Synthesis of fused cyclic chromene and alicyclic chromene derivatives from *2*-amino-*4-[4*-(dimethylamino)phenyl*]5*-oxo-*4H,5H*-pyrano *[3,2-c]*chromene-*3*-carbonitrile

Hamid Hashim Mohammed ✉
Department of Chemistry, College of Science, University of Al-Mustansiryah, IRAQ
E-mail : hammed_sugar@yahoo.com

ArticleInfo

Received
25/2/2016

Accepted
5/6/2016

ABSTRACT

Derivatives of fused cyclic chromene and alicyclic chromene were synthesized starting from 2-amino-4-[4-(dimethylamino)phenyl]5-oxo-4*H*,5*H*-pyrano [3,2-*c*]chromene-3-carbonitrile. The structures of the synthesized compounds were elucidated by spectral data : infrared spectra (FT-IR) and ^{1}HNMR.

Keywords: coumarine, chromene, pyrmidine

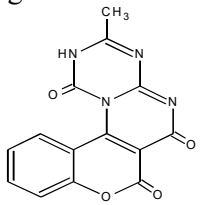
الخلاصة

- 4–[4- امينو –2حضرت سلسلة جديدة من مشتقات كرومين حلقية ملتحمة و كرومين غير حلقية من - كاربونايتريل. ان 3] كرومين –c–2، 3–بايرونو[5H، 4H- اوكسو-5(داي مثيل امينو) فنيل] تركيب المركبات المحضرة شخصت بواسطة بعض الطرق الطيفية : الاشعة تحت الحمراء (FT-IR)وطيف الرنين النووي المغناطيسي (^{1}HNMR)

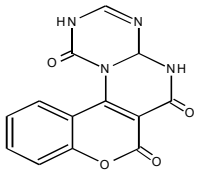
INTRODUCTION

Naturally occurring coumarins have exhibited several biomedical applications including platelet aggregation, cytotoxic activity, enzyme inhibition, antiviral, antibacterial, antifungal activities, etc. [1][2][3][4]

Coumarin and chromene derivatives are widely found in plants belonging to the families, Belliferae,Rutaceae, and Compositae [1]. New derivatives of coumarins have been isolated from plants with an ever increasing variety of uses [5][6][7][8][9][10][11][12][13]. More recently, specific studies looking at the effects of coumarins as a cytochrome P-450 inhibitor, which is a carcinogen metabolizing enzyme[14]. Based on the biological importance of several coumarins, new coumarins, chromenes, and other benzo-and-napthopyrans have been synthesized [15][16][17]. Coumarins and their derivatives may also possess valuable optical properties, especially the3-heterarylcoumarins [18][19]. By binding coumarins to biological effectors molecules, the path of the molecule through a biological system may be traced [20]. New chromene derivatives [I ,II] derived from 2-amino-4[H], 5[H]3, 4-dihydro (1) benzopyrano [4,3-d] pyrimidine-4,5-dione-1-carbonitrile were synthesized by F. K. Mohamed and coworkers [21], these compounds are important biological activities.

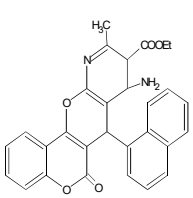


(I)

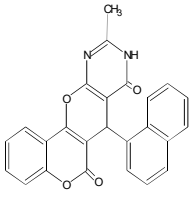


(II)

A new series of pyrano-chromene and pyrimidopyrano-chromene derivatives (III), (IV) were synthesized by Hamid H.M. and coworkers, [22][23], some of these compound have been exhibited an inhibitory activity screening against HIV-1 and HIV-2 in MT-4 cells:

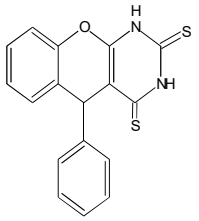


(III)

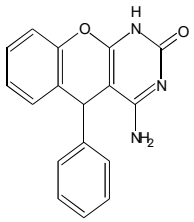


(IV)

Some novel *4-H*-Chromeno *[2,3-d]* pyrimidines (V),(VI) were synthesized via 2-amino-4-phenyl-4-chromene-3-carbonitrile [24] by Nimesh R-Kamdear and Dhaval D.H. These compounds have Exhibited pronounced antiubercular and antimicrobial activities.



(V)



(VI)

Among chromene derivatives are biologically interesting compounds showing antimicrobial [25][26][27][28][29], and antifungal activities [30][31], inhibitors of influenza virus silidoses [32][33], compounds with antihypertensive [34] and anti-allergic activity [35] and hair growth stimulant properties[36]. A new series of hydroquinolines and pyrimidoquinolines were synthesized by S.M.Abel-Gawad and coworkers [37], starting from *2*-amino-*4*-(3-bromo-phenyl)-*7, 7*-dimethyl-1-naphthalen-1-yl-5-oxo-*1, 4, 5, 6, 7, 8*-hexahydro-quinoline-3-carbonitrile, some of these compounds exhibited are mark able antifungal activity.

