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An Expeditious Synthesis of Some Novel N-Pyridyl-1,4-dihydro-4-oxo-3-quinoline Carboxylic Acids/Amides as Potential CB_2 Cannabinoid Receptor Agonists

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An expeditious synthesis of novel N-pyridyl-1,4-dihydro-4-oxo-3-quinoline carboxylic acids (**9a-e**) in 5 steps and N-pyridyl-4-oxo-1,4-dihydroquinoline-3-carboxamides (**1a-m**) were developed in six steps from a commercially available 2-bromo benzoic acid.

Key Words: Quinoline carboxylic acids, Quinoline carboxamides, Cannabinoid receptor agonists, 2-Bromobenzoic acid.

INTRODUCTION

From pharmacological point of view, up to now, a few compounds were reported that are selective for the CB_2 cannabinoid receptor subtype such as biarylpyrazoles (*e.g.*, SR-144528), 1,2-dihydro quinoline-3-carboxamide[1], 1,8-naphthyridines[2] and triaryl *bis*-sulfones[3]. In recent reports pharmacological characterization and molecular modeling studies of 4-oxo-1,4-dihydro quinoline-3-carboxamide derivatives have been reported as a new class of heterocyclic derivatives, acting as potent CB_2-selective receptor ligands[4]. In addition, 1,4-dihydro-4-oxo-3-quinoline carboxylic acids (ciprofloxacin, norfloxacin, sparfloxacin, ofloxacin *etc*.) are well known antibacterial/antifungal agents[5].

The cannabinoid receptors are a class of cell membrane receptors under the G-protein coupled receptor super family. Cannabinoid receptors are activated by ligands, which are lipid compounds known collectively as cannabinoids. There are two sub types, termed CB_1 and CB_2. Selective cannabinoid CB_1 receptor antagonists are currently under investigation for the treatment of obesity and the associated metabolic syndrome[6]. The cannabinoid CB_2 receptors are mainly expressed on T cells of the immune system, on macrophages and B cells and in hematopoietic cells. They also have a function in keratinocytes. The endocannabinoid system through CB_2 signaling plays a key role in the maintenance of bone mass. CB_2 is expressed in osteoblasts, osteocytes and osteoclasts. CB_2 agonists enhance endocortical osteoblast number and activity while restraining trabecular osteoclastogenesis. Another important effect is that CB_2 agonists attenuate ovariectomy-induced bone loss while increasing cortical thickness. These findings suggest CB_2 offers a potential molecular target for the diagnosis and treatment of osteoporosis. It was recently shown that low doses of Δ^9-THC (tetrahydrocannabinol) could reduce atherosclerosis in mice by acting at the CB_2 cannabinoid receptor. Cannabinoid agonists that selectively target CB_2 cannabinoid receptors should be devoid of psychoactive effects and also CB_2 cannabinoid receptors participate in the control of peripheralpain[7], inflammation, cough and cancer proliferation[8]. It also has an antifibrogenic role in the liver. Moreover, the recent discovery of the presence of the CB_2 cannabinoid receptors in the brain microglial cells[9] gave a rationale for prevention of Alzheimer's disease pathology by cannabinoid agents. Indeed, it was shown that CB_2 cannabinoid receptor agonists might provide neuroprotection by blockade of microglial activation[10].

Several synthetic routes have been reported for generation of quinolinone skeleton. Using tri alkyl phosphates for the alkylation of quinolinone carboxylic acids[11], reaction of aniline with 2-ethoxymethylene-malonic acid derivative[12], clay catalyzed synthesis of 2-(2,2,2-trichloro)ethylidine-3-oxo-3-(2-chlorophenyl)propionate[13]. Herein, we report a general, high yielding and scalable synthetic route for novel N-pyridyl-1,4-dihydro-4-oxo-3-quinoline carboxylic acid/amide derivatives from commercially available 2-bromo benzoic acid (**2**).

EXPERIMENTAL

Ethyl 3-(2-bromophenyl)-2-[(dimethylamino)methylene]-3-oxopropanoate (6): A mixture of 2-bromo benzoic acid (**2**) (5 g, 0.025 mol), dimethyl formamide (0.5 mL) and thionyl chloride (32 g, 0.270 mol) in dichloromethane (50 mL) was

stirred at room temperature for 3 h. Resulting mixture was evaporated under reduced pressure and dry tetrahydrofuran (20 mL) was added (solution A). A mixture of potassium salt of malonic acid ethyl ester (12.82 g, 0.075 mol), triethylamine (7.6 g, 0.075 mol) in tetrahydrofuran (50 mL) was cooled to 0-10 ºC and magnesium chloride (3.4 g, 0.035 mol) was added at same temperature. The resulting mixture was stirred at room temperature for 7-8 h. A solution of freshly prepared bromobenzoyl chloride (**3**) (solution A) was added dropwise maintaining the temperature at 0 ºC and reaction mixture was stirred overnight at room temperature. After completion of reaction, the reaction mass was quenched with 1N hydrochloric acid at 20 ºC and the product was extracted with ethyl acetate. The organic layer was washed with saturated sodium bicarbonate solution and brine solution. The organic layer was dried over anhydrous sodium sulfate and then organic layer was evaporated under reduced pressure to get ethyl 3-(2-bromophenyl)-3-oxopropanoate (**5**) as viscous syrup (3.74 g, 55 % yield). A mixture of ethyl 3-(2-bromophenyl)-3-oxopropanoate (**5**) (3.5 g, 0.012 mol) and N,N-dimethyl formamide dimethyl acetal (1.84 g, 0.015 mol) was stirred at room temperature under nitrogen. The resulting mixture was stirred at 50 ºC under nitrogen atmosphere for 1 h. After completion of the reaction, reaction mixture was concentrated under reduced pressure to get viscous material which was purified by column chromatography using ethyl acetate and hexane (25:75), to get pure ethyl-3-(2-bromophenyl)-2-[(dimethylamino)methylene]-3-oxopropanoate (**6**) (2.5 g, 60 % yield) as viscous syrup.

Ethyl 3-(2-bromophenyl)-2-[(dimethylamino)methylene]-3-oxopropanoate (6): ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.76 (t, *J* = 7.1 Hz, 3H), 2.83 (s, 3H), 3.30 (s, 3H), 3.71-3.79 (q, *J* = 7.1 Hz, 2H), 7.10-7.30 (m, 3H), 7.55 (m, 1H), 7.69 (s, 1H); ESI-MS m/z. 328 $(M + H)^+$.

General procedure for ethyl 4-oxo-1-(2-,3- or 4-pyridyl)-1,4-dihydroquinoline-3-carboxylate (8a-c): A solution of product (**6**) (1 g, 0.003 mol) in acetonitrile (10 mL) was stirred at room temperature. Selected amine (0.003 mol) and triethylamine or cesium carbonate (0.015 mol) were added, resulting mixture was stirred for 3 h at reflux and reaction mixture was evaporated under reduced pressure. The residue was dissolved in ethyl acetate and washed with water and brine. The organic layer was dried over sodium sulfate and concentrated. The residue was purified by column chromatography using dichloromethane: methanol (98:2) as eluent to afford the corresponding compound (**8a-c**) as solids.

