A Simple and Convenient Synthesis of Isolated-Fused Heterocycles Based on:
2-Imino-N-Phenyl-2H-Chromene-3-Carboxamide

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ABSTRACT
Starting from 2-imino-N-phenyl-2H-chromene-3-carboxamide, (1) a series of functionalized chromenes were achieved; such as, 2-ethoxy-2,3-dihydro-3-phenylchromeno[2,3-d]pyrimidin-4-one (2), and 2-hydrazinyl-2,3-dihydro-3-phenylchromeno-[2,3-d]pyrimidin-4-one (3). Furthermore, reactions of (3) with some of laboratory available compounds gave pyrazoles (4 - 9, 12, 13a, 13b), tetrazoles (11), 2-(2-benzylidenehydrazinyl)-3-phenyl-3H-chromeno[2,3-d]pyrimidin-4(1H)-oneisoxazoles (14), 5-chloro-1-(4-oxo-3-phenyl-4,10-dihydro-3H-chromeno[2,3-d]pyrimidin-2-yl)-3-phenyl-2,3-dihydro-1H-pyrazole-4-carbonitrile (17), pyrimidines (28a, b), pyridines (29a - 29e, 30, 33a, 33b), benzo[b][1,4]oxazepin-2- amines (32a, b), 3-chloro-4-(2-imino-2H-chromen-3-yl)-1-phenyl-4-(phenylamino) azetidin-2-one (34a-34e) and 2-(2-imino-2H-chromen-3-yl)-3-phenyl-2-(phenyl amino)thiazolidin-4-one (35a -35e). The structures of these compounds were established by elemental analysis, IR, MS and NMR spectral analysis.

Keywords: 2-Imino-2H-chromen-3-yl; Chromeno[2,3-d]pyrimidin-4-one; β-Lactam; Thiazolidin-4-ones

1. Introduction
Natural and synthetic coumarin derivatives represent, nowadays, an important group of organic compounds that are used as antibiotics [1,2] fungicides [3] anti-inflammatory [4], anticoagulant [5] and antitumor agents [6,7]. Regarding their high fluorescence ability, they are widely used as optical whitening agents, brighteners, laser dyes and also as fluorescent probes [8] in biology and medicine [9]. Also, The 4H-chromene derivatives ethyl 4-((ethoxy-carbonyl) (cyano) methyl)-2-amino-6-bromo-4H-chromene-3-carboxylate (HA 14-1) has demonstrated promising antifungal activities [10], antiviral agent [11], antiproliferation agent [12]. Due to the unique biological and pharmacological activity, chromene derivatives have attracted considerable attention thus; different processes for the synthesis of chromenes have been reported during the past few years. The importance of the chromone nucleus is evidenced by the continued appearance of new and improved methods for their synthesis, despite the several existing methods for the synthesis of chromene derivatives [13-20], there still is demand for general synthetic strategies which can efficiently provide variously substituted chromene systems.

2. Experimental
2.1. Instruments
All melting points are measured using Galenkanp melting point apparatus and are uncorrected. Elemental analyses were carried out at the Microanalytical Center of Cairo University. IR (KBr pellets \( \nu = \text{cm}^{-1} \)) spectra were determined in 1650 FT-IR instrument (Cairo University), 1H-NMR spectra (\( \delta = \text{ppm} \)) were accomplished using 300 MHz NMR Spectrometer and mass spectroscopy were recorded on GCMS-QP-1000 EX spectrometer (Cairo University).

2.2. Material and Reagents
Hydrazine hydrate, phenyldrazine, benzaldehyde and its substituted derivatives, aniline and its substituted derivatives, thioglycolic acid, acetylaceton, phosoryl chloride, ethyl acetoacetate and chloroacetyl chloride were purchased from Alderich Chemical Co.

Triethylamine, thiourea, urea, o-phenylenediamine, o-aminothiophenol and 2-cyanomethy benzimidazole were purchased from British Drug Houses (BDH).

Acetophenone, malononitrile, 2-chloro acetamide, piperidine, ethoxymethylene-malononitrile, sodium azide and

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5-amino-(1H)-1,2,4-triazole were purchased from Merck Co., Germany.

2.3. Solvents

Dimethylformamide, benzene, pyridine, ethanol and acetone were purchased from El-Nasr Pharmaceutical and Chemical Co. (ADWIC), Egypt.

2.4. Organic Preparations

Preparation of 2-ethoxy-2, 3-dihydro-3-phenylchromeno[2,3-d]pyrimidin-4-one (2).

A mixture of 1 (2.64 g, 0.01 mol) and triethylxymethane (1.48 mL, 0.05 mol) in 20 mL of dimethylformamide was refluxed for 8 h. Then the reaction mixture was poured into 150 mL of crushed ice and the resultant solid was collected by filtration to provide 2 (1.5 g, 60%) as a pale yellow solid; m.p. 285°C - 287°C. 1H NMR (CDCl3): δ 1.2 (t, 3H, CH₃), 3.9 (q, 2H, CH₂) and 6.7 - 7.9 (m, 11H, Ar-H). MS: m/z 320 ([M⁺]⁺, 66%). Calcd for C₁₇H₁₄N₄O₂: C 66.66, H 4.61, N 18.29%.

Preparation of 2-hydrazone-1, 3-dihydro-3-phenylchromen-1-ylidene-2-(3,4-dihydro-4-oxo-3-phenyl-2-chromen-1-ylidene)pyrazol-4(5H)-ylidene)propanenitrile (5), and its derivatives, (7 - 10, 11, 13a, b).

General procedure: To a solution of hydrazide 3 (3.06 g, 0.01 mol) and ethyl 3-amino-2,4-dicyanobut-2-enoate (1.79 mL, 0.01 mol) in 30 mL ethanol containing 0.1 mL piperidine was refluxed for 6 h, then allowed to cool. The formed solid was filtered off, washed with methanol to afford the pyrazole derivative 5. Analogously, diethyl malonate (1.60 mL, 0.01 mol), ethyl 2-cyanoacetate (1.13 mL), ethyl 3-oxobutanoate (1.30 mL), pentane-2,4-dione (1.00 mL), 2-(ethoxymethylene) malononitrile (1.22 gm) and 2-cyano-N-phenylacetamide (1.60 gm) were reacted with compound 3 to yield (7 - 10, 12, 13a, b), respectively.

3-Amino-3-(3-amino-5-oxo-1-(4-oxo-3-phenyl-3,4-dihydro-2H-chromeno-[2,3-d]pyrimidin-2-yl)-1H-pyrazol-4(5H)-ylidene)propanenitrile (5).

Yellow crystals (MeOH), yield 70%, m.p. 250°C - 252°C. IR: 1699 (CO), 2219 (CN), 3422 (NH₃). 1H NMR (DMSO): 2.9 (s, 2H, CH₂), 3.5 (s, 2H, NH₂), 3.7 (s, 2H, NH₂), 6.7 - 7.9 (m, 10H, Ar-H). MS: m/z 439 ([M⁺]⁺, 60%). Calcd for C₂₃H₁₄N₄O₂: C 63.33, H 3.20, N 21.89%.

1-(3,4-dihydro-4-oxo-3-phenyl-2H-chromeno-[2,3-d]pyrimidin-2-yl)pyrazolo-3,5-dione, (7). Pale yellow crystals (MeOH), yield 66%, m.p. 280°C - 282°C. IR: ν (cm⁻¹) 1685 - 1705 (C=O), 3212 (NH), 3282 (NH) and 3432 (NH₂). 1H NMR (DMSO): 4.82 (s, 2H, CH₂), 5.03 (s, 2H, CH₂), 5.1 (s, 1H, CH-methine), 6.1 - 7.8 (m, 10H, Ar-H). MS: m/z 374 ([M⁺]⁺, 55%). Calcd for C₂₀H₁₄N₄O₂: C 64.17, H 3.77, N 14.97%. Found: C 63.33, H 2.91, N 14.15%.

