-pyrano[3,2-*c*]chromen-5-yl acetates **49** and not the other expected products **50** (Scheme 22) [45].



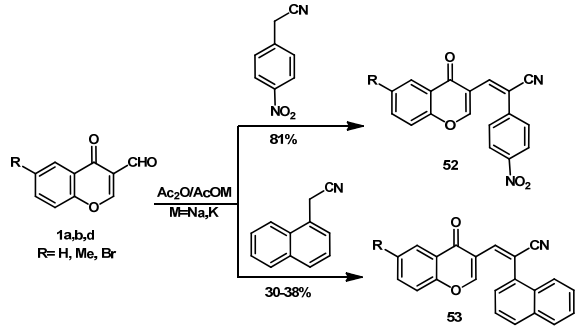

**Scheme 22**

Synthesis of *trans*-*β*-(4-oxo-4*H*-chromen-3-yl)acrylonitrile **51** was made by simple condensation of 3-formylchromones **1a**,**b** with cyanoacetic acid in dry pyridine under reflux (Scheme 23) [46,47].



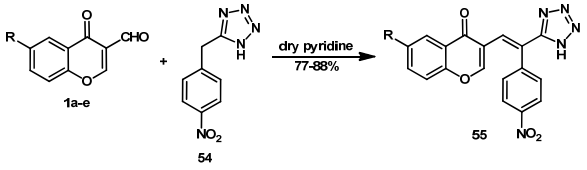

**Scheme 23**

Condensation of 3-formylchromones **1a**,**b**,**d** with *p*-nitrobenzyl cyanide and 1-naphthyl-acetonitrile in the presence of Ac2O/AcOK or Ac2O/AcONa afforded the corresponding condensation products **52** and **53**, respectively (Scheme 24) [48].



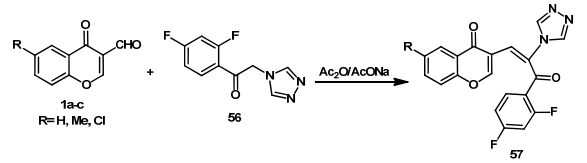

**Scheme 24**

Similarly, condensation of 3-formychromones **1a**, with tetrazolyl-*p*-nitrotoluene (**54**) in dry pyridine gave 3-[2-(4-nitrophenyl)-2-(1*H*-tetrazol-5-yl)vinyl)]-4*H*-chromen-4-one (**55**) (Scheme 25) [49].



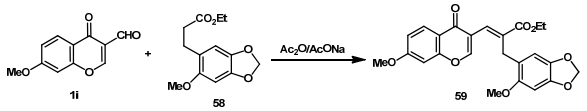

**Scheme 25**

3-Formylchromones **1a-c** condensed with 1-(2,4-difluorophenyl-2-[1,2,4]triazol-4-yl]ethanone (**56**) in acetic anhydride containing anhydrous sodium acetate to afford 3-[3-(2,4-difluorophenyl)-3-oxo-2-[1,2,4]triazol-4-yl)propenyl] chromon-4-ones (**57**) (Scheme 26) [50].



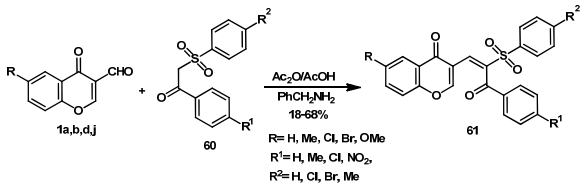

**Scheme 26**

Knoevenagel condensation of 3-formyl-7-methoxy chromone **1i** with ethyl 3-(6-methoxy-1,3-benzodioxol-5-yl) propanoate **58** gave ethyl ester **59** (Scheme 27) [51].



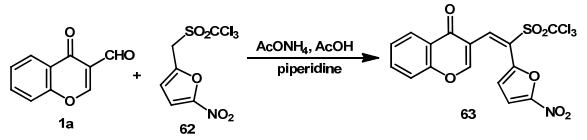

**Scheme 27**

Condensation of 3-formylchromones **1a**,**b**,**d**,**j** with phenacyl aryl sulfones **60**, in glacial acetic acid and acetic anhydride in the presence of benzylamine as catalyst, yielded 1-(aroyl)-1-(arylsulfonyl)- 2-[4-oxo-4*H*-chromen-3-yl]ethenes **61** (Scheme 28) [52].



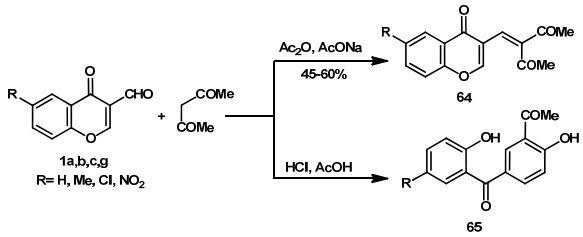

**Scheme 28**

When 3-formylchromone (**1a**) was treated with 5-nitro furyl trichloromethyl sulfone (**62**), in glacial acetic acid in the presence of ammonium acetate and piperidine, gave the condensation product **63** (Scheme 29) [52].



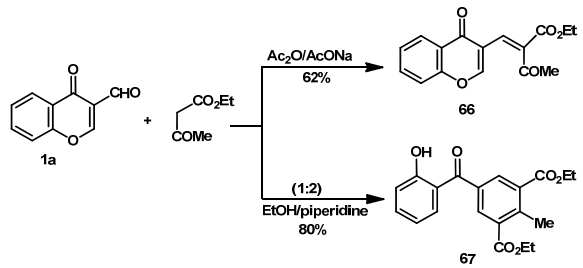

**Scheme 29**

Condensation product **64** was synthesized by reaction of 3-formylchromones **1a**,**b**,**c**,**g** and 2,4-pentanedione in acetic anhydride containing sodium acetate. While, acid catalyzed 1,4-addition of the enol form of 2,4-pentanedione to 3-formyl chromones **1a**,**b**,**c**,**g** followed by ring opening and enolization afforded 5-benzoyl-2-hydroxyacetophenones **65** (Scheme 30) [53,54].



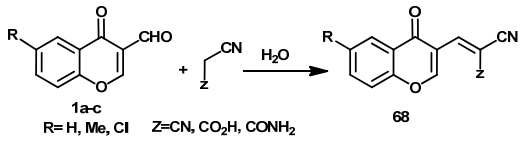

**Scheme 30**

Treatment of 3-formylchromone (**1a**) with ethyl acetoacetate in acetic anhydride containing sodium acetate yielded 3-(4-oxo-4*H*-1-chromen-3-yl)-2-(1-oxoethyl)-2-propenoic acid ethyl ester (**66**) in 62% yield. However, when the reaction was carried out with a (1:2) excess of the reagent using piperidine in ethanol, 5-(2-hydroxybenzoyl)-2-methylbenzene-1,3-dicarboxylic acid diethyl ester (**67**) was isolated in 80% yield (Scheme 31) [54,55].



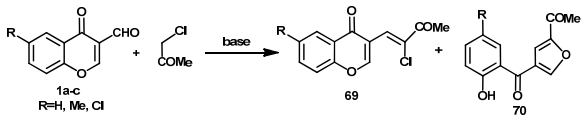

**Scheme 31**

Knoevenagel condensation of 3-formylchromones **1a-c** with malononitrile, cyanoacetic acid and cyanoacetamide were carried out in various solvents such as water, ethanol, methanol, DMF, DMSO and toluene (Scheme 32). Among these solvents, water was found to be the best solvent for the reaction to produce ylidenenitriles **68** in excellent yields [56].



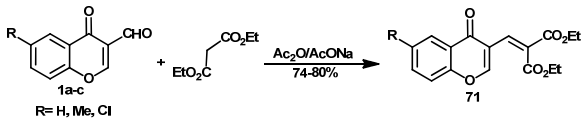

**Scheme 32**

Reaction of aldehyde **1a-c** with chloroacetone in basic medium gave a mixture of arylidine **69** (22-32%) and *o*-hydroxyphenyl furyl ketone **70** (Scheme 33) [57].



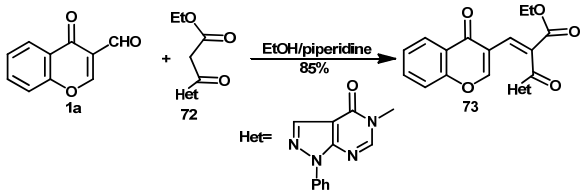

**Scheme 33**

Condensation of 3-formylchromones **1a-c** with diethyl malonate in acetic anhydride containing sodium acetate gave diethyl arylidine ester **71** in 74-80% yield (Scheme 34) [58].



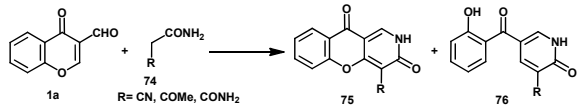

**Scheme 34**

Treatment of 3-formylchromone (**1a**) with 3(4`,5`-dihydro-4`-oxo-1`-phenylpyrazolo[3,4-*d*]pyrimidin-5`-yl)-3-oxopropionic acid ethyl ester (**72**) in ethanol containing piperidine afforded 3-{(4-oxo-4*H*-chromen-3-yl)-2-(4,5-dihydro-4-oxo-1-phenylpyrazolo[3,4-*d*]pyrimidine-5`-carbonyl}acrylic acid ethyl ester (**73**) (Scheme 35) [59].



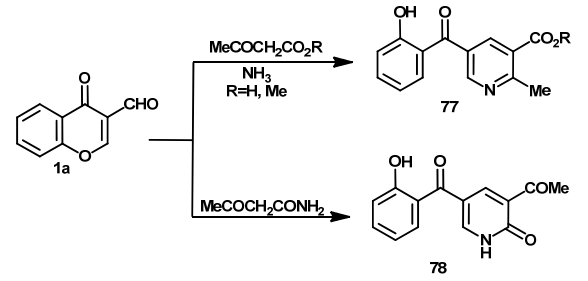

**Scheme 35**

3-Formylchromone (**1a**) reacted with acetamides **74** in dry pyridine to afford a mixture of chromenopyridones **75** and pyridone derivatives **76** (Scheme 36) [60,61].



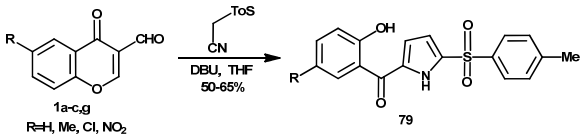

**Scheme 36**

3-Formylchromone **1a** condensed with alkyl acetoacetate or its acid in the presence of ammonia to give the pyridine derivatives **77** (46-50%). While, aldehyde **1a** condensed with acetoacetamide to produce the 2-pyridone derivative **78** (Scheme 37). The reaction involves ring opening of pyrone moiety at $C_2$ [62-64].



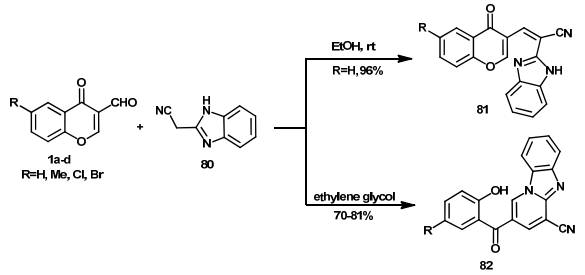

**Scheme 37**

When 3-formylchromones **1a-c**,**g** were allowed to react with equimolar amounts of tosylmethyl isocyanide (TOSMIC) in THF in the presence of mild base as 1,8-diazabicyclo[5,4,0] undec7-ene (DBU) at room temperature, the 2-tosyl-5-(2-hydroxybenzoyl)pyrroles **79** were isolated in good yields (Scheme 38) [65].



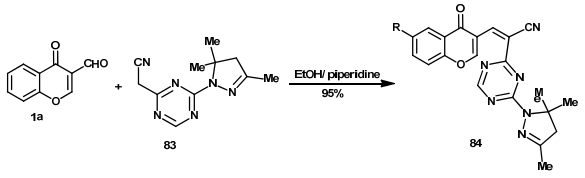

**Scheme 38**

Condensation of 3-formylchromones **1a-d** with 1*H*-benzimidazole-2-acetonitrile (**80**) in ethanol at room temperature gave the carbonitrile derivative **81** in 96%. When the reaction was carried out with in boiling ethylene glycol, 4-cyano-2-(2-hydroxybenzoyl)pyrido[1,2-*a*]benzimidazoles **82** were obtainedin 70-81% yields (Scheme 39) [66,67]



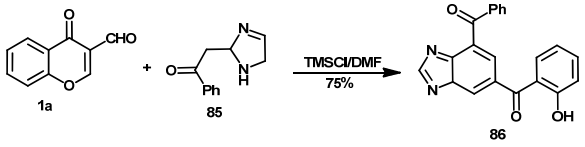

**Scheme 39**

Refluxing **1a** with pyrazolinyltriazinylacetonitrile (**83**) in ethanol containing few drops of piperidine gave the condensation product **84** in 95% yield, as antitumor agent (Scheme 40) [68].



