

Synthesis new fused and non-fused chromene [I] derivatives derived from 2-amino-4-[4-(dimethylamino)phenyl]-5-oxo-4*H*,5*H*- pyrano[3,2-*c*]chromene-3-carbonitrile

Hamid H. Mohammed^{a*}, Redha I.H.Al-bayati^a and Fatima attallah^a

^aDepartment of Chemistry, College of Science, University of Al-Mustansiryah,
P.O. Box 46136, Baghdad, Iraq

*Corresponding author. E-mail : hammed_sugar@yahoo.com

Abstract

A new series of pyrano-chromene and pyrimido pyrano-chromene derivatives were synthesized starting from 2-amino-4-[4-(dimethylamino)phenyl]-5-oxo-4*H*,5*H*-pyrano[3,2-*c*]chromene-3-carbonitrile (**5**). The structures of the synthesized compounds were elucidated by spectral data.

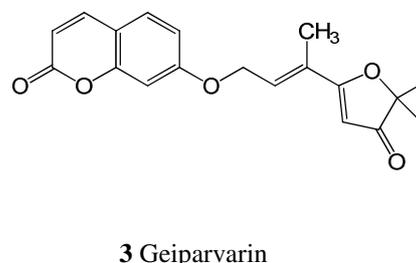
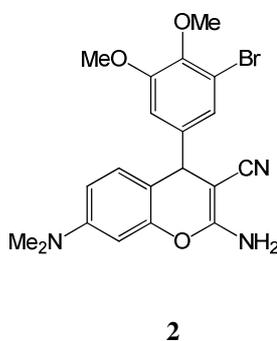
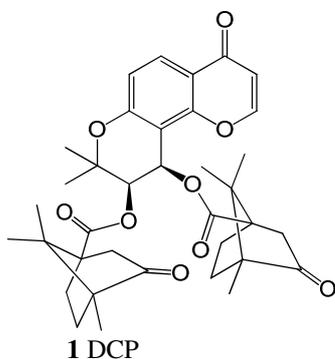
Key words: Chromenes, Pyrano-chromenes

Introduction

Chromenes and coumarins [1] have been the subject of the considerable chemical interest in the past decades. They occur widely in nature and exhibit important biological as well as pharmacological activities [2–5]. Among chromene derivatives are biologically interesting compounds showing antimicrobial [6–10], and antifungal activities [11, 12], inhibitors of influenza virus silidoses [13, 14], compounds with antihypertensive [15] and anti-allergic activity [16] and hair growth stimulant properties [17]. However, the chromenes are also well known for their biocidal [18, 19], wound healing [20], anti-inflammatory [21], and antiulcer [22] activities.

Some fused chromene derivatives were found useful as antiviral [23], antiproliferation agents [24], antioxidant [25, 26], antileishmanial [27], antitumor [28], and anti-HIV agents [29], central nervous system (CNS) activities and effects [30], as well as treatment of Alzheimer's disease [31], and Schizophrenia disorder [32]. Satyanarayana *et al.* [33] reported the synthesis and antifungal screening of new Schiff base of chromenes under conventional and microwave conditions. Furthermore, Lee *et al.* [34] have synthesized 3'*R*,4'*R*-di-(*O*)-(-)-camphanoyl-2',2'-dimethyldihydropyrano[2,3-*f*]chromone (DCP) (**1**) as a potent *in vitro* inhibitor of HIV-1 replication in H9 lymphocyte cells with an EC₅₀ of $6.78 \times 10^{-4} \mu\text{M}$. The family of 4-aryl-4*H*-chromenes has been recently reported to possess anti-cancer activity. These compounds, which are potent apoptosis inducers such as **2**, were found to be highly active in the growth inhibition MTT with the concentration causing 50 % cell growth inhibition (IC₅₀) values in the low nanomolar range [35]. Geiparvarin (**3**), a naturally occurring compound bearing a coumarin residue, has been shown to possess a significant inhibitory activity against a variety of cell lines including sarcoma 180, Lewis lung carcinoma, P-388 lymphocytic leukaemia, and Walker 256 carcinosarcoma [36].

In the present work, we report the synthesis of new chromenes derivatives .



Experimental

General

All reactants and solvents used in this study were reagents grade and they are available from Sigma-Aldrich and Fluka companies Melting points are determined in open capillary tubes in a Germany, Stuarts, SMP30 Melting points apparatus and are un corrected. Infrared spectra were recorded as KBr discs using a SHIMADZU FT-

IR8400S spectrophotometer. ¹HNMR spectra (solvent DMSO-d₆) were recorded on Bruker DMX-500 NMR spectrophotometer 300MHz spectrometer with TMS as internal standard which were made at chemistry department, Al-Bayt University, Jordan. Mass spectroscopic were recorded Shimadaza GC-Mass in the Al-Mustansiriyah University.

Synthesis of the Starting Compounds

Synthesis of 2-(4-Dimethylamino-benzylidene)-malononitrile [4]

To a mixture of *N,N* di-methyl amino benzaldehyde (0.15g, 1.0 mmol) and malono nitrile (0.07g, 1 mmol) in absolute ethanol (20 mL) was add the catalyst dipropylamine (few drops) and the reaction mixture was refluxed for 1 h., (TLC control hexane : ethyl acetate, 6:4). The reaction mixture was cooled and poured onto ice cold water, the product was filtered, dried and recrystallized from ethanol to give [4] as a yellow solid, (82% yield), m.p. 178., – GC-MS (EI, 70 eV): *m/z* (%) = 197 (100) [M]⁺, 153 (4)., FT-IR (KBr, v, cm⁻¹): 2210 cm⁻¹ (CN), 2922 cm⁻¹ (CH aliph.), 1512 cm⁻¹ (C=C).

Synthesis of 2-amino-4-(4-(dimethylamino)phenyl)-5-oxo-4, 5- dihydropyran [3,2-c]chromene-3-carbonitrile [5]

To compound [4] , (0.19g, 1.0 mmol) dissolved in ethanol (25 mL) followed a few drops of dipropylamine, was added 4-hydroxy coumarine (0.16g, 1.0 mmol) , the reaction mixture was heated under reflux for 4h., (TLC control , heptane : ethyl acetate, 6 : 4). The reaction mixture was cooled and poured onto ice cold water, the product was filtered, dried and recrystallized from 1,4-dioxane to give [5] as an orange solid, (78% yield), m.p. 167., FT-IR (KBr, v, cm⁻¹): 3323, 3406 cm⁻¹ (NH₂), 2208 cm⁻¹ (CN), 1707 cm⁻¹ (C=O). ¹HNMR, δ = 2.85 ppm [s, 6H, N(CH₃)₂], δ = 4.0 ppm [s, 1H, CH], δ = 6.60-7.78 ppm [m, 10H, Ar-H and NH₂].

