Facile and Simple Synthesis of Some New Polyfunctionally Heterocyclic Derivatives Incorporating 2-Imino-2*H*-chromene Moiety

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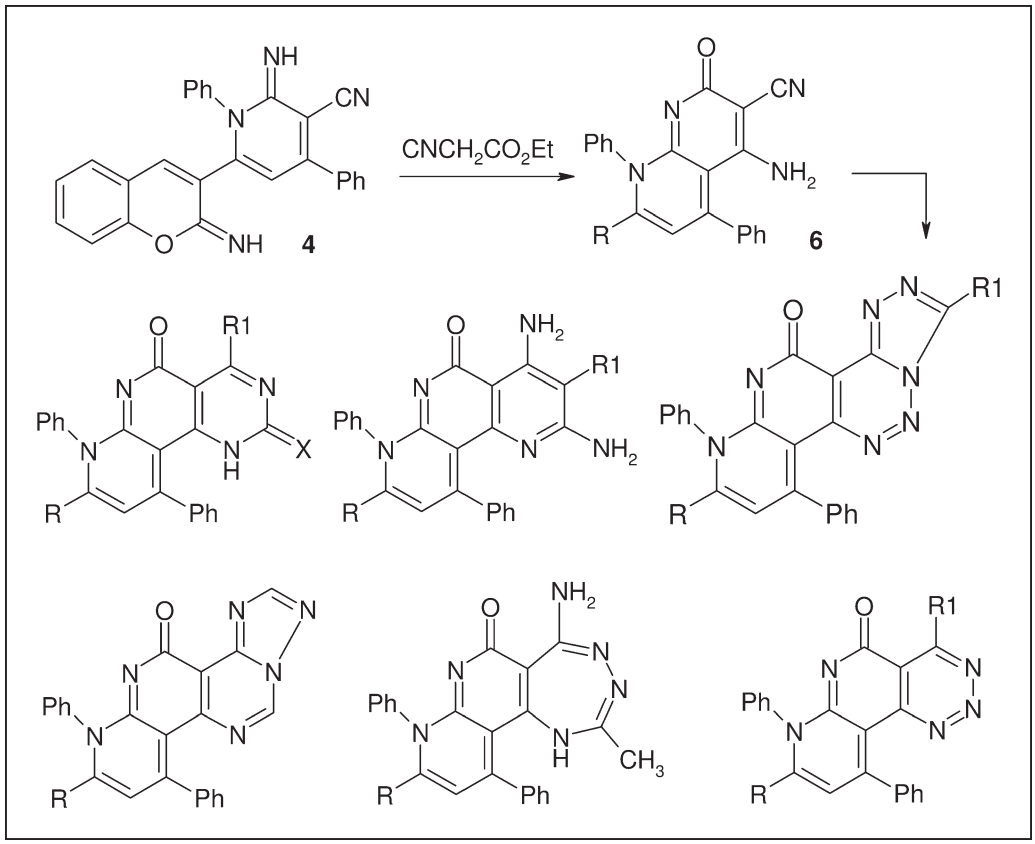

1,2-Dihydro-2-imino-6-(2-imino-2*H*-chromen-3-yl)-1,4-diphenyl-pyridine-3-carbonitrile **4** has been synthesized and reacted with ethyl cyanoacetate to yield the new 5-amino-1,7-dihydro-2-(2-imino-2*H*-chromen-3-yl)-7-oxo-1,4-diphenyl-1,8-naphthyridine-6-carbonitrile **6**, which consider a good and available starting intermediate for synthesis of series of functionalized chromenes. So, the compound **6** was utilized as a key for the synthesis of some new pyrimido[5,4-*c*][1,8]naphthyridinones, pyrido[2,3-*c*][1,6]naphthyridinones, triazolo[3′,4′:1,6]triazino][5,4-*c*][1,8]naphthyridinones, triazolo[2′,3′:1,6]pyrimido[4,5-*c*][1,8]naphthyridinones, triazepino[6,5-*c*][1,8]naphthyridinone, and triazino[5,4-*c*][1,8]naphthyridinones. The structures of these compounds were established by elemental analysis, IR, MS, and NMR spectral analysis.

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INTRODUCTION

The chromene derivatives are prominent natural products, which are widely distributed among many plants [1]. They have considerable biological importance, especially as potentially useful pesticides [2,3], inhibitors of cell proliferation and potential anticancer therapeutics [4]. The chromene derivatives was found as new PET agents for imaging of apoptosis in cancer [5], potent inhibitory activities in enzymatic and cellular assays and good selectivity to MMP-2 and MMP-9 [6], dye compounds [7–9], potent antileishmanial activity [10]. Antirhinovirus activity in cell cultures, several compounds were also proved to be both potent and selective HRV1B inhibitors [11]. The chromene compounds display high antifungal and antibacterial activities [12–15].

Also, chromene derivatives was found as anti-picornavirus capsid-binders [16], and exhibited profound antioxidant activities [17]. Infinitively, the chromene-3-carboxamide derivatives were found as potent inhibitors of AKR1B10 [18].

In addition, derivatives of chromone are important natural products possessing a wide range of valuable physiological activities [19]. And also, they represent useful synthetic building blocks in organic and medicinal chemistry [20–25]. The chromanol moiety of vitamin E (α-tocopherol) exhibits anti-androgen properties [26], chromanyl derivatives also display significant cytotoxic activity against cancer cells [27].

The importance of the chromene 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 [28–42], there is still demand for general strategies, which can efficiently provide variously substituted chromene systems.

RESULTS AND DISCUSSION

Thus, an equimolar reaction of 2-imino-*N*-phenyl-2*H*-chromene-3-carboxamide **1** with acetophenone in refluxing DMF containing a catalytic amount of piperidine for 8 h resulted in the formation of 3-(2-imino-2*H*-chromen-3-yl)-1-phenyl-3-(phenylamino)prop-2-en-1-one **2**, which allowed to react with malononitrile in ethanolic piperidine solution at reflux temperature to afford 1,2-dihydro-2-imino-6-(2-imino-2*H*-chromen-3-yl)-1,4-diphenylpyridine-3-carbonitrile **4**. The formation of **4** may proceeded *via* an initial condensation reaction of the methylene group of malononitrile and the carbonyl group of **2** to give intermediate **3**, which cyclized by nucleophilic addition of an imino function into one of the cyano group to afford pyridine derivative **4**. The structure of compound **4** was established based on analytical and spectral analysis. The IR spectrum of compound **4** confirmed the presence of intense absorption bands at ν 3282 and 2214 cm^{-1} due to imino and cyano groups, respectively. The MS of **4** showed *m*/*z* at 413 $(M-1)^+$, 20%. The ^1H NMR spectrum of **4** showed singlet signal at δ 5.40, broad singlet at δ 5.98 and a multiplet at δ 7.23−7.56 ppm attributed to pyridine *H*-5, imino function and aromatic protons, respectively.

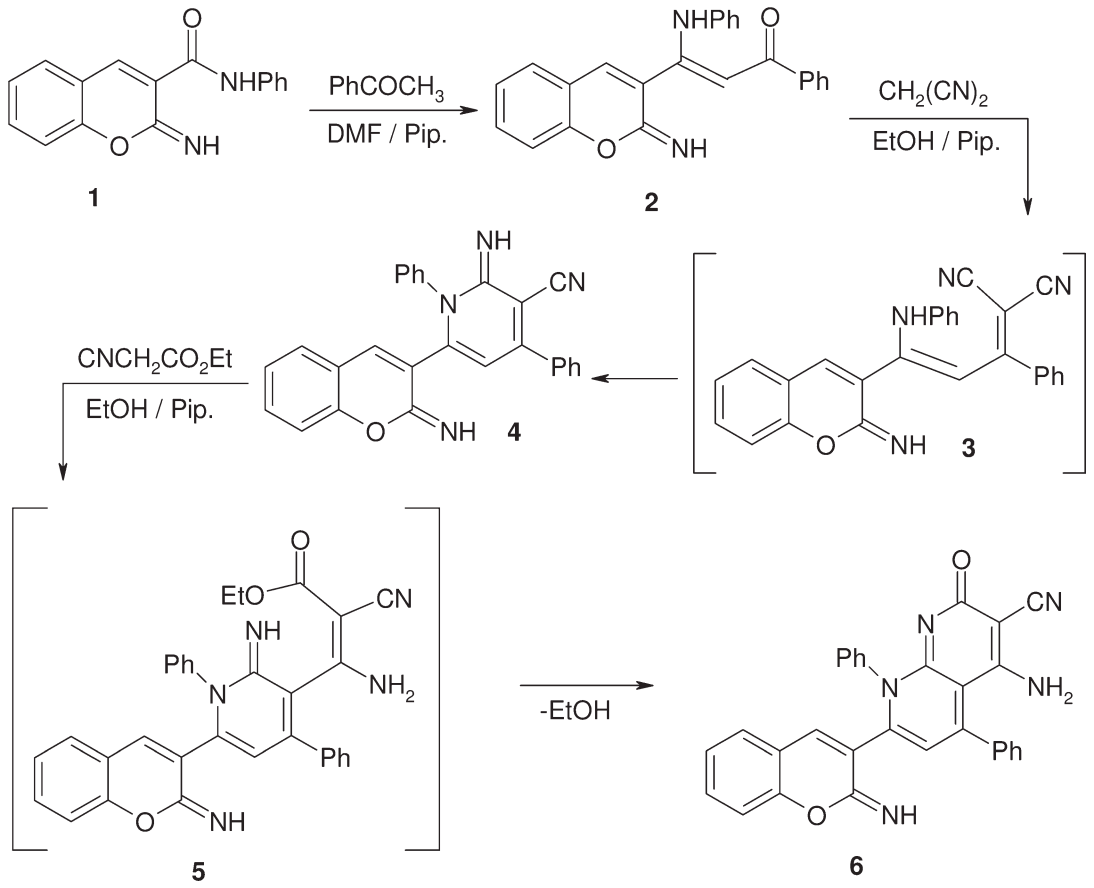
Compound **4** reacted with ethyl cyanoacetate in ethanolic piperidine solution at reflux temperature to afforded 5-amino-1,7-dihydro-2-(2-imino-2*H*-chromen-3-yl)-7-oxo-1,4-diphenyl-1,8-naphthyridine-6-carbonitrile **6**. It seemed that the addition of active methylene hydrogen of ethyl cyanoacetate to the cyano function of **4** gave the intermediate **5,** which subsequently cyclized *via* elimination of ethanol molecule yielding **6**. The MS of **6** showed *m*/*z* at 482 $(M+1)^+$, 55%. Its IR spectrum revealed absorption bands at ν 3432 (NH_2), 2217 (CN) and 1670 cm^{-1} (CO). The ^1H NMR spectrum showed a multiplet signals at δ 6.71−7.92 for aromatic protons and two singlet signals at δ 5.72 and 3.74 due to H-3 of 1,8-naphthyridine and amino protons, respectively, (Scheme 1).

