Asian Journal of Chemistry Vol. 21, No. 9 (2009), 6885-6903

Synthesis and Antimicrobial Activity of Pyrazole Derivatives of 2-Cyclopropyl-1,8-naphthyridines

ATMAKURI NARENDER, MATTEPALLY RANADHEER KUMAR, EPPKAYALAYA LAXMINARAYANA† and MARINGANTI THIRUMALA CHARY*
Kakatiya Institute of Technology and Science, Warangal-506 009, India
E-mail: mtcharya@yahoo.com

2-Amino-pyridine-3-carboxaldehyde and 3-cyclopropyl-3-oxopropionic acid ethyl ester react each other to provide 2-cyclopropyl-[1,8]-naphthyridin-3-carboxylic acid ethylester (**1**) which reacts with 99 % hydrazine hydrate to yield 2-cyclopropyl-[1,8]-naphthyridine-3-carboxylic acid hydrazide (**2**). This acid hydrazide (**2**), reacts with different acetophenones to yield respective Schiff bases (**3a-h**). Compounds **3a-h** react with Vilsmeier-Haack reagent (DMF/$POCl_3$) to furnish 1-(2-cyclopropyl-[1,8]-naphthyridine-3-carbonyl)-3-phenyl-1*H*-pyrazole-4-carbaldehydes (**4a-h**). 2-Cyclopropyl-[1,8]-naphthyridine-3-carboxylic acid hydrazide (**2**) on reaction with substituted acetylacetones and substituted ethyl acetoacetates gives substituted 2-cyclopropyl-[1,8]-naphthyridin-3-yl)-(3,5-dimethyl-pyrazol-1-yl)-methanones (**5a-d**) and 2-(2-cyclopropyl-[1,8]-naphthyridine-3-carbonyl)-5-methyl-2,4-dihydropyrazol-3-ones (**6a-c**), respectively. On the other hand, hydrazide (**2**) reacts with different aromatic aldehydes yields 2-cyclopropyl-[1,8]-naphthyridine-3-carboxylic acid benzylidene-hydrazides (**7a-g**). Compounds (**7a-g**) on reaction with mercapto-acetic acid offered 3-[(2-cyclopropyl-[1,8]-naphthyridin-3-yl-methyl)amino]phenyl-thiazolidin-4-ones (**8a-g**). Interaction of acid hydrazide (**2**) with different aromatic acid chlorides afford N'-acetyl/benzoyl-2-cyclopropyl-1,8-naphthyridine-3-carbohydrazides (**9a-d**), which on treatment with $POCl_3$ yield 2-cyclopropyl-[1,8]-naphthyridin-3-yl)-(5-phenyl-[1,3,4]-oxadiazol-2-yl)methanone (**10a-d**).

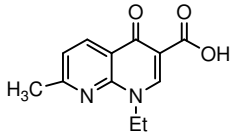
Key Words: Synthesis, Antimicrobial activity, Pyrazole derivatives, 2-Cyclopropyl-[1,8]-naphthyridine-3-carboxylic acid ethyl ester.

INTRODUCTION

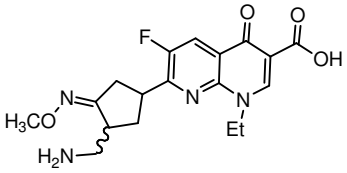
1,8-Naphthyridine derivatives have attracted considerable attention because it's skeleton is present in many compounds which have been isolated from natural sources, with various biological activities. Nalidixic acid, for example, possesses strong antibacterial activity and used mainly for the treatment of urinary tract infections with gram negative pathogens[1] and gemifloxacin has antimicrobial and antibacterial activities[2]. It is known that (E)- and (Z)-*o*-(diethylamino)ethyl oximes

†Sreenidhi Institute of Science and Technology, Ghatkesar, Hyderabad-501 301, India.

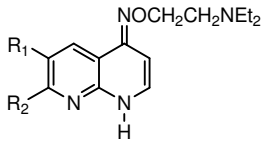
of 1,8-naphthyridine series (**A**) are potential drugs for local anesthesia[3] and 1-(2-fluorobenzyl)-3-(2-tolyl)-1,8-naphthyridin-2(1*H*)-one is used for the treatment of memory disorders, in particular, Alzheimer's disease[4]. 1,8-Naphthyridine derivatives also reacts with adenosine receptors of subtypes A_1 and A_2A[5]. These 1,8-naphthyridines are an important class of pharmaceutically active compounds as they have excellent biological activities[6,7]. The condensation of 2-amino-pyridine-3-carboxaldehyde and 3-cyclopropyl-3-oxo-propionic acid ethylester in the presence of piperidine in ethanol with activated methylene containing carbonyl compounds or β-keto esters[8]. The 1,8-naphthyridine derivatives were evaluated *in vitro* for their antimicrobial activity against *Staphylococcus aureus* as gram-positive bacteria and *E. coli* as gram-negative bacteria, using the cup diffusion technique[9-12]. The Vilsmeier-Haack reagent is an efficient, economical and mild reagent for the formylation of reactive aromatic and heteroaromatic substrates[13]. The use of Vilsmeier-Haack reactions has led to novel and convenient routes for the synthesis of various heterocyclic compounds and its importance in various synthetic methodologies[14-16].



Nalidixic Acid



Gemifloxacin



(A)

EXPERIMENTAL

All reagents used were commercial grade, melting points were determined in open capillaries and are uncorrected. IR spectra were recorded on potassium bromide disks on a Perkin-Elmer 383 spectrophotometer. ^{1}H NMR spectra were obtained on a varian 500 MHz instrument with TMS as internal standard and chemical shifts are expressed δ ppm, solvents are used $CDCl_3$ and DMSO-d_6 and mass spectrum on a Hewlett-Packard mass spectrometer operating at 70 eV, purity of the compounds were checked by TLC, which is performed with E. Merck precoated silica gel plates (60F-254) with iodine as a developing agent. Acme, India silica gel, 60-120 mesh for column chromatography is used. All compounds were recrystallized in ethyl acetate in hexane except (**4e, f, h**), (**8 c, e, f, g**) and (**10 c, d**) which were purified by column chromatography by using silica gel (60-120 mesh) eluted by using (5:1) ethyl acetate in hexane and dichloro methane in methanol.

2-Cyclopropyl-[1,8]-naphthyridine-3-carboxylic acid ethyl ester (1): To a solution of 2-amino-pyridine-3-carbaldehyde (8.19 mmol) in ethanol (10 mL) was added cyclopropyl-3-oxo-propionic acid ethyl ester (12 mL) (9.81 mmol) and piperidine (4.09 mmol) at room temperature and refluxed for *ca.* 6-8 h. The reaction completion

was monitored by TLC and recrystallized from ethyl acetate afford (**1**) as off white solid 90 % yield, IR (KBr, ν_{max}, cm^{-1}): 2200 (aliph. CH_2), 1714 (CO, ester); ^1H NMR (500 MHz, DMSO-d_6) δ: 1.12 (q, 2H, *J* = 15 Hz, CH_2), 1.21, (q, 2H, *J* = 15 Hz, CH_2), 1.39 (t, 3H, *J* = 15 Hz, CH_3), 3.01 (m, 1H, CH), 4.41 (q, 2H, *J* = 15, CH_2), 7.59, (t, 1H, *J* = 15 Hz, CH), 8.56 (d, 1H, *J* = 7.2 Hz, CH), 8.82 (s, 1H, CH), 9.12 (s, 1H, CH). ^{13}C NMR (500 MHz, DMSO-d_6/TMS) δ: 8.3 ($2CH_2$), 15.2 (CH_3), 55.8 (CH_2), 140.2 (2CH), 152.3 (2CH), 171.4 (CO). (Mass (m/z): 243 [M+1].

2-Cyclopropyl-[1,8]-naphthyridine-3-carboxylic acid hydrazide (2): The solution of 2-cyclopropyl-[1,8]-naphthyridine-3-carboxylic acid ethyl ester (**1**) (4.12 mmol) in ethanol (10 mL) was added with 99 % hydrazine hydrate (41.32 mmol) and heated for reflux for *ca.* 16 h. Reaction mixture was cooled and recrystallized from ethanol to afford (**2**) as off white solid, 95 % yield. IR (KBr, ν_{max}, cm^{-1}): 2250 (aliph. CH_2), 1700 (CO, ester), 3110 (NH), 3231 (NH_2); ^1H NMR (500 MHz, DMSO-d_6) δ: 1.05 (q, 2H, *J* = 15Hz, CH_2), 1.12 (q, 2H, *J* = 15 Hz, CH_2), 2.58 (m, 1H, CH), 4.62 (bs, 2H, NH_2), 7.56, (t, 1H, *J* = 15 Hz, CH), 8.32 (s, 1H, NH), 8.42 (d, 1H, *J* = 15 Hz, CH), 9.02 (d, 1H, *J* = 15 Hz, CH), 9.82 (s, 1H, CH). ^{13}C NMR (500 MHz, DMSO-d_6/TMS) δ: 7.3 ($2CH_2$), 138.2 (2CH), 142.3 (2CH), 165.4 (CO) Mass (m/z): 229 [M+1].

2-Cyclopropyl-[1,8]-naphthyridine-3-carboxylic acid (1-phenyl-ethylidene)-hydrazide (3a): The solution of 2-cyclopropyl-[1,8]-naphthyridine-3-carboxylic acid ethyl ester (**2**) 0.2 g (4.38 mmol) in ethanol (5 mL) was added to 1-phenyl ethanone 0.12 g (1.05 mmol) drop wise at 0 °C, warmed to room temperature and stirred for *ca.* 2 h. Recrystallized from ethyl acetate in hexane provide (**3a**) as light yellow colour solid, yield: 78 %. IR (KBr, ν_{max}, cm^{-1}): 3120 (NH), 2250 (aliph. CH_2), 1720 (CO), 1615 (C=N); ^1H NMR (500 MHz, DMSO-d_6) δ: 1.15 (m, 2H, *J* = 15 Hz, CH_2), 1.28 (m, 2H, *J* = 20 Hz, CH_2), 2.36 (s, 3H, CH_3), 2.58 (m, 1H, CH), 7.21 (t, 2H, *J* = 15 Hz, CH), 7.41, (m, 3H, CH), 7.63, (t, 1H, *J* = 15 Hz, CH), 7.86 (m, 1H, CH), 8.58 (d, 1H, *J* = 20 Hz, CH,), 9.12 (s, 1H, CH), 11.21 (s, 1H, NH). ^{13}C NMR (500 MHz, DMSO-d_6/TMS) δ: 6.9 ($2CH_2$), 19.8 (CH_3), 122.3 (2CH), 126.1 (2CH), 136.7 (2CH), 168.4 (CO) Mass (m/z): 331 [M+1].