Synthesis of (E)-ethyl N-(3-cyano-4-(4-(dimethylamino) phenyl)-5-oxo-4,5-dihydropyrano[3,2-c]chromen-2-yl)formimidate [6]

A mixture of [5] (0.36g, 1.0 mmol), triethylorthoformate (0.15g, 1mmol) add (10 ml) acetic anhydride the mixture was heated under reflux for 9 h (TLC control, hexane : ethyl acetate, 6:4) . The reaction mixture was left to cool overnight and the solid formed was recrystallized from 1,4-dioxane to give [6] as an orange solid, (65% yield), m.p. 178., FTIR (KBr, v, cm-1): 2210 cm⁻¹ (CN), 1685 cm⁻¹ (C=O), 1651 cm⁻¹ (C=N)., ¹HNMR, δ = 1.27 ppm [t, 3H, CH₃], δ = 3.08 ppm [s, 6H, N(CH₃)₂], δ = 4.24 ppm [q, 2H, CH₂], δ = 6.82-8.11 ppm [m, 9H, Ar-H and N=CH].

Synthesis of 9-amino-7-(4-(dimethylamino)phenyl)-8-imino-8,9-dihydrochromeno[3',4':5,6]pyrano[2,3-d]pyrimidin-6(7H)-one [7]

A solution of [6], (0.4 g, 1.0 mmol) and hydrazine hydrate 80% (10 ml) in methanol (25 ml) was stirred for 7 h., (TLC control, heptane : ethyl acetate, 6:4). The mixture allowed to stand overnight. The precipitate formed was, filtered, dried and recrystallized from methanol to give [7] as a brown solid, (85% yield), m.p. 127., FT-IR (KBr, v, cm⁻¹): 3294, 3311 cm⁻¹ (NH₂), 3275 cm⁻¹ (NH), 1683 cm⁻¹ (C=O), 1651 cm⁻¹ (C=N).,

Synthesis of compounds [8] , [9]

To solution of [6] (0.4g, 1.0 mmol) in methanol 25ml a solution of alkyl amine (1mmol , 5 ml) was added stirred for 1 hr. Then it is allowed to stand overnight. The precipitate formed was filtered, dried and recrystallized from methanol to give [8] or [9].

N'-(3-cyano-4-(4-(dimethylamino)phenyl)-5-oxo-4,5-dihydropyrano [3,2-c]chromen-2-yl)-N-methylformimidamide [8]

From methylamine , orange solid, (78% yield), m.p. 144., FT-IR (KBr, v, cm⁻¹): 3387 cm⁻¹ (NH), 2208 cm⁻¹ (CN), 1685 cm⁻¹ (C=O), 1650 cm⁻¹ (C=N).

N'-(3-cyano-4-(4-(dimethylamino)phenyl)-5-oxo-4,5-dihydropyrano[3,2-c]chromen-2-yl)-N-ethylformimidamide [9]

From ethylamine, orange solid, (73% yield), m.p. 151., FT-IR (KBr, v, cm⁻¹): 3336 cm⁻¹ (NH), 2210 cm⁻¹ (CN), 1732 cm⁻¹ (C=O), 1645 cm⁻¹ (C=N).

Synthesis of of compounds [10] , [11]

To solution of [5] , (0.36g, 1.0 mmol) in DMF (30 ml) , ethyl cyano- acetate or diethyl malonate (1mmole) was add. The mixture was heated under reflux for 9 h., (TLC control, hexane: ethyl acetate, 4:6). The solid product formed upon pouring on to ice / water mixture was collected by filtration and recrystallized from 1,4-dioxane to give [10] or [11].

2-cyano-N-(3-cyano-4-(4-(dimethylamino)phenyl)-5-oxo-4,5-dihydropyrano[3,2-c]chromen-2-yl)acetamide [10]

From ethyl cyano- acetate, brown solid, (89% yield), m.p. 138., FT-IR (KBr, v, cm⁻¹): weak band 3367 cm⁻¹ (NH), 2210 cm⁻¹ (CN), 1685 cm⁻¹ (C=O), 1650 cm⁻¹ (C=N).

Ethyl 3-((3-cyano-4-(4-(dimethylamino) phenyl)-5-oxo-4,5-dihydropyrano [3,2-c]chromen-2-yl)amino)-3-oxopropanoate [11]

From diethyl malonate, green solid, (92% yield), m.p. 102., FT-IR (KBr, ν , cm^{-1}): weak band at 3171 cm^{-1} (NH), 2208 cm^{-1} (CN), 1718 cm^{-1} (C=O amid), 1672 cm^{-1} (C=O lactone), 1649 cm^{-1} (C=N), $^1\text{H NMR}$, shows weak triplet signal at $\delta = 1.29 \text{ ppm}$ for (CH_3), $\delta = 3.11 \text{ ppm}$ (s, 6H, $\text{N}(\text{CH}_3)_2$), signal overlapped with signal of solvent (DMSO-d_6) at $\delta = 3.31 \text{ ppm}$ for ($-\text{CH}_2-$), $\delta = 6.85\text{-}8.06 \text{ ppm}$ [m, 9H, Ar-H and NH-CO]. Signals of ($-\text{CH}_2\text{O}-$) and (CH) of pyrone cycle not present.

Synthesis of 8-amino-7-(4-(dimethylamino)phenyl)-6,10-dioxo-6,7,10,11-tetrahydrochromeno[3',4':5,6]pyrano[2,3-b]pyridine-9-carbonitrile [12]

A solution of compound [10] (0.4g, 1.0 mmol) in 1,4-dioxane (25 mL) containing triethylamine (2 mL) was heated under reflux for 5 h., (TLC control, heptane : ethyl acetate, 7: 3). The solid product formed upon pouring onto ice / water mixture was collected by filtration and recrystallized from 1,4-dioxane to give [12] as an orange solid, (72% yield), m.p. 159., FT-IR (KBr, ν , cm^{-1}): weak band at 3360 cm^{-1} (OH), 3259 , 3281 cm^{-1} (NH_2), 2208 cm^{-1} (CN), 1699 cm^{-1} (C=O), 1676 cm^{-1} (C=N).

Synthesis of N-(3-cyano-4-(4-(dimethylamino)phenyl)-5-oxo-4,5,6a,10a-tetrahydropyrano[3,2-c]chromen-2-yl)-2-oxo-2H-chromene-3-carboxamide [13]

To a solution of [10], (0.4g, 1.0 mmol) in 1,4-dioxane (25 mL) containing dipropylamine (0.5 mL), salicylaldehyde (0.12g, 1.0mmol) was added. The reaction mixture was heated under reflux for 5h., (TLC control heptane : ethyl acetate, 6:4) . The solid products formed upon pouring onto ice/water mixture were containing few drops of hydrochloric acid was collected by filtration and recrystallized from 1,4-dioxane to give [13] as a yellow solid, (53% yield), m.p. 185., FT-IR (KBr, ν , cm^{-1}): 3269 cm^{-1} (NH), 2216 cm^{-1} (CN), 1735 cm^{-1} (C=O amid), 1683 cm^{-1} (C=O lactone), 1635 cm^{-1} (C=N).