The reactivity of *o*-aminonitrile of compound **6** was investigated towards many laboratory available reagents to synthesis of a new wide variety of fused heterocyclic compounds.

Thus, compound **6** reacted with acetic anhydride and the product obtained was depend on the reaction conditions. So, when compound **6** reacted with acetic anhydride in pyridine on water bath yielded pyrimido[5,4-*c*][1,8]naphthyridinone **8**, while under reflux in absence of pyridine gave the acetamido derivative **7**. The IR spectrum of **8** exhibited the disappearance of the absorption band due to cyano function and the appearance of absorption bands at ν 3419, 3282, and 1698 cm^{-1} due to the presence of hydroxy, imino and carbonyl groups, respectively. However, the IR spectrum of **7** showed the presence of absorption band at ν 2217 cm^{-1} due to (CN) function. The ^1H NMR spectrum of **8** showed three singlet signals at 2.52, 5.96, and 9.42 corresponding to methyl, naphthyridine and hydroxy protons, respectively, in addition a multiplet signals at 6.72–7.90 ppm due to aromatic protons. A further conformation of the prepared compound **8** was obtained *via* boiling of **7** in pyridine. Compound **7** underwent further cyclization upon treatment with hydrazine hydrate in ethanol containing a catalytic amount of piperidine at reflux temperature affording [1,2,4]triazepino[6,5-*c*][1,8]naphthyridinone **9**, (Scheme 2). The IR spectrum of compound **9** revealed the absence of absorption band at ν 2217 cm^{-1} due to the disappearance of cyano function and exhibited characteristic absorption bands at υ 3360–3385, 3282 and 1670 cm^{-1} for (NH_2), (NH), and (CO) groups, respectively. The ^1H NMR spectrum displayed singlet signals at δ 1.21, 2.24, and 5.79 due to methyl, amino, and naphthyridine protons respectively, and a multiplet signals at 6.71–7.92 ppm for aromatic protons. While the MS of **9** showed *m*/*z* at 534 (M-3, 60%).

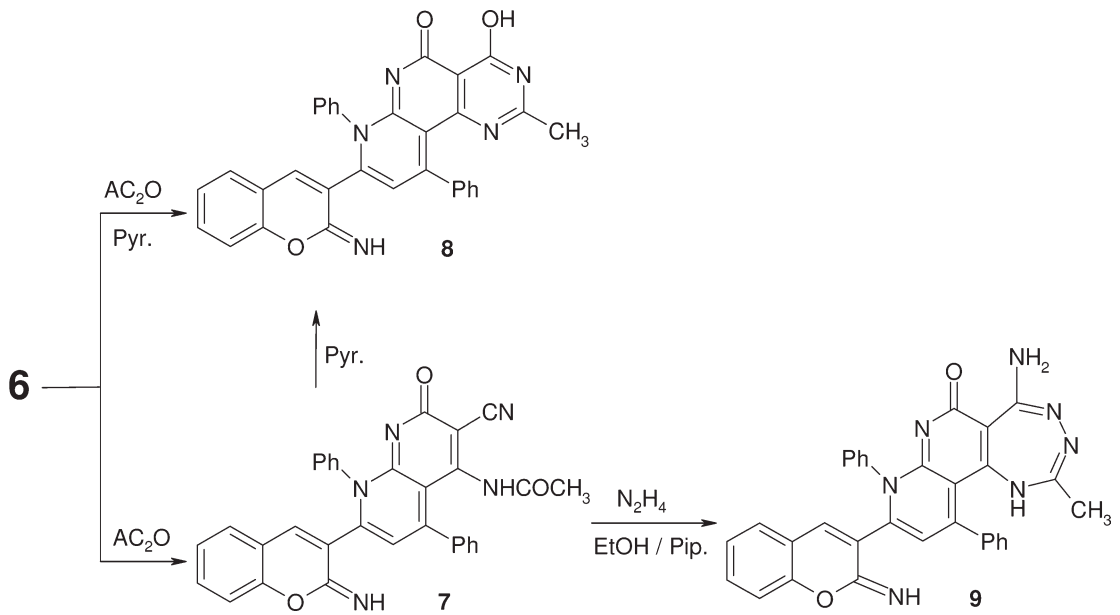
In further reactions, the enaminonitrile moiety **6** was used for preparation of pyrimido naphthyridine derivatives. Thus, **6** was fused with formamide at reflux temperature leading to amino pyrimidine derivative **11,** while the reaction with formic acid alone and/or formic acid in presence of formamide gave pyrimidindione derivative **12**. The formation of **11** may be proceeded *via* an initial condensation reaction of the carbonyl group in formamide with the amino function in **6** through intermediate **10**, which cyclized by nucleophilic addition of the amino function into the cyano group yielded amino

Scheme 1

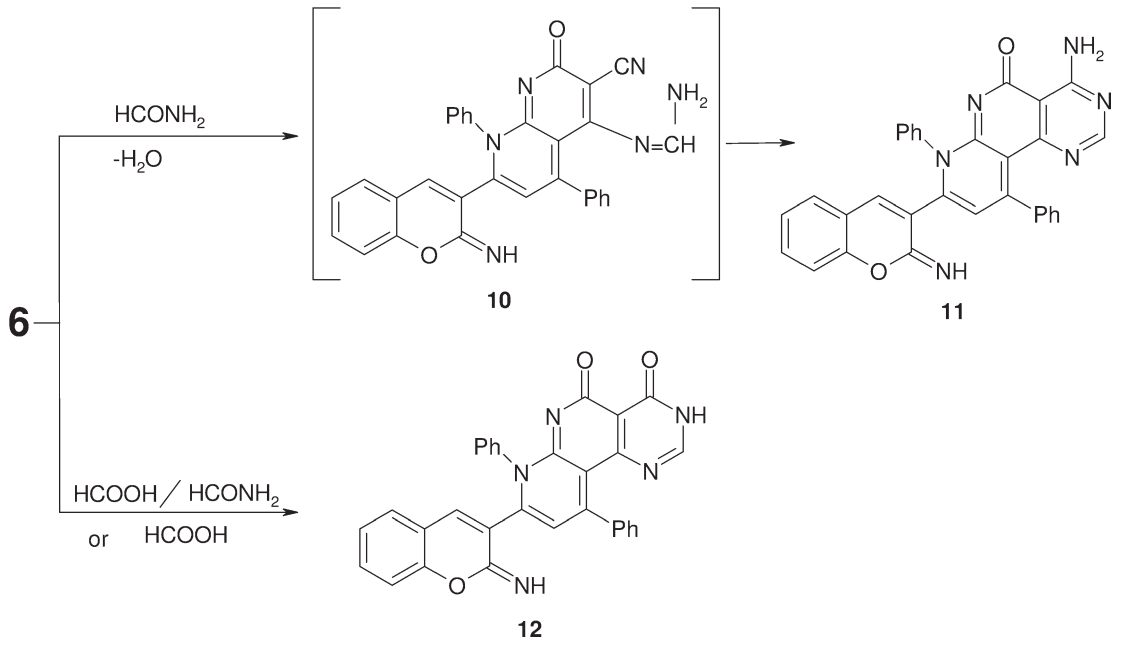


pyrimido[5,4-*c*][1,8]naphthyridinone **11**. The IR spectrum of **11** showed the presence of absorption bands at ν 3432 (NH_2), 3282 (NH), and 1670 (CO) cm^{-1}, with the absence of any characteristic absorption of (CN) group. The ^1H NMR spectrum of **11** showed new singlet signals at δ 4.21 and 6.85 ppm due to the amino and

Scheme 2



Scheme 3



pyrimidine protons, respectively, and a multiplet at δ 7.22–7.81 for aromatic protons. The MS of **11** displayed *m*/*z* at 510 (M+2, 10%).While, the IR spectrum of **12** showed the disappearance of any absorption due to amino and cyano function groups and the ^{1}H NMR spectrum of **12** showed the lack of signal attributed to amino group, (Scheme 3).

However, refluxing of **6** with 2-phenylacetyl chloride in pyridine gave 1,7-dihydro-5-phenylacetamide-2-(2-imino-2*H*-chromen-3-yl)-7-oxo-1,4-diphenyl-1,8-naphthyridin-5-yl)-6-carbonitrile **13**, treatment of the latter with H_2O_2 followed by hydrolysis with sodium hydroxide [36] gave pyrimido[5,4-*c*][1,8]naphthyridine-4,5-dione **15** *via* intermediate **14**. The IR spectrum of **13** showed the presence of absorption bands at ν 3188–3244, 2220 and 1689–1707 cm^{-1} due to (NH), (CN), and (CO) functions, respectively. While, the IR spectrum of **15** exhibited the disappearance of absorption band attributed to (CN) function.