Compound 5. Yield 70%, m.p. 257°C - 259°C. IR: 1699 (CO), 2219 (CN), 3422 (NH₃). 1H NMR (DMSO): 2.9 (s, 2H, CH₂), 3.5 (s, 2H, NH₂), 3.7 (s, 2H, NH₂), 6.7 - 7.9 (m, 10H, Ar-H). MS: m/z 439 ([M⁺]⁺, 60%). Calcd for C₂₃H₁₄N₄O₂: C 63.33, H 3.20, N 21.89%.

Compound 9. Yellow crystals (Ethanol), yield 55%, m.p. 190°C - 192°C. IR: ν (cm⁻¹) 1685-1705 (C=O), 3212 (NH), 3282 (NH) and 3432 (NH₂). 1H NMR (DMSO): 2.9 (s, 2H, CH₂), 3.5 (s, 2H, NH₂), 3.7 (s, 2H, NH₂), 6.7 - 7.9 (m, 10H, Ar-H). MS: m/z 370 ([M⁺]⁻, 60%). Calcd for C₂₃H₁₄N₄O₂: C 67.73, H 4.33, N 15.05%. Found: C 67.17, H 3.31, N 14.15%.

Compound 10. Pale green crystals (Ethanol), yield 59%, m.p. 270°C-272°C. IR: ν (cm⁻¹) 1685-1705 (C=O), 3212 (NH), 3282 (NH) and 3432 (NH₂). 1H NMR (DMSO): 2.9 (s, 2H, CH₂), 3.5 (s, 2H, NH₂), 3.7 (s, 2H, NH₂), 6.7 - 7.9 (m, 10H, Ar-H). MS: m/z 369 ([M⁺]⁻, 66%). Calcd for C₂₃H₁₄N₄O₂: C 67.3, H 4.9, N 15.13%. Found: C 70.17, H 3.31, N 14.15%.

Preparation of 1-phenyl-tetrazolo[4',5':5,2]pyrimido[4,5-b]chromen-12-one, (11).

To a stirred cold solution of 3 (0.306 g, 0.001 mol) in 30 mL of glacial acetic acid, a cold solution of sodium nitrite (0.7 g, 0.01 mol) in 10 mL of H₂O was added drop wise stirring at 5°C. The mixture was stirred for further four hours at room temperature. The solid that precipitated was collected by filtration, washed with water and air dried to afford 55% yield of the tetrazolo derivative 11. Yield 55%, m.p. 250°C - 252°C. IR: 1699 (CO), MS: m/z 317 ([M⁺]⁺, 60%). Calcd for C₂₃H₁₄N₄O₂: C 63.35, H 3.49, N 22.07%. Found: C 63.01, H 2.20, N 21.89%.
21.98%. Found: C 64.17, H 2.31, N 20.15%.

Compound 13a. Yellow crystals (Ethanol), yield 62%, m.p. 150˚C - 152˚C. IR: ν (cm–1) 1685 - 1705(C=O), 3212 - 3432 (NH2), 1HNMR (CDCl3): δ 4.1 (s, 2H, NH2), 4.3 (s, 1H, NHP), 6.2 (s, 1H, =CH-), 6.7 - 7.9 (m, 10H, Ar-H). MS: m/z 448[M]+, 40%. Calcd for C27H20N5O2S (448.48). Calcd: C 66.12, H 3.61, N 17.15%. Found: C 66.17, H 3.31, N 17.15%.

Compound 13b. Pale yellow crystals (MeOH), yield 50%, m.p. 180˚C - 182˚C. IR: ν (cm–1) 1685 - 1705(C=O), 3212 - 3432 (NH2), MS: m/z 456 ([M + 1] +, 35%). Calcd for C27H19N5O2 (455.49). Calcd: C 60.65, H 3.76, N 71.53, S 7.04%. Found: C 59.17, H 2.66, N 70.26, S 6.54%.

Preparation of 2-(2-benzylidenehydrazinyl)-3-phenyl-3H-chromeno[2,3-d]pyrimidin-2-yl)-3-phenyl-2,3-dihydro-1H-pyrazole-4-carbonitrile, (16). A suspension of 1.0 g of 151-yl)-3-phenyl-3H-chromeno[2,3-d]pyrimidin-4(10H)-one, (18). Amixture of 17 (4.79 g, 0.01 mol) and 5-amino-1,2,4-1H-triazole (0.84 g) in 30 mL ethanol containing 0.1 mL piperidine was refluxed for 3 hr. then allowed to cool. The formed brownish solid was filtered off, washed with methanol to afford the pyrazole derivative 18 (2.4 g, 50%) as a brownish solid; m.p. 156˚C - 158˚C. IR: ν (cm–1) 1670 (C=O), 3432 (NH). 1HNMR (DMSO): δ 3.98 (s, br, 1H, NH), 5.21 (s, 1H, C-3 pyrazole), 6.13 (s, br, 2H, NH2) and 6.7 - 7.9 (m, 14H, Ar-H) and 8.71 (s, 1H, methine proton of triazole ring). MS: m/z 527 ([M]+, 25%). Calcd for C28H21N5O2 (527.54). Calcd: C 76.63, H 4.01, N 23.90 %. Found: C 65.31, H 3.22, N 22.84%.

Preparation of 2-(2-benzylidenehydrazinyl)-3-phenyl-3H-chromeno[2,3-d]pyrimidin-2-yl)-3-phenyl-2,3-dihydro-1H-dipyrazole [15-2a:4’,3’-e] pyrimidine-6-carbonitrile, (19). Amixture of 17 (4.79 g, 0.01 mol) and 5-amino-3-(methylthio)-1H-pyrazole-4-carbonitrile (1.54 g, 0.01 mol) in 30 mL ethanol containing 0.1 mL piperidine was refluxed for 5 h. then allowed to cool. The formed pale yellow solid was filtered off, washed with methanol to afford the pyrazole derivative 19 (2.4 g, 50%) as a pale yellow solid (MeOH); m.p. 240˚C - 242˚C. IR: ν (cm–1) 1670 (C=O), 2221 (CN), 3432 (NH). 1HNMR (DMSO): δ 3.54 (s, 3H, SCH3), 3.98 (s, br, 1H, NH), 5.21 (s, 1H, C-3 pyrazole), 6.13 (s, br, 2H, NH2) and 6.7 - 7.9 (m, 14H, Ar-H) and 8.71 (s, 1H, methine proton of triazole ring). MS: m/z 597 ([M]+, 35 %). Calcd for C33H21N5O2S (597.65). Calcd: C 64.31, H 3.88, N 21.09 %. Found: C 63.56, H 2.52, N 20.78%.

Preparation 5-methoxy-1-(4-oxo-3-phenyl-4,10-dihydro-3H-chromeno[2,3-d]pyrimidin-2-yl)-3-phenyl-2,3-dihydro-1H-pyrazole [15-2a:4’,3’-e] pyrimidine-6-carbonitrile, (20). A solution of 10 mmol of freshly prepared sodium methoxide and 1.0 mmol of the chloro derivatives 17 in 10 mL of anhydrous methanol was refluxed for 4 hr then the reaction mixture was evaporated to dryness in vacuo. The crude residue was treated with water and neutralized with 10% hydrochloric acid, and the solid precipitate, collected by filtration, was purified by crystallization to obtain 20 as yellow crystals (DMSO-HCl); yield 30%. m.p. 288˚C - 290˚C. IR: ν (cm–1) 1699 (C=O), 2219 (CN), 3422 (NH). 1HNMR (DMSO): δ 3.82 (s, 3H, OCH3), 3.98 (s, br, 1H, NH), 4.61 (s, 1H, C-3 pyrazole) and 6.7 - 7.9 (m, 14H, Ar-H). MS: m/z 475 ([M]+, 62%). Calcd for C24H18N3O3S (597.65). Calcd: C 64.31, H 3.88, N 21.09 %. Found: C 63.56, H 2.52, N 20.78%.