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. ^{1}HNMR 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.

Synthesis of compounds

Synthesis of 2-(4-Dimethylamino-benzylidene)-malononitrile(1)[38]

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 (1) as a yellow solid, (82% yield), m.p. 178., – GC-MS (EI, 70 eV): *m/z* (%) = 197 (100) $[M]^+$, 153 (4)., FT-IR (KBr, ν, 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*(2)**[38]

To compound (1), (0.19g, 1.0 mmol) dissolved in ethanol (25 mL) followed a few drops of dipropylamine, was added 4-hedroxy 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 cooledand poured onto ice cold water, the product was filtered, dried and recrystallized from 1,4-dioxane to give (2) as an orange solid, (78% yield), m.p. 167., FT-IR (KBr, ν, cm^{-1}): 3323, 3406 cm^{-1} (NH_2), 2208 cm^{-1} (CN), 1707 cm^{-1} (C=O). ^{1}HNMR, δ = 2.85 ppm [s, 6H, $N(CH_3)_2$], δ = 4.0 ppm [s, 1H, CH],δ = 6.60-7.78 ppm [m, 10H, Ar-H and NH_2].

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

A mixture of (2) (0.36g, 1.0 mmol), powdered anhydrous $AlCl_3$ and acetonitrile (5 mL) was heated with stirred the under reflux for 10 h.,

(TLC control, hexane : ethyl acetate, 6:4), The contents were cooled and decomposed in ice-cold HCl .The product obtained was filtered ,washed with water and recrystallized from ethanol to give (3) as an orange solid, (67% yield), m.p. 103-105 ^{o}C. FT-IR(KBr, ν, cm^{-1}): 3360 cm^{-1} (NH), 2208 cm^{-1} (CN), 1701 cm^{-1} (C=Olacton)

Synthesis of ethyl 8-amino-7-(4-(dimethylamino) phenyl)- 10-methyl-6-oxo-6,7,8,9-tetrahydrochromeno [3',4':5,6] pyrano [2,3-b]pyridine-9-carboxylate (4)

Compound **(2)** (1mmole, 0.36g) and $SnCl_4$ (2 mL, 1mmol) were added to a stirred solution of ethyl acetoacetate (1 mmol) in dry toluene (20 mL). The reaction mixture was stirred under nitrogen at room temperature for 30 min and then heated under reflux for 6 h. The reaction mixture was cooled and dispersed into water and titrated to pH 12–13 with a saturated aqueous solution of Na_2CO_3. After filtration, the filtrate was extracted three times with ethyl acetate (3×15), the organic layers were dried and evaporated at reduced pressure to give the solid product, which recrystallized from ethanol to give (4) as a brown solid, (65% yield), m.p. 180-182^{o}C. FT-IR(KBr, ν, cm^{-1}):1722 cm^{-1} (C=O lacton), 1705 cm^{-1} (C=O).

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

To a solution of (2) (0.36 g, 1.0 mmol) in dry pyridine (1 mL) was added acetic anhydride (3 mL) and the mixture was refluxed for 3 h., (TLC control, hexane : ethyl acetate, 5:5). On cooling, a precipitate was separated and washed in EtOH. Recrystallized from 1,4-dioxane afforded (5) as a brown solid, (81% yield), m.p. 182-184^{o}C. FT-IR(KBr, ν, cm^{-1}):2212 cm^{-1} (CN), 1718 cm^{-1} (C=O lacton), 1681 cm^{-1} (C=O amide) .

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

A solution of (2) (0.36 g, 1.0 mmol) in acetic anhydride (10 mL) containting conc. H_2SO_4 (5 mL)was heated under reflux for 10 h.A precipitate was formed after keeping the mixture at room temperature for 24 h, which was filtered and washed with water and EtOH. The product was recrystallized from EtOH to give (6) as a brown solid, (79% yield), m.p. 179-181^{o}C. FT-IR(KBr, ν, cm^{-1}): 3390 cm^{-1} (NH), 1712 cm^{-1} (C=O lacton), 1675 cm^{-1} (C=O amid).

Synthesis of* 7-(4-(dimethylamino) phenyl)-9,11-dihydro-6H-spiro [chromeno[3',4':5,6]pyrano[2,3-d]pyrimidine-10,1'-cyclohexane]6,8(7H)-dione*(7)

To a solution of (2), (0.36g,1mmol) cyclohexanone (5ml), anhydrous $FeCl_3$ (0.16g ,1 mmol) and DMF (10 mL) were added into a 50-mL flask. The reaction mixture was refluxed for 24 h., (TLC control, heptane : ethyl acetate, 4:6). Then the mixture was diluted with H_2O to afford product, recrystallized from diethyl ether gave (7) as a green solid, (91% yield), m.p. 110-112^{o}C. FT-IR(KBr, ν, cm^{-1}): 3362 cm^{-1} (NH), 1768 cm^{-1} (C=O lacton) .