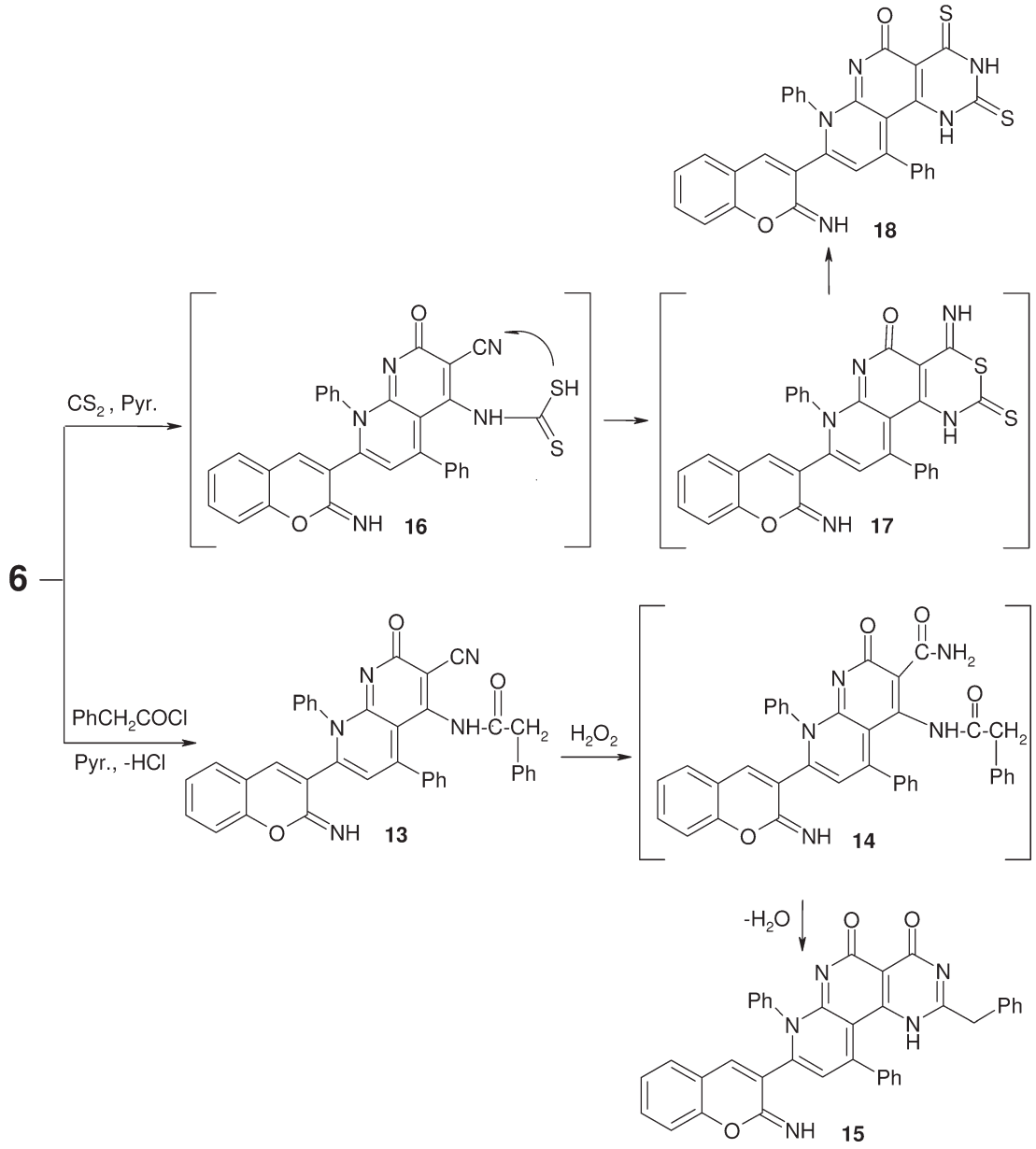
The reactivity of amino group in compound **6** is also explored through its reaction with carbon disulfide. Thus, refluxing of **6** with carbon disulfide in pyridine gave dithioxopyrimido[5,4-*c*][1,8]naphthyridinone **18**. IR spectrum of **18** showed the absence of absorption bands assignable to amino and cyano functional groups and displayed absorption bands due to NH, CO, and CS functions. Formation of **18** may be proceeded through the addition of the amino group to CS_2 followed by a nucleophilic attack of the thiol group to the cyano function forming the intermediate **17**. Rearrangement of **17** gave the pyrimidine dithione derivative **18**, (Scheme 4).

However, heating of compound **6** with ammonium thiocyanate in boiling acetic acid [37] gave pyrimido[5,4-*c*][1,8]naphthyridine **21**. The IR spectrum of **21** revealed the absence of absorption band for cyano function and showed the presence of absorption bands at ν 3419, 3282, 1689, and 1330 cm^{-1} due to (NH_2), (NH), (CO), and (CS) functions, respectively. The ^{1}H NMR spectrum displayed singlet signals at δ 2.22, 3.87, 4.20, and 57.4 due NH_2, 2 NH, and naphthyridine protons. The MS of compound **21** showed *m*/*z* at 599 (M^+, 35%).

Similarly, the reaction of compound **6** with phenyl isocyanate in pyridine at reflux temperature afforded pyrimido[5,4-*c*][1,8]naphthyridinone **22**. The IR spectrum for **22** showed the absence of absorption bands assignable to amino and cyano functional groups and showed the presence of absorption bands at ν 3180–3282, 1689 and 1320 cm^{-1} due to (NH), (CO), and (CS) functions, respectively. The MS of compound **22** showed *m*/*z* at 616 (M^+, 40%), (Scheme 5).

The condensation of *o*-aminonitrile **6** with triethyl orthoformate in refluxing acetic anhydride yielded the corresponding 1,4-diphenyl-5-ethoxymethyleneamino-2,8-dihydro-2-(2-imino-2*H*-chromen-3-yl)-7-oxo-1,8-naphthyridine-6-carbonitrile **23**, which underwent further cyclization upon treatment with hydrazine hydrate in ethanol at room temperature under stirring afforded 7-amino-8-imino-7,8-dihydro-2-(2-imino-2*H*-chromen-3-yl)-1,4-diphenylpyrimido[5,4-*c*][1,8]naphthyridin-9(1*H*)-one **24**. The IR spectrum of **23** showed the absence of any absorption due to amino function and showed the presence of (NH) at 3282, (CN) at 2220, and (CO) at 1698 cm^{-1}. The ^{1}H

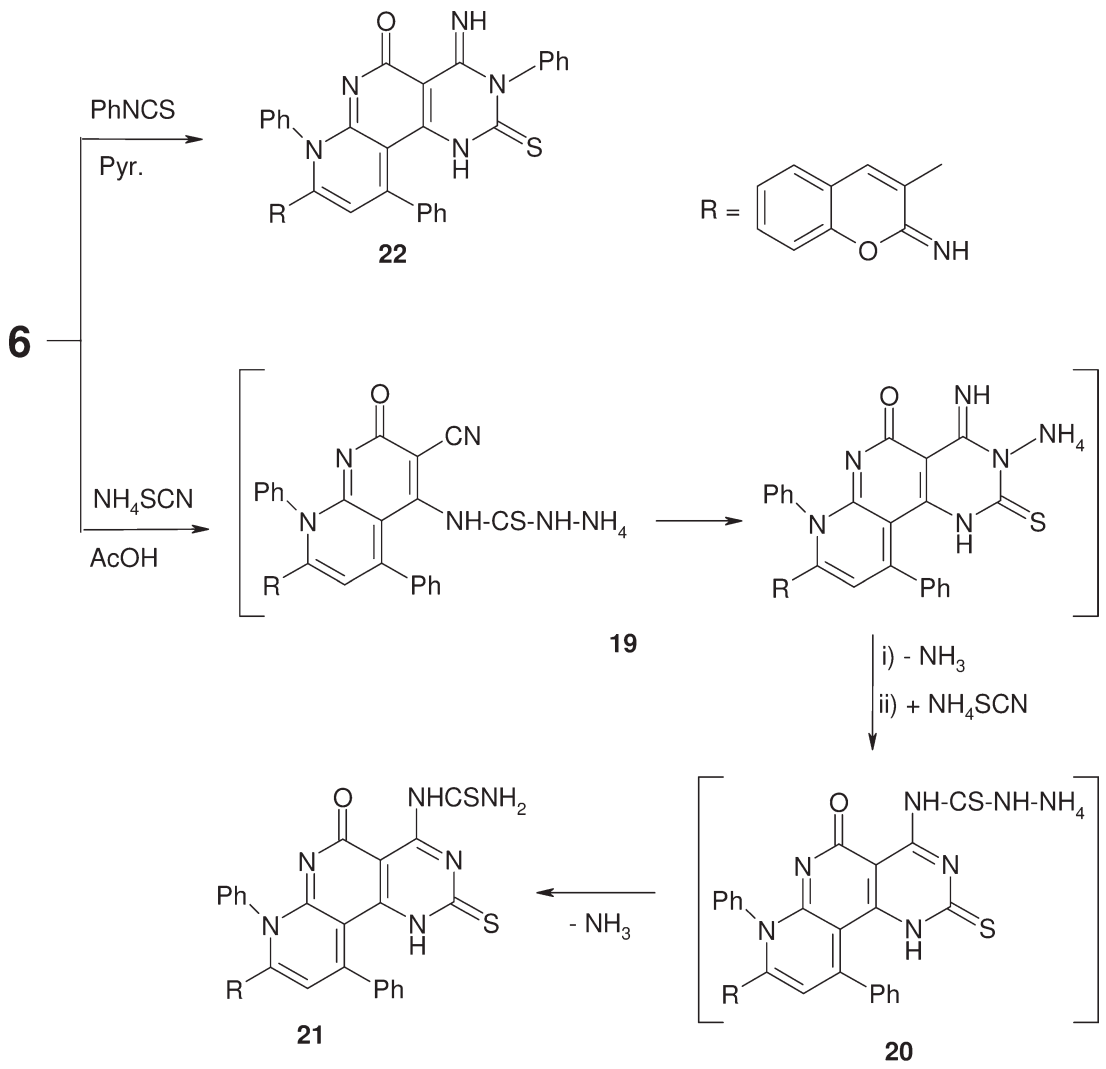
Scheme 4



NMR spectrum of **23** revealed the presence of triplet and quartet signals at δ 1.21 and 3.94 ppm due to ethoxy group. The MS of **23** showed *m*/*z* at 537 (M^+, 40%). However, the IR spectrum of **24** showed the absence of cyano and the presence of amino at 3432 cm^{-1}, while the ^1H NMR spectrum of **24** displayed singlet signals at δ 3.75, 5.11, 5.70, and 5.99 due to NH_2, pyrimidine, naphthyridin, and NH protons, with the disappearance of that due to ethoxy group. The MS of **24** showed *m*/*z* at 523 (M^+, 70%). Further cyclization of **24** was achieved by the reaction of **24** with triethyl orthoformate in acetic anhydride at reflux afforded 2-(2-imino-2*H*-chromen-3-yl)-1,4-diphenyl[1,2,4]triazolo[2′,3′:1,6]pyrimido[4,5-*c*][1,8]naphthyridin-10-one **25**. The IR spectrum of **25** showed the absence of any absorption bands may be attributed due to the presence of NH_2 function. The MS of **25** exhibited a molecular ion peak *m*/*z* 533 (M^+, 60%) and 535 (M+2, 14%).