Preparation 5-azido-1-(4-oxo-3-phenyl-4,10-dihydro-3H-chromeno[2,3-d]pyrimidin-2-yl)-3-phenyl-2,3-dihydro-1H-pyrazole-4-carbonitrile, (21). A mixture of 5-azido-amino-1-(4-oxo-3-phenyl-4,10-dihydro-3H-chromeno[2,3-d]pyrimidin-2-yl)-3-phenyl-2,3-dihydro-1H-pyrazole [15-2a:4’,3’-e] pyrimidine-6-carbonitrile, (19) and 5-azido-1-(4-oxo-3-phenyl-4,10-dihydro-3H-chromeno[2,3-d]pyrimidin-2-yl)-3-phenyl-2,3-dihydro-1H-dipyrazole [15-2a:4’,3’-e] pyrimidine-6-carbonitrile, (20). A solution of 10 mmol of freshly prepared sodium methoxide and 1.0 mmol of the chloro derivatives 17 in 10 mL of anhydrous methanol was refluxed for 4 hr then the reaction mixture was evaporated to dryness in vacuo. The crude residue was treated with water and neutralized with 10% hydrochloric acid, and the solid precipitate, collected by filtration, was purified by crystallization to obtain 20 as yellow crystals (DMSO-HCl); yield 30%. m.p. 288˚C - 290˚C. IR: ν (cm–1) 1699 (C=O), 2219 (CN), 3422 (NH). 1HNMR (DMSO): δ 3.82 (s, 3H, OCH3), 3.98 (s, br, 1H, NH), 4.61 (s, 1H, C-3 pyrazole) and 6.7 - 7.9 (m, 14H, Ar-H). MS: m/z 475 ([M]+, 62%). Calcd for C24H18N3O3S (597.65). Calcd: C 64.31, H 3.88, N 21.09 %. Found: C 63.56, H 2.52, N 20.78%.
dro-3H-chromeno[2,3-d][pyrimidin-2-yl]-3-phenyl-2,3-dihydro-1H-pyrazole-4-carbonitrile, (21). A solution of the chloro compound 17 (1.437 g, 3 mmol) in acetone (5 mL) was stirred and ice-cooled. The solution of Na2S (0.13 g, 2 mmol) in water (1 mL) was added drop wise in the solution and this mixture was stirred for 1 hr at room temperature. After evaporation of acetone, the crude product was separated by filtration and recrystallized from dichloromethane. We have obtained (0.9 g, 62%) of 21 as Yellow solid with mp 150°C - 152°C. IR: ν (cm⁻¹) 1699 (C=O), 2217 (CN), 3422 (NH). ¹HNMR (DMSO): δ 3.98 (s, br, 1H, NH), 4.61 (s, 1H, C-3 pyrazole) and 6.7 - 7.9 (m, 14H, Ar-H). MS: m/z 486 ([M⁺], 32%). Calcd for C27H18N8O2 (486.48). Calcd: C 65.76, H 2.56, N 23.73%. Found: C 65.76, H 2.56, N 23.03%. Preparation of 2-(4-amino-3-phenyl-2,3-dihydro-pyrazolo[3,4-c][1H-pyrazol-1(6H)-yl]-3-phenyl-3H-chromeno[2,3-d][pyrimidin-4(1H)-one], (23). A mixture of 17 (3.20 g, 0.01 mol) and hydrazine hydrate (0.5 mL, 0.01 mol) in 20 mL DMF containing 0.1 mL.piperidine was refluxed for 8 hr. The reaction mixture was concentrated under reduced pressure and the residue was washed with acidi-fied cold water and then triturated with methanol. The formed yellow product was filtered, washed well with methanol. Yield 58%, m. p. 150°C - 152°C. IR: 1670 (C=O), 3432 (NH) and 3455 (NH₂). ¹HNMR (DMSO): 3.98 (s, br, 1H, NH), 5.21 (s, 1H, CH- methine), 6.7 - 7.9 (m, 1H, Ar-H) and 9.21 (s, 1H, NH). MS: m/z 475 ([M⁺], 64%). Calcd for C25H21N2O2 (475.50). C 68.20, H 4.45, N 20.62%. Found: C 67.03, H 3.32, N 19.23%. Preparation of 3-(2-imino-2/-chromen-3-yl)-1-phenyl-(3-phenylamino) prop-2-en-1-one, (24a) and its derivatives (24b-e).

General procedure: A mixture of the 2-imino-N-phenyl-2H-chromene-3-carboxamide 1 (2.64 g, 0.01 mol) and acetylene and p-hydrazineacetophenone (1.36 g, 0.01 mol), p-nitroacetophenone (1.65 g, 0.01 mol), o-nitroacetophenone (1.65 g, 0.01 mol) and p-chloroacetophenone (1.54 g, 0.01 mol) respectively, in 20 mL DMF containing 0.1 mL of piperidine was refluxed for 8 hr. The reaction mixture was concentrated, poured into iced/H₂O mixture and the solid product thus formed was filtered, washed for several times with water and crystallized from methanol.

Compound 24a. Yellow crystals (MeOH), yield 60%. m.p. 182°C - 184°C. IR: ν (cm⁻¹) 1665 - 1705(C=O), 3322 (NH). ¹HNMR (DMSO): δ 4.1 (s, 1H, NH-amine), 6.5 (s, 1H, CH-ethylen), 7.1-7.6 (m, 15H, Ar-H), 11.5 (s, 1H, =NH). MS: m/z 366 ([M⁺],40%). Calcd for C24H18N2O2 (366.41). Calcd: C 78.67, H 4.95, N 7.65%. Found: C 77.17, H 4.01, N 8.15%. Compound 24b. Pale green crystals (MeOH), yield 55%, m.p. 220°C - 222°C. IR: ν (cm⁻¹) 1665 - 1705(C=O), 3445 (OH). ¹HNMR (CDCl₃): δ 4.1 (s, 1H, NH-amine), 6.5 (s, 1H, CH-ethylene), 7.1 - 7.6 (m, 14H, Ar-H), 11.5 (s, 1H, =NH) and 9.9 (s, 1H, phenolic OH). MS: m/z 383 ([M + 1]⁺, 60%). Calcd for C21H₁₆N₄O₂ (382.41). Calcd: C 75.38, H 4.74, N 7.33%. Found: C 74.17, H 3.91, N 6.15%.

Compound 24c. Brown crystals (Ethanol), yield 65%, m.p. 190°C - 192°C. IR: ν (cm⁻¹) 1665 - 1705(C=O), 1HNMRS (DMSO): δ 4.1 (s, 1H, NH-amine), 6.5 (s, 1H, CH-ethylen), 7.1 - 7.6 (m, 14H, Ar-H), 11.5 (s, 1H, =NH). MS: m/z 411 ([M⁺], 62%). Calcd for C23H₁₉N₃O₂ (411.41). Calcd: C 70.07, H 4.16, N 10.21%. Found: C 69.17, H 3.31, N 9.15%.

Compound 24d. Brown crystals (Ethanol), yield 59%, m.p. 170°C - 172°C. IR: ν (cm⁻¹) 1665 - 1705(C=O), MS: m/z 410 ([M-1]⁺, 52%). Calcd for C23H₁₉N₃O₂ (411.41). Calcd: C 70.07, H 4.16, N 10.21%. Found: C 69.17, H 3.31, N 9.15%.

Compound 24e. Yellow crystals (Ethanol), yield 55%, m.p. 255°C - 257°C. IR: ν (cm⁻¹) 1665 - 1705(C=O), ¹HNMR (DMSO): δ 4.1 (s, 1H, NH-amine), 6.5 (s, 1H, CH-ethylen), 7.1 - 7.6 (m, 14H, Ar-H), 11.5 (s, 1H, =NH). MS: m/z 400 ([M⁺],60%). Calcd for C23H₁₉N₂OCl (400.86). Calcd: C 71.91, H 4.27, N 6.99, CI8.84%. Found: C 70.17, H 3.31, N 5.15, Cl7.18%.

Preparation of 2-imino-N,N'-diphenyl-2H-chromene-3-carboxamidines, (25a) and its derivatives (25b-25e).

General procedure: A mixture of equimolar amount of compound 1 (2.64 g, 0.01 mol) aniline (0.93 ml, 0.01 mol), p-hydroxyaniline (1.09 g, 0.01 mol), p-nitroaniline (1.38 g, 0.01 mol), o-nitroaniline (1.38 g, 0.01 mol) and p-chloroaniline (1.27 g, 0.01 mol), respectively in 30 mL ethanol containing 0.1 mL of piperidine was refluxed for 5 hr. The reaction mixture was concentrated, poured into ice/H₂O mixture, and the solid product thus formed, filtered, washed for several times with water and crystallized from methanol.