Synthesis of Compound (8-10)

To an ice-cold solution of (2) (0.36g,1.0mmol), glacial acetic acid (30ml) and phosphoric acid (10ml) was added dropwise a solution of sodium nitrite (0.10g ,1.0 mmol) dissolved in the minimum amount of water in, an ice bath at temperature (-5 ^{o}C). This previously prepared diazonium salts was added dropwise to a mixture of active methylene (malononitrile, ethylcyanoacetate, diethylmalonate) (1.0 mmole), and anhydrous sodium acetate in ethanol. The reaction mixture was allowed to stand overnight at room temperature, then it was poured into water. The formed solid was filtered off, washing with water, dried and recrystallized from ethanol to give (8, 9, 10).

Synthesis of 2-[3-Cyano-4-(4-dimethyl amino-phenyl)-5-oxo-4, 5-dihydro pyrano [3,2-c] chromen-2-yl)diazenyl)-malononitrile (8)

Frommalonitrile, (88 % yield), m.p. 105-107 ^{o}C, FT-IR(KBr, ν, cm^{-1}): 2220 cm^{-1} (CN), 1732 cm^{-1} (C=O lacton), 1508 cm^{-1} (N=N).

^{1}HNMR, δ = 3.01 ppm [s, 6H, $N(CH_3)_2$], δ = 3.34 ppm [s, 1H, $CH(CN)_2$], δ = 3.45 ppm [s, 1H, CH], δ = 7.35-8.42 ppm [m, 8H, Ar-H]

Synthesis of Ethyl 2-cyano-2-((3-cyano-4-(4-(dimethyl amino) phenyl)-5-oxo-4,5-dihydropyrano [3,2-c] chromen-2-yl) diazenyl) acetate (9)

From *ethylcyanoacetate*, (78 % yield), m.p. 113-115 °C, FT-IR(KBr, ν, cm^{-1}): 2208 cm^{-1} (CN), 11643 cm^{-1} (C=O lacton), 1566 cm^{-1} (N=N).

Synthesis of Diethyl 2-((3-cyano-4-(4-(dimethylamino) phenyl)-5-oxo-4,5-dihydro pyrano[3,2-c] chromen-2-yl) diazenyl) malonate(10)

From *diethylmalonate*, (83 % yield), m.p. 121 - 123 °C, FT-IR(KBr, ν, cm^{-1}): 2218 cm^{-1} (CN), 1705 cm^{-1} (C=O lacton), 1506 cm^{-1} (N=N).

Synthesis of compound (11-13)

Compound of (2) (0.36 g, 1.0 mmol) was dissolved in aliphatic carboxylic acid (*formic acid, glacial acetic acid, propionic acid)* (3 mL, 1.0 mmol),then $POCl_3$ (0.2 mL) was added quickly. The mixture was refluxed for 12 h., (TLC control hexane : ethyl acetate, 5:5). After the mixture was cooled, added ice water (50 mL). A mass of white precipitate was produced. K_2CO_3 was added to neutralize the acid till no bubble occurs. The reaction mixture was filtered, and washed with a small amount of ethanol, dried to give (11,12, 13).

Synthesis of* 7-(4-(dimethylamino) phenyl) chromeno [3',4':5,6] pyrano[2,3-d]pyrimidine-6,8(7H,9H)-dione *(11)

From formic acid, green solid, (72 % yield), m.p. 182-184 °C, FT-IR(KBr, ν, cm^{-1}): 3400 cm^{-1}(NH), 1718 cm^{-1} (C=O lacton), 1610 cm^{-1} (C=O amid).

***Synthesis of 7-(4-(dimethylamino) phenyl)-10-Methyl chromeno [3',4':5,6]pyrano [2,3-d] pyrimidine-6,8(7H,9H)-dione* (12)**

From *glacial acetic acid*, brown green, (78 % yield),m.p. 191 -193 °C. FT-IR(KBr, ν, cm^{-1}): 3396 cm^{-1} (NH), 1716 cm^{-1} (C=O lacton), 1670 cm^{-1} (C=O amid).

Synthesis *7-(4-(dimethylamino) phenyl)-10-Ethyl chromeno [3',4':5,6]pyrano [2,3-d] pyrimidine-6,8(7H,9H)-dione(13)*

From *propionic acid*, green solid, (69 % yield), m.p. 195 -197 °C. FT-IR(KBr, ν, cm^{-1}): 3424 cm^{-1} (NH), 1735 cm^{-1} (C=O lacton), 1678 cm^{-1} (C=O amid),^{1}HNMR, δ = 2.52 ppm [s, 6H, $N(CH_3)_2$], δ = 2.35 ppm [s, 3H, CH_3], δ = 4.50 ppm [s, 1H, CH], δ = 6.30-7.80 ppm [m, 9H, Ar-H and NH].