In addition, the *N*-(ethoxymethylene) amine **23** gave 7,8-dihydro-8-imino-2-(2-imino-2*H*-chromen-3-yl)-7-methyl-1,4-diphenylpyrimido[5,4-*c*][1,8]naphthyridin-9(*1H*)-one **26** upon treatment with methylamine in ethanol at room temperature. The IR spectrum of **26** showed the absence of any absorption band may be attributed due to the presence of cyano function. The ^1H NMR spectrum of **26** showed new singlet signals at δ 2.72 and 5.47

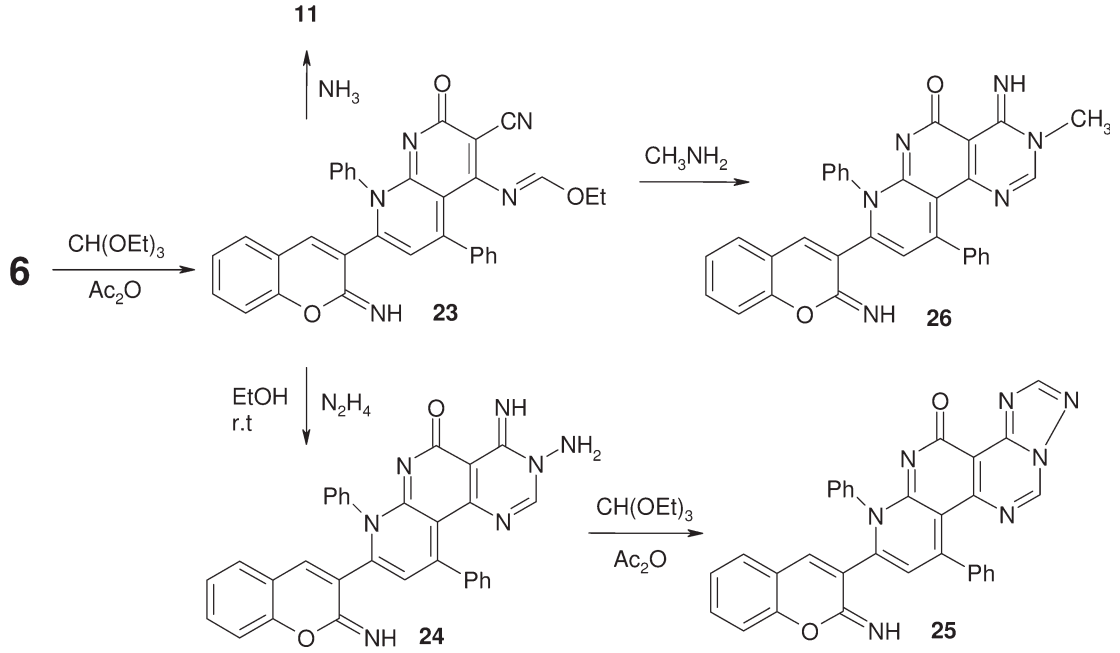
Scheme 5



ppm due to the methyl and imino groups, respectively. The MS of **26** showed a peak at *m*/*z* 522 (M^+, 45%). It is worth mentioned that, compound **23** was successfully transferred into **11** *via* ammonolysis in dioxan solution for 2 hour, (Scheme 6).

Diazotization and self coupling of the amino group of compound **6** with sodium nitrate and HCl [38,39] gave 8-chloro-2-(2-imino-2*H*-chromen-3-yl)-1,4-diphenyl[1,2,3]triazino[5,4-*c*][1,8]naphthyridin-9(1*H*)-one **27**. The IR spectrum of **27** showed the absence of any absorption bands that may be attributed to the amino and cyano function. Moreover, the ^{1}H NMR spectrum of **27** revealed the disappearance of the signal due to amino protons. The MS of **27** showed the *m*/*z* at 531 (M+2, 65%). The formation of **27** was assumed to be proceeded *via* an initial diazotization of **6** and spontaneously undergoes intramolecular cyclization through a nucleophilic addition of chlorine ion on the positive carbon of cyano function. Furthermore, compound **27** was allowed to react with hydrazine hydrate in ethanolic solution using piperidine as a catalyst yielding 4-hydrazinyl[1,2,3]triazino[5,4-*c*][1,8]naphthyridinone **28**. The IR spectrum of **28** showed the presence of absorption bands at ν 3432, 3282, and 1689 cm^{-1} due to (NH_2), (NH), and (CO) groups, respectively. The ^{1}H NMR spectrum displayed three singlet signals at δ 3.11, 3.72, and 5.21 due to (NH), (NH_2), and naphthyridine protons, respectively. The MS of **28** showed *m*/*z* at 524 (M^+, 55%). The hydrazinyl triazinonaphthyridinone **28** underwent several cyclization reactions. Thus, treatment of **28** with formic acid, acetic anhydride, benzoyl chloride and carbon disulfide [40] gave the corresponding triazolo[3′,4′:1,6][1,2,3]triazino[5,4-*c*][1,8]naphthyridinone derivatives **29a–d**. The IR spectra of **29a–d** showed the lack of absorption band due to amino function. While, the reaction of compound **28** with nitrous acid yielded

Scheme 6



tetrazolo[4′,5′:1,6][1,2,3]triazino[5,4-*c*][1,8]naphthyridinone **30**, (Scheme 7).

Similarly, triazolopyrimidine naphthyridinone **31** may be obtained through the reaction of enaminonitrile **6** with 5-amino[1,2,4]triazole in ethanolic piperidine solution at reflux temperature. The IR spectrum of **31** revealed the absence of absorption band attributed to cyano group and appearance an absorption bands at ν 3419, 3282, and 1689 cm^{-1} due to (NH_2), (NH), and (CO) functions, respectively. The ^1H NMR of **31** showed singlet signal at δ 2.21 for amino protons and multiplate at 6.90–7.63 for aromatic protons. The MS of **31** showed *m*/*z* at 551(M+3, 70%).

Also, laboratory available active methylene compounds have been similarly reacted with the enaminonitrile **6**. Thus, 2-cyanomethylbenzimidazole and/or 2-cyanomethylbenzthiazole in ethanol containing piperidine as catalyst at reflux temperature reacted with **6** to give pyrido[2,3-*c*][1,6]naphthyridinone derivatives **32a,b**. The MS of **32a** showed *m*/*z* at 638 (M^+, 50%) and the MS of **32b** showed *m*/*z* at 656 (M+1, 60%).

Similarly compound **6** condensed smoothly with malononitrile at reflux in ethanolic piperidine solution yielded pyrido[2,3-*c*][1,6]naphthyridinone derivative **33**. The MS of **33** showed *m*/*z* at 544(M-3, 55%), (Scheme 8).

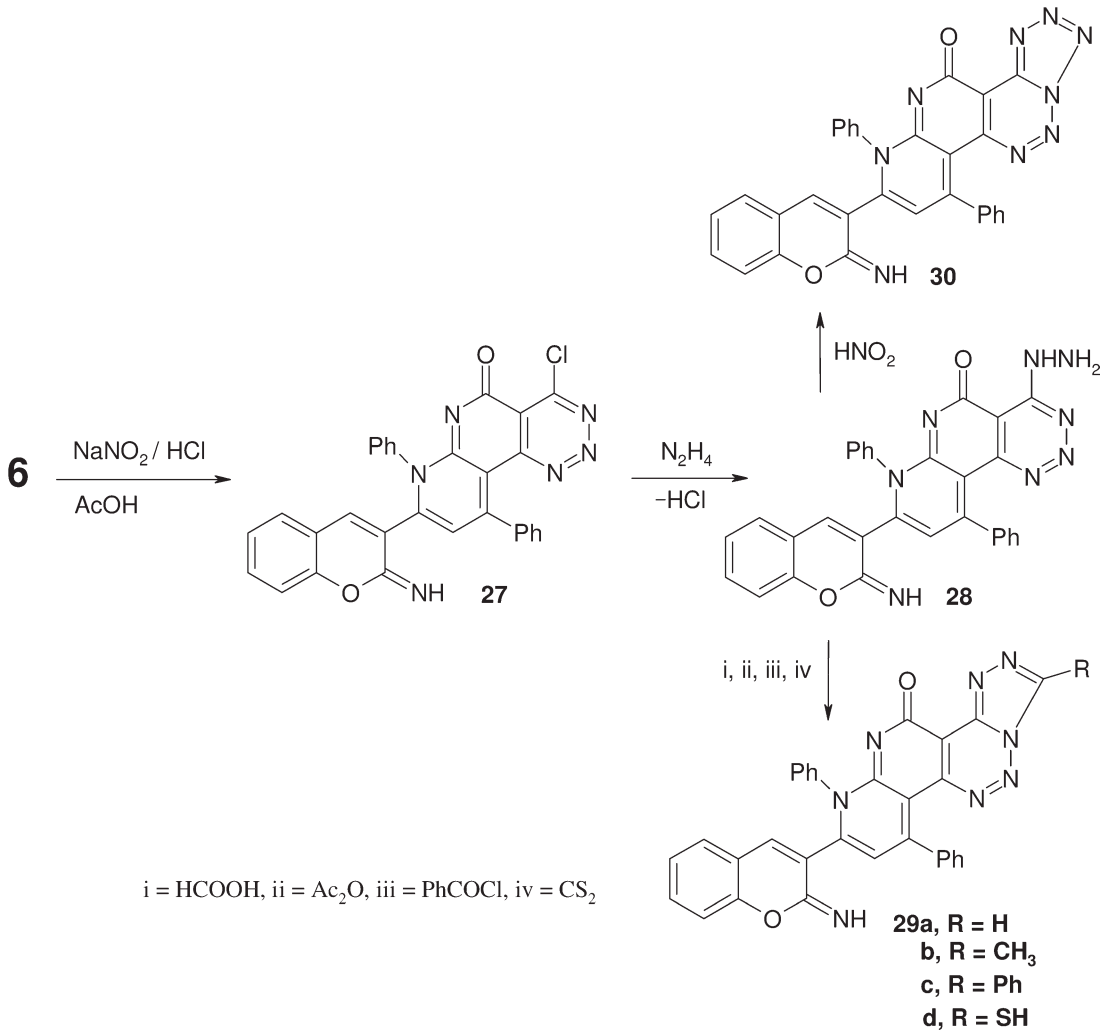
The pyrimido[5,4-*c*][1,8]naphthyridin-5-one **11** condensed easily with benzaldehyde in ethanol containing piperidine at reflux temperature affording the corresponding Schiff base **34**. The IR spectrum of **34** showed the absence of the absorption of the amino group and exhibited the presence of absorption bands at ν 3282 and 1695 cm^{-1} due to (NH) and (CO) functions, respectively. The ^1H NMR spectrum of **34** showed singlet signal at δ 6.21 ppm due to the N=CH group and a multiplet at δ 6.93–7.85 for aromatic protons. The MS of **34** showed *m*/*z* at 596 (M^+, 60%).

A β-lactam derivative **36** is formed by the addition of chloroacetyl chloride to the Schiff base **34** first generating **35** (not isolated), which in turn undergoes a condensative cyclization *via* elimination of hydrogen chloride to afford **36**. The IR spectrum of **36** showed the presence of absorption bands at ν 3289 and 1705 cm^{-1} due to (NH) and (CO) functions, respectively. The ^1H NMR spectrum of **36** showed two doublet signals at 3.92 and 4.46 ppm for the protons at C3 and C4 of the azetidinone. The MS of **36** displayed an intense ion peak at *m*/*z* 673 (M^+, 55%). A similar reactivity of Schiff base **34** is shown by the thioglycolic acid; formation of the isolated thiazolidinyl-pyrimido[5,4-*c*]naphthyridine **38** is best explain by the nucleophilic addition of thiol function on the imino carbon of **34** to give **37** (not isolated), which undergo a cyclization with loss of water generating 2-(2-imino-2*H*-chromen-3-yl)-8-(4-oxo-2-phenylthiazolidin-3-yl)-1,4-diphenylpyrimido[5,4-*c*][1,8]naphthyridin-9(1*H*)-one **38**. The MS of **38** showed a peak at *m*/*z* 670 (M^+, 50%), (Scheme 9).