Other compounds in the series were prepared similarly and their characterization data are recorded given below:

2-Cyclopropyl-[1,8]-naphthyridine-3-carboxylic acid (1-*p*-tolyl ethylidene) hydrazide (3b): Recrystallized from ethyl acetate to obtain (**3b**) as yellow colour solid, yield: 86 %. IR (KBr, ν_{max}, cm^{-1}): 3115 (NH), 2250 (aliph. CH_2), 1685 (CO), 1625 (C=N); ^1H NMR (500 MHz, DMSO-d_6) δ: 1.13 (m, 2H, *J* = 15 Hz, CH_2), 1.22 (m, 2H, *J* = 20 Hz, CH_2), 2.32 (s, 3H, CH_3), 2.46 (m, 1H, CH), 2.64 (s, 3H, CH_3), 4.25 (m, 1H, CH), 7.16, (t, 1H, *J* = 15 Hz, CH), 7.29, (s, 1H, NH), 7.28, (t, 2H, *J* = 15 Hz, CH), 7.46 (m, 2H, CH), 7.73 (d, 2H, *J* = 20 Hz, CH), 8.48 (s, 1H, CH), 9.16 (d, 1H, *J* = 15 Hz, CH), Mass (m/z): 345 [M+1].

2-Cyclopropyl-[1,8]-naphthyridine-3-carboxylic acid[1-(4-methoxy phenyl)-ethylidene]hydrazide (3c): Recrystallized from ethyl acetate in hexane provide

(**3c**) as yellow colour solid, yield: 82 %. IR (KBr ν_{max}, cm^{-1}): 3325 (NH), 3125 (OCH_3), 2280 (aliph. CH_2), 1710 (CO), 1680 (C=N); ^{1}H NMR (500 MHz, DMSO-d_6) δ: 1.11 (m, 2H, *J* = 15 Hz, CH_2), 1.21 (m, 2H, *J* = 15 Hz, CH_2), 1.80 (m, 1H, CH), 1.68 (s, 3H, CH_3), 3.36 (s, 3H, CH_3), 7.19 (t, 1H, *J* = 15 Hz, CH), 7.31, (s, 1H, CH), 7.28, (t, 1H, *J* = 15 Hz, CH), 7.56 (m, 2H, CH), 7.78 (d, 2H, *J* = 20 Hz, CH), 8.52 (s, 1H, NH), 9.18 (d, 1H, *J* = 15 Hz, CH), Mass (m/z): 361 [M+1].

2-Cyclopropyl-[1,8]-naphthyridine-3-carboxylic acid [1-(4-chloro phenyl)-ethylidene]hydrazide (3d): Recrystallized from ethyl acetate to provide (**3d**) as light green colour solid, yield: 70 %. IR (KBr, ν_{max}, cm^{-1}): 3345 (NH), 3225 (OCH_3), 2280 (aliph. CH_2), 1745 (CO), 1665 (C=N); ^{1}H NMR (500 MHz, DMSO-d_6) δ: 1.16 (m, 2H, *J* = 15 Hz, CH_2), 1.26 (m, 2H, *J* = 15 Hz, CH_2), 1.92 (s, 3H, CH_3), 2.44 (m, 1H, CH), 7.15 (t, 1H, *J* = 15 Hz, CH), 7.35 (s, 1H, CH), 7.23 (t, 1H, *J* = 15 Hz, CH), 7.52 (m, 2H, CH), 7.73 (d, 2H, *J* = 20 Hz, CH), 8.51 (s, 1H, NH), 9.24 (d, 1H, *J* = 15Hz, CH), Mass (m/z): 365 [M+1].

2-Cyclopropyl-[1,8]-naphthyridine-3-carboxylic acid [1-(4-nitro phenyl)-ethylidene]hydrazide (3e): Recrystallized from ethyl acetate in hexane (3:1) to provide (**3e**) light yellow colour solid, yield: 74 %, IR (KBr, ν_{max}, cm^{-1}): 3315 (NH), 2285 (aliph. CH_2), 1745 (CO), 1665 (C=N); ^{1}H NMR (500 MHz, DMSO-d_6) δ: 1.13 (m, 2H, *J* = 15 Hz, CH_2), 1.23 (m, 2H, *J* = 15 Hz, CH_2), 1.91 (s, 3H, CH_3), 2.42 (m, 1H, CH), 7.13 (t, 1H, *J* = 15 Hz, CH), 7.32, (s, 1H, CH), 7.21, (t, 1H, *J* = 15 Hz, CH), 7.50 (m, 2H, CH), 7.71 (d, 2H, *J* = 20 Hz, CH), 8.56 (s, 1H, NH), 9.21 (d, 1H, *J* = 15Hz, CH), Mass (m/z): 376 [M+1].

2-Cyclopropyl-[1,8]-naphthyridine-3-carboxylic acid [1-(3-nitro phenyl)-ethylidene]hydrazide (3f): Recrystallized from ethyl acetate in hexane (3:1) to provide (**3f**) Light yellow colour solid, yield: 60 %. IR (KBr, ν_{max}, cm^{-1}): 3325 (NH), 2280 (aliph. CH_2), 1755 (CO), 1670 (C=N); ^{1}H NMR (500 MHz, DMSO-d_6) δ: 1.14 (m, 2H, *J* = 15 Hz, CH_2), 1.22 (m, 2H, *J* = 15 Hz, CH_2), 1.92 (s, 3H, CH_3), 2.45 (m, 1H, CH), 7.14 (t, 1H, *J* = 15 Hz, CH), 7.31, (s, 1H, CH), 7.24, (t, 1H, *J* = 15 Hz, CH), 7.50 (m, 2H, CH), 7.72 (m, 2H, *J* = 20 Hz, CH), 8.52 (s, 1H, NH), 9.21 (d, 1H, *J* = 15 Hz, CH), Mass (m/z): 376 [M+1].

2-Cyclopropyl-[1,8]-naphthyridine-3-carboxylic acid [1-(4-amino phenyl)-ethylidene]hydrazide (3g): Recrystallized from ethyl acetate in hexane (3:1) to provide (**3g**) green colour solid, yield: 66 %. IR (KBr, ν_{max}, cm^{-1}): 3345 (NH_2), 3330 (NH), 2285 (aliph. CH_2), 1690 (CO), 1685 (C=N); ^{1}H NMR (500 MHz, DMSO-d_6) δ: 1.15 (m, 2H, *J* = 15 Hz, CH_2), 1.21 (m, 2H, *J* = 15 Hz, CH_2), 1.90 (s, 3H, CH_3), 2.41 (m, 1H, CH), 4.41 (s, 2H, NH_2), 7.13 (t, 1H, *J* = 15 Hz, CH), 7.32 (s, 1H, CH), 7.29, (t, 1H, *J* = 15 Hz, CH), 7.48 (m, 2H, CH), 7.71 (m, 2H, *J* = 20 Hz, CH), 8.50 (s, 1H, NH), 9.27 (d, 1H, *J* = 15 Hz, CH), Mass (m/z): 346 [M+1].

2-Cyclopropyl-[1,8]-naphthyridine-3-carboxylic acid [1-(2,6-dihydroxy-phenyl)ethylidene]hydrazide (3h): Recrystallized from ethyl acetate in hexane (3:1) to provide (**3h**) yellow colour solid, yield: 64 %. IR (KBr, ν_{max}, cm^{-1}): 3310 (OH), 3230 (NH), 2285 (aliph. CH_2), 1710 (CO), 1685 (C=N); ^{1}H NMR (500 MHz, DMSO-d_6) δ: 1.19 (m, 2H, *J* = 15 Hz, CH_2), 1.24 (m, 2H, *J* = 15 Hz, CH_2), 1.89 (s,

3H, CH_3), 2.51 (m, 1H, CH), 4.42 (s, 2H, NH_2), 7.13 (t, 1H, *J* = 15 Hz, CH), 7.32, (d, 2H, CH), 7.29, (m, 1H, *J* = 15 Hz, CH), 7.48 (m, 1H, CH), 7.73 (m, 1H, *J* = 20 Hz, CH), 8.54 (s, 1H, NH), 9.22 (d, 1H, *J* = 15Hz, CH), Mass (m/z): 363 [M+1].

1-(2-Cyclopropyl-[1,8]-naphthyridine-3-carbonyl)-3-phenyl-1*H*-pyrazole-4-carbaldehyde (4a): 2-Cyclopropyl-[1,8]-naphthyridine-3-carboxylic acid (1-phenyl ethylidene)hydrazide (**3a**, 0.01 mol) was dissolved in DMF (5 mL) and cooled to 0 ºC. To this contents $POCl_3$ was added drop wise at 0 ºC. The reaction mixture was stirred at 80-85 ºC for 5-6 h, cooled the reaction mass was cooled to room temperature then poured into crushed ice. The solid that separated on neutralized with $NaHCO_3$, filtered the solid and washed twice with cold water and recrystallized from ethanol to afford (**4a**). Cream colour solid, yield: 77 %. IR (KBr, ν_{max}, cm^{-1}): 2385 (aliph. CH_2), 1700, 1725 (CO), 1645 (C=N); ^{1}H NMR (500 MHz, DMSO-d_6) δ: 0.94 (m, 4H, *J* = 20 Hz, $2CH_2$), 2.16 (m, 1H, *J* = 20 Hz, CH), 7.16 (m, 1H, CH), 7.31 (m, 2H, CH), 7.41 (m, 2H, *J* = 15 Hz, CH), 7.46, (s, 1H, CH), 7.46 (t, 1H, *J* = 15 Hz, CH), 7.55 (m, 1H, CH), 8.26 (s, 1H, CH), 8.38 (s, 1H, CH), 9.12 (s, 1H, CH), 9.68 (s, 1H, CHO), ^{13}C NMR (500 MHz, DMSO-d_6/TMS) δ: 8.1 ($2CH_2$), 8.4 (CH), 95.8 (CH), 123.1 (2CH), 128.2 (2CH), 132.5 (6CH), 152.3 (2CH), 191.4 (CO, CHO). Mass (m/z): 369 [M+1].

Other compounds in the series were prepared similarly and their characterization data are recorded given below:

1-(2-Cyclopropyl-[1,8]-naphthyridine-3-carbonyl)-3-*p*-tolyl-1*H*-pyrazole-4-carbaldehyde (4b): Purified by column chromatography eluted by using 5 % methanol in DCM, to provide light cream colour solid (**4b**), yield: 65 %, IR (KBr, n_{max}, cm^{-1}): 2275 (aliph. CH_2), 1710, 1715 (2CO); ^{1}H NMR (500 MHz, DMSO-d_6) δ: 0.94 (m, 4H, *J* = 20 Hz, $2CH_2$), 2.16 (m, 1H, *J* = 20 Hz, CH), 2.36 (s, 3H, CH_3), 7.12 (m, 1H, CH), 7.34 (m, 2H, CH), 7.42 (m, 2H, *J* = 15 Hz, CH), 7.48, (s, 1H, CH), 7.51, (t, 1H, *J* = 15 Hz, CH), 7.58 (m, 1H, CH), 8.21 (s, 1H, CH), 8.38 (s, 1H, CH), 9.12 (s, 1H, CH), 9.78 (s, 1H, CHO), ^{13}C NMR (500 MHz, DMSO-d_6/TMS) δ: 7.3 ($2CH_2$), 7.9 (CH), 21.3 (CH_3) 93.8 (CH), 118.1 (2CH), 126.2 (2CH), 130.5 (6CH), 151.3 (2CH), 181.4 (CO, CHO). Mass (m/z): 383 [M+1].