Synthesis of compounds [14 -16]

A solution of compound [5], (0.36 g, 1 mmol) in 1,4-dioxane (20 mL) and dipropylamine (0.5 mL) was treated with available aromatic aldehydes (1mmol) under reflux for 3-5 h., (TLC control, heptane : ethyl acetate, 4:6). The solid product formed upon pouring onto ice / water was collected by filtration and recrystallized from available solvent to give [14] or [15] or [16].

2-((4-bromobenzylidene)amino)-4-(4-(dimethylamino)phenyl)-5-oxo-4,5-dihydropyrano[3,2-c]chromene-3-carbonitrile [14]

From *p*-bromobenzaldehyde, orange solid, (77% yield), m.p. 179., FT-IR (KBr, ν , cm^{-1}): 2206 cm^{-1} (CN), 1678 cm^{-1} (C=O), 1654 cm^{-1} (C=N).

2-((4-chlorobenzylidene)amino)-4-(4-(dimethylamino)phenyl)-5-oxo-4,5-dihydropyrano[3,2-c]chromene-3-carbonitrile [15]

From *p*-chlorobenzaldehyde, yellow solid, (71% yield), m.p. 181., FT-IR (KBr, ν , cm^{-1}): 2208 cm^{-1} (CN), 1681 cm^{-1} (C=O), 1653 cm^{-1} (C=N).

2-((4-(dimethylamino)benzylidene)amino)-4-(4-(dimethylamino) phenyl) -5-oxo-4,5-dihydropyrano[3,2-c]chromene-3-carbonitrile [16]

From *p*-*N,N*-dimethylamino benzaldehyde, orange solid, (85% yield), m.p. 169., FT-IR (KBr, ν , cm^{-1}): 2206 cm^{-1} (CN), 1681 cm^{-1} (C=O), 1653 cm^{-1} (C=N), $^1\text{H NMR}$, $\delta = 3.11 \text{ ppm}$ [s, 9H, $\text{N}(\text{CH}_3)_2$], $\delta = 3.57 \text{ ppm}$ [s, 1H, CH], $\delta = 6.84\text{-}8.04 \text{ ppm}$ [m, 13H, Ar-H and N=CH].

Synthesis of 7-(4-(dimethylamino)phenyl)-10-(pyridin-4-yl)chromeno [3',4':5,6]pyrano[2,3-d]pyrimidine-6,8(7H,9H)-dione [17]

A solution of compound [5], (0.36 g, 1 mmol) in 1, 4-dioxane (20 mL) and dipropylamine (0.5 mL) was treated with carboxy pyridine (1 mmol) under reflux for 3-5 h., (TLC control, heptane: ethyl acetate, 4:6). The solid product formed upon pouring onto ice / water was collected by filtration and recrystallized from ethanol to give [17] as an orange solid, (53% yield), m.p. 110., FT-IR (KBr, ν , cm^{-1}): 1724 cm^{-1} (C=O), 653 cm^{-1} (C=N).

Synthesis of 10-amino-12-(4-(dimethylamino)phenyl)-2-oxo-3,12-dihydro-2H-pyrano[3,2-c][1,2,4]triazolo[1,5-a]quinoline-11-carbonitrile [18]

To a solution of [5], (0.36 g, 1.0 mmol) in pyridine (20 ml), semicarbazide hydrochloride (0.11 g, 1 mmol, 1.0 mmol) was added and the reaction was heated under reflux for 18 h., (TLC control, hexane : ethyl acetate, 5:5). After cooling, the mixture was poured into cold water. The solid crude product was filtered, dried, and recrystallized from DMSO to give [18] as a yellow solid, (83% yield), m.p. 184., FTIR (KBr, ν , cm^{-1}): 3304 , 3398 cm^{-1} (NH_2), 3203 cm^{-1} (NH), 2210 cm^{-1} (CN), 1683 cm^{-1} (C=O), 1660 cm^{-1} (C=N).

Synthesis of N-(3-cyano-4-(4-(dimethylamino)phenyl)-5-oxo-4,5-dihydropyrano[3,2-c]chromen-2-yl)benzamide [19]

A mixture of [5], (0.36 g, 1.0 mmol), and benzoyl chloride (1mmol, 0.14g) in pyridine (20 ml) was refluxed for 10 h., (TLC control, hexane : ethyl acetate, 4:6). The solid product formed upon pouring onto ice / water was collected by filtration and recrystallized from 1,4-dioxane to give [19] as a green solid, (92% yield), m.p. 191., FT-IR (KBr, ν , cm^{-1}): 3371 cm^{-1} (NH), 2210 cm^{-1} (CN), 1724 cm^{-1} (C=O amid), 1688 cm^{-1} (C=O lactone), 1614 cm^{-1} (C=N).

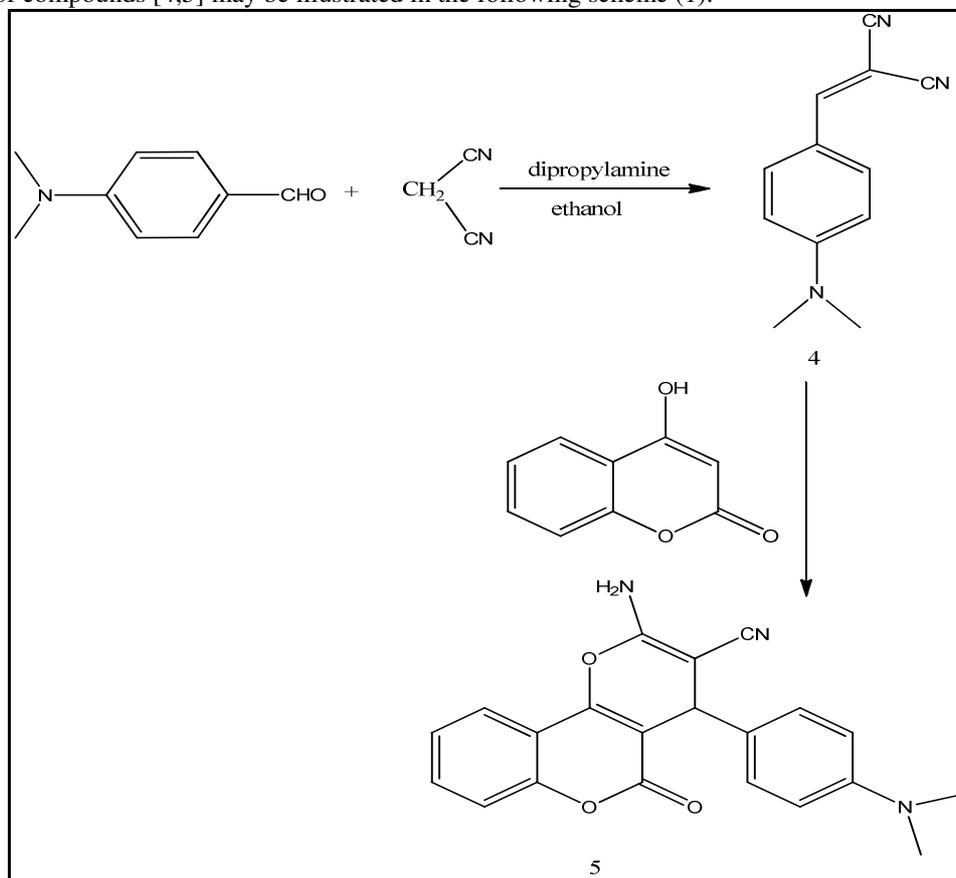
Synthesis of 7-(4-(dimethylamino)phenyl)-10-(4-methoxyphenyl) chromeno[3',4':5,6]pyrano[2,3-d]pyrimidine-6,8(7H,9H)-dione [20]

