4. Experimental

All the reagents and solvents required for synthesis were purified by general laboratory techniques before use. Compounds were purified by passing them through silica gel H (100-200 mesh) purifying column using mixture of ethyl acetate and hexane or methanol as eluent. Melting points were determined using a Labindia make melting point apparatus (heating block type) and are uncorrected. Purity of the compounds and completion of reactions were monitored by thin layer chromatography (TLC) on silica gel plates (60 F_{254}; Merck), visualizing with ultraviolet light or iodine vapors. The yields reported here are un-optimized. The IR spectra were recorded using KBr disc method on a Bruker FT-IR, model alpha. The ^{1}H-NMR spectra (on a Bruker 400 MHz spectrometer) were recorded in DMSO-d_6 (chemical shifts in δ ppm). The assignments of exchangeable protons were confirmed by the D_2O exchange studies wherever required. Mass spectral data was obtained on a Waters Micromass ESCi spectrometer.

4.1. Chemical studies

4.1.1 Synthesis of 4*H*-pyrido[1,2-*a*]pyrimidin-4-one intermediates (**4a-c** & **6a-c**)

• Synthesis of 4-oxo-4*H*-pyrido[1,2-*a*]pyrimidine-3-carboxylic acid (4a)

Diethyl 2-pyridylaminomethylenemalonate (2a)

A mixture of 2-aminopyridine (**1a**) (10 g, 10.6 mmole) and diethyl ethoxymethylenemalonate (24.47 g, 10.6 mmole) was refluxed for 2 h. The reaction mixture was cooled to RT to get (**2a**) as a light brown solid (14 g, 50%), m. p. 68-69 °C (Lit. [217,218] 67.5-68 °C).

Anal.:

TLC : R_f 0.85 (EtOAc)

IR : 3274, 1686, 1649, 1601, 1558, 1414, 1248 and 1147 cm^{-1}

^{1}H-NMR : 1.22-1.29 (m, 6H), 4.12-4.18 (q, 2H), 4.20-4.25 (q, 2H), 7.14-7.17 (m, 1H), 7.39-7.41 (d, 1H), 7.79-7.83 (m, 1H), 8.36-8.37 (d, 1H), 9.05-9.08 (d, 1H), 10.79-10.82 (d, 1H)

MS : (*m/z*) 265 (M^++1)

Ethyl 4-oxo-4*H*-pyrido[1,2-*a*]pyrimidine-3-carboxylate (3a)

The pyridine derivative (**2a**) (13 g, 5.9 mmole) was refluxed in diphenyl ether (100 ml) using air condenser for 8 h in a two-neck round-bottom flask (250 ml). The reaction mixture was cooled to RT and hexane (500 ml) was added in to it to get a solid precipitate. The precipitated solid was filtered, washed with hexane and dried to obtain the compound (**3a**) (10 g, 93.1%), m. p. 112-13 °C (Lit.[217] 110-11 °C).

Anal.:

TLC : R_f 0.48 (EtOAc)

IR : 1730, 1482, 1288, 1227 and 1103 cm^{-1}

^{1}H-NMR : 1.29-1.32 (t, 3H), 4.25-4.30 (m, 2H), 7.56-7.59 (m, 1H), 7.84-7.87 (d, 1H), 8.19-8.23 (m, 1H), 8.87 (s, 1H), 9.16-9.18 (d, 1H)

MS : (*m/z*) 219 (M^++1)

4-Oxo-4*H*-pyrido[1,2-*a*]pyrimidine-3-carboxylic acid (4a)

A solution of the ester (**3a**) (10 g, 5.2 mmole) in conc. HCl (15 ml) was refluxed for 6 h. The reaction mixture was cooled to RT to get a solid precipitate. The solid precipitate was filtered, washed with ether and dried to get compound (**4a**) as a dark brown solid (8 g, 85.5%), m. p. 268 °C (decomp.) [Lit.[217] 265 °C (decomp.)].

Anal.:

TLC : R_f 0.1 (EtOAc)

IR : 3221, 3091, 1757, 1677, 1636, 1519, 1483, 1275, 1247 cm^{-1}

^{1}H-NMR : 7.67-7.71 (m, 1H), 7.97-8.00 (d, 1H), 8.31-8.35 (m, 1H), 8.96 (s, 1H), 9.22-9.23 (d, 1H)

MS : (*m/z*) 191 (M^++1)

• Synthesis of 3-isocyanato-4*H*-pyrido[1,2-*a*]pyrimidin-4-one (6a)

4-Oxo-4*H*-pyrido[1,2-*a*]pyrimidine-3-carbonylazide (5a)

In a two-neck round-bottom flask (250 ml), compound (**4a**) (8 g, 4.2 mmole) and triethylamine (8.5 g, 8.4 mmole) were dissolved in DMF (25 ml). The reaction mixture was cooled to 0 ^oC. Ethyl chloroformate (5.03 g, 4.6 mmole) was added to the reaction mixture and stirred for 15 min followed by addition of

aqueous solution of sodium azide (10.95 g, 16.8 mmole) resulting into a yellow solid precipitate. The solid precipitate was filtered, washed with cold water, hexane and then air dried affording the compound (**5a**) as brown solid (6.8 g, 75.1%) m. p. 130-31 °C.

Anal.:

TLC : R_f 0.28 (EtOAc)

IR : 2310, 1725, 1472, 1185 and 1012 cm^{-1}

^{1}H-NMR : 7.61-7.64 (m, 1H), 7.87-7.91 (d, 1H), 8.24-8.35 (m, 1H), 8.94 (s, 1H), 9.10-9.28 (d, 1H)

MS : (*m/z*) 214 (M^+-1)

3-Isocyanato-4*H*-pyrido[1,2-*a*]pyrimidin-4-one (6a)

The acid azide (**5a**) (4 g, 1.8 mmole) in toluene was refluxed for 2 h. Work up of the reaction mixture was done by removing toluene under vacuum to get the compound (**6a**) (3.2 g, 40.6%), m. p. 180-81 °C.

Anal.:

TLC : R_f 0.5 (EtOAc)

IR : 2140, 1687, 1650, 1575, 1550, 1490 and 1190 cm^{-1}

MS : (*m/z*) 188 (M^++1)

- **Synthesis of 8-methyl-4-oxo-4*H*-pyrido[1,2-*a*]pyrimidine-3-carboxylic acid (4b)**

Diethyl (4-methyl-2-pyridylamino)methylenemalonate (2b)

4-Methyl-2-aminopyridine (10 g, 9.25 mmole) was reacted with diethyl ethoxymethylenemalonate (21.29 g, 9.25 mmole) as described above for compound (**2a**)**,** offering compound (**2b**) (15 g, 58.2%), m. p. 73-74 °C (Lit.[217] 72-73 °C).

Anal.:

TLC : R_f 0.9 (EtOAc)

IR : 1731, 1682, 1648, 1605, 1548, 1374 and 1218 cm^{-1}

MS : (*m/z*) 279 (M^++1)

Ethyl 8-methyl-4-oxo-4*H*-pyrido[1,2-*a*]pyrimidine-3-carboxylate (3b)

In analogy to compound (**3a**), **2b** (10 g, 4.31 mmole) was refluxed in diphenyl ether to obtain compound (**3b**) (10 g, 88.4%), m. p. 174-75 °C (Lit.[217] 171-72 °C).