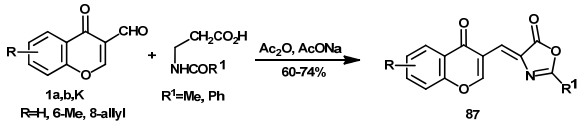

**Scheme 40**

Condensation of **1a** with imidazole derivative **85** in $Me_3SiCl$/DMF produced the imidazo[1,2-*a*] pyridine **86** in 75% yield (Scheme 41) [69].




**Scheme 41**

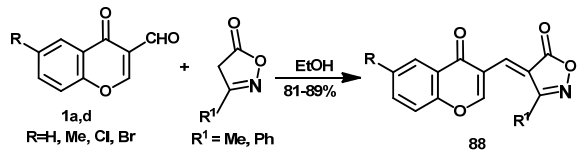
Oxazolones **87** were readily obtained from the reaction of 3-formylchromones **1a**,**b** and *N*-acetyl/ benzoylglycine in acetic anhydride containing freshly fused sodium acetate (Scheme 42) [17,70,71].




**Scheme 42**

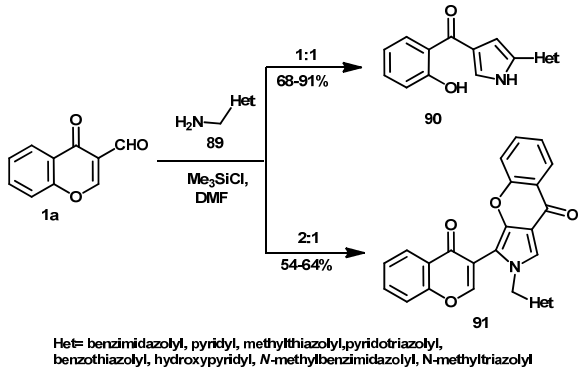
On the other hand, the isoxazolone derivatives **88** were obtained in good yields (81-89%) from the Knoevenagel condensation of 3-formylchromones **1a-d** with 3-methyl (or

phenyl)-5-isoxazolone in ethanol at room temperature (Scheme 43) [72].



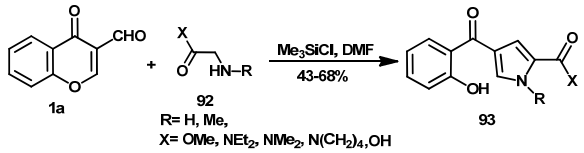

**Scheme 43**

3-Formylchromone **1a** reacted with hetarylmethylamines **89** in DMF under heating by molar ratio 1:1 in the presence of 4 molar equivalents of $Me_3SiCl$ (trimethylsilyl chloride) to give 5-hetaryl-[1*H*-pyrrol-3-yl](2-hydroxyphenyl)methanones **90** in 68-91% yields. When the reaction carried out in molar ratio 2:1 (3-formylchromone: amines), the fused chromonopyrrolyl chromones **91** were obtainedin 54-64% yields (Scheme 44) [73].



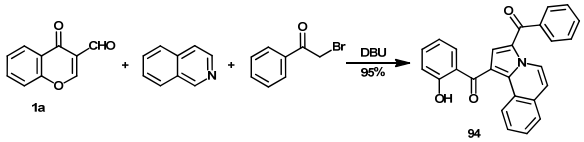

**Scheme 44**

Cyclocondensation of 3-formylchromone **1a** with glycine derivatives **92** in the presence of $Me_3SiCl$ (4 equivalents) afforded pyrrole derivatives **93** in moderated yield (Scheme 45) [73].




**Scheme 45**

A high yield of the novel pyrrolo[2,1-*a*]isoquinoline derivative **94** was prepared from the reaction of 3-formyl chromone **1a** with isoquinoline and phenacyl bromide in aqueous medim containing DBU as a catalyst as reported by Naskar *et al*. (Scheme 46) [74].

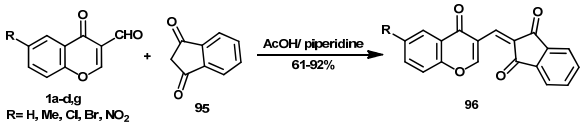



**Scheme 46**

Therefore, condensation of 3-formylchromones with acyclic active methylene compounds produced the corresponding condensation products or a variety of products depending on the reagent used and the reaction conditions.

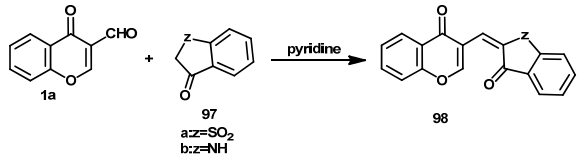
### *2.1.3. Condensation reactions with cyclic active methylene compounds*

Condensation of 3-formylchromones **1a**-**d**,**g** with 1,3-indandione **95** in glacial acetic acid containing piperidine afforded the condensation products **96** in 61-92% yields (Scheme 47) [75].



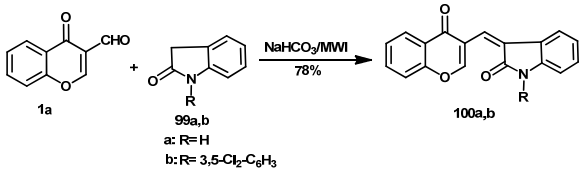

**Scheme 47**

Treatment of 3-formylchromone **1a** with 3-oxo-2,3-dihydrobenzo[*b*]thiophene-1,1-dioxide **97a** and oxindole (indolone) **97b** in dry pyridine afforded the corresponding condensation products **98** (Scheme 48) [76].



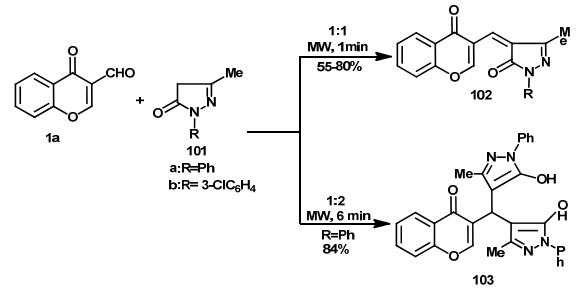

**Scheme 48**

Simple condensation of aldehyde **1a** with indolinone **99a**,**b** in the presence of sodium bicarbonate under microwave irradiationyielded (1*H*)-3-(4-oxo-4*H*-chromen-3-yl) methylene] indolin-2-one (**100a**) and 1-[(2,6-dichlorophenyl)-3-(4-oxo-4*H*-chromen-3-yl)methylene] indolin-2-one (**100b**), respectively (Scheme 49) [76,77].




**Scheme 49**

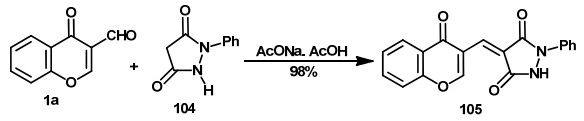
Condensation reaction of **1a** and pyrazolone derivatives **101a**,**b** in 1:1 molar ratio, under classical method or microwave irradiation, afforded 1-aryl-3-methyl-4-(4-oxo-4*H*-chromen-3-yl)methylene]pyrazol-5(4*H*)-ones (**102a**,**b**), [77,78] while using 1:2 molar ratio afforded the new 1-(chromon-3-yl)-1,1-*bis*(4-hydroxy-6-methyl-2-oxo-2*H*-pyran-3-yl)methane **103** (Scheme 50) [79].




**Scheme 50**

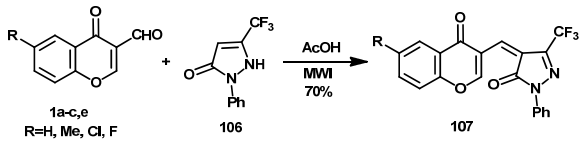
Condensation of 3-formylchromone (**1a**) with 1-phenylpyrazolidine-3,5-dione (**104**) in glacial acetic acid containing freshly fused sodium acetate, gave 4-[(4-oxo-4*H*-

chromen-3-yl)methylene]-1-phenyl-pyrazolidine-3,5-dione (**105**) (Scheme 51) [80].



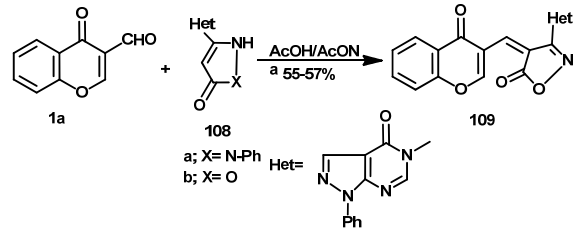

**Scheme 51**

Also, treatment of 3-formylchromones **1a-c,e** with 3-(trifluoromethyl)-1-phenyl-1*H*-pyrazol-5(4*H*)-one (**106**) in acetic acid yielded 3-(trifluoromethyl)-4-[(6-substituted 4-oxo-4*H*-chromon-3-yl)methylene]-1-phenyl-1*H*-pyrazol-5(4*H*)-ones **107** in70% yield (Scheme 52) [81].



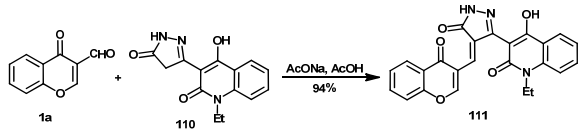

**Scheme 52**

Condensation of **1a** with pyrazolinone **108a** and isoxazolinone **108b** in acetic acid containing fused sodium acetate gave 5{4-[(4-oxo-4*H*-chromen-3-yl)methylene-5-oxo-4,5-dihydro-1*H*-pyrazol-3-yl)]}-1-phenylpyrazolo[3,4-*d*] pyrimidin-4-one **109a** and 5-{4-[(4-oxo-4*H*-chromen-3-yl)methylene-5-oxo-4,5-dihydroisoxazol-3-yl)]}-1-phenyl pyrazolo[3,4-*d*]pyrimidin-4-one **109b**, respectively (Scheme 53) [59].




**Scheme 53**

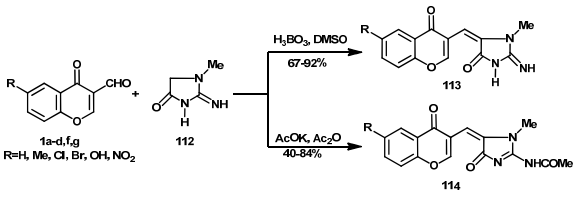
Similarly, condensation of 3-formylchromone (**1a**) with pyrazol-3-ylquinoline derivative **110** in glacial acetic acid containing sodium acetate afforded chromenylpyrazolinone **111** (Scheme 54) [82].



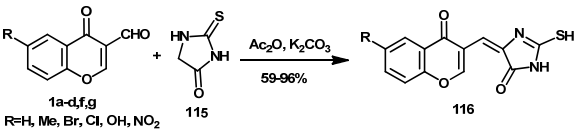

**Scheme 54**

Also, condensation of **1a-d,f,g** with creatinine **112** in DMSO using boric acid as a catalyst yielded 2-imino-1-methyl-5-(6-substituted 4-oxo-4*H*-chromen-3-yl)methylidene]imidazolin-4-one (**113**). While, 2-acetamido-1-methyl-5-[(6-substituted 4-oxo-chromen-3-yl)methylidene]-4,5-dihydroimidazol-4-one **114** was obtained when the reaction took place in acetic anhydride and potassium acetate (Scheme 55) [83].

3-Formylchromones **1a-d,f,g** condensed with thiohydantion **115** in acetic anhydride in the presence of potassium acetate under both irradiation and classical condition yielded 2-thioxo-5-[(6-substituted-4-oxo-chromen-3-yl)methylidene]imidazolidine-4-ones (**116**) (Scheme 56) [83].

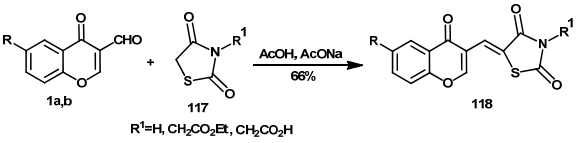



**Scheme 55**



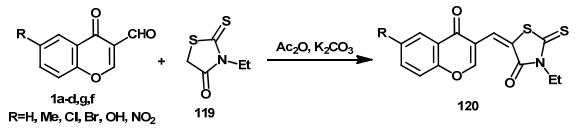

**Scheme 56**

Chromonyl-2,4-thiazolidinediones **118** were prepared by the Knoevenagel condensation of 2,4-TZDs (2,4-thiazolidine diones) **117** with 3-formylchromones **1a**,**b**,**n** in glacial acetic acid containing freshly fused sodium acetate (Scheme 57) [84-86].