A mixture of [5], (0.36 g, 1.0 mmol), and *p*-methoxy benzoyl chloride (1 mmol, 0.17g) in pyridine (20 ml) was refluxed for 18 h., (TLC control, hexane : ethyl acetate, 4:6). The solid product formed upon pouring onto ice / water was collected by filtration and recrystallized from 1,4-dioxane to give [20] as a green solid, (89% yield), m.p. 134., FT-IR (KBr, ν , cm^{-1}): weak band at 3330 cm^{-1} (NH), 1681 cm^{-1} (C=O), 1650 cm^{-1} (C=N), $^1\text{H NMR}$, $\delta = 3.09 \text{ ppm}$, [s, 6H, $\text{N}(\text{CH}_3)_2$], $\delta = 3.58 \text{ ppm}$, [s, 3H, OCH_3], $\delta = 6.76\text{-}7.67 \text{ ppm}$, [m, 12H, Ar-H], $\delta = 12.30 \text{ ppm}$, [s, 1H, NH], signal of CH of pyrone cycle not present.

Results and discussion

Preparation and characterization of 2-amino-4-[4-(dimethylamino) phenyl]-5-oxo-4H,5H-pyrano[3,2-c]chromene-3-carbonitrile [5]

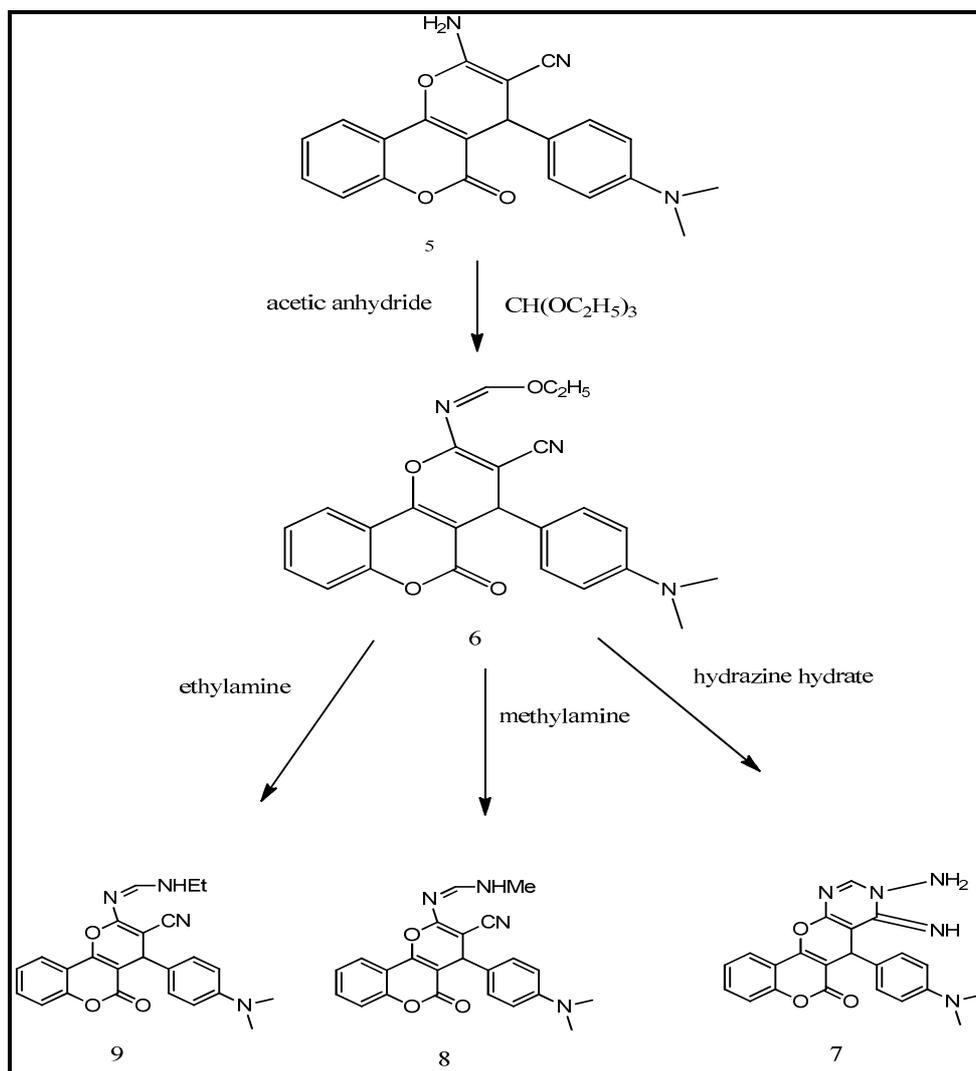
In the present study, we report on the synthesis of 2-amino-4-[4-(dimethylamino) phenyl]-5-oxo-4H,5H-pyrano [3,2-c] chromene-3-carbonitrile *via* reaction of molononitrile with 4-(dimethylamino) benzaldehyde to produced [4-(dimethylamino) benzylidene] propanedinitrile [4], which upon condensation with 4-hydroxycoumarin in presence of dipropylamine gave 2-amino-4-[4-(dimethylamino) phenyl]-5-oxo-4H,5H-pyrano[3,2-c]chromene-3-carbonitrile[5]. These results are similar to the results obtained in literatures^(37,38). The formation of compounds [4,5] may be illustrated in the following scheme (1).



Scheme (1)

Compound [4] was characterized by FT-IR and mass spectra, the FT-IR spectrum of compound [4] shows (CN) stretching band at 2210 cm^{-1} , (C=C) stretching band at 1612 cm^{-1} and (C-H)aliphatic stretching band at 2922 cm^{-1} . The mass spectrum shows the molecular ion peak at $m/z = 197$ which is in agreement with the molecular formula of this compound $\text{C}_{12}\text{H}_{11}\text{N}_3$. Compound [5] was characterized by FT-IR and $^1\text{H NMR}$, the FT-IR spectrum of compound [5] shows the (NH_2) stretching bands at 3406 and 3323 cm^{-1} and (CN) stretching band at 2208 cm^{-1} and (C=O) stretching band of lactone at 1707 cm^{-1} . The $^1\text{H NMR}$ spectrum shows singlet signal at $\delta = 2.85 \text{ ppm}$ for $\text{N}(\text{CH}_3)_2$, singlet signal at $\delta = 4.0 \text{ ppm}$ for CH of pyrone cycle, and multi- signal at $\delta = 6.60\text{-}7.78 \text{ ppm}$ for Ar-H and NH_2 .