1-(2-Cyclopropyl-[1,8]-naphthyridine-3-carbonyl)-3-(4-methoxy phenyl)-1*H*-pyrazole-4-carbaldehyde (4c): Purified by column chromatography eluted by using 2-5 % methanol in DCM, to provide light cream colour solid (**4c**), yield: 70 %. IR (KBr, ν_{max}, cm^{-1}): 2245 (aliph. CH_2), 1700, 1725 (2CO); ^{1}H NMR (500 MHz, DMSO-d_6) δ: 0.92 (m, 4H, *J* = 20 Hz, $2CH_2$), 2.24 (m, 1H, *J* = 20 Hz, CH), 3.39 (s, 3H, CH_3), 7.15 (m, 1H, CH), 7.32 (m, 2H, CH), 7.46 (m, 2H, *J* = 15 Hz, CH), 7.51, (s, 1H, CH), 7.58, (t, 1H, *J* = 15 Hz, CH), 7.61 (m, 1H, CH), 8.24 (s, 1H, CH), 8.48 (s, 1H, CH), 9.23 (s, 1H, CH), 9.83 (s, 1H, CHO), ^{13}C NMR (500 MHz, DMSO-d_6/TMS) δ: 7.3 ($2CH_2$), 7.9 (CH), 51.3 (CH_3), 91.8 (CH), 123.1 (2CH), 129.6 (2CH), 131.5 (6CH), 154.3 (2CH), 184.4 (CO, CHO). Mass (m/z): 399 [M+1].

3-(4-Chloro phenyl)-1-(2-cyclopropyl-[1,8]-naphthyridine-3-carbonyl)-1*H*-pyrazole-4-carbaldehyde (4d): Purified by column chromatography eluted by using 2-5 % methanol in DCM, to provide light cream colour solid (**4d**), yield: 64 %. IR

(KBr, ν_{max}, cm^{-1}): 2285 (aliph. CH_2), 1690, 1725 (2CO); ^{1}H NMR (500 MHz, DMSO-d_6) δ: 0.97 (m, 4H, *J* = 20 Hz, $2CH_2$), 2.26 (m, 1H, *J* = 20 Hz, CH), 7.15 (m, 1H, CH), 7.32 (m, 1H, CH), 7.46 (m, 2H, *J* = 15 Hz, CH), 7.51, (s, 1H, CH), 7.58, (t, 1H, *J* = 15 Hz, CH), 7.61 (m, 1H, CH), 8.24 (s, 1H, CH), 8.48 (s, 1H, CH), 9.23 (s, 1H, CH), 9.83 (s, 1H, CHO), ^{13}C NMR (500 MHz, DMSO-d_6/TMS) δ: 7.8 ($2CH_2$), 8.2 (CH), 92.8 (CH), 122.1 (2CH), 129.4 (2CH), 131.2 (6CH), 151.3 (2CH), 188.4 (CO, CHO). Mass (m/z): 399 [M+1]. Mass (m/z): 403 [M+1].

1-(2-Cyclopropyl-[1,8]-naphthyridine-3-carbonyl)-3-(4-nitro phenyl)-1*H*-pyrazole-4-carbaldehyde (4e): Purified by column chromatography eluted by using 2-5 % methanol in DCM, to provide light cream colour solid (**4e**), yield: 72 %. IR (KBr, ν_{max}, cm^{-1}): 2265 (aliph. CH_2), 1700, 1715 (2CO); ^{1}H NMR (500 MHz, DMSO-d_6) δ: 0.96 (m, 4H, *J* = 20 Hz, $2CH_2$), 2.23 (m, 1H, *J* = 20 Hz, CH), 7.25 (m, 1H, CH), 7.36 (m, 1H, CH), 7.56 (m, 2H, *J* = 15 Hz, CH), 7.61, (s, 1H, CH), 7.68, (t, 1H, *J* = 15 Hz, CH), 7.71 (m, 1H, CH), 8.34 (s, 1H, CH), 8.46 (s, 1H, CH), 9.26 (s, 1H, CH), 9.87 (s, 1H, CHO), ^{13}C NMR (500 MHz, DMSO-d_6/TMS) δ: 7.6 ($2CH_2$), 8.1 (CH), 90.8 (CH), 125.1 (2CH), 128.4 (2CH), 130.2 (6CH), 154.3 (2CH), 189.2 (CO, CHO). Mass (m/z): 414 [M+1].

1-(2-Cyclopropyl-[1,8]-naphthyridine-3-carbonyl)-3-(3-nitro phenyl)-1*H*-pyrazole-4-carbaldehyde (4f): Purified by column chromatography (60-120 mesh silica gel), eluted by using 2-5 % methanol in DCM, to provide light cream colour solid (**4f**), yield: 70 %. IR (KBr, ν_{max}, cm^{-1}): 2265 (aliph. CH_2), 1720, 1735 (2CO); ^{1}H NMR (500 MHz, DMSO-d_6) δ: 0.95 (m, 4H, *J* = 20 Hz, $2CH_2$), 2.24 (m, 1H, *J* = 20 Hz, CH), 7.21 (m, 1H, CH), 7.36 (m, 1H, CH), 7.55 (m, 2H, *J* = 15 Hz, CH), 7.62 (s, 1H, CH), 7.63 (t, 1H, *J* = 15 Hz, CH), 7.72 (m, 1H, CH), 8.35 (s, 1H, CH), 8.42 (s, 1H, CH), 9.22 (s, 1H, CH), 9.86 (s, 1H, CHO), ^{13}C NMR (500 MHz, DMSO-d_6/TMS) δ: 7.3 ($2CH_2$), 8.5 (CH), 92.8 (CH), 121.1 (2CH), 129.4 (2CH), 132.2 (6CH), 158.3 (2CH), 187.2 (CO, CHO). Mass (m/z): 414 [M+1].

3-(4-Amino phenyl)-1-(2-cyclopropyl-[1,8]-naphthyridine-3-carbonyl)-1*H*-pyrazole-4- carbaldehyde (4g): Purified by column chromatography (60-120 mesh silica gel), eluted by using 2-5 % methanol in DCM, to provide light cream colour solid (**4g**), yield: 74 %. IR (KBr, ν_{max}, cm^{-1}): 2215 (aliph. CH_2), 1700, 1725 (2CO); ^{1}H NMR (500 MHz, DMSO-d_6) δ: 0.98 (m, 4H, *J* = 20 Hz, $2CH_2$), 2.34 (m, 1H, *J* = 20 Hz, CH), 4.23 (s, 2H, NH_2), 7.29 (m, 1H, CH), 7.36 (m, 1H, CH), 7.58 (m, 2H, *J* = 15 Hz, CH), 7.62 (s, 1H, CH), 7.68, (t, 1H, *J* = 15 Hz, CH), 7.82 (m, 1H, CH), 8.35 (s, 1H, CH), 8.42 (s, 1H, CH), 9.24 (s, 1H, CH), 9.86 (s, 1H, CHO), ^{13}C NMR (500 MHz, DMSO-d_6/TMS) δ: 7.8 ($2CH_2$), 8.2 (CH), 92.2 (CH), 125.3 (2CH), 128.5 (2CH), 130.9 (6CH), 154.7 (2CH), 189.8 (CO, CHO). Mass (m/z): 384 [M+1].

1-(2-Cyclopropyl-[1,8]-naphthyridine-3-carbonyl)-3-(2,6-dihydroxy phenyl)-1*H*-pyrazole 4-carbaldehyde (4h): Purified by column chromatography (60-120 mesh silica gel), eluted by using 2-5 % methanol in DCM, to provide light cream colour solid (**4h**), yield: 68 %. IR (KBr, ν_{max}, cm^{-1}): 2285 (aliph. CH_2), 1725, 1700 (2CO); ^{1}H NMR (500 MHz, DMSO-d_6) δ: 0.99 (m, 4H, *J* = 20 Hz, $2CH_2$), 2.24 (m,

1H, *J* = 20 Hz, CH), 3.63 (s, 2H, 2 OH), 7.19 (m, 1H, CH), 7.26 (m, 1H, CH), 7.48 (m, 1H, *J* = 15 Hz, CH), 7.68 (t, 1H, *J* = 15 Hz, CH), 7.82 (m, 1H, CH), 8.35 (s, 1H, CH), 8.42 (s, 1H, CH), 9.24 (s, 1H, CH), 9.86 (s, 1H, CHO), ^{13}C NMR (500 MHz, DMSO-d_6/TMS) δ: 7.4 ($2CH_2$), 8.3 (CH), 94.8 (CH), 122.1 (2CH), 129.2 (2CH), 132.9 (6CH), 153.7 (2CH), 189.9 (CO, CHO). Mass (m/z): 401 [M+1].

(2-Cyclopropyl-[1,8]-naphthyridin-3-yl)-(3,5-dimethyl pyrazol-1-yl)-methanone (5a): To a solution of 2-cyclopropyl[1,8]naphthyridine-3-carboxylic acid hydrazide (**2**) (0.01 mol) in dry methanol (10 mL) was added acetyl acetone (0.015 mol) and few drops of conc. HCl. The resulting solution was refluxed for *ca.* 2-3 h and cooled to room temperature. Recrystallized from ethylacetate in hexane (5:1) to provide light green colour solid (**5a**). Yield: 72 %, IR (KBr, ν_{max}, cm^{-1}): 2245 (aliph. CH_2), 1700, (CO); ^{1}H NMR (500 MHz, DMSO-d_6) δ: 1.07 (m, 2H, *J* = 15 Hz, CH_2), 1.24 (m, 2H, *J* = 15 Hz, CH_2) 2.04 (m, 1H, *J* = 20 Hz, CH), 2.07 (s, 3H, *J* = 15 Hz, CH_3), 2.66 (s, 3H, *J* = 15 Hz, CH_3), 3.96 (s, 1H, CH), 7.75 (t, 1H, CH), 8.67 (s, 1H, CH), 8.70 (m, 1H, *J* = 15 Hz, CH), 9.15 (s, 1H, CH), ^{13}C NMR (500 MHz, DMSO-d_6/TMS) δ: 6.8 ($2CH_2$), 7.3 (CH_3), 12.7 (CH_2), 104.8 (CH), 123.1 (2CH), 127.2 (2CH), 134.9 (6CH), 153.8 (2CH), 189.9 (CO). Mass (m/z): 293 [M+1].

2-Cyclopropyl-[1,8]-naphthyridin-3-yl)-(3,5-diethyl pyrazol-1-yl)methanone (5b): Light brown colour solid, yield: [0.120 g, 70 %, IR (KBr, ν_{max}, cm^{-1}): 2245 (aliph. CH_2), 1700, (CO); ^{1}H NMR (500 MHz, DMSO-d_6) δ: 1.17 (m, 4H, *J* = 20 Hz, $2CH_2$), 1.24 (m, 6H, *J* = 20 Hz, $2CH_3$) 1.98 (m, 1H, *J* = 20 Hz, CH), 2.67 (m, 4H, *J* = 20 Hz, $2CH_2$), 6.42 (s, 1H, *J* = 15 Hz, CH), 7.75 (m, 1H, CH), 8.71 (m, 2H, 2CH), 9.18, (s, 1H, *J* = 15 Hz, CH), ^{13}C NMR (500 MHz, DMSO-d_6/TMS) δ: 6.3 ($2CH_2$), 7.1 ($2CH_2$), 7.8 ($2CH_3$), 12.7 (CH), 104.8 (CH), 120.1 (2CH), 126.2 (2CH), 131.9 (6CH), 151.8 (2CH), 187.9 (CO) Mass (m/z): 322 [M+1].