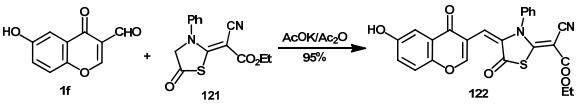

**Scheme 57**

Similarly, condensation of 3-formylchromone **1a-d**,**f**,**g** with 3-ethylrhodanine **119** in acetic anhydride/potassium acetate under both irradiation and classical condition, gave 2-thioxo-5-[(6-substituted-4-oxo-4*H*-chromen-3-yl)methylidene] thiazolidin-4-ones **120** (Scheme 58) [83].




**Scheme 58**

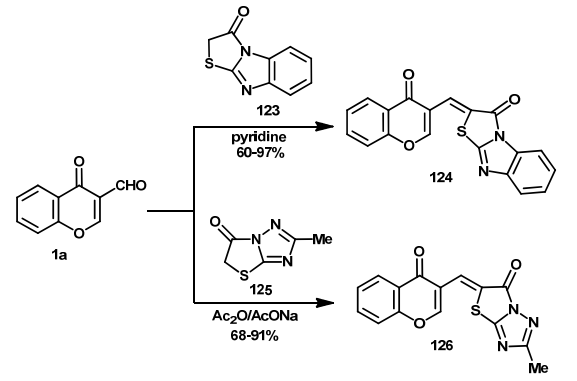
Condensation of carboxaldehyde **1f** with ethyl 2-cyano-2-(3-phenyl-5-oxo-1,3-thiazolan-2-ylidene) acetate (**121**) gave the corresponding arylidene derivative **122** (Scheme 59) [61].



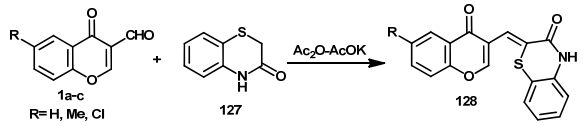

**Scheme 59**

Reaction of 3-formylchromone (**1a**) with [1,3]thiazolo[3,2-*a*]benzimidazol-3(2*H*)-one (**123**) in glacial acetic acid containing fused sodium acetate afforded the condensation product **124** in high yield (60-97%) [87].Similarly, treating **1a** with 2-methyl[1,3]thiazolo[1,2,4]triazol-5(6*H*)-one (**125**) in acetic anhydride/sodium acetate yielded the condensation product **126** in 68-91% yields (Scheme 60) [88].

Knoevenagel products **128** were obtained in low yields (15-43%) by heating 3-formylchromones **1a-c** with 2*H*-1,4-benzothiazin-3(4*H*)-one (**127**) in acetic anhydride/potassium acetate medium for 6-10 h. Using microwave the yields were increased (33-62%) in short time (7-20 min) (Scheme 61) [87].

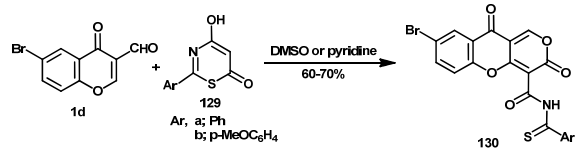



**Scheme 60**




**Scheme 61**

Reaction of 6-bromo-3-formylchromone **1d** with 2-aryl-4-hyrdoxy-6*H*-1,3-thiazin-6-ones **129a**,**b** in DMSO or pyridine gave 8-bromo-3,10-dioxo-*N*-(arylcarbonothioyl)-4,4a-dihydro-3*H*,10*H*-pyrano[4,3-*b*]-chromene-4-carboxamides (**130a**,**b**) in 60-70% yields (Scheme 62) [89].




**Scheme 62**

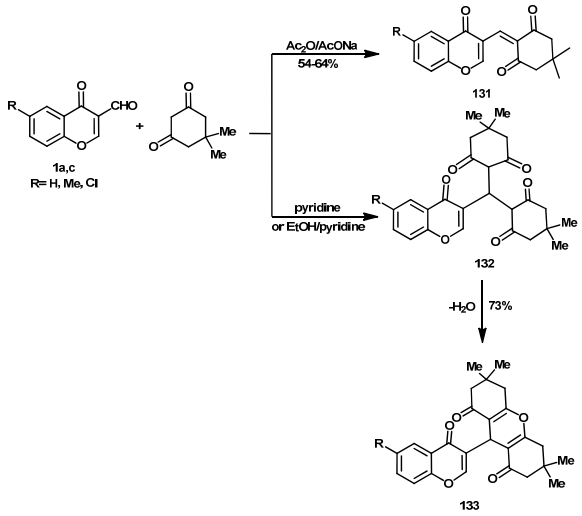
Also, condensation of 3-formylchromone **1a** with dimedone (5,5-dimethylcyclohexane-1,3-dione) in acetic anhydride containing sodium acetate yielded the condensation products **131** in 54-64% [87]. When the reaction took place in aqueous ethanol containing pyridine or aqueous pyridine by molar ratio (1:2) afforded the adduct **132** which dehydrated to formxanthone **133** in 73% yield (Scheme 63) [60,76,90].

Meldrum's acid (2,2-dimethyl-1,3-dioxane-4,6-dione) undergoes Knoevenagel condensation with 3-formylchromone **1a-c**,**e** producing the corresponding condensation product derivatives **134** in 90-95% yields (Scheme 64) [91-93].

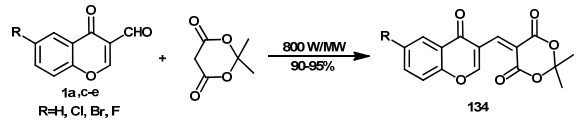
Reaction of 3-formylchromones **1a**,**c** with 4-chromanone **135** in ethanol containing triethylamine gave benzopyrano-2,3-dihydrobenzopyranones **136** in 67-80% yields (Scheme 65) [94].

Treatment of 3-formylchromone (**1a**) with barbituric acid **137a**, thiobarbituric acids **137b** and 1,3-dimethylbarbituric acid **138** gave 5-[(4-oxo-4*H*-chromen-3-yl)methylene] pyrimidine derivatives **139** and **140**,respectively (Scheme 66) [76,77].

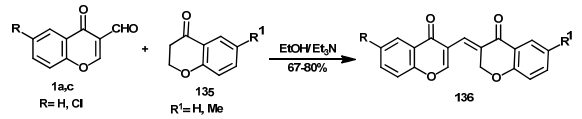
*N*-Methylpyrrole reacted with 3-formylchromones **1a**,**c**,**d**,**g** under solvent–free conditions exclusively *via* 1,4-addition followed by recyclization to form 2-hydroxy-3-(1-methyl-pyrrol-2-ylmethylene)chroman-4-ones **141** in good yield (Scheme 67) [95].



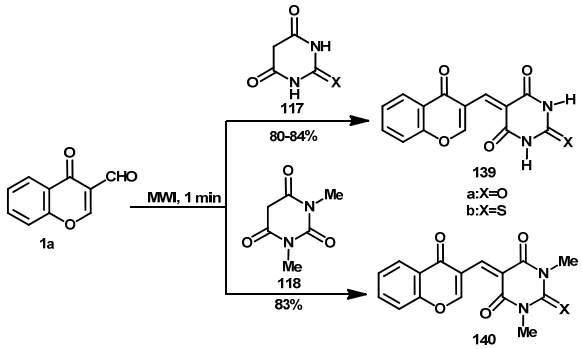

**Scheme 63**



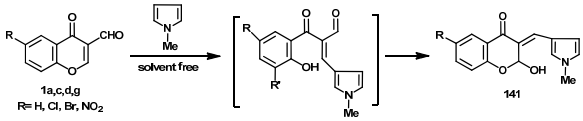

**Scheme 64**




**Scheme 65**

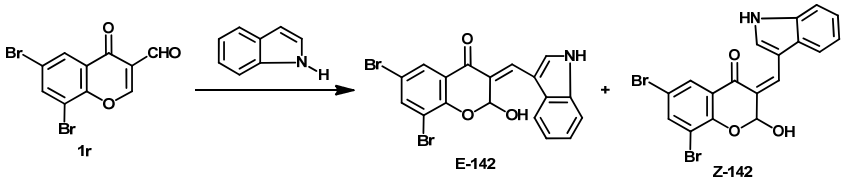



**Scheme 66**

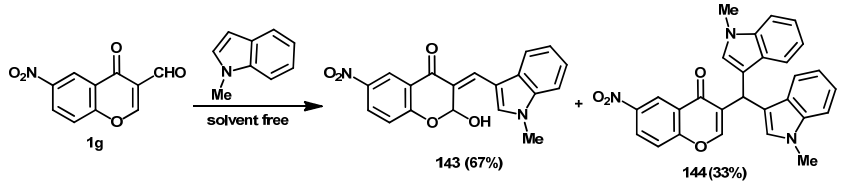



**Scheme 67**

A similar reaction of 6,8-dibromo-3-formylchromone (**1r**) with indole proceeded exclusively *via* 1,4-addition followed by recyclization to form a mixture of *E*-isomer **142** (91%) and *Z*-isomer **142** (9%) (Scheme 68) [95].



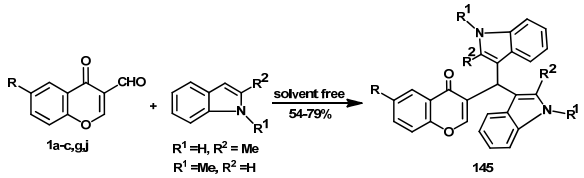

**Scheme 68**




**Scheme 69**

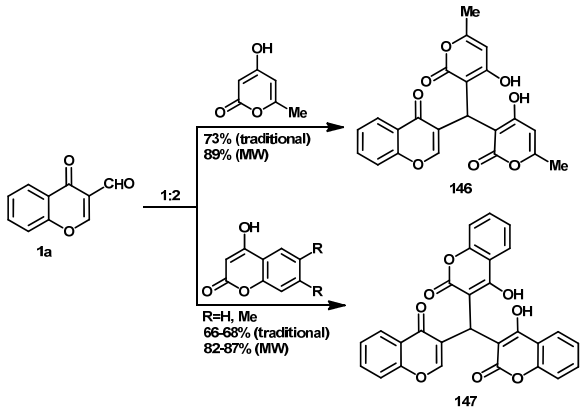
Reaction of 3-formyl-6-nitrochromone (**1g**) with *N*-methylindole afforded a mixture of *E*-(2-hydroxy-6-nitro-3-(1-methyindol-3-ylmethylene)chroman-4-one (**143**)and the *bis*-adduct **144** (Scheme 69) [95].

On the other hand, 3-formylchromones **1a-c,g,j** reacted without solvent with excess indole, 1-methyl or 2-methylindoles (2 equivalents) to give (chromon-3-yl)-*bis*-(indol-3-yl)methanes **145** (Scheme 70) [95].




**Scheme 70**

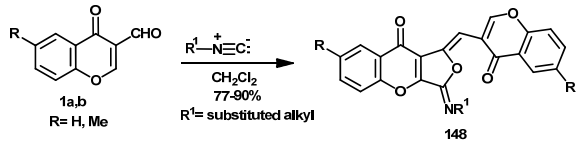
Also, 3-formylchromones **1a** reacted with triacetic acid lactone and 4-hydroxycoumarin derivatives (2 equivalents), under conventional and solvent free methods, to give (chromon-3-yl)-*bis*-(hetaryl)methanes **146** and **147**, respectively (Scheme 71) [79].



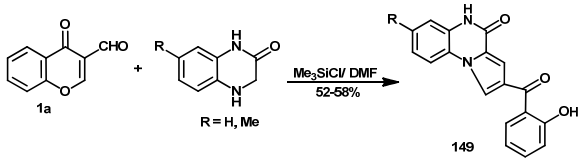

**Scheme 71**

Condensation of 3-formylchromones **1a**,**b** with alkyl isocyanides in dry dichloromethane at room temperature afforded (1*Z*)-3-(alkylimino)-1-[(chromon-3-yl)methylene]-1,3-dihydro-9*H*-furo [3,4-*b*]chromen-9-ones **148** in good yields (77-90%) (Scheme 72) [96].

The reaction of 3-formylchromone **1a** with 3,4-dihydroquinoxalin-2(1*H*)-ones gave 2-(2-hydroxy-benzoyl) pyrrolo[1,2-*a*]quinoxalin-4(5*H*)-ones **149**in 52-58% yields, respectively (Scheme 73) [73].