Compound 25a. Pale brown crystals (Methanol), yield 58%, m.p. 205°C - 207°C. IR: ν (cm⁻¹) 3380(NH), ¹HNMR (CDCl₃): δ 4.1 (s, 1H, NH-amine), 7.1 - 7.6(m, 15H, Ar-H), 11.5(s, 1H, =NH). MS: m/z 339 ([M⁺], 65%). Calcd for C22H₁₇N₄O3 (339.39). C 77.86, H 5.05, N 12.38%. Found: C 77.66, H 4.52, N 11.12%.

Compound 25b. Yellow crystals (Methanol), yield 60%, m.p. 210°C - 212°C. IR: ν (cm⁻¹) 3380(NH), 3445 (OH), ¹HNMR (DMSO): δ 4.1(s, 1H, NH-amine), 7.1 - 7.6(m, 14H, Ar-H), 11.5 (s, 1H, =NH) and 9.9 (s, 1H, phenolic OH). MS: m/z 357 ([M+2]⁺), 50%. Calcd for C22H₁₇N₃O (355.39). C 74.35, H 4.82, N 11.82%. Found: C 73.45, H 3.52, N 10.12%.

Compound 25c. Pale yellow crystals (Methanol), yield 64%, m.p. 285°C - 287°C. ¹HNMR (DMSO): δ 4.1 (s, 1H, NH-amine), 7.1 - 7.6 (m, 14H, Ar-H), 11.5 (s, 1H, =NH). MS: m/z 385 ([M + 1]⁺, 55%). Calcd for C22H₂₁N₃O₂Cl (384.39). C 68.74, H 4.20, N 14.58%. Found: C 67.72, H 6.15%.
Compound 25d. Yellow crystals (Methanol), yield 60%, m.p. 215°C - 117°C. MS: m/z 384([M]+, 55%). Calcd for C27H20N4OCl (393.6). C 67.32, H 4.10, N 10.74%.

Preparation of 4,5-dihydro-5-(2-imino-2H-chromen-3-yl)-N3-diphenyl-1H-pyrazol-5-amine, (26a) and its derivatives (26b and 27).

General procedure: A mixture of 24a (3.66 g, 0.01 mol) and hydrazine hydrate (0.05 ml, 0.01 mol), phenyl hydrazine (1.08 ml, 0.01 mol) and hydroxylamine hydrochloride (0.69 gm, 0.01 mol) containing 0.1 ml pipericidine was refluxed for 8 hr. The reaction mixture was concentrated under reduced pressure and the residue was washed with acidified cold water and then triturated with methanol, and the solid product thus formed, filtered, washed for several times with water and crystallized from methanol.

Compound 26a. Pale brown crystals (methanol), yield 66%, m.p. 155°C - 157°C. IR: 3117 - 3293 (NH). 1H NMR (DMSO): 2.9 (s, 2H, CH2), 4.1 (s, 1H, NH-amine), 7.1 (s, 1H, NH-hydrazide), 7.2 - 7.8 (m, 15H, Ar-H), 11.5 (s, 1H, =NH). MS: m/z 383([M]+3]+, 55%). Calcd for C25H20N4O3Cl (448.54): C 71.11, H 3.20, N 11.66%, S 6.55%.

Compound 26b. Brown crystals (Methanol), yield 50%, m.p. 295°C - 297°C. IR: 3117 - 3293 (NH). 1H NMR (DMSO): 1.9 (s, 2H, CH2), 4.1 (s, 1H, NH-amine), 7.1 (s, H, NH hydrazide), 7.2 - 7.8 (m, 20H, Ar-H) and 11.5 (s, 1H, =NH). MS: m/z 456([M]+), 75%). Calcd for C25H20N4O (456.54): C 78.92, H 5.30, N 12.27%. Found: C 77.01, H 4.20, N 11.66%.

Preparation of 4,5-dihydro-4-(2-imino-2H-chromen-3-yl)-6-phenyl-4-(phenyl-amino) pyrimidine-2(1H)-one, (28a), and its derivative (28b).

General procedure: A mixture of equimolar amounts of 24a (3.66 g, 0.01 mol) and urea (0.60 g, 0.01 mol) or thiourea (0.76 g, 0.01 mol) and 0.1 ml piperidine was refluxed for 8 h, in 30 mL of ethanol. The solvent was evaporated under vacuum, and the residue was poured to 30 ml acidified cold water and then triturated with methanol. The product were filtered and crystallized from ethanol.

Compound 28a. Brown crystals (Ethanol); yield 67%, m.p. 196°C - 198°C. IR: 1685 - 1705 (C=O), 3063 - 3288 (NH). 1H NMR (DMSO): 2.9 (s, 2H, CH2), 4.1 (s, 1H, NH-amine), 7.2 - 7.8 (m, 15H, Ar-H), 8.1 (s, H, NH-amide) and 11.5 (s, 1H, =NH), MS: m/z 408 ([M]+, 45%). Calcd for C25H20N4O2 (408.45): C 73.51, H 4.94, N 13.72%. Found: C 72.01, H 3.20, N 12.66%.

Preparation of 1, 2, 5, 6-tetrahydro-6-(2-imino-2H-chromen-3-yl)-2-oxo-4-phenyl-6-(phenylamino) pyrido-carbonitrile, (29a) and its derivatives (29b - 29e) and (30).

General procedure: A mixture of 24a (3.66 g, 0.01 mol) and cyanoacetamide (0.84 g, 0.01 mol) in 30 ml of ethanol in the presence of 0.1 ml of piperidine was refluxed for 8 h. The reaction mixture was concentrated under vacuum and the residue washed with acidified cold water and then triturated with methanol. The solid product formed was filtered and crystallized from ethanol to afford 29a in 65% yield. In analogously, the Chalcone 24a was reacted with cyanothioacetamide (1.0 g, 0.01 mol), 2-cyano-N-p-tolylacetamide (1.74 g, 0.01 mol), 2-cyanoacetohydrazide (0.99 g, 0.01 mol), 2-cyano-N-phenylacetamide (1.6 g, 0.01 mol) and 2-chloroacetamide (0.93 g, 0.01 mol) to yield the pyridine derivatives 29b - 29e and 30 respectively.

Compound 29a. Yellow crystals (Methanol), yield 56%, m.p. 184°C - 186°C. IR: 1689 - 1705 (C=O), 422.5 (CN). 1H NMR (DMSO): 2.9 (s, 2H, CH2), 4.1 (s, 1H, NH-amine), 7.2 - 7.8 (m, 15H, Ar-H), 8.1 (s, H, NH-amide) and 11.5 (s, 1H, =NH), MS: m/z 432 ([M]+, 65%). Calcd for C25H20N4OS (432.47): C 74.98, H 4.66, N 12.95%. Found: C 73.01, H 4.20, N 11.66%.

Preparation of the pyridine derivatives 29b - 29e and 30 respectively.
m.p. 280°C - 282°C. IR: 1689 - 1705 (C=O), 2210 (CN), 3188 - 3444 (NH and NH2). ^1H NMR (DMSO): 1.9 (s, 2H, CH2), 2.1 (s, 2H, NH), 4.1 (s, 1H, -NHPh), 7.2 - 7.8 (m, 20H, Ar-H) and 11.5 (s, 1H, =NH), MS: m/z 510 ([M + 2]^+), 50%). \textit{Calcd} for C_{26}H_{20}N_{3}O_{2}Cl (508.57). C 77.93, H 4.76, N 11.02%. \textit{Found}: C 76.41, H 3.10, N 10.06%.

**Compound 30.** Brown crystals (Methanol), yield 50%, m.p. 220°C - 222°C. IR: 1699 - 1705 (C=O), 3188 - 3244 (NH). ^1H NMR (DMSO): 1.9 (s, 2H, CH2), 4.1 (s, 1H, NH-amine), 7.2 - 7.8 (m, 15H, Ar-H), 8.1 (s, H, NH) and 11.5 (s, 1H, =NH), MS: m/z 441 ([M]^+, 55%). \textit{Calcd} for C_{24}H_{18}N_{3}O_{2}Cl (441.91). C 76.75, H 4.20, N 13.86%. \textit{Found}: C 76.11, H 3.20, N 13.66%.