Anal.:

TLC : R_f 0.55 (EtOAc)

IR : 1689, 1639, 1556, 1501, 1284 and 1143 cm^{-1}

^{1}H-NMR : 1.30 (t, 3H), 2.51 (s, 3H), 4.23-4.29 (m, 2H), 7.42-7.44 (m, 1H), 7.67 (s, 1H), 8.82 (s, 1H), 9.04-9.05 (d, 1H)

MS : (*m/z*) 233 (M^++1)

8-Methyl-4-oxo-4*H*-pyrido[1,2-*a*]pyrimidine-3-carboxylic acid (4b)

A solution of the ester (**3b**) (10 g, 4.3 mmole) in conc. HCl (15 ml) was refluxed for 2 h. The reaction mixture was cooled to RT to get a solid precipitate. The solid so obtained was filtered, washed with ether (100 ml) and dried to offer 8-methyl-4-oxo-4*H*-pyrido[1,2-*a*]pyrimidin-3-carboxylic acid (**4b**) (8.5 g, 96.7%), m. p. 225 °C [Lit.[219] 223 °C].

Anal.:

TLC : R_f 0.11 (EtOAc)

IR : 2645, 1764, 1696, 1620, 1522, 1268, 1204 and 1152 cm^{-1}

^{1}H-NMR : 2.62 (s, 3H), 7.62-7.64 (m, 1H), 7.89 (s, 1H), 8.88-8.90 (d, 1H), 9.14-9.16 (d, 1H), 10.9 (b, 1H)

MS : (*m/z*) 203 (M^+-1)

- **Synthesis of 3-isocyanato-8-methyl-4*H*-pyrido[1,2-*a*]pyrimidin-4-one (6b)**

8-Methyl-4-oxo-4*H*-pyrido[1,2-*a*]pyrimidine-3-carbonylazide (5b)

Compound (**5b**) was prepared by reacting the acid (**4b**) (8 g, 3.9 mmole) with ethyl chloroformate (4.68 g, 4.3 mmole) and sodium azide (10.19 g, 15.7 mmole) as described above for compound (**5a**) resulting in to compound (**5b**) (7 g, 77.9%), m. p. 148-50 °C.

Anal.:

TLC : R_f 0.35 (EtOAc)

IR : 2142, 1712, 1640, 1569, 1485, 1285 and 1172 cm^{-1}

^{1}H-NMR **:** 2.56 (s, 3H), 7.49-7.51 (d, 1H), 7.75 (s, 1H), 8.84 (s, 1H), 9.09-9.13 (d, 1H)

MS **:** (*m/z*) 230 (M^++1)

3-Isocyanato-8-methyl-4*H*-pyrido[1,2-*a*]pyrimidin-4-one (6b)

The azide (**5b**) (4 g) was refluxed in toluene for 2 h. The reaction mixture was cooled to RT and the solvent was removed under *vacuo* to get 3-isocyanato-8-methyl-4*H*-pyrido[1,2-*a*]pyrimidin-4-one (**6b**) (3.34 g, 95.1%), m. p. 234-35 °C.

Anal.:

TLC **:** R_f 0.61 (EtOAc)

IR **:** 2353, 2316, 2223, 1670, 1639 and 1482 cm^{-1}

MS **:** (*m/z*) 201 (M^++1)

- **Synthesis of 7-chloro-4-oxo-4*H*-pyrido[1,2-*a*]pyrimidine-3-carboxylic acid (4c)**

Diethyl (5-chloro-2-pyridylamino)methylenemalonate (2c)

Compound (**2c**) was prepared by reacting compound (**1c**) (10 g, 7.8 mmole) with diethyl ethoxymethylenemalonate (17.96 g, 7.8 mmole) as described above for compound (**2a**)**,** affording the compound (**2c**) (15 g, 42.9%), m. p. 133-34 °C (Lit.[220] 131-32 °C).

Anal.:

TLC **:** R_f 0.91 (EtOAc)

IR **:** 3270, 1676, 1644, 1588, 1552, 1395, 1219 and 1007 cm^{-1}

^{1}H-NMR **:** 1.11-1.29 (m, 6H), 4.13-4.26 (m, 4H), 7.47-7.49 (d, 1H), 7.91-7.94 (m, 1H), 8.41 (s, 1H), 8.94-8.97 (d, 1H), 10.79-10.82 (d, 1H)

MS **:** (*m/z*) 299 (M^++1)

Ethyl 7-chloro-4-oxo-4*H*-pyrido[1,2-*a*]pyrimidine-3-carboxylate (3c)

With a procedure similar to that adopted for compound (**3a**) compound (**3c**) was prepared from compound (**2c**) (15 g, 5.03 mmole) providing the titled compound (**3c**) (10 g, 78.8%), m. p. 146-47 °C (Lit.[220] 147-48 °C).

Anal.:

TLC : R_f 0.54 (EtOAc)

IR : 1681, 1645, 1591, 1552, 1466, 1366, 1222 and 1091 cm^{-1}

MS : (*m/z*) 253 (M^++1)

7-Chloro-4-oxo-4*H*-pyrido[1,2-*a*]pyrimidine-3-carboxylic acid (4c)

In analogy to compound (**4a**), compound (**4c**) was obtained by employing the same procedure using **3c** (10 g, 3.9 mmole) to get 7-chloro-4-oxo-4*H*-pyrido[1,2-*a*]pyrimidine-3-carboxylic acid (**4c**) (8 g, 89.9%), m. p. 256-57 °C.

Anal.:

TLC : R_f 0.12 (EtOAc)

IR : 3063, 1756, 1661, 1612, 1510, 1418, 1263 and 1163 cm^{-1}

MS : (*m/z*) 225.6 (M^++1)

- **Synthesis of 7-chloro-3-isocyanato-4*H*-pyrido[1,2-*a*]pyrimidin-4-one (6c)**

7-Chloro-4-oxo-4*H*-pyrido[1,2-*a*]pyrimidine-3-carbonylazide (5c)

Compound (**5c**) was prepared by reacting compound (**4c**) (8 g, 6.25 mmole) with ethyl chloroformate (6.78 g, 6.87 mmole) and sodium azide (16.25 g, 25 mmole) as described above for compound (**5a**) producing the compound (**5c**) (6.5 g, 74.2%), m. p. 159-60 °C.

Anal.:

TLC : R_f 0.25 (EtOAc)

IR : 2158, 1732, 1563, 1472, 1296, 1201 and 1023 cm^{-1}

MS : (*m/z*) 250.6 (M^++1)

7-Chloro-3-isocyanato-4*H*-pyrido[1,2-*a*]pyrimidin-4-one (6c)

5c (4 g, 1.8 mmole) was refluxed in toluene for 2 h. The reaction mixture was concentrated to obtain 7-chloro-3-isocyanato-4*H*-pyrido[1,2-*a*]pyrimidin-4-one (**6c**) (3.34 g, 98.5%), m. p. 312-13 °C.