Ethyl 4-oxo-1-(2-pyridyl)-1,4-dihydroquinoline-3-carboxylate (8a): m.p. 158-160 ºC; IR (KBr, ν_{max}, cm^{-1}): 3370, 3186, 2978, 1726, 1693, 1626, 1553 and 1482; ^{1}H NMR (300 MHz, DMSO-d_6): δ 1.24 (t, *J* = 7.2 Hz, 3H), 4.20 (q, *J* = 7.2 Hz, 2H), 7.14 (d, *J* = 8.7 Hz, 1H), 7.51 (t, *J* = 7.2 Hz, 1H), 7.62-7.70 (m, 2H), 7.82 (d, *J* = 7.8 Hz, 1H), 8.18 (td, *J* = 7.8 Hz, 1.8, 1H), 8.28 (dd, *J* = 8.1 Hz, 1.2 Hz, 1H), 8.63 (s, 1H), 8.72 (d, *J* = 4.2 Hz, 1H); ESI-MS m/z. 295 $(M + H)^+$, 317 $(M + Na)^+$ and 333 $(M + K)^+$.

Ethyl 4-oxo-1-(3-pyridyl)-1, 4-dihydroquinoline-3-carboxylate (8b): m.p. 212-218 ºC; IR (KBr, ν_{max}, cm^{-1}): 3446, 3046, 1725, 1693, 1633, 1554 and 1479; ^{1}H NMR (300 MHz, DMSO-d_6): δ 1.24 (t, *J* = 7.2 Hz, 3H), 4.19 (q, *J* = 7.2 Hz, 2H), 6.93 (d, *J* = 8.4 Hz, 1H), 7.48 (t, *J* = 7.2 Hz, 1H), 7.61-7.72 (m, 2H), 8.16 (d, *J* = 8.1 Hz, 1H), 8.27 (dd, *J* = 8.1 Hz, 1.2 Hz, 1H), 8.52 (s, 1H), 8.82 (dd, *J* = 4.5 Hz, 1.2 Hz, 1H), 8.86 (d, *J* = 2.4 Hz, 1H); ESI-MS m/z. 295 $(M + H)^+$.

Ethyl 4-oxo-1-(4-pyridyl)-1,4-dihydroquinoline-3-carboxylate (8c): m.p. 240-242 ºC; IR (KBr, ν_{max}, cm^{-1}): 3425, 3056, 1724, 1629, 1555 and 1477; ^{1}H NMR (300 MHz, DMSO-d_6): δ 1.24 (t, *J* = 7.1 Hz, 3H), 4.18-4.21 (q, *J* = 7.1 Hz, 2H), 7.06 (d, *J* = 8.4 Hz, 1H), 7.5 (t, *J* = 7.1 Hz, 1H), 7.65 (t, *J* = 7.1 Hz, 1H), 7.74 (d, *J* = 7.8 Hz, 2H), 8.28 (d, *J* = 8.0 Hz, 1H), 8.49 (s, 1H), 8.88 (m, 2H); ESI-MS m/z. 295 $(M + H)^+$.

General procedure for ethyl 3-(2-bromophenyl)-2-(4-phenylbutyl-2-amino/4-pyridinemethylamino)-3-oxo propanoate (7d or 7e): A stirred solution of 3-(2-bromophenyl)-2-[(dimethylamino)methylene]-3-oxopropanoate (**6**) (1 g, 0.003 mol), selected amine (0.003 mol) and base (cesium carbonate or triethylamine) (0.006 mol) in acetonitrile (10 mL) was refluxed for 5-6 h. After completion of reaction, the reaction mixture was concentrated under reduced pressure. The residue obtained was purified by column chromatography using ethyl acetate and hexane as an eluent to afford corresponding compound (**7d** or **7e**) as viscous syrup.

Ethyl 3-(2-bromophenyl)-2-[(4-phenylbutyl-2-amino)-methylene]-3-oxopropanoate (7d): ^{1}H NMR (300 MHz, DMSO-d_6): δ 0.79 (t, *J* = 7.2 Hz, 3H), 1.29 (d, *J* = 6.6 Hz, 3H), 1.89 (m, 2H), 2.58 (m, 2H), 3.78 (q, *J* = 7.2 Hz, 2H), 7.13-7.54 (m, 8H), 8.16 (m, 1H), 10.83 (m, 1H).

Ethyl 3-(2-bromophenyl)-2-[(4-pyridinmethyl amino)methylene]-3-oxopropanoate (7e): ^{1}H NMR (300 MHz, DMSO-d_6): δ 0.78 (t, *J* = 7.2 Hz, 3H), 3.78 (q, *J* = 7.2 Hz, 2H), 4.72 (d, *J* = 6.3 Hz, 2H), 7.17-7.36 (m, 5H), 7.52 (dd, *J* = 7.8 Hz, 1.2 Hz, 1H), 8.29 (m, 1H), 8.55 (m, 2H), 11.04 (m, 1H).

General procedure for ethyl 4-oxo-1-(1-methyl-3-phenylpropyl/4-pyridinemethyl)-1,4-dihydroquinoline-3-carboxylate (8d-e): A mixture of compound (**7d** or **7e**) (0.002 mol), cesium carbonate (0.0075 mol) and catalytic amount of copper iodide (0.25 mmol) was refluxed for 4 h in acetonitrile. After completion of the reaction resulting mixture was filtered and filtrate was concentrated under reduced pressure. The residue obtained was purified by column chromatography using dichloromethane:methanol (99:1) as an eluent to afford the corresponding compound (**8d-e**).

Ethyl 4-oxo-1-(1-methyl-3-phenylpropyl)-1,4-dihydroquinoline-3-carboxylate (8d): Compound was isolated as liquid. IR (KBr, ν_{max}, cm^{-1}): 3455, 3061, 1726, 1689, 1630, 1553 and 1488; ^{1}H NMR (300 MHz, DMSO-d_6): δ 1.27 (t, *J* = 7.2 Hz, 3H), 1.52 (d, *J* = 6.3 Hz, 3H), 2.18 (m, 2H), 2.55 (m, 2H), 4.21 (q, *J* = 7.2 Hz, 2H), 4.93 (d, *J* = 6.4 Hz, 1H), 7.11-7.24 (m, 5H), 7.45 (t, *J* = 7.2 Hz, 1H), 7.73 (td, *J* = 8.1 Hz, 1.5 Hz, 1H), 7.82 (d, *J* = 9.0 Hz, 1H), 8.26 (dd, *J* = 8.1 Hz, 1.5 Hz, 1H), 8.59 (s, 1H); ESI-MS m/z. 350 $(M + H)^+$.