CONCLUSION

Despite the several existing methods for the synthesis of chromene derivatives, there still is demand for general strategies, which can efficiently provide variously

Scheme 7



substituted chromene systems. Thus, this work opened a new avenue for the synthesis of a variety of isolated chromene derivatives using 2-imino-*N*-phenyl-2*H*-chromene-3-carboxamide.

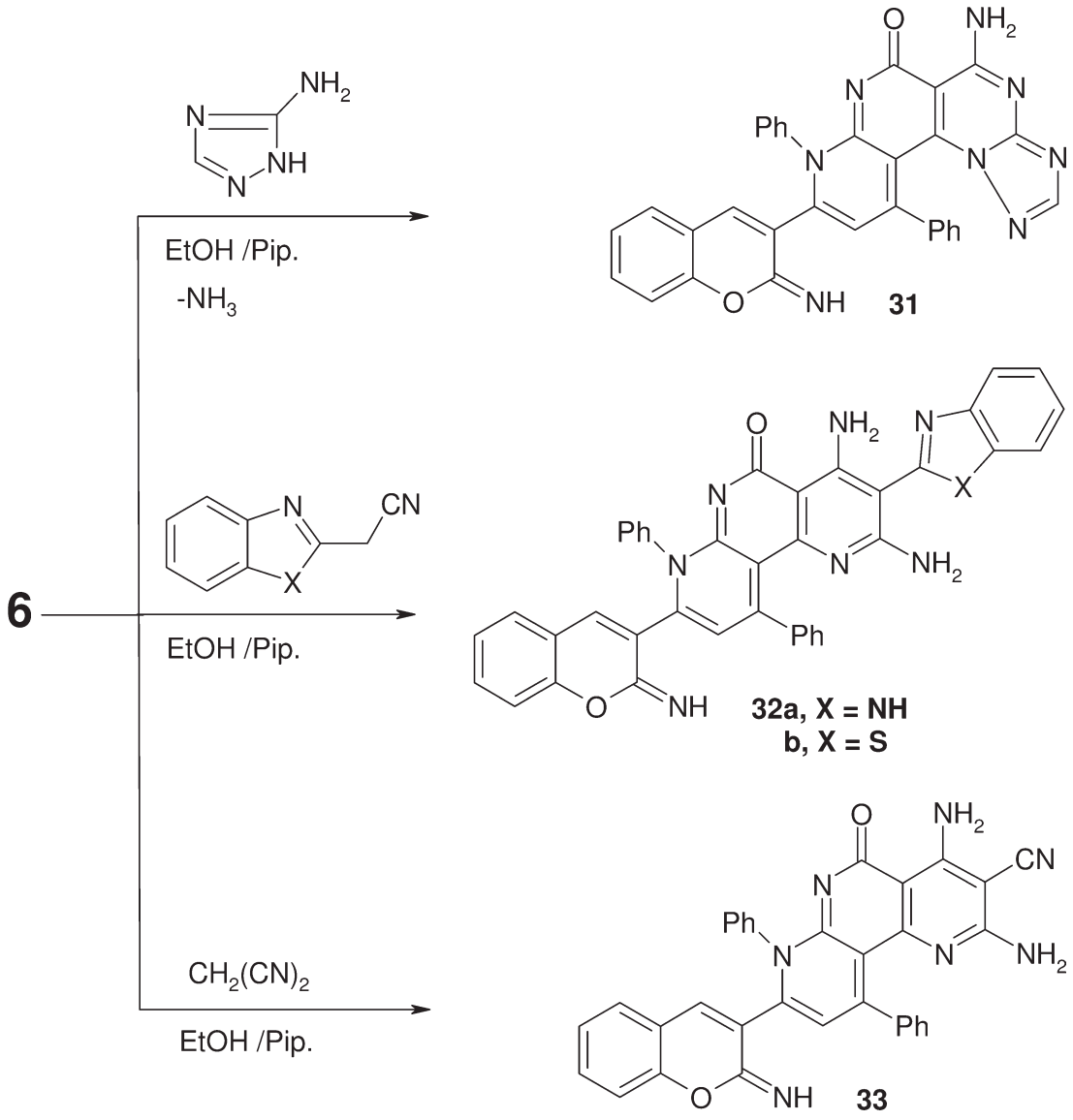
EXPERIMENTAL

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

3-(2-Imino-2*H*-chromen-3-yl)-1-phenyl-3-(phenylamino)-prop-2-en-1-one (2). A mixture of the 2-imino-*N*-phenyl-2*H*-chromene-3-carboxamide **1** (0.27 g, 1mmol) and acetophenone (0.12 mL, 1 mmol) in 30 mL DMF containing 0.1 mL of piperidine was refluxed for 8 hours. The solvent was evaporated under vacuum; the residue was triturated with 5 mL of MeOH and poured into acidified cold water (1 mL HCl, 20 mL H_2O). The resulting product was collected by filtration, washed well with 100 mL of cold water and crystallized from methanol to afford **2** as yellow crystals. Yield: 60%. m.p. 182−184°C. IR: ν (cm^{-1}) 1665−1705 (CO), 3322 (NH), ^1H NMR (DMSO): δ 4.11 (*s*, 1H, NH-amine), 6.52 (*s*, 1H, CH-ethylene), 7.12–7.62 (*m*, 15H, Ar—H), 8.52 (*s*, 1H, =NH). MS: *m*/*z* 366 (M^+, 40%). *Calcd* for $C_{24}H_{18}N_2O_2$ (366.41): C 78.67, H 4.95, N 7.65%. *Found:* C 78.77, H 5.01, N 7.76%.

1,2-Dihydro-2-imino-6-(2-imino-2*H*-chromen-3-yl)-1,4-diphenylpyridine-3-carbonitrile (4). An ethanolic solution (30 ml) containing (0.37 g, 1 mmol) of **2**, malononitrile (0.07 g, 1 mmol) and 0.1 mL of piperidine was warmed at reflux for six hours and concentrated under vacuum, the residue was poured to 30 mL acidified cold water and then triturated with methanol. The solid product was filtered and crystallized from ethanol afforded **4** as a pale yellow powder. Yield: 37%. mp. 285–287°C. IR: ν (cm^{-1}) 2214 (CN) and 3282 (NH). ^1H NMR (DMSO): δ 5.40 (*s*, 1H, CH-pyridine), 5.98 (s, 1H, NH), 7.23–7.56 (*m*, 16H, Ar—H + NH). MS: *m*/*z* 413 (M-1, 20%). *Calcd* for $C_{27}H_{18}N_4O$ (414.46): C 78.24, H 4.38, N 13.52%. *Found:* C 78.35, H 4.41, N 13.66%.

Scheme 8

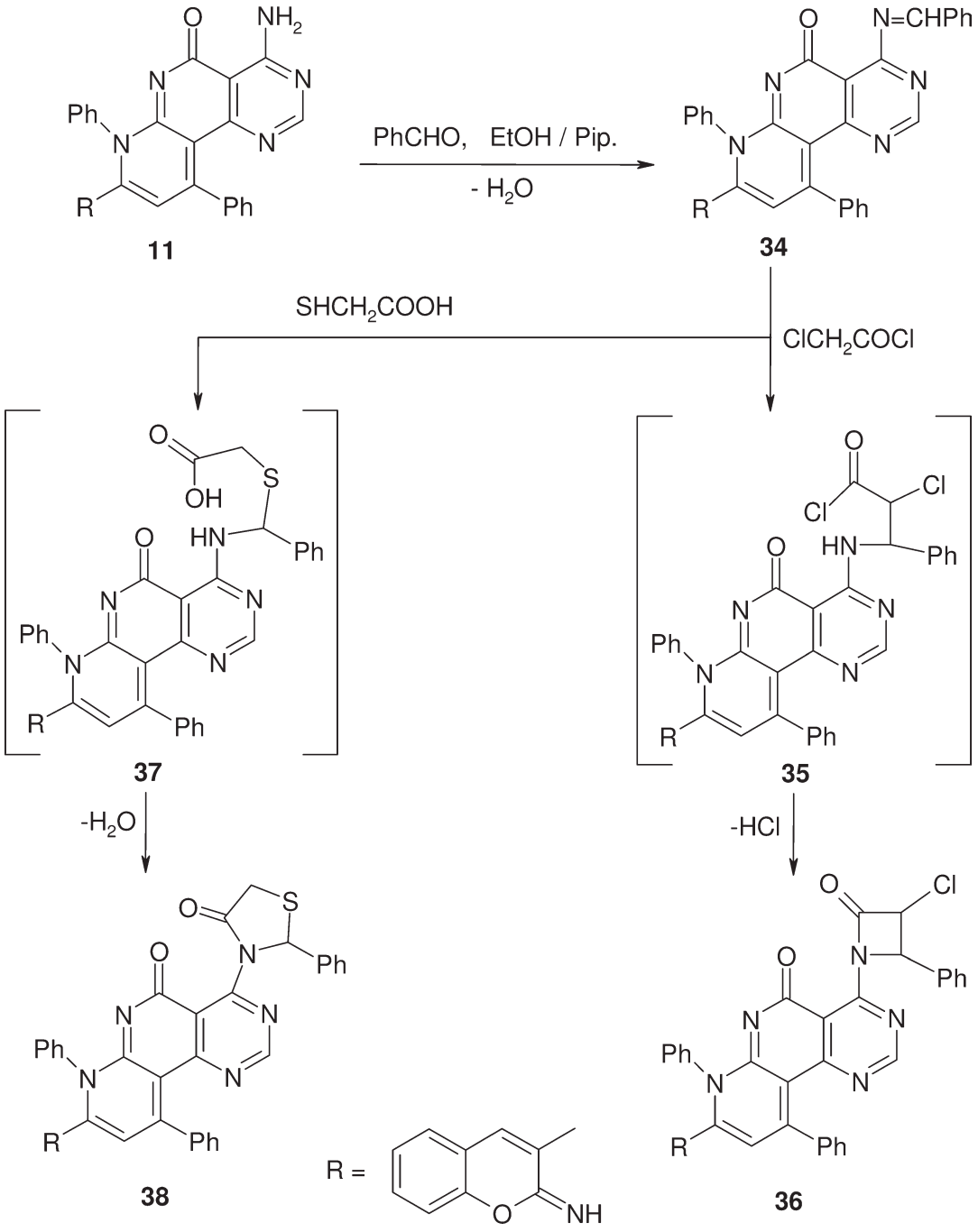


5-Amino-1,7-dihydro-2-(2-imino-2*H*-chromen-3-yl)-7-oxo-1,4-diphenyl-1,8-naphthyridine-6-carbonitrile (6). Ethanol solution (30 ml) of **4** (0.42 g, 1 mmol) containing 0.2 mL of piperidine and ethyl cyanoacetate (0.12 g, 1 mmol) was keep at reflux temperature for 6 hours. The colorless precipitate was dried, triturated with methanol, collected by filtration and crystallized from ethanol. Yield: 70%. m.p. 250–252°C. IR: ν (cm^{-1}) 1670 (CO), 2217 (CN), 3432 (NH_2). ^{1}H NMR (DMSO): δ 3.74 (*s*, 2H, NH_2), 5.72 (*s*, 1H, naphthyridine), 6.71–7.92 (*m*, 16H, Ar—H + NH). MS: *m*/*z* 482 (M+1, 55%). *Calcd* for $C_{30}H_{19}N_5O_2$ (481.15): C 74.83, H 3.98, N 14.54%. *Found:* C 74.94, H 4.01, N 14.65%.