**Preparation of 2-(2-imino-2H-chromen-3-yl)-4-phenyl-2-(phenylimino)pyrido-[1,2-a]benzimidazo-lo-5-carbonitriles, (31).** A mixture of 24a (3.66 g, 0.01 mol), 2-cyanomethylbenzimidazole (1.57 g, 0.01 mol) and 0.1 mL of piperidin-3-yl-2-(phenylamino)pyridine-3-carbonitrile, (33a) and its derivatives, (34a) and its derivatives, (34b).

**General procedure:** A mixture of an equimolar amounts of 24a (3.66 g, 0.01 mol) and (1.09 g, 0.01 mol) o-aminophenol and (1.25 g, 0.01 mol) o-aminophenol respectively, in 30 mL ethanol containing 0.1 mL of piperidine was refluxed for 8 h. The solvent was evaporated under vacuum and the residue was washed with acidified cold water and then triturated with methanol. The solid product formed was filtered and crystallized from methanol to afford 33a in 60% yield. In analogously, the Chalcone 34a was reacted with ethyl 3-amino-2, 4-dicyanobut-2-enoate (1.79 g, 0.01 mol) to yield the pyridine derivative 33b.

**Compound 33a.** Yellow crystals (Methanol), yield 60%, m.p. 184°C - 186°C. IR: 2219 (CN), 3289 (NH). ^1H NMR (DMSO): 0.9 (s, 3H, CH3), 2.2 (s, 2H, CH2), 3.7 (q, 2H, CH2), 4.1 (s, 1H, NH-amine), 6.7 - 7.9 (m, 15H, Ar-H) and 11.5 (s, 1H, =NH), MS: m/z 482 ([M+2]^2/3), 35%. \textit{Calcd} for C_{30}H_{23}N_{5}O_{2} (480.52). C 74.99, H 4.20, N 17.49%. \textit{Found}: C 73.01, H 3.20, N 16.66%.

**Compound 33b.** Pale yellow crystals (Methanol), yield 45%, m.p. 240°C - 242°C. IR: 2219 (CN), 3289 (NH). ^1H NMR (DMSO): 0.9 (s, 3H, CH3), 2.2 (s, 2H, CH2), 3.7 (q, 2H, CH2), 4.1 (s, 1H, NH-amine), 6.7 - 7.9 (m, 15H, Ar-H) and 11.5 (s, 1H, =NH), MS: m/z 527 ([M]^+, 35%). \textit{Calcd} for C_{30}H_{23}N_{5}O_{2} (527.57). C 72.85, H 4.78, N 13.27%. \textit{Found}: C 71.14, H 3.01, N 12.88%.

**Preparation of 3-chloro-4-(2-imino-2H-chromen-3-yl)-1-phenyl-4-(phenyl-amino)azetidin-2-one, (34a) and its derivatives, (34b - 34e).**

**Compound 34a.** Brown crystals (Methanol) yield 60%, m.p. 280°C - 282°C. IR: 1705 (C=O), 3289 (NH). ^1H NMR (DMSO): 4.1 (s, 1H, NH-amine), 5.2 (s, 1H, CH, C-3 of β-lactam ring), 7.1 - 7.6 (m, 15H, Ar-H) and 11.5 (s, 1H, =NH), MS: m/z 415 ([M]^+, 40%). \textit{Calcd} for C_{24}H_{17}N_{4}O_{4}Cl (415.87): C 69.31, H 4.36, N 10.10, Cl 8.5279%. \textit{Found}: C 68.19, H 3.21, N 9.18, Cl 7.12%.

**Compound 34b.** Pale yellow crystals (Methanol), yield 63%, m.p. 275°C - 277°C. IR: 1705(C=O), 3289 (NH), 3388(OH). ^1H NMR (DMSO): 4.1 (s, 1H, NH-amine), 5.2 (s, 1H, CH, C-3 of β-lactam ring), 7.1 - 7.6 (m, 14H, Ar-H), 11.5 (s, 1H, =NH) and 10.1 (s, 1H, phenolic OH). MS: m/z 431([M]^+, 55%), \textit{Calcd} for C_{24}H_{17}N_{4}O_{4}Cl (431.87): C 66.75, H 4.20, N 9.73, Cl 8.21%. \textit{Found}: C 65.09, H 3.52, N 9.08, Cl 7.12%.

**Compound 34c.** Pale brown crystals (Methanol), yield 70%, m.p. 210°C - 212°C. IR: 1705 (C=O), 3289 (NH). ^1H NMR (DMSO): 4.1 (s, 1H, NH-amine), 5.2 (s, 1H, CH, C-3 of β-lactam ring), 7.1 - 7.6 (m, 14H, Ar-H) and 11.5 (s, 1H, =NH), MS: m/z 460([M]^+, 40%), \textit{Calcd} for C_{24}H_{22}N_{4}O_{4}Cl (460.87): C 62.55, H 3.72, N 12.16, Cl 7.69%. \textit{Found}: C 61.07, H 2.22, N 11.18, Cl 6.11%.

**Compound 34d.** Brown crystals (Ethanol), yield 62%, m.p. 175°C - 177°C. IR: 1705 (C=O), 3289 (NH), MS: m/z 461 ([M + 1]^+, 55%), \textit{Calcd} for C_{24}H_{17}N_{4}O_{4}Cl (460.87): C 62.55, H 3.72, N 12.16, Cl 7.69%. \textit{Found}: C 61.17, H 2.25,
the starting compound, 2-imino-N-phenyl-2H-chromene-3-carboxamide 1, was prepared according to the previously reported procedure [18]. Thus, refluxing of compound 1 with triethyl orthoformate in dimethylformamide affording 2-ethoxy-2,3-dihydro-3-phenylchromeno[2,3-d]pyrimidin-4-one 2, (Scheme 1). The structure of the latter product was based on IR, $^1$H NMR, and mass spectra. The IR spectrum of 2 showed the lack of any absorption of the NH functions, and the $^1$H NMR spectrum (CDCl$_3$) displayed a triplet at δ 1.2 and a quartet at 3.9 ppm due to the ethoxy protons and a multiplet at 6.7 - 7.9 ppm due to aromatic protons, respectively. The MS of 2 showed the [M]$^+$ ion at m/z 320 (65%). Furthermore, compound 2 was allowed to react with hydrazine hydrate in ethanol solution using piperidine as a catalyst yielding 2-hydrazinyl-2,3-dihydro-3-phenyl-chromeno[2,3-d]pyrimidin-4-one, 3. The structure of 3 was confirmed based on elemental and spectroscopic analysis. The IR spectrum of 3 showed the presence of absorption bands at ν 1670, 3282 and 3432 cm$^{-1}$ due to CO, NH and NH$_2$ groups, respectively. The $^1$H NMR spectrum (DMSO) displayed three signals at δ 4.82, 5.1 and 8.85 due to NH$_2$, pyrimidine proton and NH respectively, and a multiplet at 6.7 - 7.9 ppm, for aromatic protons. While, the MS of 3 showed m/z at 309 [M + 3]$^+$, 45%. Compound 3 was utilized as a key intermediate for the synthesis of some new pyrazole derivatives based on mild and efficient reaction of compound 3 with some of laboratory available compounds. Thus, Compound 3 reacted with ethyl 3-amino-2,4-dicyanobut-2-enoate in boiling DMF containing a catalytic amount of piperidine. Two isomeric products seemed possible for this reaction 5 or 6, (Scheme 2). Structure 6 ruled out based on analytical and spectroscopic data (IR, $^1$H NMR and MS). Thus, the IR spectra of the product 5 showed the presence of absorption bands at ν 1699, 2219 and 3422 cm$^{-1}$ due to C=O, CN and NH$_2$ groups, respectively. Accordingly, the $^1$H NMR spectrum (DMSO) of the product 5 showed three singlet signals at δ 2.9, 3.5 and 3.7 due to the methylene and two NH$_2$ groups respectively, and a multiplet at 6.7 - 7.9 ppm, due to aromatic protons. The MS of 5 displayed [M]$^+$ at m/z 439 (60%). It is note worth that, trial to cyclise 5 in boiling pyridine was unsuccessful, (Scheme 2).