Anal.:

TLC : R_f 0.65 (EtOAc)

IR : 2317, 2243, 1668, 1625, 1547, 1525, 1475 and 1182 cm^{-1}

MS : (*m/z*) 222.6 (M^++1)

4.1.2 Synthesis of substituted (4-oxo-4*H*-pyrido[1,2-*a*]pyrimidin-3-yl)urea derivatives (Series I)

- **Synthesis of (4-oxo-4*H*-pyrido[1,2-*a*]pyrimidin-3-yl)urea derivatives**

1-(4-Chlorobenzyl)-3-(4-oxo-4*H*-pyrido[1,2-*a*]pyrimidin-3-yl)urea (I-1)

The isocyanate (**6a**) (0.5 g, 0.27 mmole) and 4-chlorobenzylamine (0.227 g, 0.16 mmole) in toluene (25 ml) were refluxed together for 6 h. The reaction mixture was cooled to RT to get a solid precipitate. The solid precipitate was filtered and washed with hexane. The product was purified by column chromatography using hexane (20%) in ethyl acetate as eluent to get the titled compound (**I-1**) (0.2 g, 37.9%), m. p. 250-51 °C.

Anal.:

TLC : R_f 0.6 (EtOAc)

IR : 3318, 3051, 1693, 1637, 1536, 1479, 1220 and 1136 cm^{-1}

^{1}H-NMR : 4.39-4.41 (d, 2H), 7.26-7.35 (m, 3H), 7.41-7.47 (m, 2H), 7.56 (t, 1H), 7.61-7.64 (d, 1H), 7.68-7.71 (m, 1H), 8.55 (s, 1H), 8.85-8.87 (d, 1H), 9.16 (s, 1H)

MS : (*m/z*) 328.9 (M^+), 330.8 (M^++2)

1-(4-Methoxybenzyl)-3-(4-oxo-4*H*-pyrido[1,2-*a*]pyrimidin-3-yl)urea (I-2)

Compound (**I-2**) was prepared by treating the isocyanate (**6a**) (0.3 g, 0.16 mmole) with 4-methoxybenzylamine (0.172 g, 0.16 mmole) as described above for compound (**I-1**). The crude product was purified by column chromatography using methanol (1%) in ethyl acetate as eluent offering the compound (**I-2**) (0.15 g, 51.9%), m. p. 229-30 °C.

Anal.:

TLC : R_f 0.68 (1% MeOH in EtOAc)

IR : 3361, 3277, 3038, 1639, 1242, 1220, 1180 and 1122 cm^{-1}

^{1}H-NMR : 3.73 (s, 3H), 4.24-4.25 (d, 2H), 6.89-6.91 (d, 2H), 7.22-7.27 (m, 3H), 7.40-7.43 (t, 1H), 7.61-7.63 (d, 1H), 7.68-7.72 (m, 1H), 8.39 (s, 1H), 8.84-8.86 (d, 1H), 9.18 (s, 1H)

MS : (*m/z*) 325 (M^++1)

1-(2-Methoxyethyl)-3-(4-oxo-4*H*-pyrido[1,2-*a*]pyrimidin-3-yl)urea (I-3)

Compound (**I-3**) was prepared by reacting the isocyanate (**6a**) (0.3 g, 0.16 mmole) with 2-methoxyethylamine (0.119 g, 0.16 mmole) as described above for compound (**I-1**). The crude product after chromatographic purification using methanol (0.9%) in ethyl acetate as eluent provided compound (**I-3**) (0.5 g, 61.1%), m. p. 196-97 °C.

Anal.:

TLC : R_f 0.65 (1% MeOH in EtOAc)

IR : 3362, 1696, 1639, 1548, 1463, 1226, 1192 and 1099 cm^{-1}

^{1}H-NMR : 3.25-3.28 (m, 5H), 3.70-3.39 (t, 2H), 7.16-7.17 (m, 1H), 7.23-7.27 (m, 1H), 7.60-7.63 (d, 1H), 7.67-7.72 (m, 1H), 8.41 (s, 1H), 8.45-8.86 (d, 1H), 9.16(s, 1H)

MS : (*m/z*) 263 (M^++1)

***N*-{2-[3-(4-Oxo-4*H*-pyrido[1,2-*a*]pyrimidin-3-yl)ureido]ethyl}acetamide (I-4)**

The isocyanate (**6a**) (0.3 g, 0.16 mmole) was reacted with 2-acetamidoethylamine (0.62 g, 0.16 mmole) as described above for compound (**I-1**). Chromatographic purification of the crude product using methanol (0.9%) in ethyl acetate as eluent furnished compound (**I-4**) (0.5 g, 61.1%), m. p. 247-49 °C.

Anal.:

TLC : R_f 0.45 (5% MeOH in EtOAc)

IR : 3317, 3251, 1726, 1633, 1536, 1467, 1219 and 1120 cm^{-1}

^{1}H-NMR : 1.81 (s, 3H), 3.11-3.16 (m, 4H), 7.09-7.11 (m, 1H), 7.23-7.27 (m, 1H), 7.61-7.63 (d, 1H), 7.68-7.72 (m, 1H), 7.94 (b, 1H), 8.35 (s, 1H), 8.84-8.86 (d, 1H), 9.17 (s, 1H)

MS : (*m/z*) 290 (M^++1)

1-(4-Oxo-4*H*-pyrido[1,2-*a*]pyrimidin-3-yl)-3-(2-trifluoromethylbenzyl)urea (I-5)

Compound (**I-5**) was prepared by reacting the isocyanate (**6a**) (0.3 g, 0.16 mmole) with 2-trifluoromethylbenzylamine (0.281 g, 0.16 mmole) as described above for compound (**I-1**). Work-up of the reaction mixture followed by chromatographic purification of the crude product using hexane (10%) in ethyl

acetate as eluent earned the titled compound (**I-5**) (0.22 g, 37.8%), m. p. 243-45 °C.

Anal.:

TLC : R_f 0.52 (EtOAc)

IR : 3315, 3047, 1667, 1638, 1548, 1478, 1328 and 1224 cm^{-1}

^{1}H-NMR : 4.51-4.52 (d, 2H), 7.25-7.28 (t, 1H), 7.47-7.51 (m, 1H), 7.56-7.64 (m, 3H), 7.68-7.74 (m, 3H), 8.59 (s, 1H), 8.86-8.88 (d, 1H), 9.17 (s, 1H)

MS : (*m/z*) 361 (M^+-1)

1-(4-Oxo-4*H*-pyrido[1,2-*a*]pyrimidin-3-yl)-3-(4-trifluoromethylbenzyl)urea (I-6)

The isocyanate (**6a**) (0.3 g, 0.16 mmole) was treated with 4-trifluoromethylbenzylamine (0.281 g, 0.16 mmole) as described above for compound (**I-1**). The crude product after chromatographic purification using hexane (10%) in ethyl acetate as eluent offered the titled compound (**I-6**) (0.21 g, 34.4%), m. p. 256-57 °C.

Anal.:

TLC : R_f 0.48 (EtOAc)

IR : 3328, 3048, 1670, 1636, 1478, 1332, 1222 and 1107 cm^{-1}

^{1}H-NMR : 4.42-4.44 (d, 2H), 7.25-7.28 (m, 1H), 7.51-7.54 (d, 2H), 7.59-7.64 (m, 2H), 7.69-7.73 (m, 3H), 8.50 (s, 1H), 8.86-8.87 (d, 1H), 9.16 (s, 1H)

MS : (*m/z*) 363 (M^++1)

1-(2,4-Difluorobenzyl)-3-(4-oxo-4*H*-pyrido[1,2-*a*]pyrimidin-3-yl)urea (I-7)

The coupling reaction of the isocynate (**6a**) (0.3 g, 0.16 mmole) was done with 2,4-difluorobenzylamine (0.229 g, 0.16 mmole) as described above for compound (**I-1**). Work-up of the reaction mixture followed by chromatographic purification of the crude product using hexane (5%) in ethyl acetate as eluent yielded compound (**I-7**) (0.1 g, 18.8%), m. p. 170-71 °C.