Synthesis of 1-(3-cyano-4-(4-(dimethylamino)phenyl)-5-oxo-4,5-dihydropyrano[3,2-c]chromen-2-yl)-3-phenylthiourea (14)

A mixture of (2) (0.36g, 1.0mmol) and phenyl isothiocynate (0.14g, 1.0 mmol) in ethanol (10ml) was refluxed for 5 h., (TLC control, hexane: ethyl acetate *6:4)*. The solid product formed upon pouring onto ice/water was collected by filtration and washed with distilled water to give (14) as a green solid, (86% yield), m.p. 197-199°C. FT-IR(KBr, ν, cm^{-1}): 3308 cm^{-1}(NH)**,** 2210 cm^{-1} (CN), 1697 cm^{-1} (C=O lacton),1232 cm^{-1} (C=S)

Synthesis of 7-(4-(dimethylamino)phenyl)-8-(phenyl-imino)-10-thioxo-8,9,10,11-tetrahydrochromeno [3',4': 5,6] pyrano [2,3-d] pyrimidin-6(7H)-one (15)

A mixture of (2) (0.36 g, 1mmol), phenyl isothiocyanate (0,14 g, 1.0 mmol) and pyridine (20 mL) was refluxedin an oil bath for 12 h., (TLC control hexan : ethyl acetate, 4:6). The reaction mixture was cooled, diluted with distilled water and the resulting solid was *recrystallized from DMF to give* (15) as a green solid, (85% yield), m.p. 215-217°C.FT-IR(KBr, ν, cm^{-1}):3362 cm^{-1}(NH)**,** 1732 cm^{-1} (C=O lacton),1242 cm^{-1} (C=S).

Synthesis of 7-(4-(dimethylamino)phenyl)-8,10-dithioxo-8,9,10,11-tetrahydrochromeno [3',4':5,6]pyrano[2,3-d]pyrimidin-6(7H)-one (16)

Mixture of compound (2)(0.36 g, 1.0 mmol) and carbon disulphide(1.0 mmol) in pyridine (10 mL) were refluxed for 6h., (TLC control hexan : ethyl acetate, 4:6). After completion of the reaction, the reaction mixture was cooled at room temperature, then poured into ice cold

water, and neutralized with hydrochloric acid. The precipitated product was filtered off, washed with distilled water and *recrystallized* from ethanol to give (16) as a white solid, (88% yield), m.p. 272-274°C. FT-IR(KBr, ν, cm^{-1}): 3414 cm^{-1} (NH), 2696, 2733 cm^{-1} (SH), 1678 cm^{-1} (C=O lacton),1232 cm^{-1} (C=S).

Synthesis of 7-(4-(dimethyl amino) phenyl)-10-(ethylthio)-8-thioxo-8,9-dihydrochromeno [3',4':5,6]pyrano[2,3-d]pyrimidin-6(7H)-one (17)

A mixture of (16) (0.45g ,1.0 mmol) and ethyl iodide (2ml, 1.0 mmol) in ethanol (30 mL) in the presence of anhydrous sodium acetate (2 g) was refluxed for 4 h., (TLC control hexan : ethyl acetate, 5:5). The reaction mixture was concentrated, poured into cold water and the solid product was collected by filtration and recrystallized from ethanol to give (17) as a brown solid, (91% yield), m.p. 189-191°C. FT-IR(KBr, ν, cm^{-1}): 3424 cm^{-1} (NH), 2750 cm^{-1} (SH), 1670 cm^{-1} (C=O lacton),1234 cm^{-1} (C=S)

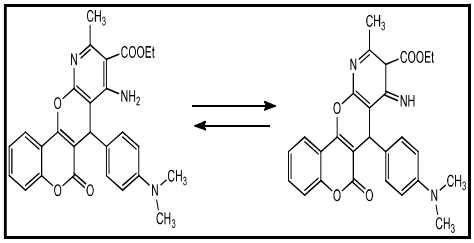
RESULTS AND DISCUSSION

Preparation and characterization of compound (1-6)

Compound (1,2) was synthesized and characterized according the literature[38]. Compound (3) was synthesized when compound (2) treated with acetonitrile in the presence $AlCl_3$, the FT--IR spectrum of compound (3), shows broad (NH) stretching band at 3360 cm^{-1} this broad band due to hydrogen bonding with (NH) group and disappearance (NH_2) stretching bands at 3281 and 3259 cm^{-1}.

When a mixture of (2) and ethyl acetoacetate in toluene was stirred under reflux in the presence of $SnCl_4$ as a Lewis acid catalyst, the fused ring product (4) was obtained in 54%. These results are similar to the results obtained in literatures[22][39].