Also, compound 3 reacted with diethyl malonate in boiling DMF containing a catalytic amount of piperidine afforded 1-(3,4-dihydro-4-oxo-3-phenyl-2H-chromen-2,3-d[pyrimidin-2-yl]pyrazolidine-3,5-dione 7, (Scheme 3). The structure of 7 was confirmed based on elemental and

3. Results and Discussion

The synthetic procedures adopted to obtain the target compounds are depicted in Schemes 1 - 10. The starting compound, 2-imino-N-phenyl-2H-chromene-3-carboxamide 1, was prepared according to the previously reported procedure [18]. Thus, refluxing of compound 1 with triethyl orthoformate in dimethylformamide affording 2-ethoxy-2,3-dihydro-3-phenylchromeno[2,3-d]pyrimidin-4-one 2, (Scheme 1). The structure of the latter product was based on IR, $^1$H NMR, and mass spectra. The IR spectrum of 2 showed the lack of any absorption of the NH functions, and the $^1$H NMR spectrum (CDCl$_3$) displayed a triplet at δ 1.2 and a quartet at 3.9 ppm due to the ethoxy protons and a multiplet at 6.7 - 7.9 ppm due to aromatic protons, respectively. The MS of 2 showed the [M]$^+$ ion at m/z 320 (65%). Furthermore, compound 2 was allowed to react with hydrazine hydrate in ethanol solution using piperidine as a catalyst yielding 2-hydrazinyl-2,3-dihydro-3-phenyl-chromeno[2,3-d]pyrimidin-4-one, 3. The structure of 3 was confirmed based on elemental and spectroscopic analysis. The IR spectrum of 3 showed the presence of absorption bands at ν 1670, 3282 and 3432 cm$^{-1}$ due to CO, NH and NH$_2$ groups, respectively. The $^1$H NMR spectrum (DMSO) displayed three signals at δ 4.82, 5.1 and 8.85 due to NH$_2$, pyrimidine proton and NH respectively, and a multiplet at 6.7 - 7.9 ppm, for aromatic protons. While, the MS of 3 showed m/z at 309 [M + 3]$^+$, 45%.

Compound 3 was utilized as a key intermediate for the synthesis of some new pyrazole derivatives based on mild and efficient reaction of compound 3 with some of laboratory available compounds. Thus, Compound 3 reacted with ethyl 3-amino-2,4-dicyanobut-2-enoate in boiling DMF containing a catalytic amount of piperidine. Two isomeric products seemed possible for this reaction 5 or 6, (Scheme 2). Structure 6 ruled out based on analytical and spectroscopic data (IR, $^1$H NMR and MS). Thus, the IR spectra of the product 5 showed the presence of absorption bands at ν 1699, 2219 and 3422 cm$^{-1}$ due to C=O, CN and NH$_2$ groups, respectively. Accordingly, the $^1$H NMR spectrum (DMSO) of the product 5 showed three singlet signals at δ 2.9, 3.5 and 3.7 due to the methylene and two NH$_2$ groups respectively, and a multiplet at 6.7 - 7.9 ppm, due to aromatic protons. The MS of 5 displayed [M]$^+$ at m/z 439 (60%). It is note worth that, trial to cyclise 5 in boiling pyridine was unsuccessful, (Scheme 2).

Also, compound 3 reacted with diethyl malonate in boiling DMF containing a catalytic amount of piperidine afforded 1-(3,4-dihydro-4-oxo-3-phenyl-2H-chromen-2,3-d[pyrimidin-2-yl]pyrazolidine-3,5-dione 7, (Scheme 3). The structure of 7 was confirmed based on elemental and
spectroscopic analysis. The IR spectra 7 showed the presence of absorption band centered between ν 1685 - 1705, 3212 cm⁻¹ due to CO and NH functions respectively. Accordingly, the 1H NMR spectrum (CDCl₃) of 7 showed three singlet signals at δ 3.2, 5.8 and 8.1 ppm due to the methylene, methine and NH pyrazole ring protons respectively, and a multiplet at δ 6.1 - 7.8 for aromatic protons. The MS of 7 displayed m/z at 374 ([M⁺], 55%).

Similarly, compound 3 was allowed to react with ethyl 2-cyanoacetate, ethyl 3-oxobutanoate and pentane-2,4-dione to afford the corresponding pyrazole derivatives 8 - 10 respectively, (Schemes 3).

Likewise, compound 3 was reacted with 2-(ethoxymethylene) malononitrile and 2-cyano-N-phenylacetamide gave the corresponding pyrazole derivatives 12, 13a, b respectively, (Scheme 4). While the reaction of compound 3 with nitrous acid afforded the tetrazolo[1,5-a]pyrimidine derivatives 11, (Scheme 4). The structure of these compounds was in agreement with analytical and spectroscopic data. The IR spectrum of 11 showed the presence of absorption bands at ν 1699 cm⁻¹ due to CO group. While, the MS of compound 11 showed m/z at 317([M⁺], 60%), (Scheme 4).

On the other hand, the hydrazine 3 reacted with aromatic aldehydes afforded 2-(2-benzylidenehydrayziny)-3-phenyl-3H-chromeno[2,3-d]pyrimidin-4-one 14, which was cyclized to 5-oxo-1-(4-oxo-3-phenyl-4,10-dihydro-3H-chromeno[2,3-d]pyrimidine)3-phenylpyrazolidine-4-carbonitrile 16 by treatment with ethyl cyanoacetate. It seemed that the addition of active methylene hydrogen of ethyl cyanoacetate to the imino carbon of 14 gave the intermediate 15, which subsequently cyclized via elimination of ethanol molecule yielding 16. The MS of 16 showed m/z at 462 (M + 1)⁺, 55%. Its IR spectrum revealed absorption bands at ν 3432 cm⁻¹ (NH), 2217 cm⁻¹ (CN) and 1670 cm⁻¹ (CO). The 1H NMR spectrum showed a multiplet signals at δ 6.71 - 7.92 for aromatic protons and three singlet signals at δ 3.98, 4.12 and 4.21 due to -NH, the two methine protons of pyrazole ring, respectively, (Scheme 5). The compound 16 was transformed in to the chloro derivatives 17, by treatment with phosphoryl chloride (Scheme 5). The MS of 17 showed at m/z at 478 ([M – 1]⁺, 16%). The IR spectrum of 17 showed the presence of absorption band at ν 1700 cm⁻¹ due to C=O, 2217 cm⁻¹ due to CN and 3425 cm⁻¹ due to NH function. The 1HNMR of compound 17 showed singlet signals at δ ppm 3.98 and 4.61 due to NH and methane proton of pyrazole ring.

Compound 17 was utilized as a useful starting material for the synthesis of a variety heterocycle-isolated coumarin derivatives based on mild and efficient reaction of compound 17 with some of laboratory available compounds. Thus, compound 17 reacted with 5-amine-1H-1,2,4-triazole in boiling DMF containing a catalytic amount of piperidine afforded 2-(4-amino-3-phenyl-2,3-dihydro-1H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-a]pyrimidin-1-yl)-3-phenyl-3H-chromeno[2,3-d]pyrimidin-4(10H)-one 18, (Scheme 6). Similarly, compound 17 reacted with 5-amino-3-(methylthio)-1H-pyrazole-4-carbonitrile yielded 4-amino-7-(methylthio)-1-(4-oxo-3-phenyl-4,10-dihydro-3H-chromeno[2,3-d]pyrimidin-2-yl)-3-phenyl-2,3-dihydro-1H-di-pyrazolo[1,5-a:4',3'-e]pyrimidine-6-carbonitrile 19.

Scheme 2. Synthetic route for prepare isolated pyrazole derivatives and reaction conditions.

Scheme 3. Synthetic route for isolated oxazole 7 and pyrazole derivatives 8 - 10, and reaction conditions.
Scheme 4. Synthetic route for isolated pyrazole derivatives and reaction conditions.

Scheme 5. Synthetic route for isolated pyrazole derivatives and reaction conditions.