Anal.:

TLC : R_f 0.48 (EtOAc)

IR : 3328, 1676, 1558, 1483, 1236 and 1127 cm^{-1}

^{1}H-NMR **:** 4.35-4.37 (d, 2H), 7.14-7.20 (m, 2H), 7.24-7.28 (m, 2H), 7.52-7.55 (t, 1H), 7.62-7.64 (d, 1H), 7.69-7.74 (m, 1H), 8.50 (s, 1H), 8.85-8.87 (d, 1H), 9.14 (s, 1H)

MS **:** (*m/z*) 331 (M^++1)

1-(4-Oxo-4*H*-pyrido[1,2-*a*]pyrimidin-3-yl)-3-[2-(thiophen-2-yl)ethyl]urea (I-8)

A mixture of isocyanate (**6a**) (0.3 g, 0.16 mmole) and 2-(2-thiophenyl)ethylamine (0.308 g, 0.16 mmole) were reacted together as described above for compound (**I-1**). The crude product was purified by column chromatography using methanol (2%) in ethyl acetate as eluent to obtain the compound (**I-8**) (0.2 g, 39.6%), m. p. 216-17 °C.

Anal.:

TLC **:** R_f 0.5 (1% MeOH in EtOAc)

IR **:** 3213, 3033, 1656, 1525, 1469, 1218, 1182 and 1127 cm^{-1}

^{1}H-NMR **:** 2.97-3.01 (t, 2H), 3.37-3.4 (t, 2H), 6.92-6.93 (b, 1H), 6.97-6.99 (m, 1H), 7.15-7.18 (t, 1H), 7.23-7.27 (m, 1H), 7.35-7.37 (d, 1H), 7.61-7.63 (d, 1H), 7.68-7.72 (m, 1H), 8.41 (s, 1H), 8.84-8.85 (d, 1H), 9.19 (s, 1H)

MS **:** (*m/z*) 315 (M^++1)

1-[3-(Morpholin-4-yl)propyl]-3-(4-oxo-4*H*-pyrido[1,2-*a*]pyrimidin-3-yl)urea (I-9)

6a (0.5 g, 0.27 mmole) and 3-(4-morpholino)propylamine (0.227 g, 0.16 mmole) were reacted together as described above for compound (**I-1**). The crude product after chromatographic purification using hexane (10%) in ethyl acetate as eluent offered the titled compound (**I-9**) (0.18 g, 40.6%), m. p. 189-90 °C.

Anal.:

TLC **:** R_f 0.67 (EtOAc)

IR **:** 3297, 3072, 1663, 1549, 1479, 1228 and 1118 cm^{-1}

^{1}H-NMR **:** 1.55-1.62 (m, 2H), 2.28-2.32 (m, 2H), 2.34 (b, 4H), 3.10-3.15 (m, 2H), 3.56-3.58 (t, 4H), 7.01-7.04 (m, 1H), 7.23-7.27 (m, 1H), 7.60-7.63 (d, 1H), 7.67-7.71 (m, 1H), 8.29 (s, 1H), 8.84-8.86 (d, 1H), 9.17 (s, 1H)

MS : (*m/z*) 332 (M^++1)

1-(3, 3-Diphenyl)propyl-3-(4-oxo-4*H*-pyrido[1,2-*a*]pyrimidin-3-yl)urea (I-10)

The isocyanate (**6a**) (0.25 g, 0.13 mmole) was reacted with 3,3-diphenylpropylamine (0.282 g, 0.13 mmole) as described above for compound (**I-1**). The chromatographic purification of the crude product using hexane (10%) in ethyl acetate as eluent afforded the urea derivative (**I-10**) (0.21 g, 39.4%), m. p. 259-60 °C.

Anal.:

TLC : R_f 0.62 (EtOAc)

IR : 3324, 3133, 3024, 1664, 1631, 1559, 1476 and 1241cm^{-1}

^{1}H-NMR : 2.18-2.23 (m, 2H), 2.97-3.05 (m, 2H), 4.01-4.05 (t, 1H), 7.11-7.34 (m, 12H), 7.60-7.63 (d, 1H), 7.67-7.74 (m, 1H), 8.32 (s, 1H), 8.85-8.92 (dd, 1H), 9.15(s, 1H)

MS : (*m/z*) 399 (M^++1)

1-(4-Oxo-4*H*-pyrido[1,2-*a*]pyrimidin-3-yl)-3-[3-(*n*.pentyloxy)pyridin-2-yl]-urea (I-11)

Compound (**I-11**) was prepared by reacting the isocynate (**6a**) (0.3 g, 0.16 mmole) with 3-*n*.pentyloxy-2-aminopyridine (0.289 g, 0.16 mmole) as described above for compound (**I-1**). The crude product after chromatographic purification using methanol (1%) in ethyl acetate as eluent offered the desired product (**I-11**) (0.2 g, 33.96%), m. p. 178-80 °C.

Anal.:

TLC : R_f 0.47 (EtOAc)

IR : 3387, 3350, 3067, 1665, 1550, 1478 and 1220 cm^{-1}

^{1}H-NMR : 0.90-0.94 (t, 3H), 1.32-1.47 (m, 4H), 1.78-1.85 (m, 2H), 4.07-4.11 (t, 2H), 7.05-7.08 (m, 1H), 7.30-7.34 (m, 1H), 7.44-7.46 (d, 1H), 7.67-7.69 (d, 1H), 7.76-7.81 (m, 1H), 7.89-7.91 (dd, 1H), 8.35 (s, 1H), 8.92-8.94 (d, 1H), 9.29 (s, 1H), 12.15 (s, 1H)

MS : (*m/z*) 368 (M^++1)

1-[3-(Benzyloxy)pyridin-2-yl]-3-(4-oxo-4*H*-pyrido[1,2-*a*]pyrimidin-3-yl)urea (I-12)

Compound (**6a**) (0.3 g, 0.16 mmole) was treated with 2-amino-3-benzyloxypyridine (0.319 g, 0.16 mmole) as described above for compound (**I-1**). The crude product was purified by column chromatography using methanol (1%) in ethyl acetate as eluent offering the titled compound (**I-12**) (0.19 g, 30.6%), m. p. 249-50 °C.