5-Acetamide-1,7-dihydro-2-(2-imino-2*H*-chromen-3-yl)-7-oxo-1,4-diphenyl-1,8-naphthyridin-5-yl)-6-carbonitrile (7). A mixture of **6** (0.38 g, 1 mmol) was refluxed in acetic anhydride (25 mL) for 3 hours, then cooled and poured into 30 mL of cold water. The brown solid product that formed was collected by filtration and washed well with 100 ml cold water. Yield: 65%. m.p. 245–247°C. IR: ν (cm^{-1}) 1698–1710 (CO), 2217 (CN), 3282 (NH). ^{1}H NMR (DMSO): δ 2.52 (*s*, 3H, CH_3), 5.30 (*s*, 1H, NH), 5.69 (*s*, 1H, naphthyridine), 6.72–7.90 (*m*, 16H, Ar—H + NH). MS: *m*/*z* 524 (M+1, 40%). *Calcd* for $C_{32}H_{21}N_5O_3$ (523.54): C 73.41, H 4.04, N 13.38%. *Found*: C 73.53, H 4.12, N 13.49%.

8-Hydroxy-2-(2-imino-2*H*-chromen-3-yl)-6-methyl-1,4-diphenylpyrimido[5,4-*c*][1,8]naphthyridin-9(*1H*)-one (8). A solution of **6** (0.48 g, 1 mmol) in acetic anhydride/pyridine mixture (20 mL: 10 mL) was heated on water bath for 8 hours, then cooled and poured into 30 mL acidified cold water. The yellow precipitate which formed was collected by filtration and washed well with 100 ml cold water. Yield: 62%. m.p. 260–262°C. IR: ν (cm^{-1}) 1698 (CO), 3282 (NH), 3419 (OH). ^{1}H NMR (DMSO): δ 2.52 (*s*, 3H, CH_3), 5.69 (*s*, 1H, naphthyridine), 6.72–7.90 (*m*, 16H, Ar—H + NH), 9.42 (*s*, 1H, OH). MS: *m*/*z* 523 (M^+, 60%). *Calcd* for $C_{32}H_{21}N_5O_3$ (523.54): C 73.41, H 4.04, N 13.38%. *Found*: C 73.53, H 4.18, N 13.48%.

Scheme 9



5-Amino-2-(2-imino-2*H*-chromen-3-yl)-6-methyl-1,4-diphenyl-5*H*-[1,2,4]-triazepino[6,5-*c*][1,8]naphthyridin-9(1*H*)-one (9). A mixture of **7** (0.52 g, 1 mmol) and hydrazine hydrate (0.05 mL, 1 mmol) in 30 mL ethanol containing 0.1 mL of piperidine was refluxed for 3 hours. The reaction mixture was concentrated under reduced pressure and the residue tritarated with methanol. The formed pale yellow product was filtered, washed well with methanol. Yield: 60%. m.p. 252–254°C. IR: ν (cm^{-1}) 1670 (CO), 3282 (NH), 3360–3385 (NH_2). ^1H NMR ($CDCl_3$): δ 1.21 (*s*, 3H, CH_3), 2.24 (*s*, 2H, NH_2), 5.79 (*s*, 1H, naphthyridine) 6.71–7.92 (*m*, 16H, Ar—H + NH), 8.32 (s, 1H, NH). MS: *m/z* 534 (M-3, 60%). *Calcd* for $C_{32}H_{23}N_7O_2$ (537.57): C 71.50, H 4.31, N 18.24%. *Found:* C 71.61, H 4.45, N 18.36%.

8-Amino-2-(2-imino-2*H*-chromen-3-yl)-1,4-diphenylpyrimido[5,4-*c*][1,8]-naphthyridin-9(*1H*)-one (11). ***Method [A].*** A mixture of **6** (0.48 g, 1 mmol) and formamide (20 mL) was refluxed for 3 hours. After cooling, the brown crystals were filtered off and washed with cold methanol, recrystallized from ethanol as brown crystals. Yield: 60%. m.p. 272–274°C. IR: ν

(cm^{-1}) 1670 (CO), 3282 (NH), 3432 (NH_2). ^1H NMR (DMSO): δ 4.21 (*s*, 2H, NH_2), 5.75 (*s*, 1H, naphthyridine), 6.85 (*s*, 1H, CH-pyrimidine), 7.22–7.81 (*m*, 16H, Ar—H + NH). MS: *m*/*z* 510 (M+2, 10%). *Calcd* for $C_{31}H_{20}N_6O_2$ (508.53): C 73.22, H 3.96, N 15.53%. *Found:* C 73.34, H 4.05, N 15.69%.

Method [B]. A stream of NH_3 gas was passed through **23** (0.54 gm, 1 mmol) in dioxan solution at room temperature for 2 hour. The mixture left in refrigerator overnight, the solid product formed upon cooling was collected by filtration to give **11**.

2-(2-Imino-2*H*-chromen-3-yl)-1,4-diphenylpyrimido[5,4-*c*]-[1,8]naphthyridine-8,9(1*H*,7*H*)-dione (12). A mixture of **6** (0.48 g, 1 mmol) and formic acid (5 mL) in formamide (20 mL) was refluxed for 3 hours. After cooling, the mixture was poured into ice/water mixture. The violet solid product that formed was collected by filtration and washed several times with cold water. Yield: 50%. m.p. 202–204°C. IR: ν (cm^{-1}) 1670 (CO), 3282 (NH). ^1H NMR (DMSO): δ 5.45 (*s*, 1H, naphthyridine), 5.99 (*s*, 1H, CH-pyrimidine), 6.71–7.93 (*m*, 16H, Ar—H + NH), 8.21 (*s*, 1H, NH-pyrimidine). MS: *m*/*z* 510 (M+1, 57%). *Calcd* for $C_{31}H_{19}N_5O_3$ (509.51): C 73.08, H 3.76, N 13.75%. *Found:* C 73.19, H 3.85, N 13.87%.

1,7-Dihydro-5-phenylacetamide-2-(2-imino-*2H*-chromen-3-yl)-7-oxo-1,4-diphenyl-1,8-naphthyridin-5-yl)-6-carbonitrile (13). To a solution of **6** (0.48 g, 1 mmol) and 2-phenylacetyl chloride (0.16 g, 1 mmol) in 20 mL of pyridine was refluxed for 6 hours, then allowed to cool, poured into acidified clod water. The solid product so formed was filtered, washed with cold water, dried and crystallized with methanol to give **13**. Yield: 70%. m.p. 280–282°C. IR: ν (cm^{-1}) 1689–1707 (CO), 2220 (CN), 3188–3244 (NH). ^1H NMR (DMSO): δ 3.81 (*s*, 2H, CH_2), 5.45 (*s*, 1H, naphthyridine), 6.43 (*s*, 1H, NH-amide), 6.70–7.91 (*m*, 21H, Ar—H + NH). MS: *m*/*z* 599 (M+1, 40%). *Calcd* for $C_{38}H_{25}N_5O_3$ (599.64): C 76.11, H 4.20, N 11.68%. *Found:* C 76.23, H 4.32, N 11.79%.

6-Benzyl-2-(2-imino-2H-chromen-3-yl)-1,4-diphenylpyrimido[5,4-*c*][1,8]-naphthyridine-8,9(1*H*,5*H*)-dione (15). To a well- stirred cold solution of **13** (0.60 g, 1 mmol) in 10 mL of (HCl:AcOH/1:1), a cold solution of H_2O_2 (10 mL) was added drop wise in an ice-bath (0–5°C), then the reaction mixture was stirred for four hours at room temperature. The solid that precipitated was collected by filtration, and then redissolved in NaOH (20 mL 10%), and heated under reflux for 30 minutes, then cooled. Acidified with HCl (15 mL) and the solid product collected and crystallized from DMF-water (3:1) as yellow crystals. Yield: 45%. m.p. 280–282°C. IR: ν (cm^{-1}) 1670 (CO), 3150–3282 (NH). ^1H NMR (DMSO): δ 2.21 (*s*, 2H, CH_2), 2.81 (*s*, 1H, NH-pyrimidine), 5.45 (*s*, 1H, naphthyridine), 7.20–7.61 (*m*, 21H, Ar—H + NH). MS: *m*/*z* 599 (M^+, 35%). *Calcd* for $C_{38}H_{25}N_5O_3$ (599.64): C 76.11, H 4.20, N 11.68%. *Found*: C 76.23, H 4.33, N 11.79%.

5,6,7,8-Tetrahydro-2-(2-imino-2*H*-chromen-3-yl)-1,4-diphenyl-6,8-dithioxopyrimido[5,4-*c*][1,8]naphthyridin-9(1*H*)-one (18). A mixture of **6** (0.48 g, 1 mmol) and carbon disulphide (2 mL) in 20 mL of pyridine was heated on water bath for 8 hours. The solid product so formed was filtered off while hot and washed several times with ethanol forming brown crystals. Yield: 50%. m.p. 270–272°C. IR: ν (cm^{-1}) 1718 (CO), 1280–1285 (CS), 3169–3190 (NH). ^1H NMR ($CDCl_3$): δ 3.98 (*s*, 1H, NH), 4.24 (*s*, 1H, NH), 5.84 (*s*, 1H, naphthyridine), 7.12–7.70 (*m*, 16H, Ar—H + NH). MS: *m*/*z* 555 (M-2, 70%). *Calcd* for $C_{31}H_{19}N_5O_2S_2$ (557.64): C 66.77, H 3.43, N 12.56%. *Found:* C 65.33, H 3.01, N 11.15%.

1,5,6,9-Tetrahydro-2-(2-imino-2*H*-chromen-3-yl)-9-oxo-1,4-diphenyl-6-thioxo-(pyrimido[5,4-*c*][1,8]naphthyridin-8-yl)thiourea (21). To a solution of **6** (0.48 g, 1 mmol) in 20 mL acetic acid, ammonium thiocyanate (0.08 g, 1 mmol) was added and the reaction mixture was refluxed for 10 hours. The solid product which formed on cooling and addition of cold water was filtered off and washed with 100 ml of cold water, dried and crystallized from methanol as brown crystals. Yield: 55%. m.p. 290–292°C. IR: ν (cm^{-1}) 1330 (CS), 1689 (CO), 3282 (NH), 3419 (NH_2). ^1H NMR ($CDCl_3$): δ 2.22 (*s*, 1H, NH_2), 3.87 (*s*, 1H, NH), 4.20 (*s*, 1H, NH), 5.74 (*s*, 1H, naphthyridine), 6.90–7.62 (*m*, 16H, Ar—H + NH). MS: *m*/*z* 599 (M^+, 35%). *Calcd* for $C_{32}H_{21}N_7O_2S_2$ (599.68): C 64.09, H 3.53, N 16.35%. *Found:* C 64.23, H 3.66, N 16.47%.