Scheme 6. Synthetic route for isolated and/or fused pyrazole derivatives 18-23, and reaction conditions.
structure of these compounds was confirmed based on elemental and spectroscopic analysis. (See experimental section). Also, the chloro derivative 17 was converted to the 5-methoxy-1-(4-oxo-3-phenyl-4,10-dihydro-3H-chromeno[2,3-d]pyrimidin-2-yl)-3-phenyl-2,3-dihydro-1H-pyrazole-4-carbonitrile 20 by refluxing with MeONa, (Scheme 6). Structure 20 confirmed based on analytical and spectroscopic data (IR, ¹H NMR and MS). Thus, the IR spectra of the product 20 showed the presence of absorption bands at ν 1699, 2219 and 3422 cm⁻¹ due to C=O, CN and NH groups, respectively. Accordingly, the ¹H NMR spectrum (DMSO) of the product 20 showed three singlet signals at δ 3.82, 3.98 and 4.61 due to the -OCH₃, -NH, and methine protons respectively, and a multiplet at 6.7 - 7.9 ppm, due to aromatic protons. The MS of 20 displayed [M]+ at m/z 475 (62%). We prepared 5-azido-1-(4-oxo-3-phenyl-4,10-dihydro-3H-chromeno[2,3-d]pyrimidin-2-yl)-3-phenyl-2,3-dihydro-1H-pyrazole-4-carbonitrile 21 from the chloro compound 17 by reaction with NaN₃ in acetone [21, 22]. The structure of 21 was in agreement with analytical and spectroscopic data. The IR spectrum of 21 showed the presence of absorption bands at ν 1699 cm⁻¹ due to CO, 2217 cm⁻¹ due to CN and 3422 cm⁻¹ due to NH groups. While, the MS of compound 21 showed m/z at 486([M]+, 32%). In further reactions, chloro compound 17 on treatment with hydrazine hydrate in DMF containing a catalytic amount of piperidine at reflux temperature afforded 2-(4-amino-3-phenyl-2,3-dihydro-pyrazol-1(6H)-yl)-3-phenyl-3H-chromeno[2,3-d]pyrimidine-4(10H)-one 23. The formation of 23 may be proceeded via an initial elimination of HCl molecule to give the intermediate 22, which cyclized by nucleophilic addition of the amino function into the cyano group yielded 23, (Scheme 6). The IR spectrum of 23 showed the presence of absorption bands at ν 1670 cm⁻¹ due to (CO) and 3432 - 3455 cm⁻¹ due to (NH, NH₂) with the absence of any characteristic absorption of (CN) group. The ¹H NMR spectrum of 23 showed four singlet at δ 3.98, 5.21, 6.53 and 9.21 ppm due to the -NH amine, methine of pyrazole ring, amino and imino group respectively, and a multiplet at δ 6.97 - 7.81 for aromatic protons. The MS of 23 displayed m/z at 475 (M⁺, 15%).

On the other hand, the carboxamide 1 easily condensed with acetophenone derivatives in DMF containing a catalytic amount of piperidine at reflux temperature to afford chromenochalcones 24a - 24e via elimination of water (Scheme 7). The IR spectrum of 24a showed absorption bands at ν 1665 - 1705 and 3322 due to CO and NH groups respectively, the Ms of 24a showed m/z at 366 ([M]+, 40%). While, the ¹HNMR spectrum of 24a (DMSO) showed three singlet signals at δ 4.1, 6.5 and 11.5 ppm due to the NH- amine, methylene and NH-imino groups respectively, and a multiplet at δ 7.1 - 7.6 for aromatic protons.

Likewise, compound 1 reacts with some aromatic amines to afford the corresponding Schiff’s base 25a - 25e, (Scheme 7). The IR spectrum of 25a showed the presence of absorption bands at ν 3380, due to NH function, with the absence of any characteristic absorption of a C=O group. The ¹H NMR spectrum (CDCl₃) displayed two signals at δ 4.1, 3.7 and 11.5 due to NH-amine, and NH-imino groups respectively, and a multiplet at 7.1 - 7.6 ppm, for aromatic protons. While, the MS of 25a showed m/z at 339([M]+, 65%).

The reactivity of exocyclic C = C conjugated with the carbonyl group in 24a - 24e was investigated by reaction with hydrazines, hydroxylamine, urea, thiourea and some laboratory available active methylene compounds. The nature of the products obtained characterized by elemental and spectroscopic data, indicates that the reaction proceeded via condensation followed by a nucleophilic attack through α, β-unsaturated ketonic group. Pyrazoles/isoazole derivatives 26a - 26b and 27 were synthesized by treating 24a with equimolar ratios of hydrazine hydrate or phenyl-hydrazine or hydroxylamine respectively in ethanol containing a catalytic amount of piperidine, (Scheme 8). The structure of these compounds was established based on analytical and spectroscopic data. The IR spectra of 26a showed the presence of absorption band centered between ν 3117 - 3293 cm⁻¹ due to NH function, with the absence of any characteristic absorption of a C=O group. Accordingly, the ¹H NMR spectrum (DMSO) of 26a showed four singlet signals at δ 2.9, 4.1, 7.1 and 11.5 ppm due to the proton at C-4 of pyrazole, NH- amine, NH- hydrazide and =NH imino respectively, and a multiplet at δ 7.2 - 7.8 for aromatic protons. The MS of 26a showed m/z at 383 ([M+3]⁺, 55%). The activation exerted by the carbonyl group on the exocyclic double bond in 24a renders them available for the cyclocondensation addition of various amino compounds such as urea and thiourea. Thus, when the chalcone 24a was reacted with an equimolar quantity of urea or thiourea respectively, (Scheme 7) an initial condensation of one amino group with the carbonyl function occurred releasing water, followed by a nucleophilic addition of the second amino group to the double bond forming 4,5-dihydro-4-(2-imino-2H-chromen-3-yl)-6-phenyl-4-(phenylamino)pyrimidin-2(1H)-ones, 28a and/or thione 28b. The structures of the synthesized compounds were confirmed by analytical and spectroscopic data (IR, ¹H NMR and MS). The IR spectra of 28a showed the presence of absorption bands centered between ν 1685 - 1705, 3063 - 3288 cm⁻¹ due to C=O and NH functions, respectively. The ¹H NMR spectrum (DMSO) of 28a showed four singlet signals at δ 2.9, 4.1, 8.1 and 11.5 ppm due to the proton at C-4 of pyrimidine, NH-amine, NH-amide and NH-imino protons , respectively and a multiplet at δ 7.2 - 7.8 for aromatic protons. The MS of 28a showed a peak at m/z 408 ([M]+, 45%). New pyridine derivatives

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have been prepared via condensation of 24a with the active methylene groups of cyanoacetamide, cyanothioacetamide, 2-cyano-N,N-tolyacetamide, 2-cyanoacetohydrazide and 2-cyano-N-phenylacetamide respectively, followed by a nucleophilic addition of the amino/imino group to the double bond, afforded 1,2,5,6-tetrahydro-6-(2-imino-2H-chromen-3-yl)-2-oxo(thioxo)-4-phenyl-6-(phenylamino)pyridine-3-carbonitriles 29a - 29e, respectively (Scheme 8). The IR spectrum of 29a showed the presence of absorption bands at ν 1689 - 1705, 2220 and 3188 - 3244 cm⁻¹ due to C=O, CN, and NH functions, respectively, and the ¹H NMR spectrum (DMSO) displayed three singlet signals at δ 2.9, 4.1 and 8.1 due to the proton at C-5 of pyridine, NH-amide and NH amide, respectively, and a multiplet at 7.2 - 7.6 ppm, respectively. The MS of 29a showed a peak at m/z 432 ([M⁺], 65%).