Anal.:

TLC : R_f 0.46 (EtOAc)

IR : 3133, 1675, 1558, 1482, 1192 and 1118 cm^{-1}

^{1}H-NMR : 5.29 (s, 2H), 7.07 (m, 1H), 7.33-7.42 (m, 3H), 7.51-7.57 (m, 3H), 7.70-7.76 (m, 1H), 7.77-7.79 (m, 1H), 7.91-7.92 (d, 1H), 8.46 (s, 1H), 8.90-8.94 (m, 1H), 9.22-9.28 (d, 1H), 9.52 (s, 1H), 12.06 (s, 1H)

MS : (*m/z*) 388 (M^++1)

1-[6-(Morpholin-4-yl)pyridin-2-yl]-3-(4-oxo-4*H*-pyrido[1,2-*a*]pyrimidin-3-yl)-urea (I-13)

Compound (**I-13**) was prepared by treating the isocyanate (**6a**) (0.3 g, 0.16 mmole) with 2-amino-6-morpholinopyridine (0.287 g, 0.16 mmole) as described above for compound (**I-1**). The chromatographic purification of the crude product using methanol (1%) in ethyl acetate as eluent offered compound (**I-13**) (0.25 g, 42.5%), m. p. 275-76 °C.

Anal.:

TLC : R_f 0.45 (EtOAc)

IR : 3118, 1688, 1558, 1484, 1440, 1229 and 1113 cm^{-1}

^{1}H-NMR : 3.66-3.68 (b, 4H), 3.95-3.97 (b, 4H), 6.17-6.20 (d, 1H), 6.29-6.31 (d, 1H), 7.11-7.15 (m, 1H), 7.48-7.52 (m, 2H), 7.58-7.62 (m, 1H), 7.67-7.70 (d, 1H), 8.97-8.99 (d, 1H), 9.53 (s, 1H), 11.48 (s, 1H)

MS : (*m/z*) 367 (M^++1)

Ethyl (2*S*)-2-{[(4-oxo-4*H*-pyrido[1,2-*a*]pyrimidin-3-yl)carbamoyl]amino}-3-phenylpropanoate (I-14)

The isocyanate (**6a**) (1.94 g, 6.1 mmole) and *L*-phenylalanine ethyl ester (2 g, 6.1 mmole) in toluene (25 ml) were refluxed together for 6 h. The reaction mixture was cooled to RT to yield a solid precipitate. The solid precipitate was filtered, washed with hexane and dried to get the titled compound (**I-14**) (2 g, 62.5%), m. p. 158-59 °C.

Anal.:

TLC : R_f 0.75 (EtOAc)

IR : 3338, 3032, 1733, 1688, 1629, 1132 and 1185 cm^{-1}

MS : 381(M^++1)

Methyl (2*S*)-4-methyl-2-{[(4-oxo-4*H*-pyrido[1,2-*a*]pyrimidin-3-yl)carbamoyl]-amino}*n*.pentanoate (I-15)

Compound (**I-15**) was obtained by reacting compound (**6a**) (2.85 g, 1.37 mmole) with *L*-leucine methyl ester (2 g, 1.37 mmole) as described above for compound (**I-14**). The crude product was recrystallized from methanol to yield compound (**I-15**) (2.1 g, 45.8%), m. p. 129-30 °C.

Anal.:

TLC : R_f 0.78 (EtOAc)

IR : 3325, 3276, 1745, 1657, 1634, 1550, 1528 and 1191 cm^{-1}

MS : (*m/z*) 333 (M^++1)

(2*S*)-2-{[(4-Oxo-4*H*-pyrido[1,2-*a*]pyrimidin-3-yl)carbamoyl]amino}-3-phenyl-propanamide (I-16)

A mixture of compound (**I-14**) (2 g, 0.52 mmole) and ammonia solution was stirred for 12 h. The solid precipitate so obtained was filtered, washed with water and recrystallized from methanol to furnish compound (**I-16**) (1.8 g, 97.4%), m. p. 239-40 °C.

Anal.:

TLC : R_f 0.35 (EtOAc)

IR : 3329, 1634, 1519, 1477, 1244 and 1191 cm^{-1}

MS : (*m/z*) 352 (M^++1)

(2*S*)-4-Methyl-2-{[(4-oxo-4*H*-pyrido[1,2-*a*]pyrimidin-3-yl)carbamoyl]amino}-*n*.pentanamide (**I-17**)

Compound (**I-15**) (2 g, 0.52 mmole) was stirred in ammonia solution for 12 h to get the solid precipitate. The precipitated recrystallized from methanol to obtain compound (**I-17**) (1.6 g 83.7%), m. p. 243-44 °C.

Anal.:

TLC : R_f 0.4 (EtOAc)

IR : 3361, 3320, 1672, 1628, 1528, 1469, 1437 and 1234 cm^{-1}

MS : (*m/z*) 318 (M^++1)

1-[(1*S*)-1-(Cyano-2-phenyl)ethyl]-3-(4-oxo-4*H*-pyrido[1,2-*a*]pyrimidin-3-yl)-urea (**I-18**)

The amide (**I-16**) (1.2 g, 0.34 mmole) was dissolved in dimethylformamide (2.5 ml) and cooled to 0°C. Cyanuric chloride (1.26 g, 0.68 mmole) was added in small portions and stirred for 2 h. The reaction mixture was quenched in ice-cold water (20 ml) to get solid precipitate. The solid precipitate was filtered and dried. The crude product so obtained was purified by column chromatography to earn the compound (**I-18**) (0.34 g, 29.8%), m. p. 223-25 °C.

Anal.:

TLC : R_f 0.45 (EtOAc)

IR : 3303, 2210, 1686, 1631, 1530, 1433, 1227 and 1133 cm^{-1}

^{1}H-NMR : 3.09-3.19 (m, 2H), 4.92-4.98 (m, 1H), 7.26-7.34 (m, 2H), 7.36-7.37 (m, 4H), 7.63-7.67 (m, 2H), 7.72-7.77 (m, 1H), 8.58 (s, 1H), 8.85-8.87 (d, 1H), 9.10 (s, 1H)

MS : (*m/z*) 334 (M^++1)

1-[(1*S*) 1-(Cyano-3-methyl)butyl]-3-(4-oxo-4*H*-pyrido[1,2-*a*]pyrimidin-3-yl)-urea (**I-19**)

Compound (**I-19**) was prepared by treating (**I-17**) (2.0 g, 0.63 mmole) with cyanuric chloride (2.33 g, 1.26 mmole) as described above for compound (**I-18**). The chromatographic purification of the crude product using hexane (25%) in ethyl acetate as eluent offered compound (**I-19**) (0.35 g, 18%), m. p. 237-39 °C.

Anal.:

TLC : R_f 0.55 (EtOAc)

IR : 3342, 2210, 1642, 1557, 1510, 1465, 1434 and 1235 cm^{-1}

^{1}H-NMR : 0.91-0.96 (d, 6H), 1.64-1.80 (m, 3H), 4.65-4.71(m, 1H), 7.27-7.31 (m, 1H), 7.65-7.67 (d, 2H), 7.73-7.77 (m, 1H), 8.49 (s, 1H), 8.86-8.88 (d, 1H), 9.12 (s, 1H)

MS : (*m/z*) 300 (M^++1)

1-Benzyl-1-isopropyl-3-(4-oxo-4*H*-pyrido[1,2-*a*]pyrimidin-3-yl)urea (I-20)

Isocyanate (**6a**) (0.25 g, 0.13 mmole) and *N-i*sopropylbenzylamine (0.199 g, 0.13 mmole) were reacted as described above for compound (**I-1**). The crude product by chromatographic purification using hexane (10%) in ethyl acetate offered the titled compound (**I-20**) (0.15 g, 30.6%), m. p. 145-46 °C.