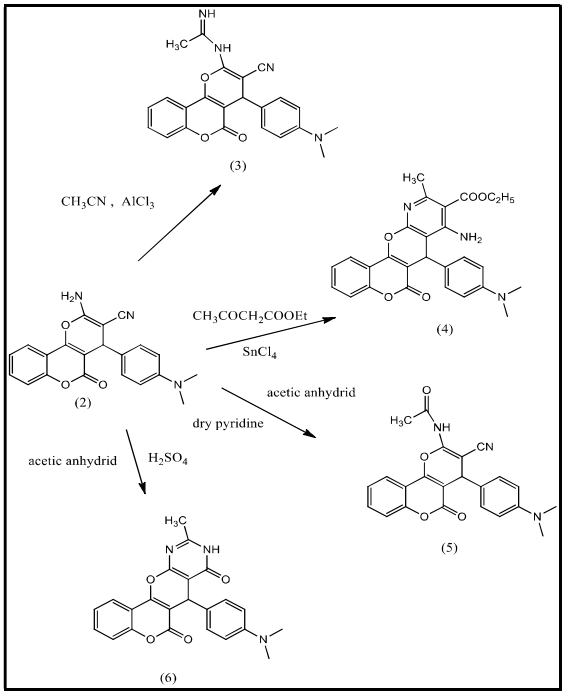
The FT-IR spectrum of compound (4), shows disappearance (CN) stretching bands at 2208 cm^{-1} and appearance (C=O) stretching bands at 1722 cm^{-1} and disappearance (NH2) stretching band of pyridine cycle this due to tautomerisim as in the following structures:



Compound (2) reacted with different reagents to give fused chromene and non fusedchromene compounds,

When treatment of compound (2) with acetic anhydride in dry pyridine for (3 h) afforded the monoacetyl derivative (5) while the reaction with acetic anhydride in the presence of sulfuric acid for (10 h) led to the pyrimidine derivative (6) in 81 and 79% yield, respectively. These results are similar to the results obtained in literatures [22].

The FT-IR spectrum of compound (5), shows (NH) stretching band at 3350 cm^{-1} and disappearance (NH_2) stretching bands at 3323 and 3406 cm^{-1}, while the FT-IR spectrum of compound (6), shows disappearance (CN) and (NH_2) stretching bands at 2208, 3323 and 3406 cm^{-1} respectively. The formation of (3-6) may be illustrated in the following scheme (1).



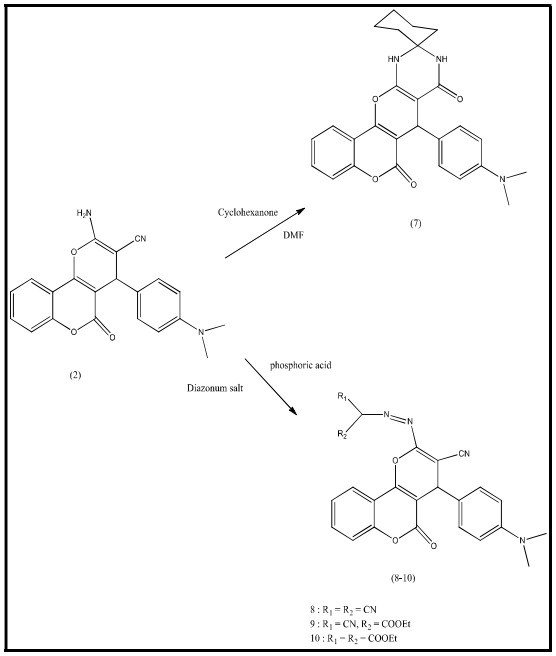
Scheme (1): preparation compounds (3-6)

Preparation and characterization of compound (7-10)

Cyclization of compound (2) with cyclohexanone in DMF in the presence of anhydrous $FeCl_3$ gave the spirocompound (7) The structure of (7) is agreement with literature [40]. The FT-IR spectrum of compound (7), shows (NH) stretching band at 3362 cm^{-1} and disappearance (CN) and (NH_2) stretching bands at 2208, 3323 and 3406 cm^{-1} respectively.

For synthesis of compound (8-10), the first step was diazotized amino derivative (2), then coupling with active methylene group compound, namely malononitral, diethyl malonate and ethyl cyanoacetate, we obtained compounds (8-10). The structures of the synthesized compounds have been characterized by FT-IR and some of them by ^{1}HNMR. The FT-IR spectra of compound (8-10), shows disappearance (NH_2) stretching bands at 3323 and 33406 cm^{-1}.