Preparation and characterization of compound [6-9]



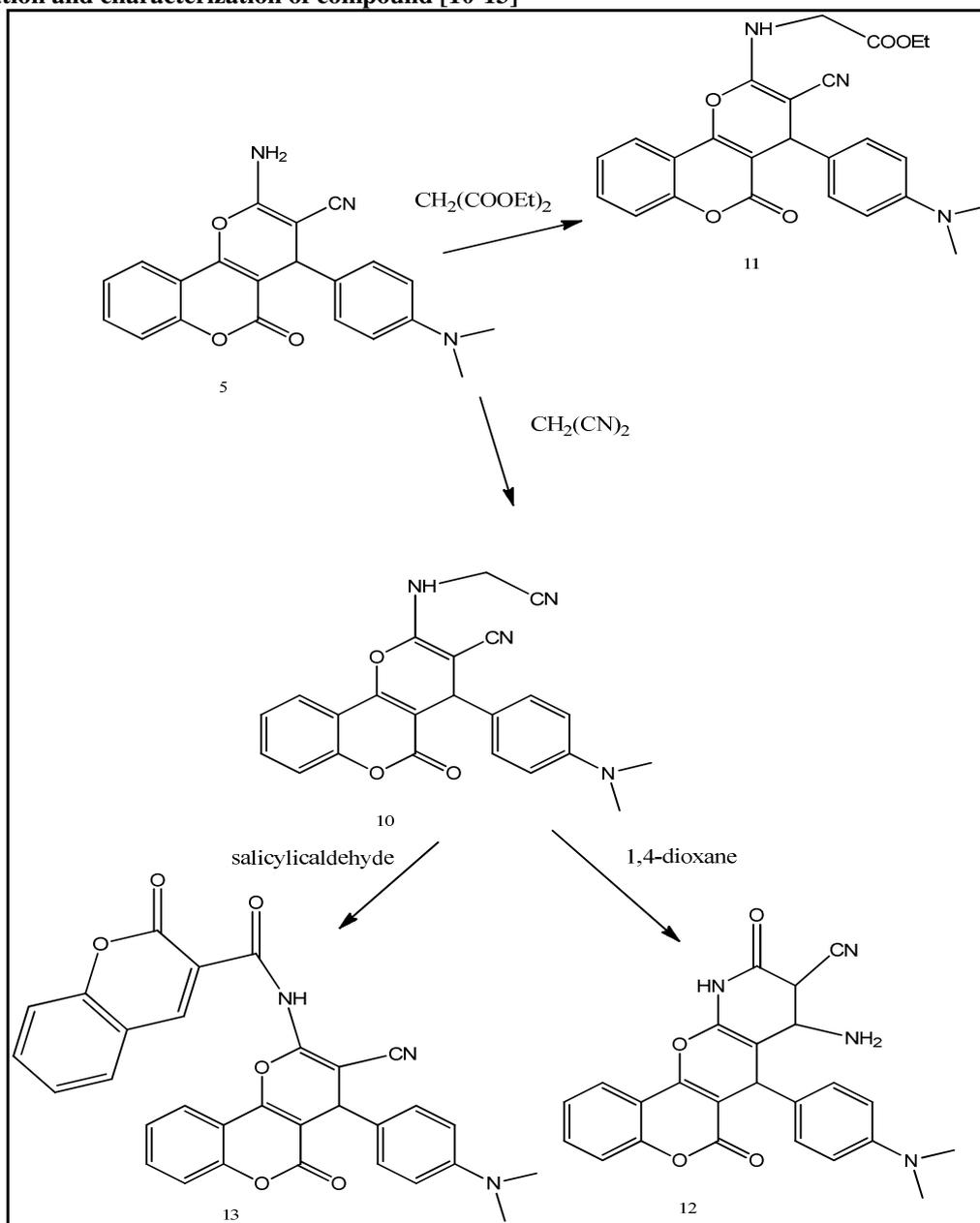
Scheme (2)

Compound [5] was selected as a key intermediate for the synthesis of new fused and non fused chromene derivatives, treatment of [5] with triethyl orthoformate in acetic anhydride gave the corresponding imidoformate derivative [6] in 65 % yield. This compound was characterized by FT-IR and ^1H NMR, the FT-IR spectrum of compound [6] shows disappearance of the amino group stretching bands at 3406 and 3323 cm^{-1} . The ^1H NMR spectrum shows triplet signal at $\delta = 1.27$ ppm for CH_3 , singlet signal at $\delta = 3.08$ ppm for $\text{N}(\text{CH}_3)_2$, quartet signal at $\delta = 4.24$ ppm for CH_2 , and multi-signal at $\delta = 6.82$ - 8.11 ppm for Ar-H and $\text{N}=\text{CH}$.

To synthesize derivatives [7-9], the compound [6] was reacted for one hour at room temperature with hydrazine hydrate to give fused chromene derivative [7], while when reacted with methyl amine or ethyl amine to gave non fused chromene derivatives [8] or [9]. These results are similar to the results obtained in literatures^(39,40). The synthetic reactions are summarized in scheme (2).

The structures of compounds [7-9] were confirmed by FT-IR spectra, The FT-IR spectrum of compound [7] shows disappearance the (CN) stretching band at 2206 cm^{-1} and appearance (NH) stretching band at 3203 cm^{-1} and (NH_2) stretching bands at 3315 and 3250 cm^{-1} , while the FT-IR spectra of compounds [8] and [9] shows appearance the cyano group (CN) stretching band 2202 or 2208 cm^{-1} and also (NH) stretching band at 3387 or 3304 cm^{-1} .

Preparation and characterization of compound [10-13]



Scheme (3)

The synthesized systems of these compounds are based on two synthetic key precursors, namely, [5] and [10]. The synthetic strategies adopted to obtain the newly synthesized [12] and [13] depended on the regioselective attack on the ethyl cyano acetate moiety of the key precursors [10] by different reagents, which, in one or two steps added a highly functionalized substituent or heterocyclic ring to the molecule. These results are similar to the results obtained in literatures⁽⁴¹⁾.

The key precursors [10] and [11] were obtained via the reaction of [5] with respective active methylene reagents ($\text{XCH}_2\text{CO}_2\text{Et}$; $\text{X}=\text{CN}$; $\text{X}=\text{CO}_2\text{Et}$).