Anal.:

TCL : R_f 0.61 (EtOAc)

IR : 3373, 1641, 1527, 1483, 1410, 1232, 1176, and 940 cm^{-1}

^{1}HNMR : 1.14-1.16 (d, 6H), 4.51-4.52 (m, 1H), 4.55 (s, 2H), 7.25-7.29 (m, 2H), 7.36-7.37 (d, 4H), 7.50 (s, 1H), 7.63-7.65 (d, 1H), 7.73-7.77 (m, 1H), 8.78-8.80 (d, 1H), 8.96 (s, 1H)

MS : (*m/z*) 337 (M^+-1)

- **Synthesis of 8-methyl-(4-oxo-4*H*-pyrido[1,2-*a*]pyrimidin-3-yl)urea derivatives**

1-(2-Methoxyethyl)-3-(8-methyl-4-oxo-4H-pyrido[1,2-a]pyrimidin-3-yl)urea (I-21)

Compound (**I-21**) was prepared by reacting compound (**6b**) (0.3 g, 0.149 mmole) with 2-methoxyethyl amine (0.111 g, 0.149 mmole) as described above for compound (**I-1**). Work up of the reaction mixture followed by chromatographic purification using hexane (5%) in ethyl acetate as eluent yielded compound (**I-21**) (**0.16** g, 38.84%), m. p. 233-34 °C.

Anal.:

TLC : R_f 0.75 (1% MeOH in EtOAc)

IR : 3388, 3305, 2890, 2360, 1633, 1534, 1452, 1228, 1179, 1088, 1006, 935, 809 and 630 cm^{-1}

^{1}HNMR : 2.39 (s, 3H), 3.22-3.25 (t, 4H), 3.35 (s, 3H), 7.09-7.11 (m, 2H), 7.41 (s, 1H), 8.30 (s, 1H), 8.73-8.75 (d, 1H), 9.06 (s, 1H)

MS **:** (*m/z*) 277 (M^+-1)

***N*-{2-[3-(8-Methyl-4-oxo-4*H*-pyrido[1,2-*a*]pyrimidin-3-yl)ureido]ethyl}acetamide (I-22)**

Compound (**I-22**) was prepared by reacting compound (**6b**) (0.3 g, 0.149 mmole) with 2-acetamidoethylamine (0.151 g, 0.149 mmole) as described above for compound (**I-1**). Chromatographic purification of the crude product was done using hexane (5%) in ethyl acetate as eluent to yield the desired porduct (**I-22**) (0.2 g, 44.2%), m. p. 269-70 °C.

Anal.:

TLC **:** R_f 0.7 (1% MeOH in EtOAc)

IR **:** 3356, 3289, 1633, 1524, 1451, 1239 and 1004 cm^{-1}

^{1}H-NMR **:** 1.81 (s, 3H), 2.41 (s, 3H), 3.1-3.15 (m, 4H), 7.03-7.06 (m, 1H) 7.11-7.13 (dd, 1H), 7.43 (s, 1H), 7.93-7.94 (m, 1H), 8.26 (s, 1H), 8.76-8.78 (d, 1H), 9.09 (s, 1H)

MS **:** (*m/z*) 304 (M^++1)

1-(8-Methyl-4-oxo-4*H*-pyrido[1,2-*a*]pyrimidin-3-yl)-3-[2-(thiophen-2-yl)ethyl]urea (I-23)

Compound (**6b**) (0.3 g, 0.149 mmole) was treated with 2-(2-thiophenyl)ethylamine (0.188 g, 0.149 mmole) as described above for compound (**I-1**). Work-up of the reaction mixture followed by chromatographic purification of the crude product using methanol (0.2%) in ethyl acetate as eluent produced 1-(8-methyl-4-oxo-4*H*-pyrido[1,2-*a*]pyrimidin-3-yl)-3-[2-(thiophen-2-yl)-ethyl]urea (**I-23**) (0.2 g, 40.8%), m. p. 249-50 °C

Anal.:

TLC **:** R_f 0.78 (1% MeOH in EtOAc)

IR **:** 3278, 1634, 1518 and 1449 cm^{-1}

^{1}H-NMR **:** 2.41 (s, 3H), 2.95-2.98 (m, 4H), 6.92 (s, 1H), 6.98 (d, 1H), 7.11-7.12 (m, 2H), 7.35-7.37 (d, 1H), 7.43 (s, 1H), 8.32 (s, 1H), 8.75-8.77 (d, 1H), 9.11 (s, 1H)

MS **:** (*m/z*) 329 (M^++1)

1-(8-Methyl-4-oxo-4*H*-pyrido[1,2-*a*]pyrimidin-3-yl)-3-[2-(morpholin-4-yl)ethyl]urea (I-24)

The isocyanate derivative (**6b**) (0.3 g, 0.149 mmole) was reacted with 2-(4-morpholinyl)ethylamine (0.163 g, 0.149 mmole) as described above for compound (**I-1**). Chromatographic purification of the crude product using methanol (0.5%) in ethyl acetate as eluent offered compound (**I-24**) (0.21 g, 42.5%), m. p. 225-26 °C.

Anal.:

TLC : R_f 0.64 (1% MeOH in EtOAc)

IR : 3334, 1632, 1569, 1460, 1235, 1145, 1104 and 1002 cm^{-1}

^{1}H-NMR : 2.37-2.41 (m, 9H), 3.21-3.24 (m, 2H), 3.58-3.59 (b, 4H), 6.98-6.99 (m, 1H), 7.11-7.12 (d, 1H), 7.42 (s, 1H), 8.37 (s, 1H), 8.76-8.78 (d, 1H), 9.08-9.09 (d, 1H)

MS : (*m/z*) 332 (M^++1)

1-Benzyl-1-isopropyl-3-(8-methyl-4-oxo-4*H*-pyrido[1,2-*a*]pyrimidin-3-yl)urea (I-25)

Isocyanate derivative (**6b**) (0.25 g, 0.12 mmole) in toluene (25 ml) was refluxed with *N-i*sopropylbenzylamine (0.185 g, 0.12 mmole) for 4 h to get a solid. The solid so obtained was filtered and washed with hexane. Chromatographic purification of the crude product using hexane (5%) in ethyl acetate provided the titled compound (**I-25**) (0.16 g, 36.7%), m. p. 161-62 °C.

Anal.:

TLC : R_f 0.62 (EtOAc)

IR : 3353, 3031, 2971, 1642, 1546, 1486, 1403 and 1242 cm^{-1}

^{1}HNMR : 1.13-1.15 (d, 6H), 2.41 (s, 3H), 4.49-4,51 (m, 1H), 4.54 (s, 2H), 7.13-7.15 (d, 1H), 7.25- 7.26 (m, 1H), 7.35-7.36 (d, 4H), 7.45 (b, 2H), 8.70-8.72 (d, 1H), 8.87 (s, 1H)

MS : (*m/z*) 349 (M^+), 350.9 (M^++2)

- **Synthesis of 7-chloro-(4-oxo-4*H*-pyrido[1,2-*a*]pyrimidin-3-yl)urea derivatives**

1-(7-Chloro-4-oxo-4*H*-pyrido[1,2-*a*]pyrimidin-3-yl)-3-[2-(morpholin-4-yl)ethyl]urea (I-26)

Compound (**I-26**) was prepared by reacting compound (**6c**) (0.3 g, 0.135 mmole) with 2-(4-morpholinyl)ethylamine (0.176 g, 0.135 mmole) as described above for compound (**I-1**). Chromatographic purification of the crude product using methanol (2%) in ethyl acetate as eluent furnished the titled compound (**I-26**) (0.22 g, 46.2%), m. p. 226-27 °C.