5,6,7,8-Tetrahydro-8-imino-2-(2-imino-2*H*-chromen-3-yl)-1,4,7-triphenyl-6-thioxopyrimido[5,4-*c*][1,8]naphthyridin-9(1*H*)-one (22). A mixture of **6** (0.48 g, 1 mmol) and phenylisothiocyanate (0.16 mL, 1 mmol) in 20 mL of pyridine was heated at reflux for 20 hours. After cooling, the solid product that formed was filtered off and recrystallized from ethanol as buff crystals. Yield: 50%. m.p. >350°C. IR: ν (cm^{-1}) 1320 (CS), 1689 (CO), 3180–3282 (NH). ^1H NMR ($CDCl_3$): δ 2.21 (*s*, 1H, NH), 4.25 (*s*, 1H, NH-pyrimidine), 5.76 (*s*, 1H, naphthyridine), 6.70–7.62 (*m*, 21H, Ar—H + NH). MS: *m*/*z* 616 (M^+, 40%). *Calcd* for $C_{37}H_{24}N_6O_2S$ (616.69). C 72.06, H 3.92, N 13.63%. *Found:* C 72.18, H 4.01, N 13.75%.

1,4-Diphenyl-5-ethoxymethyleneamino-2,8-dihydro-2-(2-imino-2*H*-chromen-3-yl)-7-oxo-1,8-naphthyridine-6-carbonitrile (23). A mixture of **6** (1.05 g, 2 mmol), triethyl orthoformate (0.30 mL, 2 mmol) and Ac_2O (30 mL) was refluxed for 4 hours. The solvent was removed under reduced pressure and the separated solid was recrystallized from ethanol to give the ethoxy methyleneamino derivative **23** as brown crystals. Yield: 65%. m.p. 236–238°C. IR: ν (cm^{-1}) 1698 (CO), 2220 (CN), 3282 (NH). ^1H NMR (DMSO): δ 1.21 (*t*, 3H, CH_3), 3.94 (*q*, 2H, CH_2), 5.73 (*s*, 1H, naphthyridine), 6.70–7.92 (*m*, 16H, Ar—H + NH). MS: *m*/*z* 537 (M^+, 40%). *Calcd* for $C_{33}H_{23}N_5O_3$ (537.57): C 73.73, H 4.31, N 13.03%. *Found:* C 73.84, H 4.33, N 13.16%.

7-Amino-8-imino-7,8-dihydro-2-(2-imino-2*H*-chromen-3-yl)-1,4-diphenyl-pyrimido[5,4-*c*][1,8]naphthyridin-9(1*H*)-one (24). To a solution of **23** (0.54 g, 10 mmol), in absolute ethanol (40 mL), hydrazine hydrate (0.2 mL, excess) was added. The reaction mixture was refluxed for 2 hours, the reaction solution was concentrated, and the solid product that separated out was filtered off and recrystallized from ethanol as yellow crystals. Yield: 62%. m.p. 258–260°C. IR: ν (cm^{-1}) 1698 (CO), 3282 (NH), 3432 (NH_2). ^1H NMR (DMSO): δ 3.75 (*s*, 2H, NH_2), 5.11 (*s*, 1H, CH-pyrimidine), 5.70 (*s*, 1H, naphthyridine), 5.99 (*s*, 1H, =NH), 6.70–7.91 (*m*, 16H, Ar—H + NH). MS: *m*/*z* 523 (M^+, 70%). *Calcd* for $C_{31}H_{21}N_7O_2$ (523.54): C 71.12, H 4.04, N 18.73%. *Found:* 71.22, H 4.16, N 18.85%.

2-(2-Imino-2*H*-chromen-3-yl)-1,4-diphenyl[1,2,4]triazolo[2′,3′:1,6]pyrimido[4,5-*c*][1,8]naphthyridin-10-one (25). A mixture of **24** (0.53 g, 1 mmol), excess of triethyl orthoformate (5 mL) and Ac_2O (20 mL) was refluxed for 1 hour. The solvent was removed under reduced pressure and the separated solid was filtered off and recrystallized from ethanol to give

triazolo-pyrimidine derivative **25** as pale brown crystals. Yield: 55%. m.p. >300°C. IR: ν (cm^{-1}) 1698 (CO), 3282 (NH). ^1H NMR (DMSO): δ 4.75 (*s*, 1H, CH-triazole), 5.54 (*s*, 1H, CH-pyrimidine), 5.75 (*s*, 1H, naphthyridine), 6.70–7.91 (*m*, 16H, Ar—H + NH). MS: *m*/*z* 533 (M^+, 60%). *Calcd* for $C_{32}H_{19}N_7O_2$ (533.55): C 72.04, H 3.59, N 18.38%. *Found:* C 72.14, H 3.65, N 18.47%.

7,8-Dihydro-8-imino-2-(2-imino-2*H*-chromen-3-yl)-7-methyl-1,4-diphenyl-pyrimido[5,4-*c*][1,8]naphthyridin-9(*1H*)-one (26). A solution of **23** (0.54 g, 10 mmol) and methylamine (0.04 mL, 10 mmol) in EtOH (30 mL) was stirred at room temperature for 1 hour. The resulting product was collected by filtration and recrystallized from ethanol to give yellow crystals. Yield: 55%. m.p. 282–284°C. IR: ν (cm^{-1}) 1685–1705 (CO), 3063–3288 (NH). ^1H NMR (DMSO): δ 2.72 (*s*, 3H, CH_3), 5.36 (*s*, 1H, CH-pyrimidine), 5.47 (*s*, 1H, =NH), 5.70 (*s*, 1H, naphthyridine), 6.94–7.82 (*m*, 16H, Ar—H + NH). MS: *m*/*z* 522 (M^+, 45%). *Calcd* for $C_{32}H_{22}N_6O_2$ (522.56): C 73.55, H 4.24, N 16.08%. *Found:* C 73.68, H 4.36, N 16.20%.

8-Chloro-2-(2-imino-2*H*-chromen-3-yl)-1,4-diphenyl[1,2,3]-triazino[5,4-*c*][1,8]naphthyridin-9(1*H*)-one (27). To an ice-cooled solution of **6** (0.48 g, 1 mmol) in 30 mL (HCl//AcOH : v/v), a solution of sodium nitrite (0.01 mol) in water (10 mL) was added dropwise. The solution was stirred at room temperature for an additional 2 hours, the crude product obtained was filtered off and recrystallized from ethanol as yellow crystals. Yield: 65%. m.p. 205–207°C. IR: ν (cm^{-1}) 1689 (CO), 3282 (NH), ^1H NMR ($CDCl_3$): δ 5.65 (*s*, 1H, naphthyridine), 7.12–7.63 (*m*, 16H, Ar—H + NH). MS: *m*/*z* 531 (M+2, 65%). *Calcd* for $C_{30}H_{17}N_6O_2Cl$ (528.95): C 68.12, H 3.24, N 15.89, Cl 6.70%. *Found:* C 68.26, H 3.32, N 15.98, Cl 6.88%.

8-Hydrazinyl-2-(2-imino-2*H*-chromen-3-yl)-1,4-diphenyl-[1,2,3]triazino[5,4-*c*][1,8]naphthyridin-9(1*H*)-one (28). A mixture of **27** (0.53 g, 1 mmol) and hydrazine hydrate (2 mL) in ethanol (20 mL) containing 0.1 mL of piperidine was refluxed for one hour. The reaction mixture was concentrated under reduced pressure and the residue triturated with methanol. The formed pale brown product was filtered and washed well with methanol. Yield: 66%. m.p. 200–202°C. IR: ν (cm^{-1}) 1689 (CO), 3282 (NH), 3432 (NH_2). ^1H NMR (DMSO): δ 3.11 (*s*, 1H, NH), 3.72 (*s*, 2H, NH_2), 5.21 (*s*, 1H, naphthyridine), 6.72–7.90 (*m*, 16H, Ar—H + NH). MS: *m*/*z* 524 (M^+, 55%). *Calcd* for $C_{30}H_{20}N_8O_2$ (524.53): C 68.69, H 3.84, N 21.36%. *Found:* C 68.79, H 3.96, N 21.48%.

General procedure for preparation of compounds (29a–d). A mixture of **28** (1.05 g, 2 mmol) and formic acid (10 mL) R = H, or acetic anhydride (25 mL) R = CH_3, or benzoyl chloride (15 mL) R = Ph, or carbon disulphide (10 mL) R = SH, was heated at reflux for 4 hours and then it allowed to cool. The solid product was collected by filtration and recrystallized from proper solvent.

2-(2-Imino-2*H*-chromen-3-yl)-1,4-diphenyl[1,2,3]triazolo-[3′,4′:1,6][1,2,3]triazino[5,4-*c*][1,8]naphthyridin-10(*1H*)-one (29a). Pale yellow crystals (EtOH) Yield: 55%. m.p. >350°C. IR: ν (cm^{-1}) 1698 (CO), 3282 (NH). ^1H NMR (DMSO): δ 4.45 (*s*, 1H, CH-triazole), 5.65 (*s*, 1H, naphthyridine), 7.11–7.73 (*m*, 16H, Ar—H + NH). MS: *m*/*z* 535 (M+1, 60%). *Calcd* for $C_{31}H_{18}N_8O_2$ (534.54): C 69.66, H 3.39, N 20.96%. *Found:* C 69.75, H 3.48, N 21.01%.

2-(2-Imino-2*H*-chromen-3-yl)-7-methyl-1,4-diphenyl[1,2,3]-triazolo[3′,4′:1,6][1,2,3]triazino[5,4-*c*][1,8]naphthyridin-10(1*H*)-one (29b). Yellow crystals (MeOH). Yield: 60%. m.p. 286–288°C. IR: ν (cm^{-1-1}) 1698 (CO), 3282 (NH). ^1H NMR (DMSO): δ 2.31 (*s*, 3H, CH_3), 5.60 (*s*, 1H, naphthyridine), 6.71–7.90 (*m*, 16H, Ar—H + NH). MS: *m*/*z* 546 (M-2, 70%). *Calcd* for $C_{32}H_{20}N_8O_2$ (548.57): C 70.06, H 4.04, N 20.43%. *Found:* C 70.15, H 4.18, N 20.56%.