Ethyl 4-oxo-1-(4-pyridinemethyl)-1,4-dihydroquinoline-3-carboxylate (8e): Compound was isolated as solid. m.p. 178-182 ºC; IR (KBr, ν_{max}, cm^{-1}): 3426, 3048, 1720, 1679, 1644, 1555 and 1489; ^{1}H NMR (300 MHz, DMSO-*d*6): δ 1.27 (t, *J* = 7.2 Hz, 3H), 4.22 (q, *J* = 7.2 Hz, 2H), 5.72 (s, 2H), 7.16 (d, *J* = 6.0 Hz, 2H), 7.39-7.47 (m, 2H), 7.64 (t, *J* = 7.8 Hz, 1H), 8.24 (d, *J* = 7.8 Hz, 1H), 8.50 (d, *J* = 4.5 Hz,

2H), 8.90 (s, 1H); ESI-MS m/z. 309 $(M + H)^+$ and 331 $(M + Na)^+$.

General procedure for 4-oxo-1-(2-,3- or 4-pyridyl/ 1-methyl-3-phenylpropyl/4-pyridinemethyl)-1,4-dihydroquinoline-3-carboxylic acid (9a-e): A mixture of product (**8a-e**) (0.003 mol) in 10 % aqueous sodium hydroxide solution (10 vol) was refluxed for 3 h. After cooling, resulting mixture was neutralized with hydrochloric acid and then extracted with ethyl acetate. The organic layer was dried over sodium sulfate and concentrated under reduced pressure. Crude product was washed with dichloromethane and methanol (1:1) mixture to afford the corresponding compound (**9a-e**) as solids.

4-Oxo-1-(2-pyridyl)-1, 4-dihydroquinoline-3-carboxylic acid (9a): Compound was isolated as a sodium salt, m.p. 265-266 ºC; IR (KBr, ν_{max}, cm^{-1}): 3442, 3049, 1731, 1613, 1551, 1512 and 1477; ^{1}H NMR (300 MHz, D_2O): δ 7.13 (d, *J* = 8.7 Hz, 1H), 7.44 (t, *J* = 7.8 Hz, 1H), 7.57-7.63 (m, 2H), 8.10 (td, *J* = 7.8 Hz, 1.5 Hz, 1H), 8.25 (d, *J* = 7.2 Hz, 1H), 8.41 (s, 1H), 8.55 (d, *J* = 3.6 Hz, 1H); ^{13}C NMR (75 MHz, D_2O): δ 117.5, 118.5, 122.3, 125.4, 125.7, 125.8, 126.3, 132.9, 139.4, 141.2, 145.5, 149.5, 151.8, 168.4, 172.3, 177.4; ESI-MS m/z. 267 $(M + H)^+$ and 289 $(M + Na)^+$. Anal. calcd. (%) for $C_{15}H_{10}N_2O_3$: C, 67.67; H, 3.79; N, 10.52. Found (%): C, 67.58; H, 3.81; N, 10.53.

4-Oxo-1-(3-pyridyl)-1, 4-dihydroquinoline-3-carboxylic acid (9b): Compound was isolated as a sodium salt, m.p.: 262-263 ºC; IR (KBr, ν_{max}, cm^{-1}): 3445, 3028, 1730, 1617, 1549, 1506 and 1474; ^{1}H NMR (300 MHz, D_2O): δ 7.04 (d, *J* = 8.7 Hz, 1H), 7.42 (t, *J* = 7.8 Hz, 1H), 7.55 (t, *J* = 8.4 Hz, 1H), 7.60-7.65 (m, 1H), 7.95 (d, *J* = 8.4 Hz, 1H), 8.23 (d, *J* = 8.1 Hz, 1H), 8.31 (s, 1H), 8.60 (d, *J* = 2.4 Hz, 1H), 8.65 (d, *J* = 5.1 Hz, 1H); ^{13}C NMR (75 MHz, D_2O): δ 120.1, 120.9, 127.9, 128.4, 129.0, 135.5, 139.0, 140.0, 142.8, 149.3, 149.8, 152.6, 170.9, 174.7, 179.7, 183.9; ESI-MS m/z. 267 $(M + H)^+$ and 289 $(M + Na)^+$. Anal. calcd. (%) for $C_{15}H_{10}N_2O_3$: C, 67.67; H, 3.79; N, 10.52. Found (%): C, 67.68; H, 3.71; N, 10.50.

4-Oxo-1-(4-pyridyl)-1, 4-dihydroquinoline-3-carboxylic acid (9c): Compound was isolated as a sodium salt, m.p. 276-280 ºC; IR (KBr, ν_{max}, cm^{-1}): 3411, 3030, 1739, 1612, 1550, 1507 and 1466; ^{1}H NMR (300 MHz, D_2O): δ 7.18 (d, *J* = 8.7 Hz, 1H), 7.44 (d, *J* = 7.8 Hz, 1H), 7.56 (m, 3H), 8.25 (d, *J* = 8.1 Hz, 1H), 8.33 (s, 1H), 8.71 (d, *J* = 5.7 Hz, 2H); ^{13}C NMR (75 MHz, D_2O): δ 117.6, 118.9, 122.7, 125.5, 125.9, 126.5, 133.0, 139.4, 145.7, 148.6, 151.2, 168.3, 172.3, 177.2; ESI-MS m/z. 272 $(M + H)^+$ and 289 $(M + Na)^+$. nal. calcd. (%) for $C_{15}H_{10}N_2O_3$: C, 67.67; H, 3.79; N, 10.52. Found (%): C, 67.62; H, 3.65; N, 10.49.

4-Oxo-1-(1-methyl-3-phenylpropyl)-1,4-dihydroquinoline-3-carboxylic acid (9d): m.p. 107-110 ºC; IR (KBr, ν_{max}, cm^{-1}): 3425, 3027, 2933, 1717, 1615, 1547, 1515 and 1469 cm^{-1}; ^{1}H NMR (300 MHz, DMSO-d_6): δ 1.59 (d, *J* = 6.6 Hz, 3H), 2.26 (m, 2H), 2.6-2.8 (m, 2H), 5.1-5.2 (m, 1H), 7.07-7.20 (m, 5H), 7.65 (t, *J* = 7.5 Hz, 1H), 7.92 (t, *J* = 7.2 Hz, 1H), 8.08 (d, *J* = 8.7 Hz, 1H), 8.40 (d, *J* = 7.2 Hz, 1H), 8.86 (s, 1H), 15.2 (acid protan); ^{13}C NMR (75 MHz, DMSO-d_6): δ 20.2, 31.8, 37.1, 46.1, 56.0, 94.9, 108.3, 117.7, 126.0, 126.3, 126.5, 126.6, 128.5, 128.6, 134.6, 140.3, 140.9, 144.9, 166.3, 177.8; ESI-MS m/z. 322 $(M + H)^+$, 344 $(M + Na)^+$ and 360 $(M + K)^+$. Anal. calcd. (%) for $C_{20}H_{19}NO_3$: C, 74.75; H, 5.96; N, 4.36. Found (%): C, 74.68; H, 5.92; N, 4.38.