2-Cyclopropyl-[1,8]-naphthyridin-3-yl)-(3-methyl-5-trifluoromethyl-pyrazol-1-yl)methanone (5c): Light brown colour solid, yield: 74 %, IR (KBr, ν_{max}, cm^{-1}): 2285 (aliph. CH_2), 1725, (CO); ^{1}H NMR (500 MHz, DMSO-d_6) δ: 1.27 (m, 2H, *J* = 20 Hz, CH_2), 1.58 (m, 2H, *J* = 20 Hz, CH_2) 1.88 (s, 3H, *J* = 15 Hz, CH_3), 2.31 (m, 1H, *J* = 20 Hz, CH), 7.91 (t, 1H, *J* = 15 Hz, CH), 8.42 (s, 1H, CH), 8.91 (d, 1H, CH), 9.23, (s, 1H, *J* = 15 Hz, CH), ^{13}C NMR (500 MHz, DMSO-d_6/TMS) δ: 6.6 ($2CH_2$), 6.9 (CH), 7.1 (CH_3), 12.4 (CH_2), 103.8 (CH), 124.1 (2CH), 128.2 (2CH), 133.9 (6CH), 151.8 (2CH), 188.9 (CO) Mass (m/z): 347 [M+1].

2-Cyclopropyl-[1,8]-naphthyridin-3-yl)-(3,5-diphenyl-pyrazol-1-yl)methanone (5d): Light brown colour solid, yield: 68 %, IR (KBr, ν_{max}, cm^{-1}): 2275 (aliph. CH_2), 1715, (CO); ^{1}H NMR (500 MHz, DMSO-d_6) δ: 1.27 (m, 4H, *J* = 20 Hz, $2CH_2$), 2.36 (m, 1H, *J* = 20 Hz, CH), 6.341 (s, 1H, *J* = 15 Hz, CH), 7.41 (m, 4H, *J* = 20 Hz, 4CH), 7.52 (m, 4H, *J* = 20 Hz, 4CH), 7.64 (m, 3H, *J* = 20 Hz, 3CH), 8.22 (s, 1H, CH), 8.58 (d, 1H, CH), 9.21, (s, 1H, *J* = 15 Hz, CH), ^{13}C NMR (500 MHz, DMSO-d_6/TMS) δ: 6.4 ($2CH_2$), 6.6 (CH), 103.8 (CH), 121.1 (2CH), 128.2 (10, CH), 133.9 (2CH), 152.8 (2CH), 187.9 (CO) Mass (m/z): 417 [M+1].

2-(2-Cyclopropyl-[1,8]-naphthyridine-3-carbonyl)-5-methyl-2,4-dihydro-pyrazol-3-one (6a): A mixture of 2-cyclopropyl-[1,8]-naphthyridine-3-carboxylic acid hydrazide (**2**) (0.01 mol) and ethyl acetoacetate (0.01 mol) was refluxed in dry methanol (25 mL) for *ca.* 16 h and recrystallized from ethyl acetate in hexane (5:1) to provide green colour solid (**6a**). Yield: 70 %, IR (KBr, ν_{max}, cm^{-1}): 2285 (aliph. CH_2), 1725, 1700 (2CO); ^{1}H NMR (500 MHz, DMSO-d_6) δ: 0.98 (m, 4H, *J* = 20 Hz, $2CH_2$), 1.21 (s, 3H, *J* = 15 Hz, CH_3), 2.12 (m, 1H, CH), 3.02 (s, 2H, CH_2), 7.56 (s, 1H, CH), 8.59 (t, 1H, CH), 8.81 (s, 1H, CH), 9.14 (s, 1H, CH), ^{13}C NMR (500 MHz, DMSO-d_6/TMS) δ: 6.8 ($2CH_2$), 7.2 (CH), 20.8 (CH_3), 32.4 (CH_2), 122.1 (2CH), 128.2 (CH), 136.9 (2CH), 142.8 (2CH), 157.9 (CH), 164.5 (CO), 169.5 (CO). Mass (m/z): 295 [M+1].

3-Cyclopropyl-5-hydroxy-pyrazol-1-yl)-(2-cyclopropyl-[1,8]-naphthyridin-3-yl)methanone (6b): Recrystallized from ethyl acetate in hexane provide (**6b**) as brown colour solid, yield: 75 %. IR (KBr, ν_{max}, cm^{-1}): 2245 (aliph. CH_2), 1700, 1725 (2CO); ^{1}H NMR (500 MHz, DMSO-d_6) δ: 0.86 (m, 4H, *J* = 20 Hz, $2CH_2$), 1.21 (m, 6H, *J* = 20 Hz, $2CH_2$, 2CH), 4.12 (s, 1H, OH), 7.58 (s, 1H, CH), 8.54 (m, 2H, 2CH), 9.08 (d, 1H, *J* = 15 Hz, CH), ^{13}C NMR (500 MHz, DMSO-d_6/TMS) δ: 1.4 ($2CH_2$), 1.9 (CH), 6.4 ($2CH_2$), 11.2 (CH), 28.4 (CH_2), 123.4 (2CH), 127.2 (CH), 134.8 (CH), 136.2 (CH), 144.8 (CH), 146.2 (CH), 166.2 (CH), 166.3 (CO), 168.5 (CO). Mass (m/z): 321 [M+1].

2-(2-Cyclopropyl-[1,8]-naphthyridine-3-carbonyl)-5-trifluoromethyl-2,4-dihydropyrazol-3-one (6c): Recrystallized from ethyl acetate in hexane provide (**6c**) as dark brown colour solid, yield: 72 %, IR (KBr, ν_{max}, cm^{-1}): 2265 (aliph. CH_2), 1700, 1715 (2CO); ^{1}H NMR (500 MHz, DMSO-d_6) δ: 1.24 (m, 2H, *J* = 20 Hz, CH_2), 1.56 (m, 2H, *J* = 20 Hz, CH_2), 1.96 (s, 3H, CH_3), 2.31 (m, 1H, CH), 7.91 (t, 1H, CH), 841, (s, 1H, CH), 8.91, (d, 1H, *J* = 15 Hz, CH), 9.26, (d, 1H, *J* = 15 Hz, CH), ^{13}C NMR (500 MHz, DMSO-d_6/TMS) δ: 6.8 ($2CH_2$), 8.2 (CH), 15.4 (CH_2), 121.4 (CF_3), 124.2 (CH), 126.8 (CH), 131.2 (CH), 134.8 (CH), 136.2 (CH), 141.2 (CH), 143.8 (CH), 166.8 (CH), 169.3 (CO), 171.5 (CO). Mass (m/z): 347 [M+1].

2-(2-Cyclopropyl-[1,8]-naphthyridine-3-carbonyl)-5-phenyl-2,4-dihydro-pyrazol-3-one (6d): Recrystallized from ethanol to provide (**6d**) as brown colour solid, yield: 70 %, IR (KBr, ν_{max}, cm^{-1}): 2245 (aliph. CH_2), 1710,1725 (2CO); ^{1}H NMR (500 MHz, DMSO-d_6) δ: 1.04 (m, 2H, *J* = 20 Hz, CH_2), 1.46 (m, 1H, *J* = 20 Hz), 2.96 (s, 2H, CH_2), 7.41 (m, 6H, 6CH), 821, (s, 1H, CH), 8.61, (d, 1H, *J* = 15 Hz, CH), 9.26 (d, 1H, *J* = 15 Hz, CH), ^{13}C NMR (500 MHz, DMSO-d_6/TMS) δ: 6.2 ($2CH_2$), 7.7 (CH), 35.4 (CH_2), 123.2 (CH), 125.8 (CH), 132.2 (CH), 133.8 (CH), 135.2 (CH), 136.2 (CH), 141.8 (CH), 156.8 (CH), 167.3 (CO), 174.5 (CO). Mass (m/z): 357 [M+1].

2-Cyclopropyl-[1,8]-naphthyridine-3-carboxylic acid benzylidene hydrazide (7a): A mixture of 2-cyclopropyl-[1,8]-naphthyridine-3-carboxylic acid hydrazide (**2**) (0.01 mol) and benzaldehyde (0.012 mol) was refluxed in dry methanol (10 mL)

for *ca.* 6 h and cooled to room temperature. Recrystallized in ethylacetate in hexane to provide light yellow coloured solid (**7a**), yield 74 %. IR (KBr, ν_{max}, cm^{-1}): 2285 (aliph. CH_2), 1715 (CO), 1615 (C=N); ^{1}H NMR (500 MHz, DMSO-d_6) δ: 1.21 (m, 4H, *J* = 25 Hz, $2CH_2$), 2.46 (s, 1H, CH), 7.18 (t, 2H, *J* = 15 Hz, CH), 7.44 (m, 3H, CH), 7.68 (t, 1H, *J* = 15 Hz, CH), 7.92 (m, 1H, CH), 8.64 (d, 1H, *J* = 20 Hz, CH), 9.15 (s, 1H, CH), 11.12 (s, 1H, NH), Mass (m/z): 317 [M+1].

2-Cyclopropyl-[1,8]-naphthyridine-3-carboxylic acid-(4-methoxy benzylidene)hydrazide (7b): Recrystallized from ethyl acetate in hexane provide (**7b**) as light yellow colour solid, yield: 68 %. IR (KBr, ν_{max}, cm^{-1}): 2275 (aliph. CH_2), 1700 (CO), 1645 (C=N); ^{1}H NMR (500 MHz, DMSO-d_6) δ: 1.24 (m, 4H, *J* = 25 Hz, $2CH_2$), 2.48 (m, 1H, CH), 3.68 (s, 3H, CH_3), 7.28 (t, 2H, *J* = 15 Hz, CH), 7.48 (m, 2H, CH), 7.58 (t, 1H, *J* = 15 Hz, CH), 7.96 (m, 1H, CH), 8.62 (d, 1H, *J* = 20 Hz, CH), 9.17 (s, 1H, CH), 9.86 (s, 1H, NH), Mass (m/z): 347 [M+1].

2-Cyclopropyl-[1,8]-naphthyridine-3-carboxylic acid-(4-nitro benzylidene)-hydrazide (7c): Recrystallized from ethyl acetate in hexane provide (**7c**) as yellow colour solid, yield: 72 %, IR (KBr, ν_{max}, cm^{-1}): 2285 (aliph. CH_2), 1725 (CO), 1635 (C=N); ^{1}H NMR (500 MHz, DMSO-d_5) δ: 1.26 (m, 4H, *J* = 25 Hz, $2CH_2$), 2.41 (m, 1H, CH), 7.25 (t, 2H, *J* = 15 Hz, CH), 7.42 (m, 2H, CH), 7.59 (t, 1H, *J* = 15 Hz, CH), 7.92 (m, 1H, CH), 8.42 (d, 1H, *J* = 20 Hz, CH), 9.07 (s, 1H, CH), 9.46 (s, 1H, NH), Mass (m/z): 362 [M+1].

2-Cyclopropyl-[1,8]-naphthyridine-3-carboxylic acid(4-ethyl benzylidene)-hydrazide (7d): Recrystallized from ethyl acetate in hexane provide (**7d**) as yellow colour solid, yield: 70 %. IR (KBr, ν_{max}, cm^{-1}): 2265 (aliph. CH_2), 1725 (CO), 1665 (C=N); ^{1}H NMR (500 MHz, DMSO-d_6) δ: 1.22 (m, 4H, *J* = 25 Hz, $2CH_2$), 1.31 (t, 3H, *J* = 15 Hz, CH), 2.26 (m, 1H, CH), 2.66 (q, 2H, CH_2), 7.21 (t, 2H, *J* = 15 Hz, CH), 7.43 (m, 2H, CH), 7.58 (t, 1H, *J* = 15 Hz, CH), 7.91 (m, 1H, CH), 8.41 (d, 1H, *J* = 20 Hz, CH), 9.07 (s, 1H, CH), 9.26 (s, 1H, NH), Mass (m/z): 345 [M+1].