Anal.:

TLC : R_f 0.5 (2% MeOH in EtOAc)

IR : 3285, 1729, 1646, 1552, 1464, 1284, 1247 and 1117 cm^{-1}

^{1}H-NMR : 2.39 (b, 6H), 3.23-3.24 (m, 2H), 3.60 (b, 4H), 7.08 (b, 1H), 7.63-7.65 (d, 1H), 7.70-7.73 (dd, 1H), 8.57 (s, 1H), 8.84 (s, 1H), 9.17 (s, 1H)

MS : (*m/z*) 352.1 (M^+), 354.1 (M^++2)

1-(7-Chloro-4-oxo-4*H*-pyrido[1,2-*a*]pyrimidin-3-yl)-3-[2-(thiophen-2-yl)ethyl]urea (I-27)

Compound (**I-27**) was obtained by treating compound (**6c**) (0.3 g, 0.135 mmole) with 2-(2-thiophenyl)ethylamine (0.17 g, 0.135 mmole) as described above for compound (**I-1**). Work-up of the reaction mixture followed by chromatographic purification of the crude product using hexane (10%) in ethyl acetate as eluent offered compound (**I-27**) (0.24 g, 50.8%), m. p. 216-17 °C.

Anal.:

TLC : R_f 0.75 (1% MeOH in EtOAc)

IR : 3387, 1651, 1544, 1510, 1470, 1224 and 1189 cm^{-1}

^{1}H-NMR : 2.97-3.00 (t, 2H), 3.37-3.40 (t, 2H), 6.92-6.93 (d, 1H), 6.97-6.99 (m, 1H), 7.18-7.20 (m, 1H), 7.35-7.37 (m, 1H), 7.63-7.66 (d, 1H), 7.71-7.74 (dd, 1H), 8.51 (s, 1H), 8.83-8.84 (d, 1H), 9.19 (s, 1H)

MS : (*m/z*) 349 (M^+), 350.9 (M^++2)

1-(7-Chloro-4-oxo-4*H*-pyrido[1,2-*a*]pyrimidin-3-yl)-3-(thiophen-2-yl)methyl-urea (I-28)

Isocyanate derivative (**6c**) (0.25 g, 0.11 mmole) in toluene was refluxed

with (2-thiophenyl)methylamine (0.127 g, 0.11 mmole) to get a solid. The solid so obtained was filtered and washed with hexane. The crude product was purified by column chromatography using 1% methanol in ethyl acetate to obtain the compound (**I-28**) (0.15 g, 39.76%), m. p. 285-87 °C.

Anal.:

TLC : R_f 0.6 (EtOAc)

IR : 3272, 3024, 1652, 1562, 1472, 1337, 1240, and 1155 cm^{-1}

^{1}HNMR : 4.49-4.50 (d, 2H), 6.97-6.98 (m, 1H), 7.00 (s, 1H), 7.40-7.41 (d, 1H), 7.56 (b, 1H), 7.64-7.66 (d, 1H), 7.72-7.74 (d, 1H), 8.51 (s, 1H), 8.89 (s, 1H), 9.18 (s, 1H)

MS : (*m/z*) 335.34(M^++1), 337.38 (M^++2)

1-(7-Chloro-4-oxo-4*H*-pyrido[1,2-*a*]pyrimidin-3-yl)-3-(2-methoxyethyl)urea (I-29)

A mixture of isocyanate derivative (**6c**) (0.25 g, 0.11 mmole), 2-methoxyethylamine (0.162 g, 0.11 mmole) and toluene was refluxed for 4 h to get solid precipitate. The solid so obtained was filtered and washed with hexane. Chromatographic purification of the product using hexane (15%) in ethyl acetate accomplished the desired compound (**I-29**) (0.22 g, 65.74%), m. p. 254-56 °C.

Anal.:

TLC : R_f 0.65 (5% MeOH in EtOAc)

IR : 3370, 3116, 2972, 1702, 1649, 1557, 1528, 1434, 1354, 1229, 1199, 1106, 817, 757 and 593 cm^{-1}

^{1}HNMR : 3.24-3.39 (m, 7H,), 7.19-7.21 (m, 1H), 7.63-7.65 (d, 1H), 7.70-7.73 (dd, 1H), 8.51 (s, 1H), 8.83-8.84 (b, 1H), 9.16 (s, 1H)

MS : (*m/z*) 297.39 (M^+), 299.38 (M^++2)

1-(7-Chloro-4-oxo-4*H*-pyrido[1,2-*a*]pyrimidin-3-yl)-3-(4-trifluoromethyl)benzylurea (I-30)

A mixture of isocyanate derivative (**6c**) (0.25 g, 0.11 mmole) and 4-trifluoromethylbenzylamine (0.197 g, 0.11 mmole) in toluene was refluxed for 4 h. Solid precipitate so obtained was filtered and washed with hexane.

Chromatographic purification of the crude product using 1% methanol in ethyl acetate yielded the titled compound (**I-30**) (0.23 g, (51.4%), m. p. 287-89 °C.

Anal.:

TLC : R_f 0.61 (1% MeOH in EtOAc)

IR : 3397, 3187, 1692, 1656, 1632, 1364 and 1226 cm^{-1}

^{1}HNMR : 4.42-4.44 (d, 2H), 7.57-7.66 (m, 6H), 7.72-7.75 (dd, 1H), 8.58 (s, 1H), 8.84-8.85 (d, 1H), 9.16 (s, 1H)

MS : (*m/z*) 397.34(M^+), 399.38 (M^++2)

1-(7-Chloro-4-oxo-4*H*-pyrido[1,2-*a*]pyrimidin-3-yl)-3-(3-trifluoromethyl)benzylurea (**I-31**)

A mixture of isocyanate derivative (**6c**) (0.25 g, 0.11 mmole) and 3-trifluoromethylbenzylamine (0.197 g, 0.11 mmole) and toluene (50 ml) was refluxed for 4 h. Solid precipitate so obtained was filtered and washed with hexane. The crude product was purified by column chromatography using hexane (5%) in ethyl acetate to furnish the titled compound (**I-31**) (0.22 g, 49.1%), m. p. 260-62 °C.

Anal.:

TLC : R_f 0.6 (1% MeOH in EtOAc)

IR : 3312, 3282, 3085, 1677, 1646, 1564, 1488, 1433, 1331, 1243, 1160, 1107, 1016, 821, 765 and 644 cm^{-1}

^{1}HNMR : 4.42-4.43 (d, 2H), 7.51-7.53 (d, 2H), 7.61-7.63 (m, 2H), 7.70-7.75 (m, 3H), 8.60 (s, 1H), 8.84-8.85 (d, 1H), 9.17 (s, 1H)

MS : (*m/z*) 397.34(M^+), 399.32 (M^++2)

1-(7-Chloro-4-oxo-4*H*-pyrido[1,2-*a*]pyrimidin-3-yl)-3-(2-trifluoromethyl)benzylurea (**I-32**)

Isocyanate derivative (**6c**) (0.25 g, 0.11 mmole) in toluene was refluxed with 2-trifluoromethylbenzylamine (0.197 g, 0.11 mmole) to get solid precipitate. The solid so obtained was filtered and washed with hexane. Chromatographic purification of the crude product using hexane (5%) in ethyl acetate furnished the titled compound (**I-32**) (0.23 g, 51.4%), m. p. 276-78 °C.