4-Oxo-1-(4-pyridinemethyl)-1,4-dihydroquinoline-3-carboxylic acid (9e): Compound was isolated as a sodium salt, m.p. 264-268 ºC; IR (KBr, ν_{max}, cm^{-1}): 3442, 3045, 1721, 1614, 1547, 1517 and 1474; ^{1}H NMR (300 MHz, D_2O): δ 5.53 (s, 2H), 7.07 (d, *J* = 5.7 Hz, 2H), 7.31-7.39 (m, 2H), 7.50 (t, *J* = 7.8 Hz, 1H), 8.20 (d, *J* = 7.8 Hz, 1H), 8.28 (d, *J* = 6.0 Hz, 2H), 8.46 (s, 1H); ^{13}C NMR (75 MHz, D_2O): δ 116.7, 118.0, 121.5, 125.0, 126.1, 127.2, 132.8, 138.6, 145.5, 145.6, 148.2, 148.9, 168.4, 172.2, 176.8; ESI-MS m/z. 281 $(M + H)^+$, 303 $(M + Na)^+$ and 319 $(M + K)^+$. Anal. calcd. (%) for $C_{16}H_{12}N_2O_3$: C, 68.56, H, 4.32; N, 9.99. Found (%): C, 68.41, H, 4.32; N, 9.93.

General procedure for 4-oxo-1-(pyridyl)-1,4-dihydroquinoline-3-carboxamide (1a-m): A stirred solution of 1,4-dihydro-4-oxo-1-(alkyl/aryl)quinoline-3-carboxylic acid (**9a**, **9b**, **9c**, **9d**, **9e**)(0.0037 mol), selected amine (0.00563 mol), diisopropylethyl amine (0.0075 mol) and N,N,N',N'-tetramethyl-O-(7-azo benzotriazol-1-yl)uronium hexafluorophosphate (HATU) (0.00563 mol) in a mixture of dimethyl formamide (1 mL) and dichloromethane (10 mL) was stirred at 25-30 ºC for 2-3 h. After completion of reaction, the reaction mixture was quenched with water and extracted with ethylacetate. Organic layer was concentrated under reduced pressure. The residue obtained was purified by column chromatography using 2 % methanol in dichloromethane as an eluent to afford the corresponding pure 4-oxo-1-(pyridyl)-1,4-dihydroquinoline-3-carboxamide (**1a-m**).

4-Oxo-N-(1-phenylethyl)-1-(2-pyridyl)-1,4-dihydroquinoline-3-carboxamide (1a): Compound was isolated as solid, m.p. 133-138 ºC; IR (KBr, ν_{max}, cm^{-1}): 3434, 3217, 3057, 2979, 1663, 1604 and 1545; ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.62 (d, *J* = 7.5 Hz, 3H), 5.33 (m, 1H), 7.20-7.63 (m, 10H), 8.02 (td, *J* = 7.8 Hz, 1.2 Hz, 1H), 8.54 (dd, *J* = 7.8 Hz, 1.2 Hz, 1H), 8.71 (dd, *J* = 4.8 Hz, 1.2 Hz, 1H), 8.92, (s, 1H) and 10.42 (d, *J* = 7.5 Hz, NH); ^{13}C NMR (75 MHz, $CDCl_3$): δ 23.2, 48.4, 111.6, 118.3, 122.4, 123.9, 125.8, 126.0, 126.3, 126.6, 127.2, 128.8, 129.0, 133.5, 139.6, 140.8, 144.5, 147.0, 150.4, 152.6, 163.1, 176.5; ESI-MS m/z. 370 $(M + H)^+$ and 392 $(M + Na)^+$. Anal. calcd. (%) for $C_{23}H_{19}N_3O_2$: C,74.78; H, 5.18; N, 11.37. Found (%): C,74.71; H, 5.22; N, 11.24.

4-Oxo-1-(2-pyridyl)-N-(2-methylphenyl)-1,4-dihydroquinoline-3-carboxamide (1b): Compound was isolated as solid, m.p. 146-149 ºC; IR (KBr, ν_{max}, cm^{-1}): 3454, 3047, 2958, 1726, 1677, 1606 and 1547; ^{1}H NMR (DMSO-d_6, 300 MHz): δ 2.42 (s, 3H), 7.01 (m, 1H), 7.19 (t, *J* = 7.8 Hz, 1H), 7.26 (d, J = 7.2 Hz, 1H), 7.30 (d, *J* = 8.4 Hz, 1H), 7.61 (m, 1H), 7.74 (m, 2H), 7.88 (d, *J* = 7.8 Hz, 1H), 8.22 (td, *J* = 7.8 Hz, 2.1 Hz, 1H), 8.29 (d, *J* = 7.5 Hz, 1H), 8.47 (dd, *J* = 8.1 Hz, 1.2 Hz, 1H), 8.76 (m, 1H), 8.9 (s, 1H) and 12.20 (br, NH); ^{13}C NMR (75 MHz, DMSO-d_6): δ 18.3, 111.8, 118.4, 121.0, 122.5, 124.0, 125.9, 126.3, 126.5, 126.6, 126.7, 127.4, 130.6, 133.8, 137.4, 139.6, 140.8, 147.6, 150.5, 152.5, 162.2, 176.7; ESI-MS m/z. 356 $(M + H)^+$ and 378 $(M + Na)^+$. Anal. calcd. (%) for $C_{22}H_{17}N_3O_2$: C, 74.35; H, 4.82; N, 11.82. Found (%): C, 74.22; H, 4.83; N, 11.76.

4-Oxo-N-(1-phenylethyl)-1-(3-pyridyl)-1,4-dihydroquinoline-3-carboxamide (1c): Compound was isolated as solid, m.p. 171-173 ºC; IR (KBr, ν_{max}, cm^{-1}): 3450, 3230, 3054, 2969, 1666, 1604 and 1538; ^{1}H NMR (300 MHz, DMSO-d_6):

δ 1.49 (d, *J* = 6.9 Hz, 3H), 5.16 (m, 1H), 7.03 (d, *J* = 8.1 Hz, 1H), 7.31 (m, 1H), 7.36 (m, 3H), 7.56 (td, *J* = 8.1 Hz, 0.6 Hz, 1H), 7.71 (m, 2H), 8.16 (d, *J* = 8.4 Hz, 1H), 8.39 (dd, *J* = 8.1 Hz, 1.2 Hz, 1H), 8.61 (s, 1H), 8.83 (dd, *J* = 4.8 Hz, 1.5 Hz, 1H), 8.86 (d, *J* = 2.1 Hz, 1H) and 10.37 (d, *J* = 7.8, NH); ^{13}C NMR (75 MHz, DMSO-d_6): δ 23.2, 80.4, 111.7, 118.4, 125.2, 125.8, 126.3, 126.4, 126.8, 127.2, 128.8, 133.7, 136.0, 137.6, 140.8, 144.6, 148.3, 148.7, 151.3, 163.1, 176.5; ESI-MS m/z. 370 $(M + H)^+$ and 392 $(M + Na)^+$. Anal. calcd. (%) for $C_{23}H_{19}N_3O_2$: C,74.78; H, 5.18; N, 11.37. Found (%): C,74.69; H, 5.16; N, 11.42.