2-Cyclopropyl-[1,8]-naphthyridine-3-carboxylic acid (4-chloro benzylidene)-hydrazide (7e): Recrystallized from ethyl acetate in hexane provide (**7e**) as yellow colour solid, yield: 74 %. IR (KBr, ν_{max}, cm^{-1}): 2245 (aliph. CH_2), 1690 (CO), 1645 (C=N); ^{1}H NMR (500 MHz, DMSO-d_6) δ: 1.24 (m, 4H, *J* = 25 Hz, $2CH_2$), 2.42 (m, 1H, CH), 7.21 (t, 2H, *J* = 15 Hz, CH), 7.45 (m, 2H, CH), 7.56 (t, 1H, *J* = 15 Hz, CH), 7.91 (m, 1H, CH), 8.43 (d, 1H, *J* = 20 Hz, CH), 9.17 (s, 1H, CH), 9.46 (s, 1H, NH), Mass (m/z): 351 [M+1].

2-Cyclopropyl-[1,8]-naphthyridine-3-carboxylicacid-(4-bromo benzylidene)-hydrazide (7f): Recrystallized from ethyl acetate in hexane provide (**7f**) as yellow colour solid, yield: 68 %. IR (KBr, ν_{max}, cm^{-1}): 2235 (aliph. CH_2), 1680 (CO), 1625 (C=N); ^{1}H NMR (500 MHz, DMSO-d_6) δ: 1.26 (m, 4H, *J* = 25 Hz, $2CH_2$), 2.34 (m, 1H, CH), 7.26 (t, 2H, *J* = 15 Hz, CH), 7.41 (m, 2H, CH), 7.46 (t, 1H, *J* = 15 Hz, CH), 7.92 (m, 1H, CH), 8.41 (d, 1H, *J* = 20 Hz, CH), 9.19 (s, 1H, CH), 9.36 (s, 1H, NH), Mass (m/z): 351 [M+1].

2-Cyclopropyl-[1,8]-naphthyridine-3-carboxylic acid-(3,5-dihydroxy benzylidene)-hydrazide (7g): Recrystallized from ethyl acetate in hexane provide (**7g**) as Yellow colour solid, yield: 74 %. IR (KBr, ν_{max}, cm^{-1}): 2225 (aliph. CH_2), 1675 (CO), 1685 (C=N); ^{1}H NMR (500 MHz, DMSO-d_6) δ: 1.16 (m, 4H, *J* = 25 Hz, $2CH_2$), 2.24 (m, 1H, CH), 3.64 (s, 2H, OH), 7.16 (t, 1H, *J* = 15 Hz, CH), 7.31, (m, 2H, CH), 7.36, (s, 1H, *J* = 15 Hz, CH), 7.72 (m, 1H, CH), 8.21 (d, 1H, *J* = 20 Hz, CH), 9.09 (s, 1H, CH), 9.26 (s, 1H, NH), Mass (m/z): 349 [M+1].

2-Cyclopropyl-[1,8]-naphthyridine-3-carboxylic acid (4-oxo-2-phenyl thiazolidin-3-yl)-amide (8a): To a solution of 2-cyclopropyl-[1,8]-naphthyridine-3-carboxylic acid benzylidene hydrazide (**7a**) (0.01 mol) in ethanol (10 mL) was added mercapto-acetic acid (0.05 mol) and catalytic amount of anhydrous zinc chloride, at room temperature. The resulting clear solution was heated for reflux at 90 °C for *ca.* 6-8 h, reaction completion was monitored by TLC, after completing the starting material (**7a**) cooled to room temperature and recrystallized from ethylacetate in hexane to provide cream colour solid (**8a**). Yield 74 %. IR (KBr, ν_{max}, cm^{-1}): 3110 (NH), 2265 (aliph. CH_2), 1710 (CO), 1665 (C=N); ^{1}H NMR (500 MHz, DMSO-d_6) δ: 0.96 (m, 4H, *J* = 20 Hz, $2CH_2$), 2.26 (m, 1H, CH), 3.84 (s, 2H, CH_2), 6.21 (s, 1H, CH), 7.33 (m, 3H, CH), 7.39 (m, 2H, *J* = 20 Hz, CH), 7.70 (m, 1H, CH), 8.17 (d, 1H, *J* = 20 Hz, CH), 9.29 (s, 1H, CH), 9.36 (s, 1H, NH), ^{13}C NMR (500 MHz, DMSO-d_6/TMS) δ: 6.8 ($2CH_2$), 7.2 (CH), 38.8 (CH_2), 52.7 (CH), 124.6, 124.9 (2CH), 129.1, 129.3, 129.5, 129.8 (6CH), 136.2, 136.5 (2CH), 138.9 (2CH), 151.3 (2CH), 177.9, 179.4 (2CO) Mass (m/z): 391 [M+1].

2-Cyclopropyl-[1,8]-naphthyridine-3-carboxylic acid [2-(4-methoxy phenyl)-4-oxo-thiazolidin-3-yl]amide (8b): Recrystallized from ethanol provide (**8b**) as off white solid, yield: 68 %. IR (KBr, ν_{max}, cm^{-1}): 3410 (NH), 2245 (aliph. CH_2), 1700 (CO), 1645 (C=N); ^{1}H NMR (500 MHz, DMSO-d_6) δ: 0.98 (m, 4H, *J* = 20 Hz, $2CH_2$), 2.31 (m, 1H, CH), 3.84 (s, 2H, CH_2), 3.92 (s, 3H, CH_3), 6.24 (s, 1H, CH), 7.43 (m, 2H, CH), 7.48 (m, 2H, *J* = 20 Hz, CH), 7.80 (m, 1H, CH), 8.27 (d, 1H, *J* = 20 Hz, CH), 9.39 (s, 1H, CH), 9.46 (s, 1H, NH), ^{13}C NMR (500 MHz, DMSO-d_6/TMS) δ: 6.3 ($2CH_2$), 6.8 (CH), 35.8 (CH_2), 54.7 (CH_2), 122.6, 123.9 (2CH), 125.1, 126.3, 126.8, 127.2 (6CH), 134.2, 134.5 (2CH), 137.9 (2CH), 153.3 (2CH), 172.9, 176.4 (2CO) Mass (m/z): 421 [M+1].

2-Cyclopropyl-[1,8]-naphthyridine-3-carboxylic acid-[2-(4-nitro phenyl)-4-oxo-thiazolidin-3-yl]amide (8c): Recrystallized from ethanol provide (**8c**) as off white solid, yield: 72 %. IR (KBr, ν_{max}, cm^{-1}): 3345 (NH), 2265 (aliph. CH_2), 1715 (CO), 1655 (C=N); ^{1}H NMR (500 MHz, DMSO-d_6) δ: 1.10 (m, 4H, *J* = 20 Hz, $2CH_2$), 2.19 (m, 1H, CH), 3.46 (s, 2H, CH_2), 5.44 (s, 1H, CH), 7.13, (m, 2H, CH), 7.28, (m, 2H, *J* = 20 Hz, CH), 7.32 (m, 1H, CH), 8.17 (d, 1H, *J* = 20 Hz, CH,), 8.39 (s, 1H, NH), 9.16 (s, 1H, CH), ^{13}C NMR (500 MHz, DMSO-d_6/TMS) δ: 6.4 ($2CH_2$), 6.9 (CH), 39.8 (CH_2), 57.7 (CH), 125.6, 125.9 (2CH), 126.1, 126.3, 126.8, 127.4 (6CH), 133.2, 134.2 (2CH), 136.9 (2CH), 158.3 (2CH), 171.9, 174.4 (2CO), Mass (m/z): 436 [M+1].

2-Cyclopropyl-[1,8]-naphthyridine-3-carboxylic acid-[2-(4-ethyl phenyl)-4-oxo-thiazolidin-3-yl]amide (8d): Recrystallized from ethanol provide (**8d**) as cream colour solid, yield: 70 %. IR (KBr, ν_{max}, cm^{-1}): 3415 (NH), 2225 (aliph. CH_2), 1725, 1700 (2CO), 1645 (C=N); ^{1}H NMR (500 MHz, DMSO-d_6) δ: 1.04 (m, 4H, *J* = 20 Hz, $2CH_2$), 1.35 (t, 3H, *J* = 15 Hz, CH_3), 2.29 (m, 1H, CH), 2.69 (q, 2H, CH_2), 3.42 (s, 2H, CH_2), 5.14 (s, 1H, CH), 7.26 (m, 2H, CH), 7.29 (m, 2H, *J* = 20 Hz, CH), 7.28 (m, 1H, CH), 8.29 (d, 1H, *J* = 20 Hz, CH,), 8.19 (s, 1H, NH), 9.29 (s, 1H, CH), ^{13}C NMR (500 MHz, DMSO-d_6/TMS) δ: 6.4 ($2CH_2$), 6.9 (CH), 15.6 (CH_3), 39.8 (CH_2), 57.7 (CH), 69.8 (CH_2), 125.6, 125.9 (2CH), 126.1, 126.3, 126.8, 127.4 (6CH), 133.2, 134.2 (2CH), 136.4 (2CH), 158.1 (2CH), 170.9, 173.4 (2CO), Mass (m/z): 419 [M+1].

2-Cyclopropyl-[1,8]-naphthyridine-3-carboxylicacid-[2-(4-chloro phenyl)-4-oxo-thiazolidin-3-yl]amide (8e): Recrystallized from ethanol provide (**8e**) as off white solid, yield: 74 %. IR (KBr, ν_{max}, cm^{-1}): 3410 (NH), 2245 (aliph. CH_2), 1700, 1715 (2CO), 1655 (C=N); ^{1}H NMR (500 MHz, DMSO-d_6) δ: 1.02 (m, 4H, *J* = 20 Hz, $2CH_2$), 2.29 (m, 1H, CH), 3.32 (s, 2H, CH_2), 5.24 (s, 1H, CH), 7.23, (m, 2H, CH), 7.27, (m, 2H, *J* = 20 Hz, CH), 7.22 (m, 1H, CH), 8.27 (d, 1H, *J* = 20 Hz, CH), 8.29 (s, 1H, NH), 9.19 (s, 1H, CH), ^{13}C NMR (500 MHz, DMSO-d_6/TMS) δ: 6.4 ($2CH_2$), 6.8 (CH), 38.4 (CH_2), 57.7 (CH), 124.6, 125.9 (2CH), 125.1, 125.3, 126.8, 127.2 (6CH), 132.2, 133.2 (2CH), 135.9 (2CH), 158.2 (2CH), 172.9, 174.4 (2CO) Mass (m/z): 425 [M+1].