2-(2-Imino-2*H*-chromen-3-yl)-1,4,7-triphenyl[1,2,3]tri-azolo[3′,4′:1,6][1,2,3]triazino[5,4-*c*][1,8]naphthyridin-10(1*H*)-one (29c). Yellow crystals (DMF:H_2O/3:1). Yield: 62%. m.p. 270–272°C. IR: ν (cm^{-1}) 1698 (CO), 3282 (NH). ^1H NMR (DMSO): δ 5.55 (*s*, 1H, naphthyridine), 6.72–7.91 (*m*, 21H, Ar—H + NH). MS: *m*/*z* 610 (M^+, 35%). *Calcd* for $C_{37}H_{22}N_8O_2$ (610.64): C 72.78, H 3.63, N 18.35%. *Found:* C 72.89, H 3.75, N 18.49%.

2-(2-Imino-2*H*-chromen-3-yl)-7-mercapto-1,4-diphenyl[1,2,3]-triazolo[3′,4′:1,6][1,2,3]triazino[5,4-*c*][1,8]naphthyridin-10(1*H*)-one (29d). Yellow crystals (EtOH). Yield: 55%. m.p. 280–282°C. IR: ν (cm^{-1}) 1698 (CO), 3282 (NH). ^1H NMR ($CDCl_3$): δ 3.42 (*s*, 1H, SH), 5.65 (*s*, 1H, naphthyridine), 7.11–7.73 (*m*, 16H, Ar—H + NH). MS: *m*/*z* 566 (M^+, 50%). *Calcd* for $C_{31}H_{18}N_8O_2S$ (566.59): C 65.71, H 3.20, N 19.78%. *Found:* C 65.80, H 3.27, N 19.86%.

2-(2-Imino-2*H*-chromen-3-yl)-1,4-diphenyl[1,2,3,4]tetra-zolo[4′,5′:1,6][1,2,3]triazino[5,4-*c*][1,8]naphthyridin-10(1*H*)-one (30). It was prepared according to the procedure that described for **27**, it recrystallized from ethanol as brown crystals. Yield: 50%. m.p. 195–197°C. IR: ν (cm^{-1}) 1698 (CO), 3282 (NH). ^1H NMR ($CDCl_3$): δ 4.99 (*s*, 1H, naphthyridine), 6.96–7.73 (*m*, 16H, Ar—H + NH). MS: *m*/*z* 535 (M^+, 40%). *Calcd* for $C_{30}H_{17}N_9O_2$ (535.53): C 67.28, H 3.20, N 23.54%. *Found:* C 67.39, H 3.31, N 23.66%.

9-Amino-2-(2-imino-2*H*-chromen-3-yl)-1,4-diphenyltriazo-lo[2′,3′:2,3]pyrimido[4,5-*c*][1,8]naphthyridin-10(1*H*)-one (31). A mixture of **6** (0.48 g, 1 mmol), 5-amino-1*H*-[1,2,4]tri-azole (0.09 g, 1 mmol) in 30 mL of ethanol containing 0.2 mL of piperidine was refluxed for 8 hours. The solvent was evaporated under vacuum and the residue was triturated with methanol. The solid product was filtered and crystallized from methanol as brown crystals. Yield: 50%. m.p. 295–297°C. IR: ν (cm^{-1}) 1689 (CO), 3282 (NH), 3419 (NH_2). ^1H NMR (DMSO): δ 2.21 (*s*, 2H, NH_2), 4.87 (*s*, 1H, naphthyridine), 6.90–7.63 (*m*, 16H, Ar—H + NH). MS: *m*/*z* 551(M+3, 70%). *Calcd* for $C_{32}H_{20}N_8O_2$ (548.55): C 70.06, H 3.67, N 20.43%. *Found:* C 70.11, H 3.71, N 20.51%.

General procedure for preparation of compounds (32a,b) A mixture of **6** (0.48 g, I mmol), 2-cyanomethylbenzi-midazole (0.16 g, 1 mmol) or 2-cyanomethylbenzthiazole (0.17 g, 1 mmol) in 30 mL of ethanol containing 0.2 mL of piperidine was refluxed for 8 hours. The solvent was evaporated under vacuum, triturated the residue with methanol and the resulting solid product was collected by filtration and crystallized from the proper solvent.

6,8-Diamino-7-(1*H*-benzo[*d*]imidazol-2-yl)-2-(2-imino-2*H*-chromen-3-yl)-1,4-diphenylpyrido[2,3-*c*][1,6]naphthyridin-9(*1H*)-one (32a) Yellow crystals (EtOH). Yield: 60%. m.p. 190–192°C. IR: ν (cm^{-1}) 1690 (CO), 3189–3195 (NH), 3410, 3490 (NH_2). ^1H NMR ($CDCl_3$): δ 4.21 (*s*, 2H, NH_2), 4.42 (*s*, 2H, NH_2), 4.87 (*s*, 1H, naphthyridine), 6.55 (*s*, H, NH), 6.72–7.40 (*m*, 21H, Ar—H + 2NH). MS: *m*/*z* 638 (M^+, 50%). *Calcd*

for $C_{39}H_{26}N_8O_2$ (638.68): C 73.34, H 4.10, N 17.54%. *Found:* C 73.41, H 4.21, N 17.66%.

6,8-Diamino-7-(benzo[*d*]thiazol-2-yl)-2-(2-imino-2*H*-chromen-3-yl)-1,4-diphenylpyrido[2,3-*c*][1,6]naphthyridin-9(1*H*)-one (32b). Yellow crystals (MeOH). Yield: 40%. m.p. 156–158°C. IR: ν (cm^{-1}) 1689 (CO), 3282 (NH), 3419, 3495 (NH_2). ^1H NMR (DMSO): δ 4.25 (*s*, 2H, NH_2), 4.47 (*s*, 2H, NH_2), 6.79–7.32 (*m*, 20H, Ar—H + NH). MS: *m*/*z* 656 (M+1, 60%). *Calcd* for $C_{39}H_{25}N_7O_2S$ (655.73): C 71.43, H 3.84, N 14.95%. *Found:* C 71.54, H 3.98, N 15.01%.

6,8-Diamino-1,9-dihydro-2-(2-imino-2*H*-chromen-3-yl)-9-oxo-1,4-diphenyl-pyrido[2,3-*c*][1,6]naphthyridine-7-carbonitrile (33). It was prepared according to procedure that described for compound **4.** Yellow crystals (MeOH). Yield: 60%. m.p. 188–190°C. IR: ν (cm^{-1}) 1690 (CO), 2217 (CN), 3120 (NH), 3432–3490 (NH_2). ^1H NMR ($CDCl_3$): δ 4.12 (*s*, 2H, NH_2), 4.33 (*s*, 2H, NH_2), 4.65 (*s*, 1H, naphthyridine), 6.79–7.46 (*m*, 16H, Ar—H + NH). MS: *m*/*z* 544 (M-3, 55%). *Calcd* for $C_{33}H_{21}N_7O_2$ (547.57): C 72.38, H 3.87, N 17.91%. *Found:* C 72.49, H 3.99, N 17.99%.

8-(Benzylideneamino)-2-(2-imino-2*H*-chromen-3-yl)-1,4-diphenylpyrimido[5,4-*c*][1,8]naphthyridin-9(1*H*)-one (34). An equimolar mixture of **11** (1.2 g, 2 mmol) and benzaldehyde (0.22 g, 2 mmol) was dissolved in ethanol (30 mL) in the presence of piperidine (0.2 mL) was refluxed for 6 hours. The solid product formed after cooling was collected by filtration and recrystallized from DMF-H_2O (3:1) yielded yellow crystals. Yield: 60%. m.p. 284–286°C. IR: ν (cm^{-1}) 1695 (CO), 3282 (NH). ^1H NMR (DMSO): δ 4.69 (*s*, 1H, naphthyridine), 4.99 (*s*, 1H, CH-pyrimidine), 6.21 (*s*, 1H, -N=CH), 6.93–7.85 (*m*, 21H, Ar—H + NH). MS: *m*/*z* 596 (M^+, 60%). *Calcd* for $C_{38}H_{24}N_6O_2$ (596.64): C 76.50, H 4.05, N 14.09%. *Found:* C 76.58, H 4.17, N 14.21%.

8-(3-Chloro-2-oxo-4-phenylazetidin-1-yl)-2-(2-imino-2H-chromen-3-yl)-1,4-diphenylpyrimido[5,4-*c*][1,8]naphthyridin-9(1*H*)-one (36). To a well stirred solution of **34** (1.2 g, 2 mmol) and triethylamine (0.41 mL, 4 mmol) in dry dioxane (20 mL), chloroacetyl chloride (0.22 mL, 2 mmol) was added dropwise at room temperature, then the reaction mixture was refluxed for 8 hours. The precipitate of triethylamine hydrochloride was filtered and washed thoroughly with dioxane. The filtrate was evaporated to one-third of its original volume, cooled and poured into acidified ice/water and the precipitate formed washed with water thoroughly, dried and recrystallized from methanol as brown crystals. Yield: 60%. m.p. 255–257°C. IR: ν (cm^{-1}) 1695–1705 (CO), 3289 (NH). ^1H NMR (DMSO): δ 3.92 (*d*, 1H, azitidene-CH-4), 4.46 (*d*, 1H, azitidene-CH-3), 4.79 (*s*, 1H, naphthyridine), 7.11–7.62 (*m*, 21H, Ar—H + NH). MS: *m*/*z* 673 (M^+, 55%). *Calcd* for $C_{40}H_{25}N_6O_3Cl$ (673.12): C 71.37, H 3.74, N 12.49, Cl 5.27%. *Found:* C 71.48, H 3.81, N 12.58, Cl 5.32%.

2-(2-Imino-2*H*-chromen-3-yl)-8-(4-oxo-2-phenylthiazolidin-3-yl)-1,4-diphenylpyrimido[5,4-*c*][1,8]naphthyridin-9(1*H*)-one (38). An equimolar mixture of **34** (1.2 g, 2 mmol) and thioglycolic acid (0.28 mL, 2 mmol) in dry benzene (20 mL) was refluxed for 10 hours. The reaction mixture was evaporated to dryness under reduced pressure. The thiazolidinone was separated off, washed with ether and crystallized from ethanol as yellow crystals. Yield: 60%. m.p. 285–287°C. IR: ν (cm^{-1}) 1695–1702 (CO), 3289 (NH). ^1H NMR (DMSO): δ 3.82 (*s*, 1H, CH-thiazolidine), 4.22 (*s*, 2H, CH_2-thiazolidine), 4.88 (*s*, 1H, naphthyridine), 5.65 (*s*, 1H, CH-pyrimidine), 6.82–7.81 (*m*, 21H, Ar—H + NH). MS: *m*/*z* 670 (M^+, 50%). *Calcd* for $C_{40}H_{26}N_6O_3S$ (670.74): C 71.63, H 3.91, N 12.53%. *Found:* C 71.61, H 4.01, N 12.64%.

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