4-Oxo-1-(3-pyridyl) N-(2-methylphenyl)-1,4-dihydroquinoline-3-carboxamide (1d): Compound was isolated as solid, m.p. 211-213 ºC; IR (KBr, ν_{max}, cm^{-1}): 3459, 3039, 1675, 1605 and 1548; ^{1}H NMR (300 MHz, DMSO-d_6): δ 2.41 (s, 3H), 7.01 (td, *J* = 7.5 Hz, 1.2 Hz, 1H), 7.08 (d, *J* = 8.4 Hz, 1H), 7.26 (d, *J* = 7.5 Hz, 1H), 7.60 (td, *J* = 7.5 Hz, 0.9, 1H), 7.75 (m, 2H), 8.21 (m, 1H), 8.28 (d, *J* = 7.2 Hz, 1H), 8.48 (dd, *J* = 8.1 Hz, 1.5 Hz, 1H), 8.79 (s, 1H), 8.86 (dd, *J* = 4.8 Hz, 1.5 Hz, 1H), 8.91 (d, *J* = 2.1 Hz, 1H) and 12.16 (s, NH); ^{13}C NMR (75 MHz, DMSO-d_6): δ 18.3, 111.8, 118.5, 121.0, 123.9, 125.3, 126.1, 126.5, 126.6, 126.7, 127.4, 130.6, 133.9, 136.1, 137.4, 137.5, 140.9, 148.7, 148.8, 151.4, 162.3, 176.7 ESI-MS m/z. 356 $(M + H)^+$ and 378 $(M + Na)^+$. Anal. calcd. (%) for $C_{22}H_{17}N_3O_2$: C, 74.35; H, 4.82; N, 11.82. Found (%): C, 74.41; H, 4.79; N, 11.75.

4-Oxo-1-(3-pyridyl)-N-(4-pyridinemethyl)-1,4-dihydroquinoline-3-carboxamide (1e): Compound was isolated as solid, m.p. 194-198 ºC; IR (KBr, ν_{max}, cm^{-1}): 3447, 3247, 3039, 1662, 1603 and 1541; ^{1}H NMR (300 MHz, DMSO-d_6): δ 4.60 (d, *J* = 6.0 Hz, 2H), 7.04 (d, *J* = 8.4 Hz, 1H), 7.30 (d, *J* = 5.7 Hz, 2H), 7.57 (t, *J* = 7.8 Hz, 1H), 7.72 (m, 2H), 8.16 (m, 1H), 8.40 (dd, *J* = 8.1 Hz, 0.6 Hz, 1H), 8.49 (d, *J* = 4.5 Hz, 2H), 8.65 (s, 1H), 8.84 (dd, *J* = 4.8 Hz, 1.5 Hz, 1H), 8.88 (d, *J* = 2.1 Hz, 1H) and 10.36 (t, *J* = 6.0 Hz, NH); ^{13}C NMR (75 MHz, DMSO-d_6): δ 41.6, 111.6, 118.4, 122.5, 125.2, 125.9, 126.4, 126.8, 133.7, 136.1, 137.5, 140.9, 148.4, 148.7, 148.8, 149.9, 151.3, 164.5, 176.3; ESI-MS m/z. 357 $(M + H)^+$. Anal. calcd. (%) for $C_{21}H_{16}N_4O_2$: C, 70.77; H, 4.53; N, 15.72. Found (%): C, 70.84; H, 4.49; N, 15.76.

4-Oxo-N-(1-phenylethyl)-1-(4-pyridyl)-1,4-dihydroquinoline-3-carboxamide (1f): Compound was isolated as solid, m.p. 190-195 ºC; IR (KBr, ν_{max}, cm^{-1}): 3422, 3238, 3056, 2963, 1667, 1607 and 1547; ^{1}H NMR (300 MHz, DMSO-d_6): δ 1.50 (d, *J* = 6.9 Hz, 1H), 5.16 (m, 1H), 7.16 (d, *J* = 8.4 Hz, 1H), 7.26 (m, 1H), 7.36 (m, 4H), 7.57 (m, 1H), 7.72 (m, 1H), 7.73 (m, 2H), 8.39 (dd, *J* = 8.1 Hz, 1.5 Hz, 1H), 8.59 (s, 1H), 8.89 (dd, *J* = 4.5 Hz, 1.5 Hz, 2H) and 10.33 (d, *J* = 7.8 Hz, NH); ^{13}C NMR (75 MHz, DMSO-d_6): δ 23.0, 48.5, 112.0, 117.9, 122.5, 125.7, 126.1, 126.5, 126.9, 127.0, 128.6, 133.3, 139.7, 144.5, 147.2, 147.8, 152.3, 163.1, 176.5; ESI-MS m/z. 370 $(M + H)^+$ and 392 $(M + Na)^+$. Anal. calcd. (%) for $C_{23}H_{19}N_3O_2$: C,74.78; H, 5.18; N, 11.37. Found (%): C, 74.60; H, 5.24; N, 11.38.

4-Oxo-1-(4-pyridyl) N-(2-methylphenyl)-1,4-dihydroquinoline-3-carboxamide (1g): Compound was isolated as solid, m.p. 209-211 ºC; IR (KBr, ν_{max}, cm^{-1}): 3455, 3041, 2921, 1678, 1608 and 1541; ^{1}H NMR (300 MHz, DMSO-d_6): δ 2.41 (s, 3H), 7.01 (td, *J* = 7.5 Hz, 0.9 Hz, 1H), 7.19 (t, *J* = 8.1 Hz, 2H), 7.26 (d, *J* = 7.2 Hz, 1H), 7.61 (td, *J* = 8.1 Hz, 0.9 Hz, 1H), 7.77 (m, 1H), 7.82 (dd, *J* = 4.5 Hz, 1.5 Hz, 2H), 8.28 (d, *J* = 7.5 Hz, 1H), 8.47 (dd, *J* = 8.1 Hz, 1.2 Hz, 1H), 8.77 (s, 1H), 8.92 (dd, *J* = 4.5 Hz, 1.5 Hz, 2H) and 12.12 (br, NH); ^{13}C NMR (75 MHz, DMSO-d_6): δ 18.3, 112.0, 118.4, 121.0, 122.7, 123.9, 126.2, 126.6, 126.7, 127.4, 130.6, 133.9, 137.4, 139.9, 147.9, 148.0, 152.4, 162.2, 176.7; ESI-MS m/z. 356 $(M + H)^+$ and 378 $(M + Na)^+$. Anal. calcd. (%) for $C_{22}H_{17}N_3O_2$: C, 74.35; H, 4.82; N, 11.82. Found (%): C, 74.30; H, 4.82; N, 11.79.