2-Cyclopropyl-[1,8]-naphthyridine-3-carboxylic acid-[2-(4-bromo phenyl)-4-oxo-thiazolidin-3-yl]amide (8f): Recrystallized from ethanol provide (**8f**) as light yellow solid, yield: 68 %. IR (KBr, ν_{max}, cm^{-1}): 3420 (NH), 2265 (aliph. CH_2), 1710, 1690 (2CO), 1645 (C=N); ^{1}H NMR (500 MHz, DMSO-d_6) δ: 1.12 (m, 4H, *J* = 20 Hz, $2CH_2$), 2.19 (m, 1H, CH), 3.22 (s, 2H, CH_2), 5.44 (s, 1H, CH), 7.33 (m, 2H, CH), 7.47 (m, 2H, *J* = 20 Hz, CH), 7.62 (m, 1H, CH), 8.17 (d, 1H, *J* = 20 Hz, CH), 8.19 (s, 1H, NH), 9.29 (s, 1H, CH), ^{13}C NMR (500 MHz, DMSO-d_6/TMS) δ: 6.6 ($2CH_2$), 7.1 (CH), 39.4 (CH_2), 57.4 (CH), 124.6, 125.6 (2CH), 126.3, 126.6, 126.9, 127.4 (6CH), 133.5, 134.6 (2CH), 137.9 (2CH), 157.3 (2CH), 174.9, 176.4 (2CO) Mass (m/z): 470 [M+12].

2-Cyclopropyl[1,8]naphthyridine-3-carboxylicacid-[2-(3,5-dihydroxy phenyl)-4-oxo-thiazolidin-3-yl]amide (8g): Recrystallized from ethanol provide (**8g**) as off white solid, yield: 56 %. IR (KBr, ν_{max}, cm^{-1}): 3520, 3465 (2OH), 3425 (NH), 2245 (aliph. CH_2), 1700, 1690 (2CO), 1645 (C=N); ^{1}H NMR (500 MHz, DMSO-d_6) δ: 1.02 (m, 4H, *J* = 20 Hz, $2CH_2$), 2.29 (m, 1H, CH), 3.32 (s, 2H, CH_2), 5.34 (s, 1H, CH), 7.33, (s, 2H, CH), 7.47, (t, 1H, *J* = 20 Hz, CH), 7.61 (s, 1H, CH), 8.37 (d, 1H, *J* = 20 Hz, CH), 8.49 (s, 1H, NH), 9.19 (s, 1H, CH), ^{13}C NMR (500 MHz, DMSO-d_6/TMS) δ: 6.6 ($2CH_2$), 6.9 (CH), 36.8 (CH_2), 54.7 (CH), 100.6 (CH), 105.6, 105.9 (2CH), 126.3, 126.5, 126.8, 127.6 (4CH), 132.2, 133.2 (2CH), 136.7 (2CH), 158.3 (1CH), 172.9, 173.4 (2CO) Mass (m/z): 423 [M+1].

TABLE-1
CHARACTERIZATION DATA OF COMPOUNDS **3-10**

Compd.	Ar	R1	R2	m.p. (ºC)	Yield (%)	m.f.	Elemental analysis (%): Found (Calcd.)		
							C	H	N
3a	C_6H_5	–	–	224-226	78	$C_{20}H_{18}N_4O$	72.71 (68.29)	5.41 (4.07)	16.96 (16.47)
3b	*p*-$CH_3C_6H_4$	–	–	226-228	86	$C_{21}H_{20}N_4O_3$	73.23 (68.93)	5.85 (4.44)	16.27 (16.18)
3c	*p*-$CH_3OC_6H_4$	–	–	222-224	82	$C_{21}H_{20}N_4O_2$	69.98 (69.17)	5.59 (5.26)	15.55 (15.44)
3d	*o*-ClC_6H_4	–	–	254-256	70	$C_{20}H_{17}N_4OCl$	65.84 (65.45)	4.70 (4.47)	15.36 (15.35)
3e	*p*-$NO_2C_6H_4$	–	–	242-244	74	$C_{20}H_{17}N_5O_3$	63.99 (63.45)	4.56 (4.47)	18.66 (18.35)
3f	*m*-$NO_2C_6H_4$	–	–	244-246	60	$C_{20}H_{17}N_5O_3$	63.99 (63.45)	4.56 (4.47)	18.66 (18.35)
3g	*p*-$NH_2C_6H_4$	–	–	232-234	66	$C_{20}H_{19}N_5O$	69.55 (69.25)	5.54 (5.13)	20.28 (20.13)
3h	o-$(OH)_2C_6H_3$	–	–	254-256	64	$C_{20}H_{18}N_4O_3$	66.29 (66.17)	5.01 (4.88)	15.46 (15.29)
4a	C_6H_5	–	–	274-276	77	$C_{22}H_{16}N_4O_2$	71.73 (71.34)	4.38 (4.23)	15.21 (15.12)
4b	*p*-$CH_3C_6H_4$	–	–	268-270	65	$C_{23}H_{18}N_4O_2$	72.24 (71.92)	4.74 (4.63)	14.65 (13.95)
4c	*p*-$CH_3OC_6H_4$	–	–	272-274	70	$C_{23}H_{18}N_4O_3$	69.34 (68.66)	4.55 (4.34)	14.06 (14.01)
4d	*o*-ClC_6H_4	–	–	284-286	64	$C_{22}H_{23}N_4O_2Cl$	65.59 (65.29)	3.75 (3.64)	13.91 (13.37)
4e	*p*-$NO_2C_6H_4$	–	–	262-264	72	$C_{22}H_{15}N_5O_4$	63.92 (63.50)	3.66 (3.58)	16.94 (16.63)
4f	*m*-$NO_2C_6H_4$	–	–	272-274	70	$C_{22}H_{15}N_5O_4$	63.92 (63.40)	3.66 (3.48)	16.94 (16.53)
4g	*p*-$NH_2C_6H_4$	–	–	284-286	74	$C_{22}H_{17}N_5O_2$	68.92 (68.76)	4.47 (3.99)	18.27 (18.13)
4h	*o*-$(OH)_2C_6H_3$	–	–	274-276	68	$C_{22}H_{16}N_4O_4$	65.99 (65.80)	4.03 (4.52)	13.99 (13.06)
5a	–	CH_3	CH_3	264-266	72	$C_{17}H_{16}N_4O$	69.85 (69.50)	5.52 (4.69)	19.17 (18.70)
5b	–	C_2H_5	C_2H_5	274-276	70	$C_{19}H_{20}N_4O$	71.23 (71.17)	6.29 (6.11)	17.49 (17.34)
5c	–	CF_3	CH_3	264-266	74	$C_{17}H_{13}N_4OF_3$	58.96 (58.64)	3.78 (3.68)	16.18 (16.09)
5d	–	C_6H_5	C_6H_5	272-274	68	$C_{27}H_{20}N_4O$	77.87 (77.23)	4.84 (4.16)	13.45 (13.03)
6a	–	CH_3	–	282-284	70	$C_{16}H_{14}N_4O_2$	65.30 (65.26)	4.79 (4.54)	19.04 (19.01)
6b	–	C_3H_5	–	268-270	75	$C_{18}H_{16}N_4O_2$	67.49 (67.29)	5.03 (4.94)	17.49 (17.37)

6c	–	CF_3	–	262-264	72	$C_{16}H_{11}N_4O_2F_3$	66.68 (66.50)	3.73 (3.78)	17.68 (17.63)
6d	–	C_6H_5	–	276-278	70	$C_{21}H_{16}N_4O_2$	70.77 (70.66)	4.53 (4.49)	15.72 (15.43)
7a	C_6H_5	–	–	204-206	74	$C_{19}H_{16}N_4O$	72.13 (72.06)	5.10 (4.99)	17.71 (17.43)
7b	*p*-$CH_3OC_6H_4$	–	–	274-276	68	$C_{20}H_{18}N_4O_2$	69.35 (69.20)	5.24 (5.12)	16.17 (16.06)
7c	*p*-$NO_2C_6H_4$	–	–	204-206	72	$C_{19}H_{15}N_5O_3$	63.15 (63.01)	4.18 (4.09)	19.38 (19.12)
7d	*p*-$C_2H_5OC_6H_4$	–	–	277-279	70	$C_{21}H_{20}N_4O_2$	69.98 (69.87)	5.59 (5.41)	15.55 (15.39)
7e	*p*-ClC_6H_4	–	–	273-275	74	$C_{19}H_{15}N_4OCl$	65.05 (64.64)	4.31 (3.98)	15.97 (16.39)
7f	*o*-BrC_6H_4	–	–	262-264	68	$C_{19}H_{15}N_4OBr$	57.74 (57.23)	3.83 (3.76)	14.17 (14.03)
8a	C_6H_5	–	–	234-236	74	$C_{21}H_{18}N_4O_2S$	64.60 (64.06)	4.65 (4.49)	14.35 (14.23)
8b	*p*-$CH_3OC_6H_4$	–	–	238-240	68	$C_{22}H_{20}N_4O_3S$	62.84 (62.80)	4.79 (4.52)	13.32 (13.06)
8c	*p*-$NO_2C_6H_4$	–	–	233-235	72	$C_{21}H_{17}N_5O_4S$	57.92 (57.50)	3.93 (3.69)	16.08 (17.70)
8d	*p*-$C_2H_5OC_6H_4$	–	–	241-243	70	$C_{23}H_{22}N_4O_3S$	63.58 (63.17)	5.10 (4.91)	12.89 (12.39)
8e	*p*-ClC_6H_4	–	–	244-246	74	$C_{21}H_{17}N_4O_2SCl$	59.36 (58.64)	4.03 (3.98)	13.19 (12.89)
8f	*o*-BrC_6H_4	–	–	238-240	68	$C_{21}H_{17}N_4O_2SBr$	53.74 (53. 23)	3.65 (3.16)	11.94 (11.03)
8g	*o*-$(OH)_2C_6H_3$	–	–	234-236	56	$C_{21}H_{18}N_4O_4S$	59.70 (58.23)	4.29 (4.01)	13.26 (13.03)
9a	C_6H_5	–	–	274-276	56	$C_{19}H_{16}N_4O_2$	68.66 (68.46)	4.85 (4.69)	16.86 (16.43)
9b	*p*-$CH_3OC_6H_4$	–	–	278-280	74	$C_{20}H_{18}N_4O_3$	66.29 (66.10)	5.01 (4.92)	15.46 (15.06)
9c	*p*-$NO_2C_6H_4$	–	–	277-279	68	$C_{19}H_{15}N_5O_4$	60.47 (60.20)	4.01 (3.89)	18.56 (18.20)
9d	*p*-ClC_6H_4	–	–	274-276	72	$C_{19}H_{15}N_4O_2Cl$	62.21 (62.17)	4.12 (3.91)	15.27 (15.19)
10a	C_6H_5	–	–	284-286	70	$C_{19}H_{14}N_4O$	72.60 (72.46)	4.49 (3.99)	17.82 (17.43)
10b	*p*-$CH_3OC_6H_4$	–	–	273-275	74	$C_{20}H_{16}N_4O_2$	69.76 (69.50)	4.68 (4.52)	16.27 (16.06)
10c	*p*-$NO_2C_6H_4$	–	–	279-281	68	$C_{19}H_{13}N_5O_3$	63.51 (63.30)	3.65 (3.49)	19.49 (18.70)
10d	*p*-ClC_6H_4	–	–	281-283	72	$C_{19}H_{13}N_4OCl$	65.43 (65.17)	3.76 (3.21)	16.06 (15.39)

N'-Acetyl/benzoyl-2-cyclopropyl-[1,8]-naphthyridine-3-carbohydrazides (9a): To a solution of 2-cyclopropyl-[1,8]-naphthyridine-3-carboxylic acid ethyl ester (**2**) (0.01 mol) in ethanol (10 mL) was added benzoyl chloride (0.01 mol) dropwise at room temperature. The solution was refluxed for *ca.* 3-4 h, reaction was monitored by TLC. After completion of reaction it was poured in to crushed ice. Solid obtained was filtered and recrystallized from ethanol to provide (**9a**) Yield: 74 %. IR (KBr, ν_{max}, cm^{-1}): 3420, 3385 (2NH), 2265 (aliph. CH_2), 1710, 1690 (2CO); ^{1}H NMR (500 MHz, DMSO-d_6) δ: 0.94 (m, 4H, *J* = 20 Hz, $2CH_2$), 1.13 (m, 1H, *J* = 20 Hz, CH), 7.23 (m, 2H, CH), 7.31 (m, 2H, 2CH), 7.41, (m, 2H, *J* = 15 Hz, 2CH), 7.46 (s, 1H, CH), 7.52 (t, 1H, *J* = 15 Hz, CH), 8.26 (s, 1H, CH,), 8.38 (s, 1H, CH), 9.12 (s, 1H, CH), 9.21 (s, 2H, 2NH), 9.26 (s, 1H, CH), Mass (m/z): 333 [M+1].