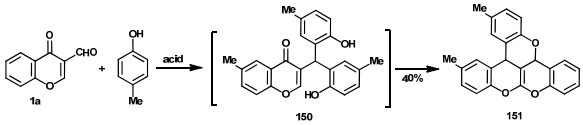



**Scheme 72**



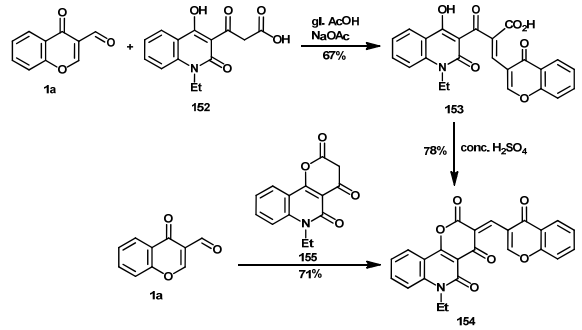

**Scheme 73**

Under acidic conditions, *p*-cresol underwent 1,2-addition through C-2 atom to thealdehyde function of 3-formyl chromone (**1a**) to produce intermediate **150** which, converted to 2,14-dimethyl-10a*H*,15a*H*-tribenzo[*b*,*e*,*i*][1,6,7] trioxaphenalene (**151**) (Scheme 74) [97].




**Scheme 74**

Treating carboxaldehyde **1a** with β-ketoacid **152**, [98] in glacial acetic acid containing freshly fused sodium acetate, yielded the Knoevenagel condensation products **153** which underwent dehydration by stirring in concentrated $H_2SO_4$ at room temperature to afford 3-chromonylmethylenepyrano[3,2-*c*]quinoline derivatives **154**. Moreover, compound **153** was obtained authentically from condensation reaction of pyrano [3,2-*c*]quinoline **155** with **1a** (Scheme 75) [99].



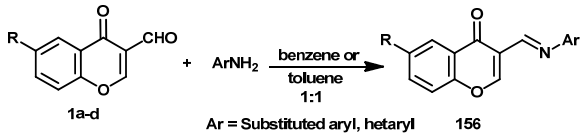
Scheme 75

Thus, a large number of chromone derivatives linked a variety of heterocyclic systems were prepared from the direct condensation of 3-formylchromones with heterocyclic compounds containing active methylene groups.

### *2.2. Chemical reactivity of 3-formylchromones towards nitrogen nucleophiles*

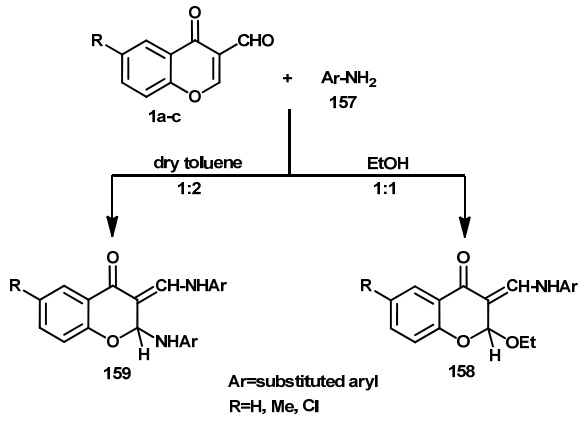
#### *2.2.1. Reactions with primary amines*

A large group of 3-(aryl/heteroaryliminomethyl)chromone derivatives **156** were prepared from condensation reactions of 3-formylchromones **1a-d** with a variety of aryl/hetaryl-aminesin non polar solvents such as benzene, toluene or xylene under reflux, in the presence of *p*-toluenesulfonic acid as a catalyst (Scheme 76) [100-108].



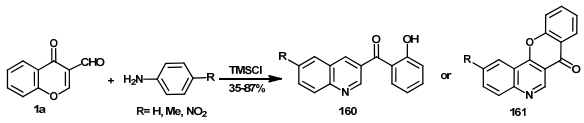
Scheme 76

On the other hand, reaction of 3-formylchromones **1a-c** with equimolar ratio of aryl/hetarylamines **157** in boiling ethanol gave 3-(aryl/hetarylaminomethylene)-2-(ethoxy) chromones **158**, but when the reaction took place with two moles of **157** in dry toluene, the 1,4-adducts **159** were obtained (Scheme 77) [105-115].



Scheme 77

Reaction of 3-formylchromone **1a** with various anilines in the presence of $Me_3SiCl$/DMF led to either 3-(2-hydroxybenzoyl)quinolines **160** or 7*H*-chromeno[3,2-*c*]quinolin-7-ones **161** (Scheme 78), depending on the structure of the starting aniline. Substituents in the aniline molecule that withdraw electrons favored the formation of **161**; on the contrary, electron-rich anilines gave only **160** [116,117].

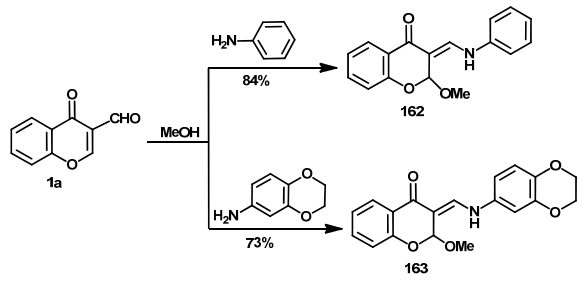


Scheme 78

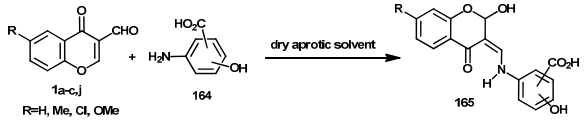
Condensation of 3-formylchromone (**1a**) with aniline and 6-amino-1,4-benzoxodioxane in methanol gave 3-(aniline methylene)-2-methoxychroman-4-one (**162**) and 3-(1,4-benzodioxane-6-aminomethylene)-2-methoxychroman-4-one (**163**), respectively (Scheme 79) [118].

Also, reaction of 6-substituted 3-formylchromone **1a-c,j** with aromatic amino carboxylic acid **164** in benzene or toluene yielded only 3-(arylaminomethylene)-2-hydroxychromon-4-ones **165** at room temperature or under reflux (Scheme 80) [113].

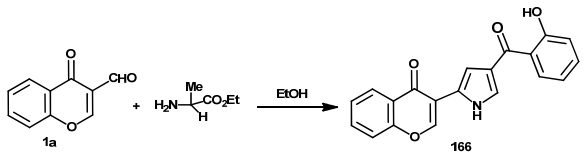
Treatment of 3-formylchromone **1a** with ethyl 2-amino-propanoate yielded pyrrole derivative **166** in high yield (Scheme 81) [119].



Scheme 79

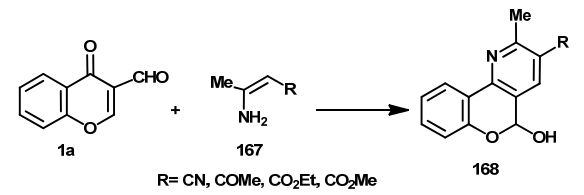


Scheme 80

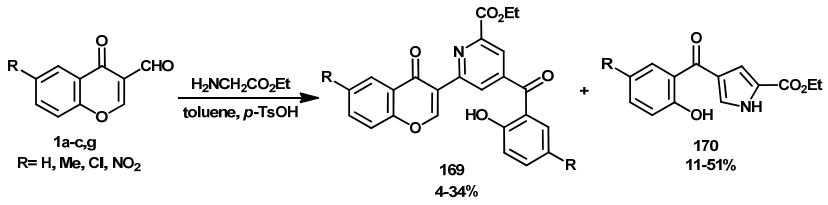


Scheme 81

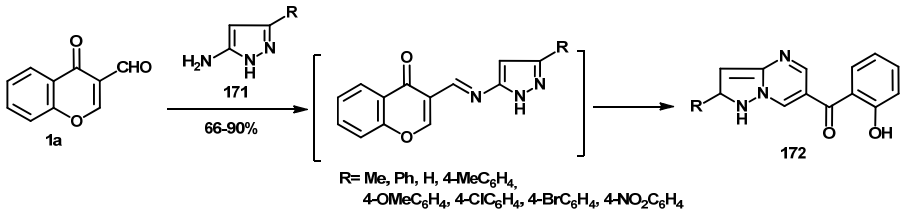
Chromenopyridines **168** were prepared by treating 3-formylchromone **1a** with enaminonitriles, enaminoketones or β-aminoesters **167** (Scheme 82) [63,64,76,120].



Scheme 82




**Scheme 83**

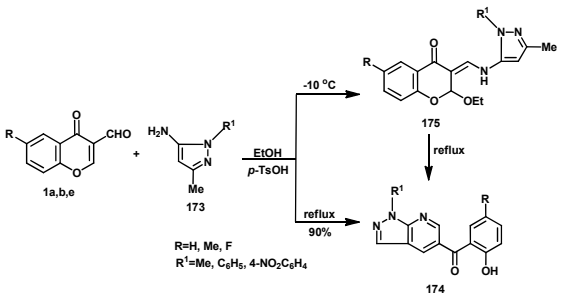



**Scheme 84**

Interaction of 3-formylchromones **1a**-**c**,**g** with ethyl glycinate in boiling toluene in the presence of *p*-toluenesulfonic acid gave a mixture of ethyl 4-(2-hydroxybenzoyl)-6-(4-oxo-chromen-3-yl)-pyridine-2-carboxylates **169** and ethyl 4-(2-hydroxybenzoyl)pyrrole-2-carboxylates **170** (Scheme 83) [62,65,76,121].

Also, the reaction of 3-formylchromone (**1a**) with equimolar amount of aminopyrazoles **171** in absolute ethanol afforded 6-(2-hydroxybenzoyl)pyrazolo[1,5-*a*]pyrimidines **172**, *via* iminomethyl derivative (Scheme 84) [122].

Treatment of 3-formylchromones **1a**,**b**,**e** with 5-amino pyrazoles **173** in boiling ethanol containing *p*-toluenesulfonic acid gave 2-hydroxybenzoylpyrazolo[3,4-*b*]pyridines **174**. While, when this reaction was carried out at lower temperature (-10 °C), the enamine-adducts **175** were isolated. Enamine-adducts rearrange into pyrazolo[3,4-*b*]pyridines **174** after prolonged refluxing (Scheme 85) [123].



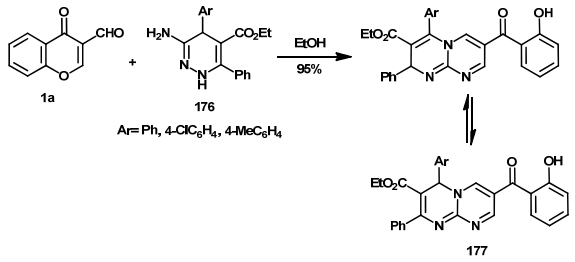

**Scheme 85**

Reaction of 3-formylchromone **1a** with ethyl 2-aminopyrimidine carboxylate**s** **176** in ethanol gave ethyl 7-(2-hydroxybenzoyl)-2*H*-(4*H*)pyrimido[1,2-*a*]pyrimidine-3-carboxylate **177** (Scheme 86) [124].

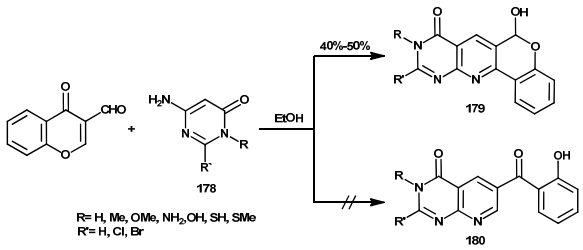
On the other hand, aminopyrimidones **178** reacted with aldehyde **1a** in refluxing ethanol to afford the unexpected pyrido[2,3-*d*]pyrimidines **179** but not the predicted pyridopyrimidines **180** (Scheme 87) [125].

Acetic acid catalyzed condensation of aldehyde **1a** with 1-(2-aminophenyl)pyrrole (**181**) led to the pyrrolo[1,2-*a*] quinoxaline derivative **182** (Scheme 88) [126].

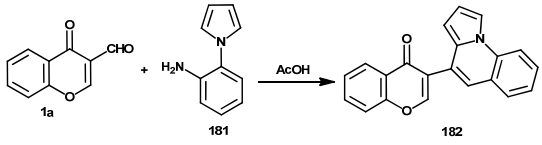
2-(4*H*-4-Chromen-3-yl)-3-aryl-1,2-dihydroquinazolin-4(3*H*)-ones **184** are the final products from the reaction of carboxaldehyde **1a** and amino amides **183** in both ethanolic and nonpolar medium (Scheme 89) [127].