4-Oxo-1-(4-pyridyl)-N-(4-pyridinemethyl)-1,4-dihydroquinoline-3-carboxamide (1h): Compound was isolated as solid, m.p. 194-199 ºC; IR (KBr, ν_{max}, cm^{-1}): 3445, 3216, 3056, 2921, 1660, 1605 and 1544; ^{1}H NMR (300 MHz, DMSO-d_6): δ 4.60 (d, *J* = 6.0 Hz, 2H), 7.17 (d, *J* = 8.4 Hz, 1H), 7.30 (dd, *J* = 4.5 Hz, 1.5, 2H), 7.57 (td, *J* = 7.8 Hz, 0.9 Hz, 1H), 7.73 (m, 1H), 7.78 (dd, *J* = 4.5 Hz, 1.5 Hz, 2H), 8.40 (dd, *J* = 8.1 Hz, 1.5 Hz, 1H), 8.49 (dd, *J* = 4.5 Hz, 1.5 Hz, 2H), 8.63 (s, 1H), 8.89 (dd, *J* = 4.5 Hz, 1.5 Hz, 2H) and 10.32 (t, *J* = 6.0 Hz, NH); ^{13}C NMR (75 MHz, DMSO-d_6): δ 41.6, 111.7, 118.3, 122.5, 122.7, 126.0, 126.4, 126.8, 133.7, 139.8, 147.6, 147.9, 148.8, 149.9, 152.4, 164.4, 176.3; ESI-MS m/z. 357 $(M + H)^+$ and 379 $(M + Na)^+$. Anal. calcd. (%) for $C_{21}H_{16}N_4O_2$: C, 70.77; H, 4.53; N, 15.72. Found (%): C, 70.60; H, 4.49; N, 15.69.

4-Oxo-1-(1-methyl-3-phenylpropyl)-N-(1-phenylethyl)-1, 4-dihydroquinoline-3-carboxamide (1i): Compound was isolated as viscous syrup, IR (KBr, ν_{max}, cm^{-1}): 3450, 3231, 2929, 1660, 1603 and 1543; ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.61 (d, *J* = 6.9 Hz, 3H), 1.62 (d, *J* = 6.9 Hz, 3H), 2.22 (m, 1H), 2.33 (m, 1H), 2.64 (m, 2H), 4.72 (m, 1H,) 5.31 (m, 1H), 7.00-7.63 (m, 12H), 8.56 (d, *J* = 8.1 Hz, 1H), 8.93 (d, *J* = 3.0 Hz, 1H) and 10.54 (d, *J* = 7.5 Hz, NH); ^{1}H NMR (75 MHz, $CDCl_3$): δ 20.2, 22.9, 31.9, 37.2, 48.9, 53.8, 112.0, 114.9, 124.7, 126.0, 126.4, 126.8, 127.4, 128.2, 128.4, 128.5, 139.5, 142.9, 144.2, 164.1, 176.2; ESI-MS m/z. 425 $(M + H)^+$. Anal. calcd. (%) for $C_{28}H_{28}N_2O_2$: C, 79.22; H, 6.65; N, 6.60. Found (%): C, 79.16; H, 6.63; N, 6.59.

4-Oxo-1-(1-methyl-3-phenylpropyl) N-(2-methylphenyl)-1, 4-dihydroquinoline-3-carboxamide (1j): Compound was isolated as viscous syrup, IR (KBr, ν_{max}, cm^{-1}): 3452, 2926, 1676, 1605 and 1543; ^{1}H NMR (300 MHz, DMSO-d_6): δ 1.59 (d, *J* = 6.3, 3H), 2.25 (m, 2H), 2.39 (s, 3H), 2.62 (m, 2H), 5.10 (m, 1H), 7.01 (td, *J* = 7.5 Hz, 1.2, 1H), 7.10-7.23 (m, 7H), 7.57 (t, *J* = 7.5 Hz, 1H), 7.83 (m, 1H), 7.98 (d, *J* = 9.0 Hz, 1H), 8.34 (m, 1H), 8.45 (dd, *J* = 7.5 Hz, 1.5 Hz, 1H), 8.96 (s, 1H) and 12.25 (br, NH); ^{13}C NMR (75 MHz, DMSO-d_6): δ 18.4, 20.3, 31.8, 37.3, 55.2, 111.5, 117.0, 120.9, 123.7, 125.6, 126.3, 126.6, 126.9, 127.3, 127.4, 128.5, 128.6, 130.6, 133.6, 137.6, 139.9, 140.9, 143.8, 162.7, 175.8; ESI-MS m/z. 411 $(M + H)^+$ and 433 $(M + Na)^+$. nal. calcd. (%) for $C_{27}H_{26}N_2O_2$: C, 79.00; H, 6.34; N, 6.82. Found (%): C, 79.09; H, 6.38; N, 6.79.

4-Oxo-N-(1-phenylethyl)-1-(4-pyridinemethyl)-1,4-dihydroquinoline-3-carboxamide (1k): Compound was isolated as solid, m.p. 216-218 ºC; IR (KBr, ν_{max}, cm^{-1}): 3434, 3043, 2961, 1668, 1609 and 1561; ^{1}H NMR (300 MHz, DMSO-d_6): δ 1.49 (d, *J* = 6.9 Hz, 3H), 5.19 (m, 1H), 5.83 (s, 2H), 7.14 (d, *J* = 6.0 Hz, 2H), 7.25 (m, 1H), 7.38 (m, 4H),

7.50 (t, *J* = 7.8 Hz, 1H), 7.58 (d, *J* = 8.7 Hz, 1H), 7.71 (m, 1H), 8.35 (dd, *J* = 8.1 Hz, 1.5, 1H), 8.48 (d, *J* = 6.0 Hz, 2H), 9.05 (s, 1H) and 10.43 (d, *J* = 7.8 Hz, NH); ^{13}C NMR (75 MHz, DMSO-d_6): δ 116.7, 118.0, 121.5, 125.0, 126.1, 127.2, 132.8, 138.6, 145.5, 145.6, 148.2, 148.9, 168.4, 172.2, 176.8; ESI-MS m/z. 384 $(M + H)^+$. Anal. calcd. (%) for $C_{24}H_{21}N_3O_2$: C, 75.18; H, 5.52; N, 10.96. Found (%): C, 75.14; H, 5.53; N, 11.01.

4-Oxo-1-(4-pyridinemethyl)-N-(2-methylphenyl)-1,4-dihydroquinoline-3-carboxamide (1l): Compound was isolated as solid, m.p. 230-232 ºC; IR (KBr, ν_{max}, cm^{-1}): 3449, 3210, 3037, 2977, 1668, 1608 and 1534; ^{1}H NMR (300 MHz, DMSO-d_6): δ 2.41 (s, 3H), 5.91 (s, 2H), 7.00 (td, *J* = 7.5 Hz, 0.9, 1H), 7.20 (m, 3H), 7.25 (d, *J* = 7.5 Hz, 1H), 7.54 (t, *J* = 7.2 Hz, 1H), 7.63 (d, *J* = 8.7 Hz, 1H), 7.76 (m, 1H), 8.34 (d, *J* = 8.1 Hz, 1H), 8.44 (dd, *J* = 8.1 Hz, 1.2 Hz, 1H), 8.50 (d, *J* = 4.5 Hz, 2H), 9.24 (s, 1H) and 12.24 (br, NH); ^{13}C NMR (75 MHz, DMSO-d_6): δ 18.4, 55.3, 111.8, 118.1, 121.0, 121.7, 123.7, 125.9, 126.7, 126.8, 127.3, 127.5, 130.6, 133.7, 137.6, 139.4, 145.4, 150.0, 150.4, 162.6, 176.5; ESI-MS m/z. 370 $(M + H)^+$ and 392 $(M + Na)^+$. Anal. calcd. (%) for $C_{23}H_{19}N_3O_2$: C, 74.78; H, 5.18; N, 11.37. Found (%): C, 74.68; H, 5.18; N, 11.41.