The structures of the synthesized compounds have been characterized by FT-IR and some of them by ¹HNMR. The FT-IR spectrum of compounds [10] and [11] shows disappearance of the amino group stretching bands at 3406 and 3323 cm^{-1} and appearance (NH) stretching band at 3367 - 3396 cm^{-1} . The ¹HNMR spectrum of [11] shows weak triplet signal at $\delta = 1.29$ ppm for (CH_3), singlet signal at $\delta = 3.11$ ppm for $\text{N}(\text{CH}_3)_2$, signal overlapped with signal of solvent (DMSO- d_6) at $\delta = 3.31$ ppm for ($-\text{CH}_2-$), and multi - signal at $\delta = 6.85$ -8.06 ppm for Ar-H and NH-CO]. Signals of ($-\text{CH}_2\text{O}-$) and (CH) of pyrone cycle not present.

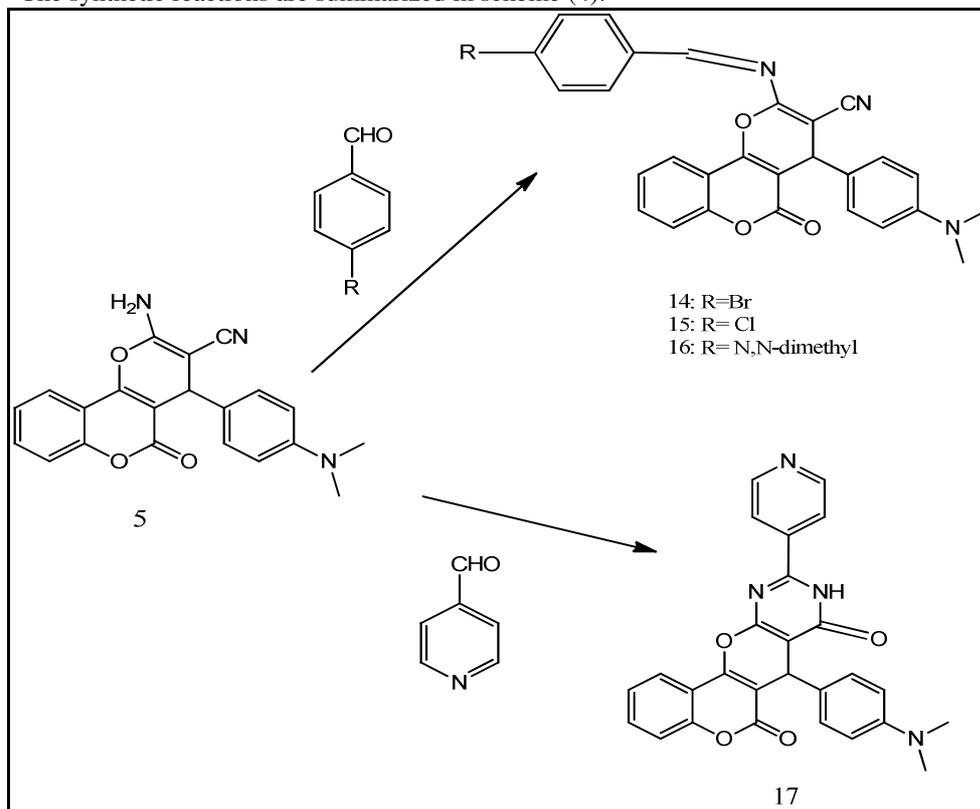
Compound [10] underwent ready cyclization when heated in 1,4-dioxane containing triethylamine to give chromene pyridine derivative [12]. The FT-IR spectrum of compound [12] shows weak (NH) stretching band at 3360 cm^{-1} in the keto form and (NH_2) stretching bands at 3281 and 3259 cm^{-1} .

Thus, the reaction of [10] with salicylaldehyde gave the coumarine derivative [13]. The FT-IR spectrum shows disappearance (NH_2) stretching bands at 3323 and 3406 cm^{-1} .

Preparation and characterization of compound [14-17]

The Schiff bases compounds [14-17] were synthesized by reaction compound [5] with substituted aromatic aldehydes in 1,4-dioxane. The reaction with carboxy pyridine gave fused chromene derivative (17) while the reaction other substituted aromatic aldehydes gave non-fused chromene derivatives (14-16), this due to the high activity of carboxy pyridine. These results are similar to the results obtained in literatures^(42,43)

The synthetic reactions are summarized in scheme (4).