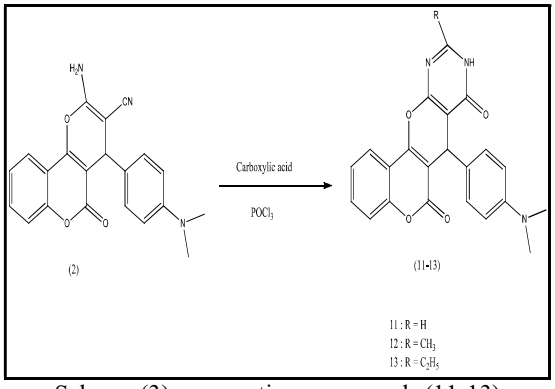
The ^{1}HNMR spectrum of compound (8), shows singlet signal at δ = 3.01 ppm for $N(CH_3)_2$, singlet signal at δ = 3.34 ppm for $CH(CN)_2$, singlet signal at δ = 3.45 ppm for (CH), multi-signals at δ = 7.35-8.42 ppm for Ar-H. The formation of (7-10) may be illustrated in the following scheme (2).



Scheme (2): preparation compounds (7-10)

Preparation and characterization of compound (11-13)

For synthesis these compounds, compound **(2)** was also selected as a key intermediate for the synthesis of new fused and non-fused chromene derivatives. The synthetic reactions are summarized in Scheme (3).



Scheme (3): preparation compounds (11-13)

The importance biological activities of pyrimidinone derivatives (11-13) had resulted in the development of several synthetic methods for their construction[41][42], where these method requires two steps and suffer from several disadvantages such as vigorous conditions, long reaction times and low yields[43][44]. The development of one – step and efficient syntheses of pyrimidinone derivatives under mild conditions using $POCl_3$ remained a work in progress.

In our reaction system $POCl_3$ acted not only as a chlorinating reagent, but also an oxidant. Thus we concluded that the compound (2) were first oxidized to give the corresponding n-substituted 5-amino-pyrazole-4-carboxamide, which immediately reacted with the acyl chloride which might be generated *in situ* from the reaction of the carboxylic acid with $POCl_3$. Followed by cyclization and condensation of the intermediate, the target products were formed. The reaction went smoothly by controlling the amount of $POCl_3$, and the products were obtained in good yields. These results are similar to the results obtained in literatures[45].

The structures of the synthesized compounds have been characterized by FT-IR and some of them by ^{1}HNMR. The FT-IR spectra of compound (11-13), shows (NH) stretching band at 3442-3396 cm^{-1} and disappearance

(CN) and (NH_2) stretching bands at 2208, 3323 and 3406 cm^{-1}respectively.The ^{1}HNMR spectrum of compound (13), shows singlet signal at δ = 2.52 ppm for $N(CH_3)_2$, singlet signal at δ = 2.35 ppm for (CH_3), singlet signal at δ = 4.50 ppm for (CH), multi- signals at δ = 6.30-7.80 ppm for (NH) and Ar-H.

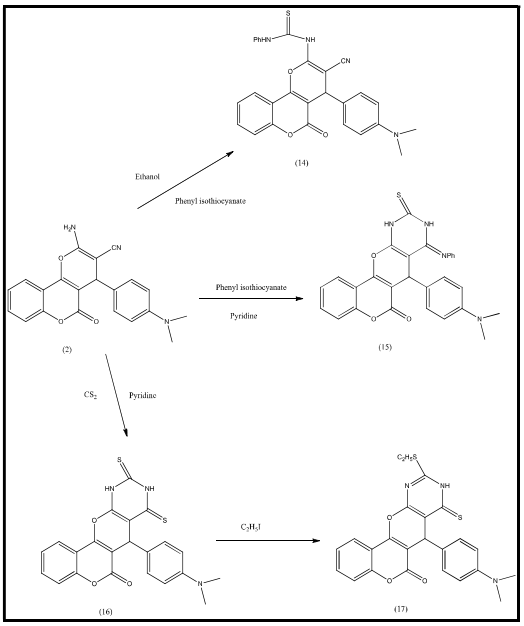
Preparation and characterization of compound (14-17)

When treatment of compound (2) with phenyl isothiocyanate in ethanol for 5h led to the non-fused chromene derivative (14) in 86% yield, while the reaction with phenyl isothiocyanate in pyridine for 12h afforded pyrimidoquinoline derivative (15) in 85% yield. These results are similar to the results obtained in literatures [46].

The structures of the synthesized compounds have been characterized by FT-IR. The FT-IR spectrum of compound (14), shows (NH) stretching band at 3308 cm^{-1} and disappearance (NH_2) stretching bands at 3323 and 3406 cm^{-1} respectively, while the FT-IR spectrum of compound (15), shows and disappearance (CN) and (NH_2) stretching bands at 2208, 3323 and 3406 cm^{-1} respectively.

The reaction of compound (2) with carbon disulfide in pyridine proceeded through the addition of CS_2 on the amino group followed by cyclization by nuclophilic attack of the sulfur atom on the cyano group which underwent rearrangement to give pyrimidinrdithiol derivative (16).