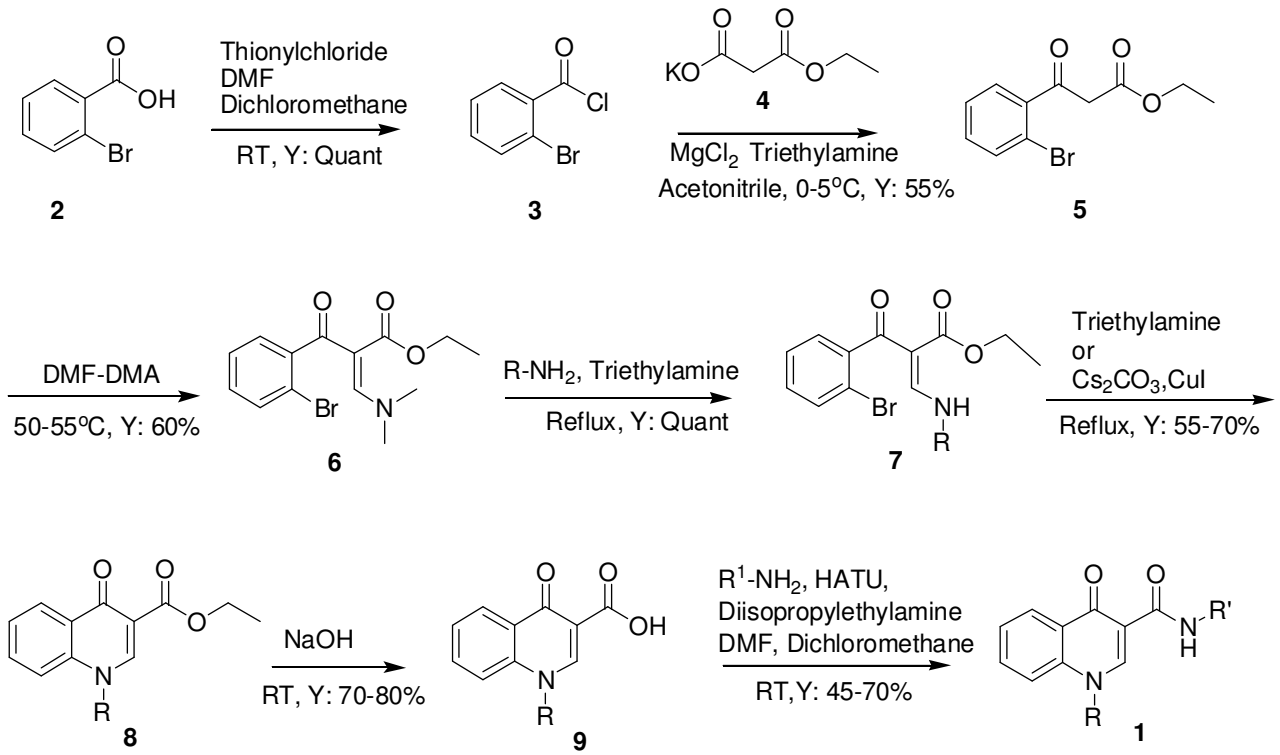
4-Oxo-N, 1-*bis*(4-pyridinemethyl)-1,4-dihydroquinoline-3-carboxamide (1m): Compound was isolated as solid m.p. 245-249 ºC; IR (KBr, ν_{max}, cm^{-1}): 3434, 3044, 2924, 1663, 1602 and 1562; ^{1}H NMR (300 MHz, $CDCl_3$): δ 4.71 (d, *J* = 6.0 Hz, 2H), 5.48 (s, 2H), 7.05 (d, *J* = 6.0 Hz, 2H), 7.25 (d, *J* = 8.4 Hz, 2H), 7.31 (d, *J* = 6.0 Hz, 2H), 7.50 (td, *J* = 7.8 Hz, 0.6 Hz, 1H), 7.65 (m, 1H), 8.57 (m, 3H), 8.61 (dd, *J* = 4.8 Hz, 1.8 Hz, 2H), 8.92 (s, 1H) and 10.53 (t, *J* = 6.0 Hz, NH); ^{13}C NMR (75 MHz, $CDCl_3$): δ 42.0, 56.3, 112.0, 116.2, 120.6, 122.1, 125.5, 127.5, 127.9, 133.2, 138.9, 143.1, 147.7, 148.5, 149.8, 150.7, 165.0, 176.8; ESI-MS m/z. 371 $(M + H)^+$ and 393 $(M + Na)^+$. Anal. calcd. (%) for $C_{22}H_{18}N_4O_2$: C, 71.34; H, 4.90; N, 15.13. Found (%):C, 71.29; H, 4.89; N, 15.15.

RESULTS AND DISCUSSION

2-Bromo benzoic acid (**2**) was converted into corresponding acid chloride (**3**) in the presence of thionyl chloride followed by condensation with potassium salt of monoethyl malonate (**4**) to obtain bromobenzoyl β-keto ester (**5**), which was further reacted with N,N-dimethyl formamide dimethyl acetal to give ethyl-3-(2-bromophenyl)-2-[(dimethylamino)methylene]-3-oxopropanoate (**6**) (**Scheme-I**) in about 33 % yield.

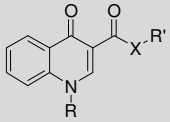
In presence of triethylamine or cesium carbonate, ethyl-3-(2-bromophenyl)-2-[(dimethylamino)methylene]-3-oxopropanoate (**6**) on condensation with 2-aminopyridine, 3-aminopyridine or 4-aminopyridine undergoes *in situ* cyclisation to afford ethyl-1,4-dihydro-4-oxo-(N-pyridyl quinoline)-3-carboxylate (**8a-c**) derivatives as shown in **Scheme-I**. However, ethyl-3-(2-bromophenyl)-2-[(dimethylamino)methylene]-3-oxopropanoate (**6**) when treated with 4-phenylbutane-2-amine, 4-(aminomethyl)pyridine in the presence of bases such as triethylamine or cesium carbonate obtained an intermediate bromo derivative ethyl-3-(2-bromophenyl)-2-[(N-pyridylamino)methylene]-3-oxopropanoate (**7d**, **7e**) and which was then converted to quinolinone ester (**8d**, **8e**) by further treatment with cesium carbonate and adding by catalytic amount of copper iodide (**Scheme-I**).