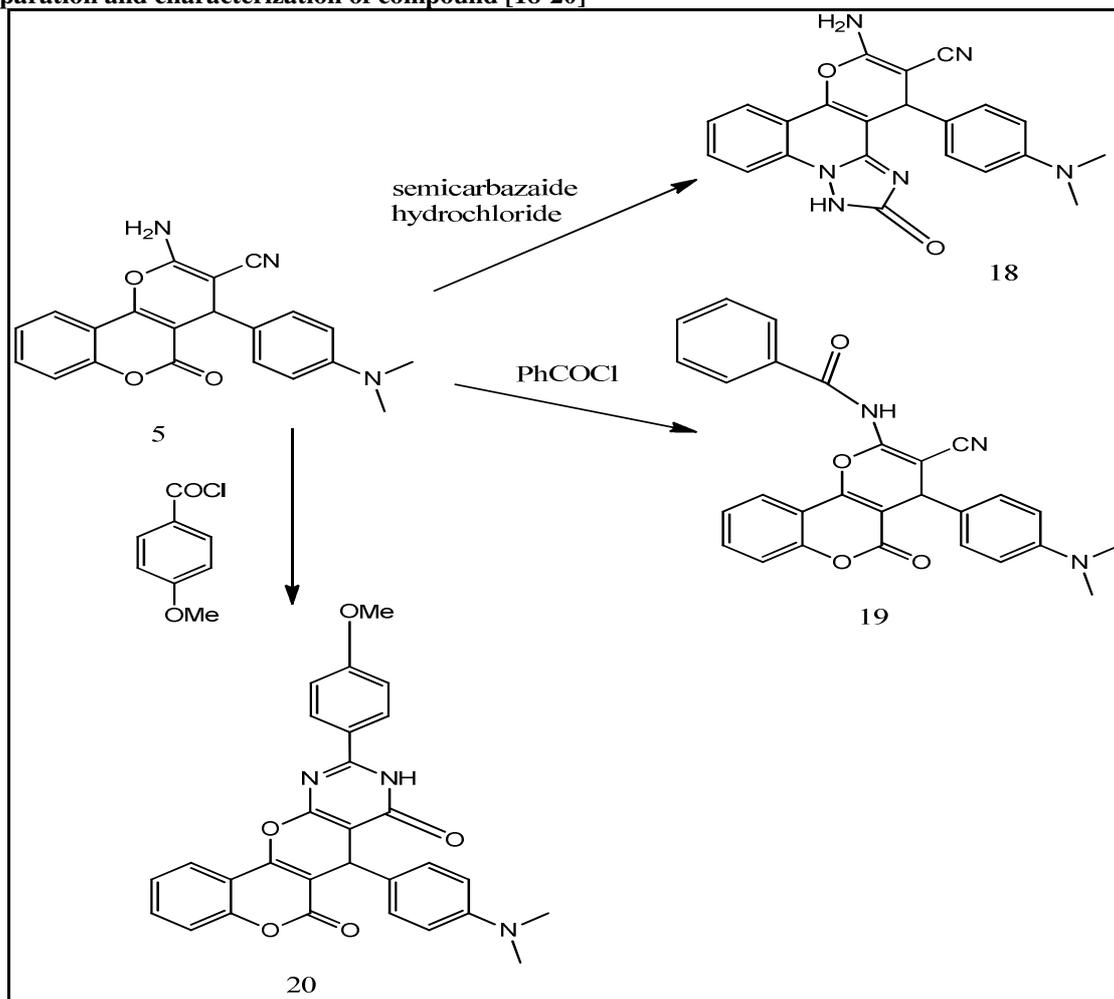


Scheme (4)

The structures of the synthesized compounds have been characterized by FT-IR and some of them by ^1H NMR. The FT-IR spectra of these compounds shows disappearance (NH_2) stretching bands at 3323 and 3406 cm^{-1} , while compound [17] shows disappearance the (CN) stretching band at 2208 cm^{-1} and disappearance (NH_2) stretching bands at 3323 and 3406 cm^{-1} .

Compound [16] was characterized by ^1H NMR, the ^1H NMR spectrum shows singlet signal at $\delta = 3.11$ ppm for $\text{N}(\text{CH}_3)_2$, singlet signal at $\delta = 3.57$ ppm for CH of pyrone cycle, and multi-signal at $\delta = 6.84$ - 8.04 ppm for Ar-H and $\text{N}=\text{CH}$.

Preparation and characterization of compound [18-20]



Scheme (5)

To synthesize these derivatives, an attempt to construct a third heterocyclic ring condensed with coumarin was successful *via* reaction of [5] with semicarbazide hydrochloride in refluxing dry pyridine to give triazolo[1,5-*a*]quinolone [18] in 83 % yield.

The FT-IR spectrum of compound [18] shows appearance of (NH) stretching band at 3203 cm^{-1} and (C=O) of lactam at 1693 cm^{-1} and disappearance of (C=O) of lactone at 1707 cm^{-1} .

Thus, Benzoylation of [5] with benzoylchloride or *p*-methoxy Benzoyl chloride afforded the non fused chromene derivative [19] and fused chromene - pyrimido derivative [20] respectively. These results are similar to the results obtained in literatures^(42,44).

The FT-IR spectrum of compound [19] shows appearance of (NH) stretching band at 3416 cm^{-1} and disappearance (NH₂) stretching bands at 3323 and 3406 cm^{-1} , while the FT-IR spectrum for compound [20] shows disappearance stretching bands of the (CN) at 2208 cm^{-1} and (NH₂) at 3323 and 3406 cm^{-1} . The ¹HNMR spectrum of [20] shows singlet signal at $\delta = 3.09\text{ ppm}$ for N(CH₃)₂, singlet signal at $\delta = 3.58\text{ ppm}$ for OCH₃, and multi-signal at $\delta = 6.76\text{-}7.67\text{ ppm}$, for Ar-H], $\delta = 12.30\text{ ppm}$, [s, 1H, NH], signal of CH of pyrone cycle not present.

References

1. G. P. Ellis in *Chromenes, Chromanones and Chromones*, (Eds.: A. Weissberger, E. Taylor), John Wiley & Sons, New York, **1977**, pp. 1–10.
2. W. C. Cutting, R. H. Dreisbach, M. Azima, B. J. Neff, B. J. Brown, J. Wray, *Stanford Med. Bull.* **1951**, 9, 236–242.
3. C. Mentzer, P. Meunier, J. Lecocq, D. Billet, D. Xuong, *Bull. Soc. Chim. Fr.* **1945**, 12, 430–437.
4. J. S. G. Cox, *Nature (London)* **1967**, 216, 1328–1329.
5. T. S. C. Orr, M. C. Pollard, J. Gwilliam, J. S. G. Cox, *Clin. Exp. Immunol.* **1970**, 7, 745–757.