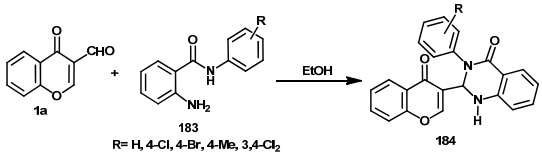

**Scheme 86**



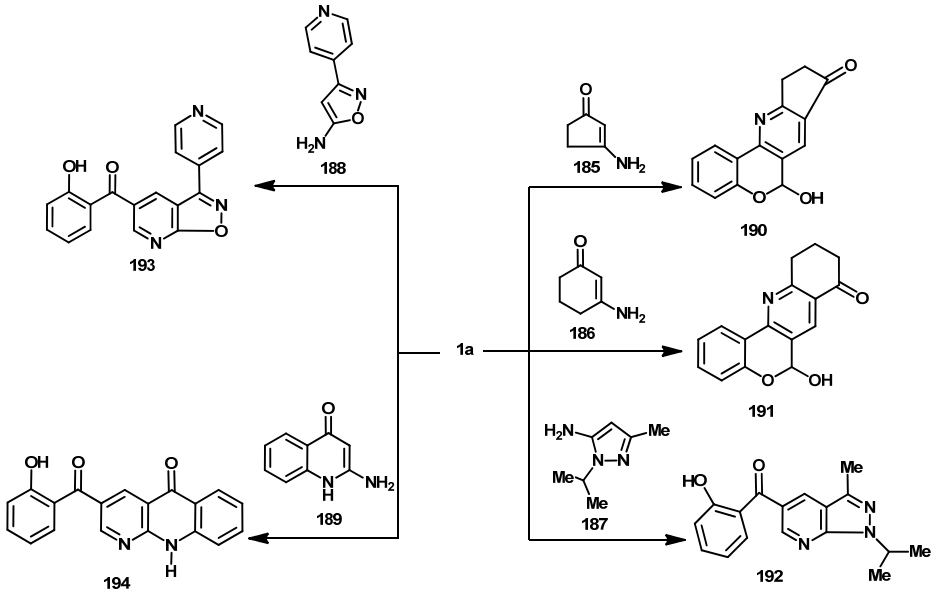

**Scheme 87**




**Scheme 88**




**Scheme 89**

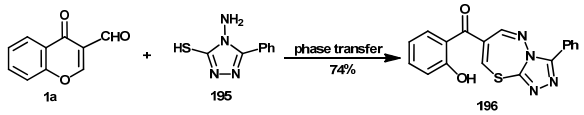


**Scheme 90**

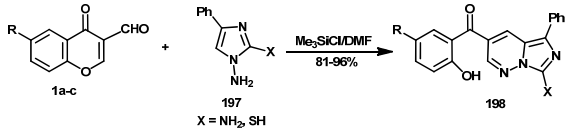
Reaction of 3-formylchromone **1a** with enamine derivatives **185**-**189** in pyridine or glacial acetic acid led to fused pyridine derivatives **190**-**194** in one step, respectively (46-82% yields) (Scheme 90) [76].

Reaction of 3-formylchromone **1a** with 4-amino-3-mercapto-5-phenyl-1,2,4-triazole (**195**) under phase transfer condition yielded ring-opened thiadiazepine **196** (Scheme 91) [128].

Condensation of **1a**-**c** with 4-phenyl-1*H*-imidazole-1-amines **197** in the presence of $Me_3SiCl$/DMF gave imidazo[1,5-*b*]pyridazines **198** in 81-96% yields (Scheme 92) [129].

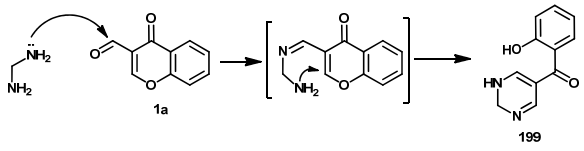


**Scheme 91**



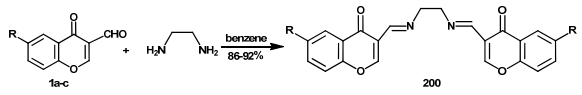
**Scheme 92**

Diaminomethane reacted with 3-formylchromone **1a** to yield pyrimidine derivative **199**. The reaction initially takes place on the formyl group and is followed by an intramolecular attack of the second amine function on the C-2 atom of the pyrone ring followed by the ring opening (Scheme 93) [130].



**Scheme 93**

Condensation of equimolar amountsof **1a**-**c** with ethylenediamine in benzene gave the 1,2-*bis*[(chromon-3-yl)methyleneamino]ethane **200**, using excess of ethylenediamine afforded poor yield of 1:1 condensation product (Scheme 94) [130].



**Scheme 94**

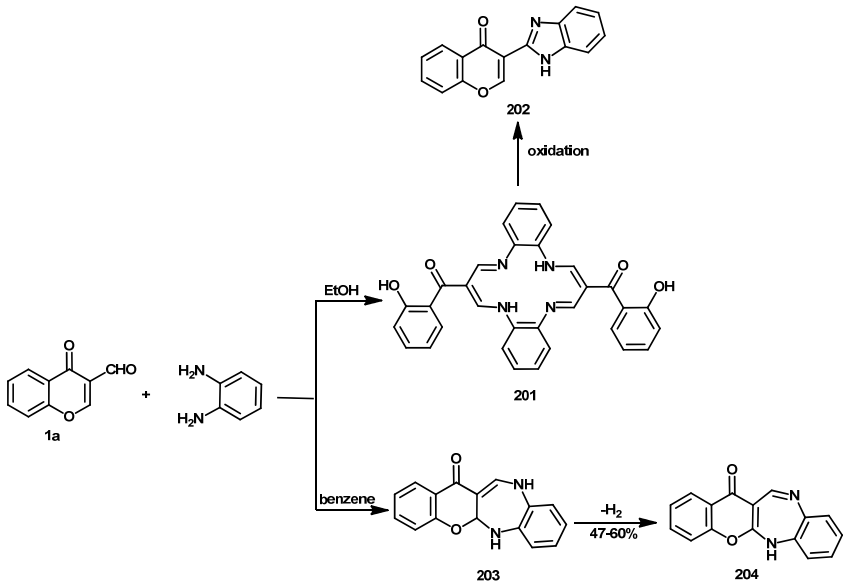
Reaction of aldehyde **1a** with *o*-phenylenediamine in boiling ethanol gave 7,16-*bis*(2-hydroxybenzoyl)-5,14-dihydrodibenzo[*b*-*i*][1,4,8,11]tetraazacyclotetradecine (**201**), which then oxidized to 3-(2-benzimidazolyl)chromone **202**, while in boiling benzene, benzodiazepino chromone **204** was obtained during dehydrogenation ofthe initially formed dihydro analogous **203**, through air oxidation or boiling in nitrobenzene (Scheme 95) [130-141].

On the other hand, cyclocondensation of 6-chloro-3-formylchromone (**1c**) with diaminopyridone derivative **205** in DMF under reflux containing few drops of piperidine afforded the 1,2,3,5-tetrahydro[1,2,4]triazolo[1,5-*a*]pyridine derivative **206** (Scheme 96) [142].

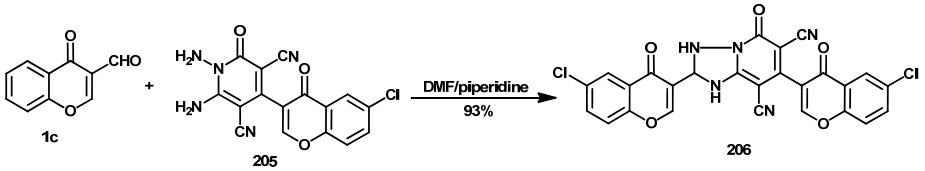
Condensation reaction of 6-chloro-3-formylchromone (**1c**) with *p*-phenylenediamine in dry benzene containing *p*-toluenesulfonic acid in 1:1 and 2:1 molar ratio gave 3-[(4-aminophenylimino)methyl]-6-chloro-4-oxo-4*H*-chromene (**207**) and the *bis* compound **208**, respectively (Scheme 97) [143].

On the other hand, condensation reaction of 3-formyl chromone (**1a**) with 2-aminophenol and 2-aminothiophenol in ethanol afforded compound **209** *via* the formation of the simple condensation product followed by 1,4-addition of ethanol molecules (Scheme 98) [132].

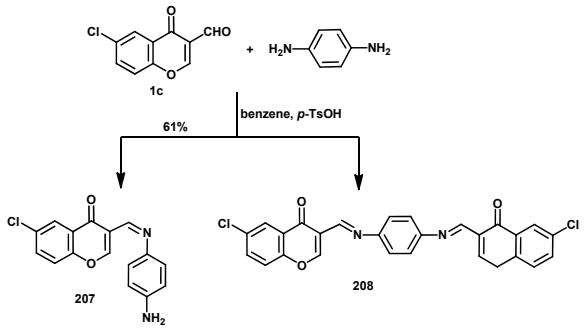
Consequently, the products obtained from the reaction of 3-formylchromones with primary amines depend mainly on the type of amine, molar ratio and the solvent used. Also, a diverse number of heterocyclic systems were obtained from the condensation of 3-formylchromones with bifunctional nucleophiles.



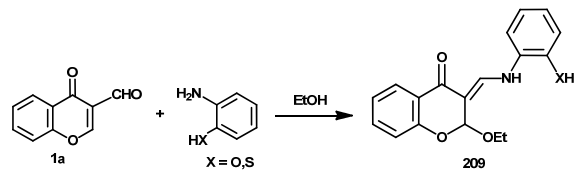

**Scheme 95**




**Scheme 96**



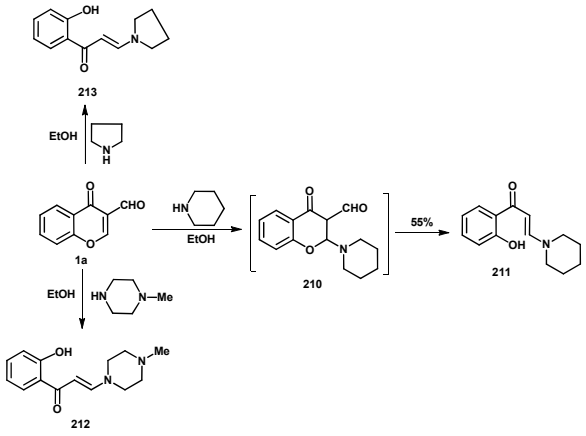

**Scheme 97**




**Scheme 98**

### *2.2.2. Reactions with secondary amines*

When 3-formylchromone **1a** treated with secondary amine like piperidine, an unstable 1,4-adduct **210** is formed, this adduct undergoes base catalyst deformylation to give the enaminoketone **211** in 55% yield [151]. Further, 3-formylchromones **1a** when heated with *N*-methylpiperazine in ethanol furnished 1-(2-hydroxyphenyl)-3-(4-methylpiperazin-1-yl)propenone (**212**) [41].Similarly, 1-(2-hydroxyaryl)-3-(pyrrolidin-1-yl)prop-2-en-1-one (**213**) was synthesized by the reaction of 3-formlylchromones **1a** with pyrrolidine in dry ethanol (Scheme 99) [145,146].



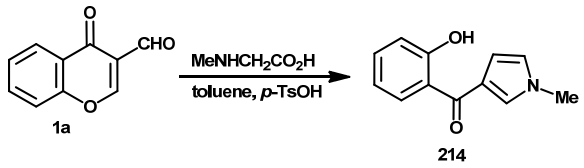

**Scheme 99**

Treatment of 3-formylchromone (**1a**) with *N*-methylglycine in boiling toluene in the presence of *p*-toluenesulfonic acid

produces *N*-methyl-3-salicyloyl pyrrole **214** in high yield (Scheme 100) [119].

Condensation of 3-formylchromone **1a** with $N^1$,$N^2$-dimethyl glycinamide (**215**) and L-pyrrolinamide **216** afforded chromonylimidazolinone **217** (79% yield) and pyrroloimidazolinone **218** (84% yield), respectively, these reactions proceed *via* [4+1] recyclization (Scheme 101) [73,147].