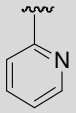
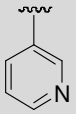
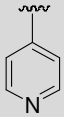
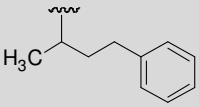
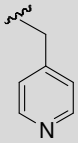
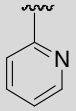
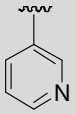
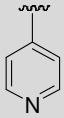
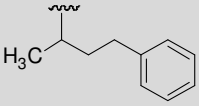
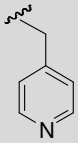
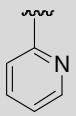
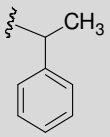
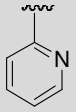
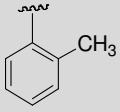
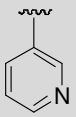
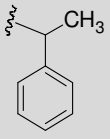
Compounds (**8a-e**) undergo hydrolysis in presence of aqueous NaOH to give N-pyridyl-1,4-dihydro-4-oxo-3-quinoline carboxylic acids (**9a-e**), respectively as shown in Table-1

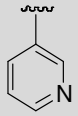
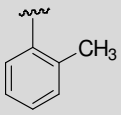
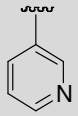
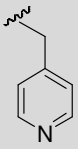
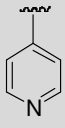
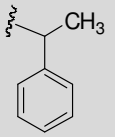
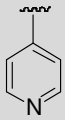
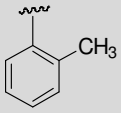
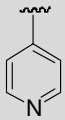
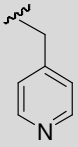
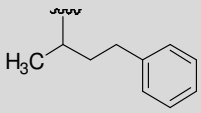
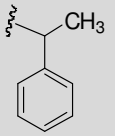
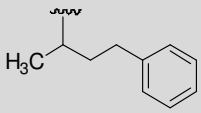
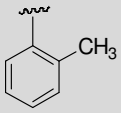
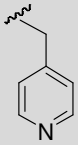
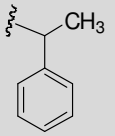
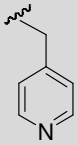
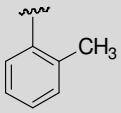
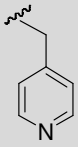
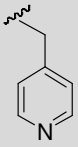


Scheme-I

TABLE-1
CHEMICAL STRUCTURES OF SYNTHESISED COMPOUNDS (**8a-e**), (**9a-e**), (**1a-m**) AND YIELDS



Entry	-R	-R'	-X-	Compound	Yield (%)
1		C_2H_5	O	**8a**	75
2		C_2H_5	O	**8b**	55
3		C_2H_5	O	**8c**	60
4		C_2H_5	O	**8d**	75
5		C_2H_5	O	**8e**	65
6		H	O	**9a**	75
7		H	O	**9b**	55
8		H	O	**9c**	60
9		H	O	**9d**	75
10		H	O	**9e**	65
11			N	**1a**	55
12			N	**1b**	55
13			N	**1c**	65

14			N	**1d**	75
15			N	**1e**	68
16			N	**1f**	45
17			N	**1g**	65
18			N	**1h**	53
19			N	**1i**	50
20			N	**1j**	60
21			N	**1k**	46
22			N	**1l**	60
23			N	**1m**	69

in about 70-80 % yield. N-Pyridyl-1,4-dihydro-4-oxo-3-quinoline carboxylic acid (**9a**, **9b**, **9c**, **9d**, **9e**) were treated with variety of amines like 4-(aminomethyl)pyridine, phenylethylamine and 2-methyl-aniline in presence of N,N,N',N'-tetramethyl-O-(7-azobenzotriazol-1-yl)uronium hexa fluorophosphate (HATU) in a mixture of dimethylfarmamide and dichloromethane gave amides 4-oxo-N-(pyridyl)-1-(aryl/alkyl)-1,4-dihydroquinoline-3-carboxamides (**1a-m**), respectively as shown in Table-1 in about 45-70 % yield.

The structure of compounds **8a-e**, **9a-e**, **1a-m** were confirmed by mass spectra, IR, ^{1}H and ^{13}C NMR, mass spectra of compound showed (M + 1) peak, in arrangement with their molecular formula. In the 300 MHz ^{1}H NMR spectrum of compounds, =CH proton was observed as singlet at 8.30-9.50 ppm. The proton of amide NH group of carboxamides observed at different regions for aliphatic attached amide proton at 10.32-10.48 ppm and for aromatic attached amide proton at 12.10-12.35 ppm (for aromatic attached) and all the other aromatic and aliphatic protons were observed at expected regions.

Conclusion

We have developed an efficient synthesis for the preparation of various novel N-pyridyl-1,4-dihydro-4-oxo-3-quinoline carboxylic acids (**9a-e**) and novel 4-oxo-N-(pyridyl)-1,4-dihydroquinoline-3-carboxamides (**1a-m**).

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REFERENCES

1. E. Stern, G.G. Muccioli, R. Millet, J.F. Goossens, A. Farce, P. Chavatte, J.H. Poupaert, D.M. Lambert, P. Depreux and J.P. Henichart, *J. Med. Chem*., **49**, 70 (2006).
2. P.L. Ferrarini, V. Calderone, T. Cavallini, C. Manera, G. Saccomanni, L. Pani, S. Ruiu and G.L. Gessa, *Bioorg. Med. Chem*., **12**, 1921 (2004).
3. B.J. Lavey, J.A. Kozlowski, R.W. Hipkin, W. Gonsiorek, D.J. Lundell, J.J. Piwinski, S. Naruba and C.A. Lunn, *Bioorg. Med. Chem. Lett*., **15**, 783 (2005).
4. E. Stern, G.G. Muccioli, B. Bosier, L. Hamtiaux, R. Millet, J.H. Poupaert, J.P. Hnichart, P. Depreux, J.F. Goossens and D.M. Lambert, *J. Med. Chem*., **50**, 5471 (2007).
5. J.N. Kim, K.Y. Lee, H.S. Kim, T.Y. Kim, *Org. Lett*., **2**, 343 (2000); O. Tabarrini, M. Stevens, V. Cecchetti, S. Sabatini, M. Dell'Uomo, G. Manfroni, M. Palumbo, C. Pannecouque, E. D. Clercq and A. Fravolini, *J. Med. Chem*., **47**, 5567 (2004).
6. G.G. Muccioli and D.M. Lambert, *Curr. Med. Chem*., **12**, 1361 (2005).
7. S.J.R. Elmes, M.D. Jhaveri, D. Smart, D.A. Kendall and V. Chapman, *Eur. J. Neurosci*., **20**, 2311 (2004).
8. S. Sarfaraz, F. Afaq, V. M. Adhami and H. Mukhtar, *Cancer Res*., **65**, 1635 (2005).
9. A. Franklin and N. Stella, *Eur. J. Pharmacol*., **474**, 195 (2003).
10. B.G. Ramirez, C. Blazquez, T. Gomez del Pulgar, M. Guzman and M.L. de Ceballos, *J. Neurosci*., **25**, 1904 (2005).
11. J. Frank, Z. Meszaros, F. Dutka, T. Komives and A.F. Marton, *Tetrahedron Lett*., **18**, 4545 (1977).
12. C.C. Price and R.M. Roberts, *Org. Synth. Coll*., **3**, 272 (1955); N. Yokoma, B. Ritter and A. Neubert, *J. Med. Chem*., **25**, 337 (1982).
13. I.A. Sayyed, D.G. Panse, B.M. Bhawal and A.R.A.S. Deshmukh, *Synth. Commun*., **30**, 2533 (2000).