The FT-IR spectra of compound (16), shows (NH) stretching band at 3411 cm^{-1}, two (SH) stretching bands at 2696 and 2733 cm^{-1} and disappearance (CN) and (NH_2) stretching bands at 2208, 3281 and 3259 cm^{-1} respectively. Alkylation of compound (16) with one mole of ethyl iodide gave compound (17), the FT-IR spectra of compound (17), shows one (SH) stretching band at 2750 cm^{-1}. The formation of (14-17)may be illustrated in the following scheme (4).



Scheme (4): preparation compounds (14-17)

CONCLUSION

In conclusion, we have reported a convenient synthesis of fused pyridine, pyrmidine and pyrimidine derivatives from chromenecoumarine and alicyclic chromenecoumarine derivatives.

REFERENCES

[1] MurrayR. D. H., MendezJ., and BrownS. A. "The Natural Coumarins: Occurrence, Chemistry and Biochemistry ،"John Wiley and Sons, Chichester, 1982.

[2] M. M. Khafagy, A. H. F. Abd El-Wahab, F. A. Eid, and A. M. El-Agrody, IlFarmaco,, 2002, 57, p. 715.

[3] .A. H. Bedair, H. A. Emam, N. A. El-Hady, K. A. R. Ahmed, and A. M. El-Agrody, Il Farmaco, 2001,56, p. 965 .

[4] M. E. Cromheecke, M. Levi, L. P. Colly, B. M. J. De Mol, and M. H. Prins, Lancet, 2000,97, p. 356 .

[5] .J. H. Kwak, K. B. Lee, and F. J. Schmitz, J. Nat. Prod., 2001, 64, p. 1081 .

[6] C. Mahidol, W. Kaweetripob, H. Prawat, and S. Ruchirawat, J. Nat. Prod., 2002, 65, p. 757.

[7] S. D. Ibadullaeva and S. V. Serkerov,

Chem. Nat. Comp., 2000, 36, p. 534 .

[8] L. V. Upyr and A. N. Kommisarenko, Chem. Nat. Comp., 2002,38, p. 97.

[9] V. S. P. Chaturvedula, J. K. Schilling, and D. G. I. Kingston, J. Nat. Prod., 2002, 65, p. 965.

[10] E. Scio, A. Ribeiro, T. M. A. Alves, A. J. Romanha, Y. G. Shin, G. A. Cordell, and C. L. Zani, J.Nat. Prod., 2003, 66, p. 634 .

[11] *J. Cai, P. Basnet, Z. Wang, K. Komatsu, L. Xu and T. Tani, J. Nat. Prod., 2000,63, p. 485.*

[12] .J. F. Bukuru, L. Van Puyvelde, S. G. Mathenge, F. P. Mudida and N. De Kimpe, J. Nat. Prod., 2002, 65, p. 783 .

[13] G. Honda, M. Itoh, Y. Takeda, O. K. Kodzhimatov, and O. Ashurmetov, J.Nat. Prod., 2000, 63, p. 436

[14] Y. Miyake, A. Murakami, Y. Sugiyama, M. Isobe, K. Koshimizu, and H. Ohigashi, J. Agric. FoodChem., 1999, 47, p. 3151.

[15] .Amantini, F. Fringuelli, and F. Pizzo, J. Org. Chem., 2002, 67: 7238.

[16] V. Y. Sosnovskikh, B. I. Usachev, and I. I. Vorontsov, J. Org. Chem., 2002, 67, 6738

[17] K. A. Parker and T. L. Mindt ." ‹K. A. Parker and T. L. Mindt, Org. Lett., 2001, 3,p. 3875 .

[18] S. Nad and H. Pal, J. Phys. Chem..,2001,105,p. 1097

[19] "O. V. Khilya, M. S. Frasinyuk, A. V. Turov, and V. P. Khilya, Chem. OfHeter. Comp., 2001,37, p. 1029.

[20] A. R. Newcombe, R. W. Stockley, J. L. Hunter, and M. R. Webb, Biochemistry ‹ 1999, 38, p. 6879 .

[21] F.K.Mohamed, A.I.Essawy ,A.Y.Soliman, andM.G.Badrey .Der ,pharma chemical, 2009, 1 (1) ‹p. 1-11 .

[22] N.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-4H,5H-pyrano[3,2-c] chromene-3 "‹*z.naturforsch* ‹ 2013, 68b, pp. 229-238.

[23] "E. A.Bell andR. G Foster, Nature, 1962, 194, p. 91

[24] E.Perspicace ,S.Marchais, and R.W.Hartmann, "Synthesis and biological evaluation ofthieno [3,2-d]pyrimidinones ,thieno [3,2-d]pyrimines and quinazolinones " Molecules, 2013, 18 ,No.4, p. 4487-4509‹.

[25] A. M. El Agrody, M. S. Abd El Latif, N. A. El Hady, A. H. Fakery, A. H. Badair, Molecules ‹2001,6,p. 519-527

[26] A. H. Badair, N. A. El Hady, M. S. Abd El Latif, A. H. Fakery, A. M. El Agrody, Farmaco, 2000,55, p. 708 .