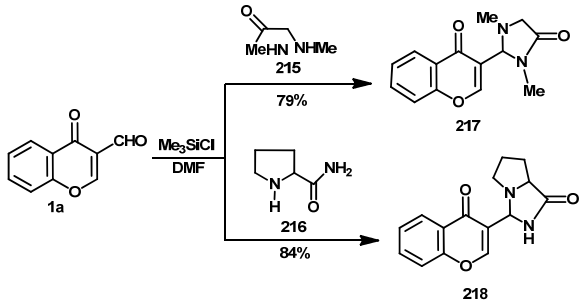
As a result, a variety of products were obtained from the reaction of 3-formylchromones with secondary amines depending on the nucleophile used.



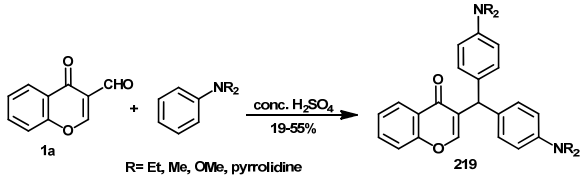

**Scheme 100**

### *2.2.3. Reactions with tertiary amines*

The acid-catalyzed condensation of 3-formylchromone (**1a**) with a range of tertiary aromatic amines gave the 3-[*bis*(4-aminophenyl)methyl]chromones **219** in moderate yield (Scheme 102) [148].



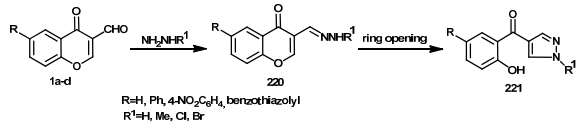

**Scheme 101**




**Scheme 102**

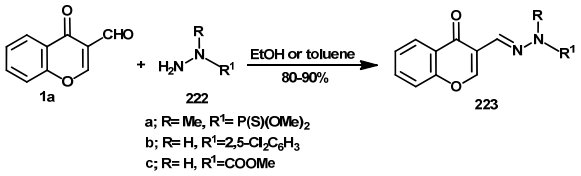
### *2.2.4. Reactions with hydrazines*

The reaction of 3-formylchromones **1a-d** with hydrazines gave initially hydrazones **220** which then reacted further at the C-2 position to give 4-(2-hydroxybenzoyl)pyrazoles **212** (Scheme 103) [149-151].




**Scheme 103**

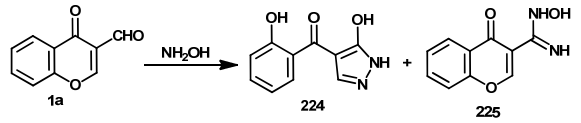
Treatment of 3-formylchromone **1a** with substituted hydrazines **222a-c** in absolute ethanol or toluene afforded the corresponding hydrazones **223a-c** (Scheme 104) [152,153].




**Scheme 104**

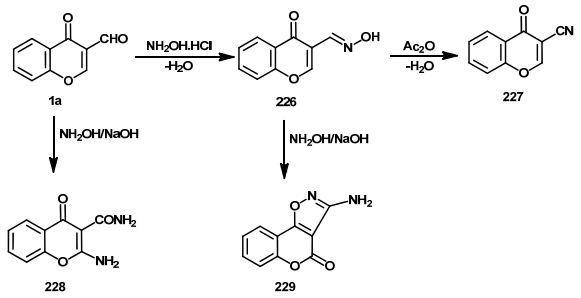
### *2.2.5. Reactions with hydroxylamine*

The reaction of 3-formylchromone (**1a**) with hydroxylamine hydrochloride (1:2 molar ratio) afforded a mixture of pyrazole **224** and chromone **225** (Scheme 105) [154,155].



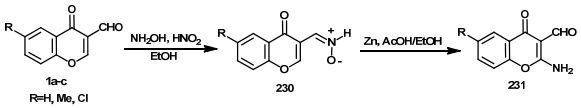

**Scheme 105**

Treatment of 3-formylchromones (**1a-d**) with hydroxylamine hydrochloride in ethanol gave the corresponding oximes **226** which on dehydration by acetic anhydride gave chromone-3-carbonitriles **227**. When the reaction of **1a-d** with hydroxylamine hydrochloride took place in the presence of sodium formate containing HCl, the carbonitriles **227** were obtained directly. On the other hand, Oximation of **1a** and its oxime **225** using hydroxylamine in sodium hydroxide led to 2-aminochromone-3-carboxamide (**228**) and 3-amino-4*H*-chromeno[3,4-*d*] isoxazol-4-one (**229**), respectively (Scheme 106) [156-158].



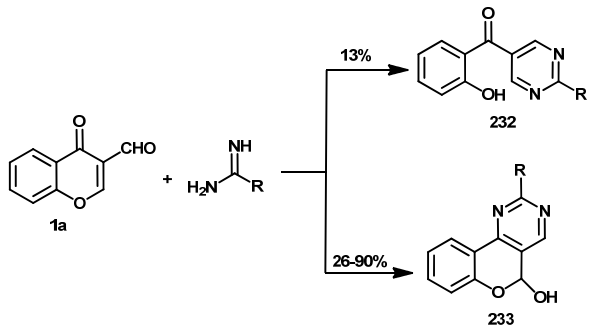

**Scheme 106**

Nitrones **230** were prepared from the reaction of aldehydes **1a-c** with hydroxylamine in ethanol. Nitrones **230** rearranged to 2-amino-3-formylchromones **231** in ethanol containing few drops of acetic acid in the presence of zinc (Scheme107) [159,160].




**Scheme 107**

Hence, hydroxylamine on reactions with 3-formylchromones gave diverse types of products depending on the reaction conditions.




**Scheme 108**

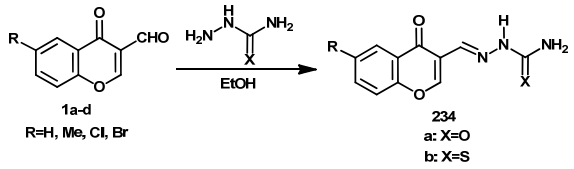
### *2.2.6. Reactions with amidines*

Reaction of 3-formylchromone **1a** with formamidine gave a mixture of 5-(2-hydroxybenzoyl) pyrimidine **232** (R=H, 13%) and 5-hydroxy-5*H*-chromeno[4,3-*d*]pyrimidine **233** (R=H, 31%) as reported by Loewe [161] While, reaction of **1a** with several *C*-substituted formamidines (R=alkyl, aryl, hetaryl, $NH_2$, NHCN, SH, SMe, OH, OMe, 1-pyrrolidinyl, 1-piperidinyl, 4-morpholinyl) gave only chromeno-pyrimidines **233** in 26-90% yields (Scheme108) [161-166].

Thus, 3-formylchromones are a good precursors for the synthesis of pyrimidine derivatives *via* treatment with amidine derivatives as 1,3-bifunctional nucleophiles.

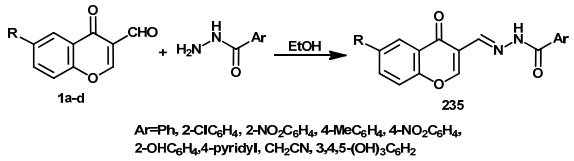
### *2.2.7. Reactions with hyrazides*

3-Formylchromones **1a-d** reacted with semicarbazide and thiosemicarbazide in ethanol to give the corresponding semicarbazones **234a** (X=O) and thiosemicarbazone **234b** (X=S), respectively (Scheme109) [150,167,168].




**Scheme 109**

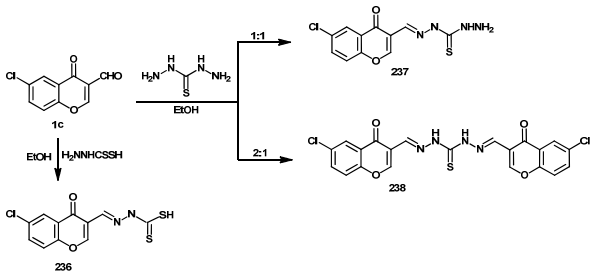
The reaction of 3-formylchromone **1a-d** with aroylhydrazines gave the corresponding aroylhydrazone **235** (Scheme110) [169-172].



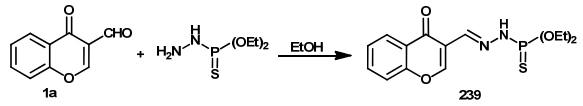

**Scheme 110**

3-Formylchromone **1c** condensed with equimolar amount of hydrazine carbodithioic acid and thiocarbohydrazide in ethanol to give the corresponding hydrazones **236** and **237**, respectively. Also, condensation of **1c** with two equivalents of thiocarbohydrazide gave *bis* thiocarbohydrazone derivative **238** (Scheme111) [173].

Phosphorohydrazone of chromone **239** was obtained from stirring 3-formylchromone **1a** with diethoxythiophosphoryl-hydrazide inethanol (Scheme112) [159].




**Scheme 111**




**Scheme 112**

## 3. Conclusion

In the present work, the chemical reactivity of 3-formylchromones was evaluated and summarized towards all types of carbon and nitrogen nucleophiles under different reaction conditions.3-Formylchromones are very active toward the nucleophilic reagents, due to the availability of three electron deficient sites, the aldehydes carbon, *C*-2 carbon, and the *C*-4 carbon of the carbonyl group. A variety of fused heterocyclic systems were prepared directly from the reaction of 3-formylchromones with some bifunctional nucleophiles, these reactions mainly proceed *via* condensation with the aldehydic function followed by nucleophilic attack at C-2 position of the chromone moiety.

## References

[1]. Reynolds, G. A.; Van Allan, J. A. *J. Heterocycl. Chem.* **1969**, *6*, 375-377.
[2]. Harnisch, H. *Liebigs Ann. Chem.* **1973**, *765*, 8-14.
[3]. Nohara, A.; Umetani, T.; Sanno, Y. *Tetrahedron Lett.* **1973**, *14*, 1995-1998.
[4]. Nohara, A.; Umetani, T.; Sanno, Y. *Tetrahedron* **1974**, *30*, 3553-3561.
[5]. Prakash, O.; Kumar, R.; Sharma, D.; Bhardwaj, V. *J. Indian Chem. Soc.* **2004**, *81*, 888-890.
[6]. Klutchko, S.; Cohen, M. P.; Shavel J. J.; Von Standtmann, M. *J. Heterocycl. Chem.* **1974**, *11*, 183-188.
[7]. Becket, G. J. P.; Ellis, G. P. *Tetrahedron Lett.* **1976**, *17*, 719-720.
[8]. Ellis, G. P. *J. Chem. Res (S).* **1978**, 47-48.
[9]. El-Shaaer, H. M. E.; Prejessy, A.; Zahradik, P.; Lacova, M.; Sustekova, Z. *Monatch Chem.* **1993**, *124*, 539-548.
[10]. Eiden, F.; Haverland, H. *Arch. Pharm.* **1996**, *5*, 29-33.
[11]. Paul, S.; Gupta, R.; Gupta, M.; Loupy, A. *Synthesis* **2002**, 75-78.
[12]. Shim, Y. S.; Kim, K. C.; Chi, D. Y.; Lee, K. H.; Cho, H. *Bioorg. Med. Chem. Lett.* **2003**, *13*, 2561-2563.