4-Methoxy benzoic acid N'-(2-cyclopropyl-[1,8]-naphthyridine-3-carbonyl)-hydrazide (9b): Recrystallized from ethanol provide (**9b**) as off white solid, yield: 68 %. IR (KBr, ν_{max}, cm^{-1}): 3425, 3395 (2NH), 2255 (aliph. CH_2), 1710, 1700 (2CO); ^{1}H NMR (500 MHz, DMSO-d_6) δ: 0.99 (m, 4H, *J* = 20 Hz, $2CH_2$), 1.23 (m, 1H, *J* = 20 Hz, CH), 3.46 (s, 3H, CH_3), 7.21 (m, 2H, CH), 7.46 (m, 2H, CH), 7.72 (m, 2H, *J* = 15 Hz, CH), 7.96 (s, 1H, CH), 8.36 (s, 1H, CH), 8.58 (s, 1H, CH), 9.22 (s, 1H, CH), 9.31 (s, 1H, NH), 9.386 (s, 1H, CH), 9.28 (s, 1H, NH) Mass (m/z): 363 [M+1].

4-Nitro benzoic acid N'-(2-cyclopropyl-[1,8]-naphthyridine-3-carbonyl)-hydrazide (9c): Recrystallized from ethanol provide (**9c**) as brown colour solid, yield: 72 %. IR (KBr, ν_{max}, cm^{-1}): 3425, 3395 (2NH), 2285 (aliph. CH_2), 1700, 1690 (2CO); ^{1}H NMR (500 MHz, DMSO-d_6) δ: 0.98 (m, 4H, *J* = 20 Hz, $2CH_2$), 1.24 (m, 1H, *J* = 20 Hz, CH), 7.21 (m, 2H, 2CH), 7.44 (m, 2H, CH), 7.72 (m, 1H, *J* = 15 Hz, CH), 7.96 (s, 1H, CH), 8.36 (s, 1H, NH), 8.58 (s, 1H, CH), 9.38 (s, 1H, CH), 9.28 (s, 1H, NH) Mass (m/z): 378 [M+1].

4-Chloro benzoic acid N'-(2-cyclopropyl-[1,8]-naphthyridine-3-carbonyl)-hydrazide (9d): Recrystallized from ethanol provide (**9d**) as light green colour solid, yield: 70 %. IR (KBr, ν_{max}, cm^{-1}): 3395, 3375 (2NH), 2265 (aliph. CH_2), 1725, 1710 (2CO); ^{1}H NMR (500 MHz, DMSO-d_6) δ: 0.91(m, 4H, *J* = 20 Hz, $2CH_2$), 1.14 (m, 1H, *J* = 20 Hz, CH), 7.24 (m, 2H, 2CH), 7.48 (m, 2H, CH), 7.71, (m, 1H, *J* = 15 Hz, CH), 7.98 (s, 1H, CH), 8.36 (s, 1H, NH), 8.54 (s, 1H, CH), 9.34 (s, 1H, CH), 9.18 (s, 1H, NH) Mass (m/z): 367 [M+1].

2-Cyclopropyl-3-(5-phenyl-[1,3,4]-oxadiazol-2-yl)-[1,8]-naphthyridine (10a): To a solution of compound (**9a**) (0.01 mol) in $POCl_3$ (5 mL), was stirred for *ca.* 5-6 h at 70 °C. The reaction mass was poured on crushed ice. The solid was filtered and washed with aq. $NaHCO_3$ solution and recrystallized in ethyl acetate in hexane to afford (**10a**) yield: 74 %, IR (KBr, ν_{max}, cm^{-1}): 2265 (aliph. CH_2); ^{1}H NMR (500 MHz, DMSO-d_6) δ: 0.96 (m, 4H, *J* = 20 Hz, $2CH_2$), 1.12 (m, 1H, *J* = 20 Hz, CH), 7.26 (m, 2H, 2CH), 7.32 (m, 2H, 2CH), 7.41 (m, 2H, *J* = 15 Hz, 2CH), 7.76 (s, 1H, CH), 7.72 (t, 1H, *J* = 15 Hz, CH), 8.26 (s, 1H, CH), 8.38 (s, 1H, CH), 9.12 (s, 1H, CH), ^{13}C NMR (500 MHz, DMSO-d_6/TMS) δ: 6.9 ($2CH_2$), 7.3(CH),

121.8, 122.2 (2CH), 132.7, 132.9, 133.4, 134.5, 134.9, 135.6 (6CH), 144.6, 145.2 (2CH), 165.6 (1CH), 166.3 (1CH), Mass (m/z): 315 [M+1].

2-Cyclopropyl-3-[5-(4-methoxy phenyl)-[1,3,4]-oxadiazol-2-yl]-[1,8]-naphthyridine (10b): Light brown colour solid, yield: 68 %, ^{1}H NMR (500 MHz, DMSO-d_6) δ: 0.94 (m, 4H, J = 20 Hz, 2CH_2), 1.12 (m, 1H, J = 20 Hz, CH), 3.92 (s, 3H, CH_3), 7.26 (m, 2H, 2CH), 7.35 (m, 2H, 2CH), 7.41 (m, 1H, J = 15 Hz, CH), 7.76 (s, 1H, CH), 7.72 (t, 1H, J = 15 Hz, CH), 8.26 (s, 1H, CH), 9.02 (s, 1H, CH), ^{13}C NMR (500 MHz, DMSO-d_6/TMS) δ: 6.4 (2CH_2), 7.1(CH), 67.3 (1CH), 122.8, 124.2 (2CH), 133.7, 134.9, 135.4, 136.5, 136.9, 137.6 (6CH), 146.6, 147.2 (2CH), 164.6 (1CH), 166.2 (1CH), Mass (m/z): 345 [M+1].

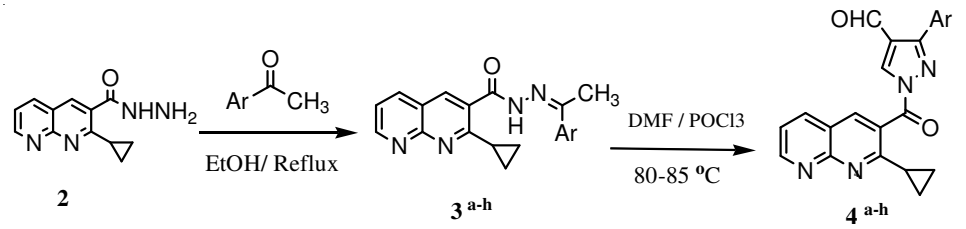
2-Cyclopropyl-3-[5-(4-nitro phenyl)-[1,3,4]-oxadiazol-2-yl]-[1,8]-naphthyridine (10c): Light brown colour solid, yield: 72 %, ^{1}H NMR (500 MHz, DMSO-d_6) δ: 0.94 (m, 4H, J = 20 Hz, 2CH_2), 1.12 (m, 1H, J = 20 Hz, CH), 3.92 (s, 3H, CH_3), 7.26 (m, 2H, 2CH), 7.35 (m, 2H, 2CH), 7.41 (m, 1H, J = 15 Hz, CH), 7.76 (s, 1H, CH), 7.72 (t, 1H, J = 15 Hz, CH), 8.26 (s, 1H, CH), 9.02 (s, 1H, CH), ^{13}C NMR (500 MHz, DMSO-d_6/TMS) δ: 6.2 (2CH_2), 6.8 (CH), 119.8, 120.1 (2CH), 131.7, 132.4, 133.2, 134.9, 135.3, 135.8 (6CH), 141.6, 142.2 (2CH), 164.6, (1CH), 166.3 (1CH), Mass (m/z): 360 [M+1].

3-[5-(4-Chloro phenyl)-[1,3,4]-oxadiazol-2-yl]-2-cyclopropyl-[1,8]-naphthyridine (10d): Light brown colour solid, yield: 70 %, ^{1}H NMR (500 MHz, DMSO-d_6) δ: 0.94 (m, 4H, J = 20 Hz, 2CH_2), 1.12 (m, 1H, J = 20 Hz, CH), 3.92 (s, 3H, CH_3), 7.26 (m, 2H, 2CH), 7.35 (m, 2H, 2CH), 7.41 (m, 1H, J = 15 Hz, CH), 7.76 (s, 1H, CH), 7.72 (t, 1H, J = 15 Hz, CH), 8.26 (s, 1H, CH), 9.02 (s, 1H, CH), ^{13}C NMR (500 MHz, DMSO-d_6/TMS) δ: 6.7 (2CH_2), 7.4 (CH), 129.8, 130.1 (2CH), 134.7, 135.4, 136.2, 136.9, 137.3, 138.8 (6CH), 144.6, 145.2 (2CH), 168.6 (1CH), 169.3 (1CH), Mass (m/z): 349 [M+1].

RESULTS AND DISCUSSION

The chemistry of 1,8-naphthyridine derivatives continues to draw the attention of synthetic organic chemists due to their varied biological activities (**3d-e**). Studies on the synthesis of 1,8-naphthyridines have served as a fertile field of research in the perusal for antibacterial agents. Many 1,8-naphthyridine compounds have demonstrated important antibacterial activity (**3d-e**) and (**8a-c**). The actual resurgence of interest in naphthyridines and related compounds has resulted in an enormous account of research on new structural modifications to improve the overall spectrum of antibacterial activity. Herein, the preparation of various substituted 1,8-naphthyridines with a potentially biological interest are reported. Aromatic amino aldehyde are valuable starting material for a wide variety of N-heterocyclic compounds. Annelation reactions with heterocyclic amino aldehydes provide synthetic entry into new heterocyclic systems attached to naphthyridine. The general synthetic procedure used in the preparation of these compounds involved the Friedlander condensation of 2-amino-pyridine-3-carbaldehyde with 3-cyclopropyl-3-oxo-pro-

pionic acid ethyl ester gives 2-cyclopropyl-[1,8]-naphthyridine-3-carboxylic acid ethyl ester in ethanol piperidine as base. In this work, 2-amino-3-carboxaldehyde is valuable starting material for a wide variety of nitrogen containing heterocyclic compounds. A series of naphthyridine derivatives which possessed excellent broad-spectrum activity against gram-positive and gram-negative bacteria as well as good pharmacokinetic properties have been reported in this paper.