6. A. M. El Agrody, M. S. Abd El Latif, N. A. El Hady, A. H. Fakery, A. H. Badair, *Molecules* **2001**, *6*, 519–527.
7. A. H. Badair, N. A. El Hady, M. S. Abd El Latif, A. H. Fakery, A. M. El Agrody, *Farmaco* **2000**, *55*, 708–714.
8. A. M. El Agrody, M. H. El Hakim, M. S. Abd El Latif, A. H. Faker, E. S. El Sayed, K. A. El Ghareab, *Acta Pharm.* **2000**, *50*, 111–120.
9. M. C. Yimdjo, A. G. Azebaze, A. E. Nkengfack, A. M. Michele, B. Bodo, Z. T. Fomum, *Phytochemistry* **2004**, *65*, 2789–2795.
10. V. Jeso, K. C. Nicolaou, *Tetrahedron Lett.* **2009**, *50*, 1161–1163.
11. T. Mouri, T. Yano, S. Kochi, T. Ando, M. Hori, *J. Pestic. Sci.* **2005**, *30*, 209–213.
12. S. Sardari, Y. Mori, K. Horita, R. G. Micetich, S. Nishibe, M. Daneshtalab, *Bioorg. Med. Chem.* **1999**, *7*, 1933–1940.
13. W. P. Smith, L. S. Sollis, D. P. Howes, C. P. Cherry, D. I. Starkey, N. K. Copley, *J. Med. Chem.* **1998**, *41*, 787–797.
14. R. N. Taylor, A. Cleasby, O. Singh, T. Sharzynski, J. A. Wonacott, W. P. Smith, L. S. Sollis, D. P. Howes, C. P. Cherry, R. Bethell, P. Colman, *J. Med. Chem.* **1998**, *41*, 798–807.
15. D. A. Quagliato, US Patent 5171857, **1993**.
16. D. R. Buckle, S. Harry, US Patent 4263299, **1981**.
17. H. Koga, H. Nabata, H. Nishina (Chugai Seiyaku K. K., Japan), PCT Int. Appl. WO 9214439, **1992**.
18. M. Weidenbörner, H. Hindrof, H. C. Jha, P. Tsotsonos, H. Egg, *Phytochemistry*, **1990**, *29*, 1103–1105.
19. M. Weidenbörner, H. C. Jha, *Pestic. Sci.* **1993**, *38*, 347–351.
20. R. H. Davis, J. J. Donato, G. M. Hartman, R. C. Haas, *J. Am. Podiatr. Med. Assoc.* **1994**, *84*, 77–81.
21. T. Hirata, T. Suga, *Bull. Chem. Soc. Jap.* **1978**, *51*, 842–849.
22. D. Womble, J. H. Helderman, *Int. J. Immunopharmac.* **1988**, *10*, 967–974.
23. C. Conti, N. Desideri, *Bioorg. Med. Chem.* **2009**, *17*, 3720–3722; and ref. cited therein.
24. C. P. Dell, C. W. Smith, Eur. Pat. Appl. 537 949, **1993**.
25. S. V. Jovanovic, S. Steenken, M. Tosic, B. Marjanovic, M. G. Simic, *J. Am. Chem. Soc.* **1994**, *116*, 4846–4851.
26. T. Symeonidis, M. Chamilos, D. J. Hadjipavlou-Litina, M. Kallitsakis, K. E. Litinas, *Bioorg. Med. Chem. Lett.* **2009**, *19*, 1139–1142.
27. T. Narender, S. S. Gupta, *Bioorg. Med. Chem. Lett.* **2009**, *14*, 3913–3916.
28. D. O. Moon, C. Park, M. S. Heo, Y. M. Park, Y. H. Choi, G. H. Kim, *Int. Immunopharmacol.* **2007**, *7*, 36–45.
29. Y. A. Al-Soud, I. A. Al-Masoudi, S. Saeed, U. Beifuß, N. A. Al-Masoudi. *Chem. Heterocyc. Comp.* **2006**, *467*, 669–676.
30. F. Eiden, F. Denk, *Arch. Pharm. (Weinheim)* **1991**, *324*, 353–354.
31. C. Bruhlmann, F. Ooms, P.-A. Carrupt, B. Testa, M. Catto, F. Leonetti, C. Altomare, A. Carotti, *J. Med. Chem.* **2001**, *44*, 3195–3208.
32. S. R. Kesten, T. G. Heffner, S. G. Johnson, T. A. Pugsley, J. L. Wright, D. L. Wise, *J. Med. Chem.* **1999**, *42*, 3718–3725.
33. V. S. V. Satyanarayana, P. Sreevani, A. Sivakumar, V. Vijayakumar, *Arkivoc* **2008**, *17*, 221–233.
34. D. Yu, A. Brossi, N. Kilgore, C. Wild, G. Allaway, K.-H. Lee, *Bioorg. Med. Chem. Lett.* **2003**, *13*, 1575–1576.
35. W. Kemnitzer, J. Drewe, S. Jiang, H. Zhang, Y. Wang, J. Zhao, S. Jia., J. Herich, D. Labreque, R. Storer, K. Meerovitch, D. Bouffard, R. Rej, R. Denis, C., Blais, S. Lamothe, G. Attardo, H. Gourdeau, B. Tseng, S. Kasibhatla, S. X. Cai, *J. Med. Chem.* **2004**, *47*, 6299–6310.
36. T. Fujiwara, A. Sato, M. El-Farrash, K. Miki, K. Kabe, Y. Isaka, M. Kodama, Y. M. Wu, L. B. Chen, H. Harada, M. Sugimoto, M. Hatanaka, Y. Hinuma, *Antimicrob. Agents Chemother.* **1998**, *42*, 1340–1345.
37. Tu, Shujiang, " Synthesis of 2-amino-3-ethoxycarbonyl-4-aryl-4H,5H-pyrano-[3,2-c]benzopyran-5-one ", *Journal of Chemical Research*, **2004**, *6*, 396-398.
38. R. Medyouni, " Clean procedure and DFT study for the synthesis of 2-amino-3-ethoxycarbonyl-4-(aryl)-4H-pyrano[3,2-c]chromen-5-one derivatives: A novel class of potential antimicrobial and antioxidant agents ", *Journal of Chemistry*, **2013**, 472657, 9.
39. Z.H.Khalil, A.A.Abdel-Hafez, A.A.Gelies and A.M.Kamal, " Nitriles in hetero synthesis. synthesis and reaction of pyrano [3,2-h] quonoline derivatives " , *bull. Chem.. soc.. Jpn.*, **1991**, *64* ,668-670 .

40. M.E.A.Zaki ,N.M.Fawzy and S.A.Swelam , "synthesis of fused Azoles and N-Heteroaryl derivatives based on pyrano [2,3-c]pyrazole" , *molecules*, **1999**, 3 , 1-8 .
41. H.Z.shams , R.M.Mohareb, M.H.Helal and A.E.Mahmoud , "Novel synthesis and antitumor evaluation of polyfunctionally substituted heterocyclic compounds derived from 2- cyano-N-(3-cyano-4,5,6,7-tetrahydrobenzo [b]thiophen-2-yl)-acetamide" , *Molecules* , **2011**, 16 , 52-73.
42. Najim A. Al-Masoudi, H. H. Mohammed, A. M. Hamdy, O. A. Akrawi , N. Eleya, A.Spannenberg, C .Pannecouque, and P. Langer" Synthesis and anti-HIV of new fused chromene derivatives derived from 2-amino-4-(1-naphthyl)-5-oxo-4*H*,5*H*-pyrano[3,2-*c*]chromene-3-carbonitrile", *Z. Naturforsch.* **2013**, 68b, 229 – 238
43. A.M.EL-Agrody ,F.A.Hussein ,E.H.Mohamed and A.H.Bedair, "Synthesis of 9-methoxy and 9-acetoxy-3-amino-1-(4-methoxy- phenyl) -1*H*- Benzo (f) chromenes-2-carbonitriles " ,*Z. Naturforsch*, **2002**, 57b , 579-585 .
44. S.M.Abd –Gawad ,M.S.A El-Gaby , H.I.Heiba , H .M .Aly and M.M.Ghorab, "Synthesis and radiation stability of some new biologically active hydroquinoline and pyrimido [4,5-*b*]quinoline derivatives " *Journal of the Chinese chemical society*, **2005**, 52, 1227-1236 .

The IISTE is a pioneer in the Open-Access hosting service and academic event management. The aim of the firm is Accelerating Global Knowledge Sharing.

More information about the firm can be found on the homepage:

<http://www.iiste.org>

CALL FOR JOURNAL PAPERS

There are more than 30 peer-reviewed academic journals hosted under the hosting platform.

Prospective authors of journals can find the submission instruction on the following page: <http://www.iiste.org/journals/> All the journals articles are available online to the readers all over the world without financial, legal, or technical barriers other than those inseparable from gaining access to the internet itself. Paper version of the journals is also available upon request of readers and authors.

MORE RESOURCES

Book publication information: <http://www.iiste.org/book/>

Academic conference: <http://www.iiste.org/conference/upcoming-conferences-call-for-paper/>

IISTE Knowledge Sharing Partners

EBSCO, Index Copernicus, Ulrich's Periodicals Directory, JournalTOCS, PKP Open Archives Harvester, Bielefeld Academic Search Engine, Elektronische Zeitschriftenbibliothek EZB, Open J-Gate, OCLC WorldCat, Universe Digital Library , NewJour, Google Scholar