[13]. Shrestha, S.; Hwang, S. Y.; Lee, K. H.; Cho, H. *Bull. Korean Chem. Soc.* **2005**, *26*, 1138- 1140.
[14]. Nandgaonkar, R. G.; Ingle, V. N. *Asian J. Chem.* **2005**, *17*, 2016-2018.
[15]. Kamotra, P.; Gupta, A.K.; Gupta, R.*Indian J. Chem. B* **2007**, *46*, 866-868.
[16]. Hatzade, K. M.; Taile, V. S.; Gaidhane, P. K.; Umare, V. D.; Haldar, A. G. M.; Ingle, N. V. *Indian J. Chem. B* **2009**, *48*, 1548-1557.
[17]. Ibrahim, S. S.; Allimony, H. A.; Abdel-Halim, A. M.; Ibrahim, M. A. *Arkivoc* **2009**, *14*, 28-38.
[18]. Patil, L. R.; Ingle, V. S.; Bondge, S. P.; Mane, R. A. *Indian J. Chem.* **2001**, *41B*, 131-134.
[19]. Shankar, M. S. S.; Reddy, R. B.; Chandra, M. G. V. P.; Reddy, Y. D. *J. Indian Chem. Soc.* **1989**, *66*, 30-35.
[20]. Tuskaev, V. A.; Oganesyan, E. T.; Mutsueva, S. K. *Pharm. Chem. J.* **2002**, *36*, 309-312.
[21]. Hatzade, K. M.; Taile, V. S.; Gaidhane, P. K.; Halder, A. G. M.; Ingle, V. N. *Indian J. Chem. B* **2008**, *47*, 1260-1270.
[22]. Abass, M.; Abdel-Megid, M.; Hassan, M. *Synth. Commun.* **2007**, *37*, 329-352.
[23]. Abass, M.; Hassan, A. *Chem. Pap.* **2003**, *57*, 267-277.
[24]. Abdel-Megid, M.; Gabr, Y.; Awas, M. A.; Abdel-Fattah, N. M. *Chem. Heterocycl. Compds.* **2009**, *45*, 1354-1364.
[25]. Siddiqui, Z.N.; Musthafa, T. N. M. *Tetrahedron Lett.* **2011**, *52*, 4008-4013.
[26]. Mustafa, T. N. M.; Siddiqui, Z. N.; Husain, F. M.; Ahmad, I. *Med. Chem. Res.* **2010**, *19*, 1473-1481.
[27]. Siddiqui, Z. N.; Asad, M.; Praveen, S. *Med. Chem. Res.* **2008**, *17*, 318-325.
[28]. El-Shaaer, H. M. *Eur. J. Chem.* **2012**, *3*, 51-56.
[29]. Melikyan, G.; Lacova, M.; Kralova, K.; El-Shaaer, H. M.; Henselova, M.; Avetisyan, A. A. *Chem. Pap.* **1993**, *47*, 388-392.
[30]. Lacova, M.; El-Shaaer, H. M.; Loss, D.; Matulova, M.; Chovancova, J.; Furdik, M. *Molecules* **1998**, *3*, 120-131.
[31]. Caujoll, R.; Baziard-Mouysset, G.; Favort, J. D.; Payard, M.; Loiseau, P. R.; Amaroush, H.; Linas, M. D.; Seguela, J. P.; Loiseau, P. M.; Bories, C.; Gayral, P. *Eur. J. Med. Chem*. **1993**, *28*, 29-35.
[32]. Gasparova, R.; Lacova, M.; El-Shaaer, H. M.; Odlerova, Z. *Il Farmaco* **1997**, *52*, 251-352.
[33]. Achaiah, G.; Jayamma, Y.; Reddy, V. M. *Indian J. Heteterocycl. Chem.* **1991**, *1*, 139-143.
[34]. Karale, B. K.; Gill, C. H.; Ganages, K. N.; Bachute, M. T.; Shingare, M. S. *Indian J. Heterocycl. Chem*. **1999**, *9*, 153-154.
[35]. Karale, B. K.; Gill, C. H.; Ganage, K. N.; Bachute, M. T.; Shingare, M. S. *Indian J. Heterocycl. Chem*. **2003**, *12*, 267-270.
[36]. Carvaiho, S. A.; Desilva, E. F.; Desouza, M. N. N.; Lourence, M. C. S.; Reckova, R. R. F. *Bioorg. Med. Chem. Lett*. **2008**, *18*, 538-541.
[37]. Joshi, R. S.; Mandhane, P. G.; Badadhe, P. V.; Gill, C. H. *Ultrason. Sonochem.* **2011**, *18*, 735-738.
[38]. Nohara, A.; Kuriki, H.; Saijo, T.; Ukawa, K.; Murata, T.; Kanno, M.; Sanno, Y. *J. Med. Chem.* **1975**, *18*, 34-37.
[39]. Karale, B. K.; Chavan, V. P.; Hangarge, R. V.; Mane, A. S. *Indian J. Heterocycl. Chem*. **2001**, *11*, 81-82.
[40]. Halnor, V. B.; Dalvi, N. R.; Joshi, N. S.; Gill, C. H.; Karale, B. K. *Indian J. Chem. B* **2006**, *45*, 288-291.
[41]. Lacova, M.; Stankovcova, H.; Bohac, A.; Kotzianova, B. *Tetrahedron* **2008**, *64*, 9646-9653.
[42]. Lacova, M.; GaSparova, R.; Kois, P.; Bohac, A.; El-Shaaer, H. M. *Tetrahedron* **2010**, *66*, 1410-1419.
[43]. Kovacikova, L.; GaSparova, R.; Bohac, A.; Durana, M.; Lacova, M. *Arkivoc* **2010**, *11*, 188-203.
[44]. Shingare, M. S.; Karale, B. K.; Gill, C. H.; Ganage, K. N.; Bachute, M. T. *Indian J. Heterocycl. Chem*. **1999**, *9*, 153-154.
[45]. Kois, P.; El-Shaaer, H. M.; Lacova, M. 6thElectronic Conference on Synthetic Organic Chemistry, ECSOC-9, September 1-30, 2005.
[46]. Nohara, A.; Umetani, T.; Sanno, Y. *Jap. Patent,* 1975, *7*, 552067; C. A., **1976**, *84*, 105400t.
[47]. Nohara, A.; Kuriki, H.; Saijo, T.; Sugihara, H.; Kanno, M.; Sanno, Y. *J. Med. Chem.* **1977**, *20*, 141-145.
[48]. Gill, C. H.; Karale, B. K.; Dalvi, N. R. *Indian J. Chem. B* **2005**, *44*, 1522-1525.
[49]. Diwakar, S. D.; Bhagwat, S. S.; Shingare, M. S.; Gill, C. H. *Bioorg. Med. Chem. Lett*. **2008**, *18*, 4678-4681.
[50]. Luengo, J. I.; Elliott, J. D.; Xiang, J. N. PCT. Int. Appl. Wo. 97 04, 773; C. A., **1997**, *126*, 225307g.
[51]. Nadiu, M. S. R.; Nadiu, R. R. *Indian J. Chem. B* **1997**, *36*, 99-100.
[52]. Prousek, J.; Jurasek, A.; Kovac, J. *Coll. Czech. Chem. Commun.* **1980**, *45*, 1704-1706.
[53]. Jones W. D.; Albrecht, W. L. *J. Org. Chem*. **1976**, *41*, 706-707.
[54]. Bandyophadyaya, C.; Sur, K. R.; Patra, R. *J. Chem. Res. (s)*. **1998**, *12*, 802-803.
[55]. Borrell, J. I.; Teixido, J.; Schuler, E.; Michelotti, E. L. *Molecular Diversity* **2000**, *5*, 163- 166.
[56]. Hangarge, R. V.; Sonwane, S. A.; Jarikote, D. V.; Shingare, M. S. *Green Chem.* **2001**, *3*, 310-312.
[57]. Chandra, K. G.; Samita, B.; Nanda, G.; Basudeb, A. *J. Chem. Res(s)*. **1998**, 178-179.
[58]. Saha, S. S.; Ghosh, T.; Tarun, G.; Bandyopadhyay, C. *Synth. Commun.* **2008**, *38*, 2429-2436.
[59]. Awas, M. A. A. *Chem. Pap.* **2006**, *60*, 338-347.
[60]. Nohara, A.; Ishiguro, T.; Sanno, Y. *Tetrahedron Lett.* **1974**, *13*, 1183-1186.
[61]. Abdel-Rahman, A. H.; Hammouda, M. A. A.; El-Desoky, S. I. *Heteroatom. Chem.* **2005**, *16*, 20-27.
[62]. Heber, D. *Synthesis* **1978**, 691-692.
[63]. Ghosh, C. K.; Khan, S. *Synthesis* **1981**, 903-907.
[64]. Ghosh, C. K. *Heterocycles* **2004**, *63*, 2875-2898.
[65]. Terzidis, M.; Tsoleridis, C. A.; Stephanidou-Stephanatou, J. *Tetrahedron* **2007**, *63*, 7828-7862.
[66]. Von Harnish, H. *Justus Lieb. Ann. Chem*. **1972**, *765*, 25-33.
[67]. Copeland, R. A. B.; Day, A. R. *J. Am. Chem. Soc.* **1943**, *65*, 1072-1075.
[68]. Brzozowski, Z.; Saczewski, F. *Eur. J. Med. Chem. Chem.* **2002**, *37*, 709-720.
[69]. Ryabukhin, S. V.; Plaskon, A. S.; Volochnyuk, D. M.; Tolmachev, A. A. *Synthesis* **2 007**, 3155-3162.
[70]. Sarma, G. V. S. R.; Reddy, V. M. *Indian J. Heterocycl. Chem.* **1993**, *3*, 111-116.
[71]. Fitton, A. O.; Frost, J. R.; Suschitzky, H.; Houghton, P. G. *Synthesis* **1977**, 133-134.
[72]. Sabitha, G.; Reddy, M. M.; Archana, B.; Yadav, J. S. *Synth. Commun*. **1998**, *28*, 573-581.
[73]. Plaskon, A. S.; Ryabukhin, S. V.; Volochnyuk, D. M.; Shivanyuk, A. N.; Tolmachev, A. A. *Tetrahedron* **2008**, *64*, 5933-5943.
[74]. Naskar, S.; Banerjee, M.; Hazra, A.; Mondal, S.; Maity, A.; Paira, R.; Sahu, K. B.; Saha, P.; Banerjee, S.; Mondal, N. B. *Tetrahedron Lett*. **2011**, *52*, 1527-1531.
[75]. Polyakov, V. K.; Shevtsova, R. G.; Tsukerman, S. *Ukr. Khim. Zh*, **1981**, *47*, 85-87.
[76]. Haas, G.; Stanton, J. L.; Von Sprecher, A.; Wenk, P. *J. Heterocycl. Chem.* **1981**, *18*, 607- 612.
[77]. Singh, P.; Kaur, M.; Holzer, W. *Eur. J. Med. Chem.* **2010**, *45*, 4968-4082.
[78]. Karale, B. K.; Chavan, V. P.; Mane, A. S.; Hangarge, R. V.; Gill, C. H.; Shingare, M. S. *Synth. Commun.* **2002**, *32*, 497-503.
[79]. Siddiqui, Z. N.; Musthafa, T. N. M.; Praveen, S. *Med. Chem. Res.* **2013**, *22*, 127-133.
[80]. Khodairy, A. *J. Chinese Chem. Soc.* **2007**, *54*, 93-102.
[81]. Shelke, S. N.; Dalvi, N. R.; Kale, S. B.; More, M. S.; Gill, C. H.; Karale B. K. *Indian J. Chem. B* **2007**, *46*, 1174-1178.
[82]. Abbas, M.; Othman, E. S.; Hassan, A. *Synth. Commun.* **2007**, *37*, 607-621.
[83]. Lacova, M.; GaSparova, R.; Loos, D.; Liptay, T.; Pronayova, N. *Molecules* **2000**, *5*, 167- 178.
[84]. Bozdag-Dundar, O.; Evranos, B.; Das-Evcimen, N.; Sarhkaya, M.; Ertan, R. *Eur. J. Med. Chem.* **2008**, *43*, 2412-2417.
[85]. Verspohl, E. J.; Bozdağ-Dündar, O.; Kaup, R. M.; Bauer, K.; Ertan, R. *Med. Chem. Res*. **2009**, *18*, 665-670.
[86]. Ibrahim, M. A.; Abdel-megid, M.; El-Gohary, N. M. *J. Braz. Chem. Soc*. **2011**, *21*, 1130- 1139.
[87]. GaSparova, R.; Lacova, M. *Coll. Czech. Commun*. **1995**, *60*, 1178-1183.
[88]. Franz, C.; Heinisch, G.; Holzer, W.; Mereiter, K.; Strobe, B.; Zheng, C. *Heterocycles* **1995**, *41*, 2527-2551.
[89]. Shutov, R. V.; Kukline, E. V.; Ivin, B. A. *Russ. J. Gen. Chem.* **2009**, *79*, 1049-1051.
[90]. Eiden, F.; Haverland, H. *Arch. Pharm*. **1967**, *300*, 806-809.
[91]. Shelke, K. F.; Sapkal, K. S. B.; Niralwad, S.; Shingate, B. B.; Shingate, M. S. *Cent. Eur. J. Chem.* **2010**, *8*, 12-18.
[92]. Shindalkar, S. S.; Madje, B. R.; Shingare, M. S. *Indian J. Chem*. *B* **2006**, *45*, 2571-2573.
[93]. Prousek, J. *Coll. Czech. Chem. Commun*. **1991**, *56*, 1361.
[94]. Reddy, K. V.; Rao, A. V. S. *Org. Prep. Proc. Int*. **1997**, 29, 355-357.
[95]. Sosnovskikh, V. Y.; Irgashev, R. A.; Levchenko, A. A. *Tetrahedron* **2008**, *64*, 6607-6614.
[96]. Teimouri, M. B. *Tetrahedron* **2011**, *67*, 1837-1843.
[97]. Bandyopadhyay, C.; Sur, K. R. *Indian. J. Chem*. *B* **2000**, *39*, 137-140.
[98]. Ibrahim, M. A.; Hassanin, H. M.; Gabr, Y. A.; Alnamer, Y. A. *Eur. J. Chem*. **2010**, *3*, 195-199.
[99]. Hassanin, H. M.; Ibrahim, M. A.; Alnamer, Y. A. *Turkish J. Chem*. **2012**, *36*, 682-699.
[100]. Fitton, A. O.; Frost, J. R.; Suschitzky, H. *Tetrahedron Lett.* **1975**, *16*, 2099-2100.
[101]. Sigg, I.; Haas, G.; Winkler, T. *Helv. Chim. Acta* **1982**, *65*, 26.
[102]. Achaiah, C.; Reddy, V. *Indian J. Pharm. Sci.* **1991**, *53*, 253-255.
[103]. Chen, H. M.; Cao, L. H. *J. Chinese Chem. Soc*. **2009**, *56*, 1028-1034.
[104]. Kapur, A.; Kumar, K.; Singh, L.; Singh, P.; Elango, M.; Subramanian, V.; Gupta, V.; Kanwal, P.; Ishar, M. P. S. *Tetrahedron* **2009**, *65*, 4593-4603.
[105]. Khan, K. M.; Ambreen, N.; Hussain, S.; Perveen, S.; Choudhary, M. I. *Bioorg. Med. Chem.* **2009**, *17*, 2983-2988.
[106]. Khan, K. M.; Ambreen, N.; Mughal, U. R.; Jalil, S.; Perveen, S.; Choudhary, M. I. *Eur. J. Med. Chem.* **2010**, *45*, 4058-4064.
[107]. Dziewulska-Kulaczkowska, A. *J. Therm. Anal. Calorim*. **2012**, *109*, 7-15.
[108]. El-Shaaer, H. M.; Abdel-Aziz, S. A. A.; Hanafy, F. I.; Ali, T. E.; El-Fayomy, A. Z. *Eur. J. Chem*. **2011**, *2*, 158-162.
[109]. Fitton, A. O.; Haughyo, G.; Suschitzky, H. *Synthesis* **1979**, 337-339.