Scheme-I

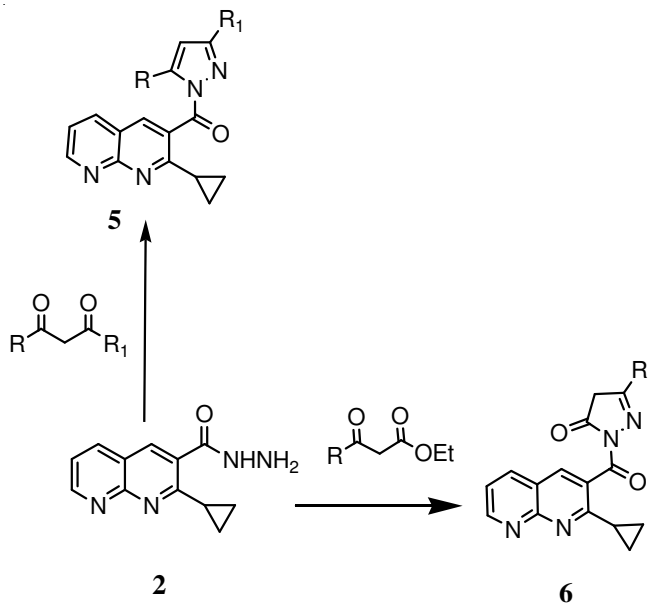
Formation of **4a-h** can be accounted for by reaction of **2** with substituted acetophenones in ethanol, refluxed for *ca.* 4 h to provide Schiff bases (**3a-h**) which on further treatment with Vills-Maier-Haack reagent yielded **3a-h** (**Scheme-II**).

In order to construct new derivatives of the interesting 1,8-naphthyridines of type **5** and **6**, that are cyclization at the hydrazine nitrogens of (**2**) by reaction with β-diketones in ethanol/methanol, containing catalytic amount of conc. HCl, we attempted reaction of the compound carboxylic acid hydrazide (**2**), with 1,3-diketones containing catalytic amount of conc. HCl in ethanol, refluxing for *ca.* 3 h to provide compound (**5a-d**). On the other hand, carboxylic acid hydrazide (**2**), with β-ketoesters in ethanol, refluxing for *ca.* 3-4 h to provide compound (**6a-d**) in good yields.

In order to extend the scope of this reaction, carboxylic acid hydrazide (**2**), is made to react with aromatic aldehydes in ethanol to yield Schiff base (**7a-g**) with high yields and purity, which on cyclization by using mercapto acetic acid and anhydrous $ZnCl_2$ in ethanol refluxing to give cyclized products (**8a-g**) in good yiels.

Carboxylic acid hydrazide (**2**) reacts with aromatic acid chlorides in ethanol to give N-Acyl compounds (**9a-d**), with high yields. Cyclization of **9a-d** by using $POCl_3$ yielded the products (**10a-d**), in good yields.

Antimicrobial activity: The compounds were dissolved in DMSO at a concentration of 1 mg/mL. Sterile nutrient agar (oxoid) was incubated with the organisms tested. Each 100 mL of the medium received 1 mL of 24 h broth culture and 3 drops of the test compounds were placed separately in cups (8 mm diameter) cut in the agar. The plates were incubated at 37 ºC for 24 h, DMSO as a blank showed no inhibition zone. A solution of 0.1 % of penicillin G or streptomycin sulfate in DMSO was used as the standard for gram-positive and gram-negative bacteria, respectively. The resulting inhibition zone diameters were measured in mm.



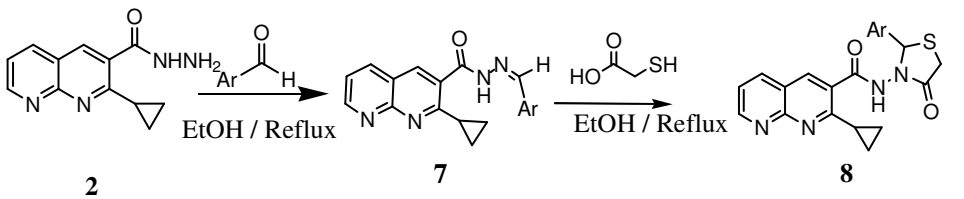
5

2 **6**

5a. R = CH_3, $R_1 = CH_3$
5b . R = C_2H_5 , $R_1 = C_2H_5$
5c. R = CF_3, $R_1 = CH_3$
5d. R = C_6H_5, $R_1 = C_6H_5$

6a. R = CH_3
6b. R = C_3H_5
6c. R = CF_3
6d. R = C_6H_5

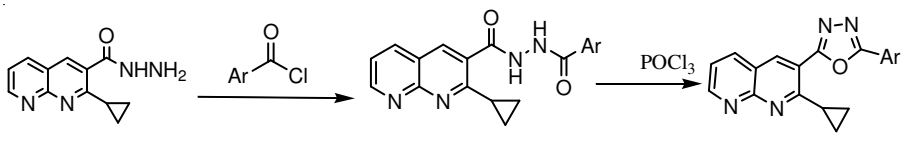
Scheme-II



2 **7** **8**

Ar = C_6H_5, p-$OCH_3C_6H_4$, p-$NO_2C_6H_4$, p-$C_2H_5OC_6H_4$,p-Cl C_6H_4, p-Br C_6H_4, o-$(OH)_2$ C_6H_3

Scheme-III



2 **9** **10**

Ar = C_6H_5 , p-$OCH_3C_6H_4$, p-$NO_2C_6H_4$, p-ClC_6H_5

Scheme-IV

The new 1,8-naphthyridine derivatives were evaluated *in vitro* for their antibacterial activity against *S. aureus*, *Klebsiella pneumoniea*, *E. coli, Salmonella paratyphi A*, *Salmonella paratyphi B*, *Micrococcus luteus* as Gram-positive bacteria and Gram-negativebacteria (Table-2). The results of the biological evaluation indicate that all the compounds tested were moderate active than the reference standards. Compound **4d, e, f** and **h**, **5a, c & d** and **6b, c** and **d** possessed a good activity with an MIC value of 15-17 and compounds **8b, c, e** and **f**, **10b, c, d** possessed a moderate activity with MIC values from 10 to 15 and compounds **4a, b & c, 5b, 6a** and **10a** have reasonable activity and some compounds in Table-2 showed a poor activity and some are to be inactive.

TABLE-2
INHIBITION ZONE (mm) AGAINST

Compd.	*S. aureus*	*E. coli*	*Klebsiella pneumoniae*	*Salmonella paratyphi A*	*Salmonella paratyphi B*	*Micrococcus luteus*
1	11	10	4	6	4	9
2	1	4	-	8	7	5
3a	17	7	5	-	6	13
3b	-	8	3	2	-	-
3c	17	-	15	12	-	9
3d	2	4	8	6	8	6
3e	15	12	10	6	12	16
3f	9	8	5	8	8	17
3g	5	6	4	-	-	2
3h	12	8	12	6	10	14
4a	8	10	-	10	4	2
4b	4	8	-	6	8	5
4c	-	4	-	-	2	10
4d	7	14	10	6	14	16
4e	8	4	-	-	6	10
4f	9	8	12	8	14	17
4g	5	4	-	-	6	3
4h	15	17	10	8	14	10
5a	10	6	-	4	-	8
5b	8	8	-	6	2	4
5c	2	4	-	-	8	7
5d	8	6	-	-	6	10
6a	-	8	-	5	-	10
6b	10	6	-	4	-	8
6c	8	4	-	6	2	4
6d	10	2	--	8	5	12
7a	2	3	-	-	8	7
7b	8	10	-	-	6	10
7c	-	8	5	-	-	6
7d	2	6	-	-	3	3
7e	4	3	--	--	4	5

7f	4	--	10	--	5	3
7g	2	8	3	4	9	8
8a	16	10	8	5	12	10
8b	10	8	10	4	16	8
8c	12	8	8	6	2	16
8d	2	5	-	8	6	17
8e	8	3	--	--	4	9
8f	12	--	10	--	5	3
8g	14	12	8	4	10	8
9a	3	4	-	-	6	6
9b	-	4	5	-	-	6
9c	5	7	-	-	6	3
9d	-	10	-	5	-	10
10a	10	6	-	4	-	8
10b	8	6	-	6	2	4
10c	2	4	-	-	8	7
10d	8	10	-	-	6	10

On the basis of these results the 1,8-naphthyridine derivatives seem to be more active against *S. aureus* and *E. coli* than *Klebsiella pneumoniea*. All the compounds reported in Table-2 were tested for their antimicrobial activity against the bacteria *Staphylococas aureus*, *Micrococcus luteus*, *E. coli*, *Klebsiella pneumoniea*, *Salmonella paratyphi A*, *Salmonella paratyphi B*, *Micrococcus luteus*.

ACKNOWLEDGEMENTS

The authors are thankful to Management and Principal of KITS and to the Management, Director, Principal and Head, Department of Science and Humanities of SNIST for providing research facilities, grants and for their encouragement.

REFERENCES

1. H.V. Patel, P.S. Fernandes, S.P. Pandey and K.A. Vyas, *Indian J. Chem.*, **29B**, 135 (1990).
2. H. Egawa, A. Miyamido, Y. Nishimra, H. Okada, H. Uno and J. Matsumato, *J. Med. Chem.*, **27**, 1543 (1984).
3. S. Jyoti, *Trends Microbiol.*, **9**, 255 (2001).
4. M.T. Chary, K. Mogilaiah and B. Sreenivasulu, *J. Indian Chem. Soc.*, **64**, 488 (1987).
5. K. Mogilaiah, K.V. Reddy and B. Sreenivasulu, *Indian J. Chem.*, **22B**, 178 (1983).
6. N. Suzuki and R. Dohmori, *Chem. Pharma. Bull.*, **27**, 410 (1979).
7. N. Suzuki, *Chem. Pharma. Bull.*, **28**, 761 (1980).
8. H. Egawa, T. Miyamoto, A. Minamida, Y. Nishimura, H. Okada, H. Uno and J. Matsumoto, *J. Med. Chem.*, **27**, 1543 (1984).
9. S.R. Jain and A. Kar, *Planta Med.*, **20**, 118 (1971).
10. F. Al-Omran, R.M. Mohareb and A.A. El-Khair, *J. Heterocycl. Chem.*, **39**, 877 (2002).
11. R. Nandhakumar, H. Vishwanathan, T. Suresh and P.S. Mohan, *Fitoterapia*, **73**, 734 (2002).
12. R. Karvembu and K. Natarajan, *Polyhedron*, **21**, 219 (2002).
13. M. Venugopal and P.T. Perumal, *Synth. Commun.*, **21**, 515 (1991).
14. K. Dinakaran and P.T. Perumal, *Indian J. Chem.*, **39B**, 135 (2000).
15. A.R. Katritzky, M. Charles and M. Marson, *J. Am. Chem. Soc.*, **105**, 3279 (1983).
16. J.M. Quintela, J. Vilar, C. Peinador, C. Veiga and V. Ojea, *Heterocycles*, **41**, 1001 (1995).

(*Received*: 22 October 2008; *Accepted*: 5 August 2009) AJC-7707