Similarly, compound 24a reacted with 2-chloroacetamide to afford 3-chloro-5, 6-dihydro-6-(2-imino-2H-chromen-3-yl)-4-phenyl-6-(phenylamino)pyridin-2(1H)-one 30, (Scheme 9). Also, 2-(cyanomethyl) benzimidazole, reacted with the chalcone 24a, in ethanol using piperidine as a catalyst gave the 2-(2-imino-2H-chromen-3-yl)-4-phenyl-2-(phenylamino) pyridin[1,2-a]benzimidazolo[5,4-f]quinazoline-3-carbonitrile and/or ethyl 3-amino-2,4-dicyanobut-2-enoate respectively, followed by a nucleophilic addition of chloro acetyl chloride to 25a - 25e, were used to prepare new compounds. Thus, cyanoacetamide, cyanothioacetamide, 2-cyano-N,N-tolyacetamide, 2-cyanoacetohydrazide and 2-cyano-N-phenylacetamide respectively, followed by a nucleophilic addition of the amino/imino group to the double bond, afforded 1,2,5,6-tetrahydro-6-(2-imino-2H-chromen-3-yl)-2-oxo(thioxo)-4-phenyl-6-(phenylamino)pyridine-3-carbonitriles, derivatives probably 32a - 32e, respectively. On the other hand, the new synthesized Schiff’s bases 2-(1-cyano-2-oxobutylidene)-1,2,5,6-tetrahydro-6-(2-imino-2H-chromen-3-yl)-4-phenyl-6-(phenylamino)pyridine-3-carbonitrile, 33a and 2-(1-cyano-2-oxobutylidene)-1,2,5,6-tetrahydro-6-(2-imino-2H-chromen-3-yl)-4-phenyl-6-(phenylamino)pyridine-3-carbonitrile 33b, respectively. The structure of these products was established based on the IR spectrum of 33a which showed the presence of absorption bands at ν 2219 and 3289 cm⁻¹ due to C=O and NH functions, respectively. The ¹H NMR spectrum (DMSO) of 33a displayed two singlet signals at δ 2.9, 4.1 and 11.5 due to the C-3 protons, NH-amine and NH-imino protons respectively, and a multiplet at δ 6.9 - 7.6 ppm, for aromatic protons. The MS showed the [M⁺] ion at m/z 505 (35%). Similarly, the chalcone 24a was reacted with amino phenols in ethanolic solution containing a catalytic amount of piperidine to give 2,3-dihydro-2-(2-imino-2H-chromen-3-yl)-N,4-diphenyl-benzimidazole, derivatives 32a, b (Scheme 9). The IR spectrum of 32a showed the presence of absorption bands at ν 3289 cm⁻¹ due to NH function, the ¹H NMR spectrum (DMSO) of 32a displayed three singlet signals at δ 2.9, 4.1 and 11.5 due to the C-3 protons, NH-amine and NH-imino protons respectively, and a multiplet at 6.7 - 7.3 ppm for aromatic protons. While, the MS of 32a showed a peak at m/z 457 ([M⁺], 55%). Also, compound 24a was reacted with 2-amino-prop-1-ene-1, 1,3-tricarbonitrile and/or ethyl 3-amino-2,4-dicyanobut-2-enoate to afford 2-(dicyano- methylene)-1,2,5,6-tetrahydro-6-(2-imino-2H-chromen-3-yl)-4-phenyl-6-(phenylamino)pyridine-3-carbonitrile, derivatives probably via initial condensation of the activated methylene group with the carbonyl function releasing water, followed by a nucleophilic addition of the NH group at the double bond of compound 24a to afford 31, (Scheme 9). The structure of 31 was assigned based on IR, ¹H NMR, and mass spectra. The IR spectrum showed the presence of absorption bands at ν 2220 cm⁻¹ and 3188 - 3244 cm⁻¹ due to CN and NH functions respectively, while that due to C=O was completely disappeared, and the ¹H NMR spectrum (CDCl₃) displayed three singlet at δ 2.9, 4.1 and 11.5 due to the C-3 proton, NH-amine and NH-imino protons respectively, and a multiplet at δ 6.9 - 7.6 ppm, for aromatic protons. The MS showed the [M⁺] ion at m/z 505 (35%). Similarly, the chalcone 24a was reacted with amino phenols in ethanolic solution containing a catalytic amount of piperidine to give 2,3-dihydro-2-(2-imino-2H-chromen-3-yl)-N,4-diphenyl-benzimidazole, derivatives 32a, b (Scheme 9). The IR spectrum of 32a showed the presence of absorption bands at ν 3289 cm⁻¹ due to NH function, the ¹H NMR spectrum (DMSO) of 32a displayed three singlet signals at δ 2.9, 4.1 and 11.5 due to the C-3 protons, NH-amine and NH-imino protons respectively, and a multiplet at 6.7 - 7.3 ppm for aromatic protons. While, the MS of 32a showed a peak at m/z 457 ([M⁺], 55%). Also, compound 24a was reacted with 2-amino-prop-1-ene-1, 1,3-tricarbonitrile and/or ethyl 3-amino-2,4-dicyanobut-2-enoate to afford 2-(dicyano-methylen)-1,2,5,6-tetrahydro-6-(2-imino-2H-chromen-3-yl)-4-phenyl-6-(phenylamino)pyridine-3-carbonitrile, 33a and 2-(1-cyano-2-oxobutylidene)-1,2,5,6-tetrahydro-6-(2-imino-2H-chromen-3-yl)-4-phenyl-6-(phenylamino)pyridine-3-carbonitrile 33b, respectively. The structure of these products was established based on the IR spectrum of 33a which showed the presence of absorption bands at ν 2219 and 3289 cm⁻¹ due to C=O and NH functions, respectively. The ¹H NMR spectrum (DMSO) of 33a displayed two singlet signals at δ 2.9, 4.1 and 11.5 due to the C-3 protons, NH-amine and NH-imino protons respectively, and a multiplet at 6.7 - 7.3 ppm for aromatic protons. While, the MS of 33a showed a peak at m/z 482 ([M + 2]⁺, 35%).

On the other hand, the new synthesized Schiff’s bases 2-(1-cyano-2-oxobutylidene)-1,2,5,6-tetrahydro-6-(2-imino-2H-chromen-3-yl)-4-phenyl-6-(phenylamino)pyridine-3-carbonitrile, derivatives 34a - 34e, (Scheme 10). The IR spectra of 34a - 34e showed the

![Scheme 7. Synthetic route for chalcones 24a-e and Schiff's bases 25a-e.](image-url)
Scheme 8. Synthetic route for isolated pyrazole, isoxazole, pyrimidine and pyridine derivatives 26ab, 27, 28a,b and 29a-e.

Scheme 9. Synthetic route for the preparation of compounds 30-33a,b.

Scheme 10. Synthetic route for the preparation of β-latame 34a,b. and thiazolidinone derivatives 35a-e.
presence of absorption bands due to C=O and NH functions respectively. The $^1$H NMR spectrum (DMSO) of $^{34}c$ showed three singlet signals at δ 4.1, 5.2 and 11.5 ppm for NH-amine, the proton at C3 of the β-lactam unit and NH-imino protons respectively and a multiplet at δ 7.1 - 7.6 for aromatic protons. The MS of $^{34}c$ showed the [M]$^+$ ion at m/z 460 (40%). Also, the Schiff’s bases $^{25}a$ - $^{25}e$ were reacted with equimolar ratio of thioglycolic acid in boiling benzene using water separator system, the thiol group of thioglycolic acid could be added to the imino carbon atoms of Schiff’s bases $^{25}a$ - $^{25}e$ followed by smooth cyclization to afford 2-(2-imino-2H-chromen-3-yl)-3-phenyl-2-(phenylamino) thiazolidinone-4-ones, $^{35}a$ - $^{35}e$ (Scheme 10). The IR spectra of $^{35}a$ showed bands due to OH at 3400 cm$^{-1}$; C=O at 1623 cm$^{-1}$; C-N at 1230 cm$^{-1}$ and C-CH$_n$ at 1515 cm$^{-1}$. The 1H NMR spectrum (DMSO) showed three singlet signals at δ 3.8, 4.1 and 5.2 for the methylene of thiazolidinone, NH-amine and NH-imino protons respectively and a multiplet at δ 6.8 - 7.8 for aromatic protons. In the MS of $^{35}a$ showed m/z 411 ([M-2]$, 35\%$).

4. Conclusion

Despite the several existing methods for the synthesis of chromene derivatives, there still is demand for general strategies, which can efficiently provide variously substituted chromene systems. Thus, this work opened a new avenue for the synthesis of a variety of 2-imino-N-phenyl-2H-chromene-3-carboxamide, derivatives.

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