[110]. Lacova, M.; Stankovicova, H.; Odlerova, Z. *II Farmaco* **1995**, *50*, 885-888.
[111]. Fitton, A. O.; Frost, J. R.; Houghton, P. G.; Suschitzky, H. *J. Chem. Soc. , Perkin Trans. 1* **1977**, 1450-1452.
[112]. El-Shaaer, H. M.; Foltinova, P.; Lacova, M.; Chovancova, J.; Stankovicova, H. *II Farmaco* **1998**, *53*, 224-232.
[113]. Stankovicova, H.; Lacova, M.; Gaplovsky, A.; Chovancova, J.; Pronayova, N. *Tetrahedron* **2001**, *57*, 3455-3464.
[114]. Al-Rashida, M.; Ashraf, M.; Hussain, B.; Nagra, S. A.; Abbas, G. *Bioorg. Med. Chem.* **2011**, *19*, 3367-3371.
[115]. Dziewulska-Kulaczkowska, A.; Mazur, L. *J. Mol. Struct.* **2011**, *985*, 233-244.
[116]. Plaskon, A. S.; Ryabukhin, S. V.; Volochnyuk, D. M.; Gavrilenko, K. S.; Shivanyuk, A. N.; Tolmachev, A. A. *J. Org. Chem.* **2008**, *73*, 6010-6013.
[117]. Ryabukhin, S. V.; Plaskon, A. S.; Volochnyuk, D. M.; Tolmachev, A. A. *Synthesis* **2007**, 1861-1871.
[118]. Kalanithi, M.; Kodimunthiri, D.; Rajarajan, M.; Tharmaraj, P. *Spectrochim. Acta A* **2011**, *82*, 290-298.
[119]. Clarke, P. D.; Fitton, A. O.; Kosmirak, M.; Suschitzky, H.; Suschitzky, J. L. *J. Chem. Soc. , Perkin Trans. 1* **1985**, 1747-1756.
[120]. Ghosh, C. K.; Ray, A.; Patra, A. *J. Heterocycl. Chem.* **2001**, *38*, 1459-1463.
[121]. Fitton, A. O.; Kosmırak, M.; Suschıtzky, H. *Tetrahedron Lett.* **1982**, *23*, 3953-3956.
[122]. Nogueras, M.; Sanchez, A.; Cobo, J.; Low, J. N. *J. Heterocycl. Chem*. **2002**, *49*, 51-54.
[123]. Lacova, M.; Puchala, A.; Solčanyova, E.; Lac, J.; Kois, S.; Chovancova, J.; Rsala, D. *Molecules* **2005**, *10*, 809-821.
[124]. Eynde, J. J. V.; Hecq, N.; Kataeva, O.; Kappe, C. O. *Tetrahedron* **2001**, *57*, 1785-1791.
[125]. Quiroga, D.; Rengifo, A.; Insuasty, B.; Abonía, R.; Nogueras, M.; Sanchez, A. *Tetrahedron Lett*. **2002**, *43*, 9061-9063.
[126]. Abonia, R.; Insusty, B.; Quiroga, J.; Kolshorn, H.; Meier, H. *J. Heterocycl. Chem.* **2001**, *38*, 671-674.
[127]. Kubicova, L.; Pour, M.; Lacova, M.; Kralova, K.; Chovancova, J.; Kaustova, J. 9thElectronic Conference on Synthetic Organic Chemistry, ECSOC-9, September 1-30, 2002.
[128]. Reddy, G. J.; Sabitha, M. G.; Rao, A. V. S. *Synth. Commun*. **1987**, *17*, 1851-1859.
[129]. Plaskon, A. S.; Ryabukhin, S. V.; Volochnyuk, D. M.; Shivanyuk, A. N.; Tolmachev, A. A. *Heterocycles* **2008**, *75*, 1765-1772.
[130]. Ghosh, C. K.; Khan, S. *Synthesis* **1980**, *9*, 701-702.
[131]. Reddy, G. J.; Rao, A. V. S. *Curr. Sci.* **1981**, *50*, 84-86.
[132]. Sigg, I.; Haas, G.; Winkler, T. *Helv. Chim. Acta* **1982**, *65*, 275-279.
[133]. Rihs, G.; Sigg, I.; Haas, G.; Winkler, T. *Helv. Chim. Acta* **1985**, *68*, 1933-1935.
[134]. Risitano, F.; Grassi, G.; Foti, F. *J. Heterocycl. Chem*. **2001**, *38*, 1083-1086.
[135]. Abdel-Rahman, A. H.; Khalil, A. M.; Keshk, E. M. *Boll. Chim. Farm*. **2001**, *140*, 387-396.
[136]. Grolik, J.; Zwolinski, K.; Eilmes, J.; Sieron, L. *Tetrahedron* **2011**, *67*, 2623-2632.
[137]. Grolik, J.; Sieron, L.; Eilmes, J. *Tetrahedron Lett.* **2006**, *47*, 8209-8213.
[138]. Das, B.; Holla, H.; Srinivas, Y. *Tetrahedron Lett.* **2007**, *48*, 61-64.
[139]. Maiti, S.; Panja, S. K.; Bandyopadhyay, C. *Indian J. Chem.* **2009**, *48B*, 1447-1452.
[140]. El-Desoky, E. I.; Al-Shihry, S. S. *J. Heterocycl. Chem*. **2008**, *45*, 1855-1864.
[141]. Das, B.; Kanth, B. S.; Reddy, K. R.; Kumar, A. S. *J. Heterocycl. Chem*. **2008**, *45*, 1499- 1502.
[142]. Ali, T. E.; Ibrahim, M. A. *J. Braz. Chem. Soc*. **2010**, *21*, 1007-1016.
[143]. Ali, T. E.; Abdel-Aziz, S. A.; El-Shaaer, H. M.; Hanafy, F. I.; El-Fauomy, A. Z. *Turk. J. Chem.* **2008**, *32*, 365-374.
[144]. Ghosh, C. K.; Khan, S. *Synthesis* **1981**, 719-720.
[145]. Shelke, S. N.; Dalvi, N. R.; Shingare, M. S.; Gill, C. H.; Karale, B. K. *Indian J. Heterocycl. Chem*. **2006**, *15*, 403-404.
[146]. Sharad, N. S.; Sonawane, M. P.; Karale, B. K.; Gill, C. H. *Nature Precedings* **2009**, *1*, 2855-2862.
[147]. Pospisil, J.; Potacek, M. *Heterocycles* **2004**, *63*, 1165-1173.
[148]. Gabbutt, C. D.; Hargrove, T. F. L.; Heron, B. M.; Jones, D.; Poyner, C.; Yildiz, E.; Horton, P. N.; Hursthouse, M. B. *Tetrahedron* **2006**, *62*, 10945-10953.
[149]. Ghosh, C. K.; Mukhopdyaya, K. K. *J. Indian Chem. Soc*. **1978**, *55*, 52-55.
[150]. Ghosh, C. K.; Mukhopdyaya, K. K. *J. Indian Chem. Soc*. **1978**, *55*, 386-388.
[151]. Reddy, G. J.; Sbitha, G.; Rao, A. V. S. *Indian J. Chem. B* **1984**, *23*, 99-103.
[152]. Nawrot-Modranka, J.; Nawrot, E.; Graczyk, J. *Eur. J. Med. Chem*. **2006**, *41*, 1301-1309.
[153]. Lazrenkow, A.; Nawrot-Modranka, J.; Brzeziska, E.; Krojewska, U. R.; Ozalski, M. *Med. Chem. Res.* **2012**, *21*, 1861-1868.
[154]. Ghosh, C. K.; Sinharoy, D. K.; Mukhopadhyaya, K. K. *J. Chem. Soc., Perkin Trans. 1* **1979**, 1981-1985.
[155]. Bosinski, W.; Jerzmanowska, Z. *Pol. J. Chem.* **1983**, *57*, 471-474.
[156]. Petersen, U.; Heitzer, H. *Liebigs Ann. Chem.* **1976**, 1663-1666.
[157]. Sosnovskikh, V. Y.; Moshkin, V. S.; Kodess, M. I.; *Tetrahedron Lett*. **2008**, *49*, 6856- 6859.
[158]. Sosnovskikh, V. Y.; Moshkin, V. S.; Kodess, M. I. *Mendeleev Commun*. **2010**, *20*, 209- 211.
[159]. Maiti, S.; Panja, S. K.; Bandyopodhyay, C. *Tetrahedron Lett*. **2009**, *50*, 3966-3969.
[160]. Ishar, M. P. S.; Kumar, K.; Singh, R. *Tetrahedron Lett.* **1998**, *39*, 6547-6550.
[161]. Lowe, W. *Synthesis* **1976**, 274-276.
[162]. Ghosh, C. K.; Khan, S. C. *Indian J. Chem. B* **1979**, *18*, 128-130.
[163]. Pene, C.; Hubert-Habart, M. *J. Heterocycl. Chem*. **1980**, *17*, 61-64.
[164]. Crowther, A. F.; Curd, F. H. S.; Richardson, D. N.; Rose, F. L. *J. Chem. Soc.* **1984**, 1636.
[165]. Borrell, J. I.; Teixido, J.; Schuler, E.; Michelotti, E. *Tetrahedron Lett.* **2001**, *42*, 5331- 5334.
[166]. Bruno, O.; Brullo, C.; Ranis, A.; Schenone, S.; Bondavalli, F.; Barocelli, E.; Chivarini, M.; Ballabeni, V.; Impicciatore, M.; Tognolini, M. *Bioorg. Med. Chem. Lett.* **2011**, *11*, 1397-1400.
[167]. Tsao, L.; Van, V.; Sun, G.; Lyu, Y. *Russ. J. Gen. Chem*. **2001**, *71*, 767-769.
[168]. Cao, L. H.; Huang, Y. L. Y. T.; Sun, G. Z. *Yingyong Huaxue* **2001**, *18*, 312-313.
[169]. Foltinova, P.; Lacova, M.; Loss, D. *II Farmaco***2000**, *55*, 21-26.
[170]. Cao, L.; Wang, W. *Chem. Heterocycl. Compd.* **2003**, *39*, 1072-1075.
[171]. Wang, B. D.; Yang, Z. Y.; Zhang, D. W.; Wang, Y. *Spectrochim. Acta A* **2006**, *63*, 213-219.
[172]. Tsao, L.; Chzhan, L.; Lyu, T. *Chem. Nat. Compd*. **2001**, *37*, 311-314
[173]. Ali, T. E.; Abdel-Aziz, S. A.; El-Shaaer, H. M.; Hanafy, F. I.; El-Fauomy, A. Z. *Phosphorous, Sulfur and Silicon Rel. Elem.* **2008**, *183*, 2139-2160.