[27] 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, p. 111

[28] M. C. Yimdjo, A. G. Azebaze, A. E. Nkengfack, A. M. Michele, B. Bodo, Z. T. Fomum, Phytochemistry, 2004, 65, p. 2789 .

[29] V. Jeso, K. C. Nicolaou, Tetrahedron Lett., 2009,50, p. 1161

[30] T. Mouri, T. Yano, S. Kochi, T. Ando, M. Hori, J. Pestic. Sci., 2005,30, p. 209

[31] S. Sardari, Y. Mori, K. Horita, R. G. Micetich, S. Nishibe, M. Daneshtalab, Bioorg. Med. Chem.,, 1999,7, p. 1933

[32] W. P. Smith, L. S. Sollis, D. P. Howes, C. P. Cherry, D. I. Starkey, N. K. Cobley, J. Med. Chem., 1998,41, p. 787 .

[33] 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, p. 798 .

[34] D. A. Quagliato, US Patent 5171857, 1993 .

[35] D. R. Buckle, S. Harry, US Patent 4263299, 1981 .

[36] H. Koga, H. Nabata, H. Nishina (Chugai Seiyaku K. K., Japan), PCT Int. Appl. WO

9214439, 1992 .

[37] H. A. Walker, S.Wilson, E.C.Atkins, H.E.Garrettand A.R. Richardson, J. Pharmacol. Exp.Ther., 1951, 101, p. 368 .

[38] H. H. Mohammed, R. I.H.Al-bayatia and F. Attallah, "Synthesis new fused and non-fused chromene [I] derivatives derived from 2-amino-4-[4-(dimethylamino)phenyl]5-oxo-4H,5Hpyrano[3,2-c]chromene-3-carbonitrile", Journal of Chemistry and Materials Resea"،*2015,7(4),*pp. 134-143

[39] H. Huanan, L. Song, Q. Fang, J. Meng and Y. Luo, "Article Tin (IV) Chloride-Promoted One-Pot Synthesis of NovelTacrine Analogues "Taizhou University, Linhai ,Molecules, 2011, 16, p. 1878-1887 .

[40] J .Li, L. Zhang, D. Shi, Q. Li, D. Wang, C. g, Q. Zhang ،and Y. Fan ,"Investigation of Reaction of o-Aminonitriles with Ketones: ew Modification of Friedländer Reaction Structures of Its Products "LETTER, 2008, , p. 0233-0236

[41] M.X.W Jiang ; N.C. Warshakoon, M.J. Miller "Chemoenzymatic AsymmetricTotal Synthesis of Phosphodiesterase Inhibitors:Preparation of a Polycyclic Pyrazolo[3,4-d]pyrimidine from an Acylnitroso Diels-Alder Cycloadduct-Derived Aminocyclopentenol ". J. O "،*J. Org. chem* ،،.pp. p. 2824-2827.

[42] J.A. Markwalder ،M.R Arnone, P.A Benfield ; M.Boisclair ،G.R Burton, C.H Chang, S.S. Cox, Czerniak, P.M Dean, C.L. Doleniak, D. Grafstrom, R. Harrison, B.A.Kaltenbach, R.F. Nugiel, D.A.Rossi, K.A.Sherk, S.R. Sisk, L.M. Stouten, P. Trainor, G" ،synthesis and biological evaluation of 1- aryl- 4,5-dihydro-1H-pyrazolo [3,4-d]pyrimidin-4-one inhibitors of cyclin - dpendent kinases "، *J.Med.Chem*، *2004,*47, P.5894- 5911 .

[43] .Schenone, S.; Bruno, O.; Radi, M.; Botta, M. "4-Amino-Substituted Pyrazolo[3,4-d]Pyrimidines: Synthesis and Biological Properties". Mini-Rev. Org. Chem., 2009, 6, p. 220-233 .

[44] R.K .Hemender, R.A. Panduranga, V. Veeranagaiah, N .Versatile .44" ،R.K . Hemender, R.A. Panduranga, V. Veeranagaiah, N .Versatile "synthesis of 6-alkyl(aryl)-1H-pyrazolo[3,4-d]pyrimidin-4[5H]ones ". Indian J. Chem. B,, 1992, 31B, p. 163-166.

[45] X.Zhang ,Q.Lin and P.Zhong, "A faciale one-pot synthesis of 1-Arylpyrazolo[3,4-d]pyrimidine-4-ones,Molecules, 2010, 15, p. 3079-3086

[46] M. Messaâd a, F. Chabchoub a, R.Ennigrou band M. Salem a "Action Disulfure Carbonet Phenylthioisocyanate surdes Derives Naphtopyraniques Naphtopyranopyrimidodithioneset Naphtopyrano pyrimidothiones", Phosphorus "،*Phosphorus, sulfur andslicon and the related elements*، 2011, 10, p. 1042 - 6507 .