Anal.:

TLC : R_f 0.62 (1% MeOH in EtOAc)

IR : 3362, 3126, 1707, 1622, 1558, 1461, 1311 and 1225 cm^{-1}

^{1}HNMR : 4.51-4.52 (d, 2H), 7.47-7.51 (m, 1H), 7.59-7.75 (m, 6H), 8.68 (s, 1H), 8.85 (b, 1H), 9.17 (s, 1H)

MS : (*m/z*) 397.34 (M^+), 399.32, (M^++2)

1-Benzyl-3-(7-chloro-4-oxo-4*H*-pyrido[1,2-*a*]pyrimidin-3-yl)-1-isopropylurea (I-33)

Isocyanate derivative (**6c**) (0.25 g, 0.11 mmole) in toluene (25 ml) was refluxed with *N-i*sopropylbenzylamine (0.168 g, 0.11 mmole) for 5 h to get solid precipitate. Chromatographic purification of the crude product using hexane (10%) in ethyl acetate offered the desired compound (**I-33**) (0.2 g, 47.8%), m. p. 158-60 °C.

Anal.:

TLC : R_f 0.64 (EtOAc)

IR : 3447, 1663, 1630, 1521, 1487, 1234, 1114 and 1070 cm^{-1}

MS : (*m/z*) 371.42 (M^+), 373.41(M^++2)

1-Benzyl-3-(7-chloro-4-oxo-4*H*-pyrido[1,2-*a*]pyrimidin-3-yl)-1-phenethylurea (I-34)

Reaction of isocyanate derivative (**6c**) (0.25 g, 0.11 mmole) and *N*-benzyl phenylethylamine (0.238 g, 0.11 mmole) was done as described above for compound (**I-1**). The crude product was purified by column chromatography using 2% methanol in ethyl acetate to obtain the titled compound (**I-34**) (0.18 g, 36.8%), m. p. 195-97 °C.

Anal.:

TLC : R_f 0.55 (1% MeOH in EtOAc)

IR : 3345, 3028, 1647, 1550, 1493, 1435, 1366 and 1233 cm^{-1}

^{1}HNMR : 2.85-2.89 (t, 2H), 3.35-3.59 (t, 2H), 4.58 (s, 2H), 7.14-7.38 (m, 11H), 7.68-7.71 (d, 1H), 7.81-7.82 (b, 2H), 8.88 (b, 1H), 8.92 (s, 1H)

MS : (*m/z*) 433.42 (M^+), 435.41 (M^++2)

3.1.3 Synthesis of *N*-(4-oxo-4*H*-pyrido[1,2-*a*]pyrimidin-3-yl)-4-(pyridin-2-yl)piperazine-1-carboxamide derivatives (Series II)

- **Synthesis of *N*-(4-oxo-4*H*-pyrido[1,2-*a*]pyrimidin-3-yl)-4-(pyridin-2-yl)- piperazine-1-carboxamide derivatives**

_N_-(4-Oxo-4_H_-pyrido[1,2-_a_]pyrimidin-3-yl)-4-(pyridin-2-yl)piperazine-1-carboxamide (II-1)

Compound (**II-1**) was prepared by reacting compound (**6a**) (0.3 g, 0.16 mmole) with 4-(2-pyridyl)piperazine (0.262 g, 0.16 mmole) as described above for compound (**I-1**). The crude product was purified by column chromatography using hexane (10%) in ethyl acetate as eluent to afford the compound (**II-1**) (0.19 g, 33.8%), m. p. 194-95 °C.

Anal.:

TLC : R_f 0.51 (1% MeOH in EtOAc)

IR : 3393, 3107, 1659, 1596, 1537, 1482 and 1238 cm^{-1}

^{1}H-NMR : 3.57-3.58 (b, 8H), 6.65-6.69 (m, 1H), 6.86-6.88 (d, 1H), 7.31-7.35 (m, 1H), 7.54-7.58 (m, 1H), 7.67-7.69 (d, 1H), 7.80-7.84 (m, 1H), 8.08 (s, 1H), 8.13-8.14 (d, 1H), 8.77 (s, 1H) 8.90-8.93 (d, 1H)

MS : (*m/z*) 351 (M^++1)

4-(4-Methoxyphenyl)-_N_-(4-oxo-4_H_-pyrido[1,2-_a_]pyrimidin-3-yl)piperazine-1-carboxamide (II-2)

The urea derivative (**II-2**) was obtained by refluxing the isocyanate (**6a**) (0.3 g, 0.16 mmole) with 1-(4-methoxyphenyl piperazine (0.308 g, 0.16 mmole) in toluene for 6 h. The reaction mixture was cooled to RT and the solid precipitate was filtered. The chromatographic purification of the crude product using hexane (10%) in ethyl acetate as eluent yielded the titled compound (**II-2**) (0.19 g 31.2%), m. p. 143-45 °C.

Anal.:

TLC : R_f 0.52 (1% MeOH in EtOAc)

IR : 3396, 3031, 2926, 1649, 1479, 1437, 1229 and 1021 cm^{-1}

^{1}H-NMR : 2.99 (b, 4H), 3.61(b, 4H), 3.81 (s, 3H), 6.87-7.01 (m, 4H),

7.32-7.35 (m, 1H), 7.67-7.69 (d, 1H), 7.80-7.84 (m, 1H), 8.06 (s, 1H), 8.77 (s, 1H), 8.91-8.93 (d, 1H)

MS : (*m/z*) 380 (M^++1)

***N*-(4-Oxo-4*H*-pyrido[1,2-*a*]pyrimidin-3-yl)-4-[3-(*N*-*c*yclopropylcarboxamido) pyridine-2-yl]piperazinecarboxamide (II-3)**

Compound (**II-3**) was prepared by reacting the isocyanate (**6a**) (0.3 g, 0.16 mmole) with *N*-cyclopropyl-2-(piperazine-1-yl)pyridine-3-carboxamide (0.319 g, 0.16 mmole) as described above for compound (**I-1**). The crude compound was purified by column chromatography using methanol (3%) in ethyl acetate as eluent to get the desired compound (**II-3**) (0.22 g, 31.6%), m. p. 140-42 °C.

Anal.:

TLC : R_f 0.4 (EtOAc)

IR : 3296, 3035, 1654, 1530, 1484, 1434, 1234 and 1134 cm^{-1}

^{1}H-NMR : 0.55-0.58 (m, 2H), 0.69-0.72 (m, 2H), 2.82-2.83 (m, 1H), 3.31-3.36 (t, 4H), 3.57-3.59 (t, 4H), 6.89-6.92 (m, 1H), 7.32-7.36 (m, 1H), 7.65-7.67 (m, 2H), 7.81-7.85 (m, 1H), 8.08 (s, 1H), 8.23-8.25 (dd, 1H), 8.51-8.53 (d, 1H), 8.76 (s, 1H), 8.91-8.93 (d, 1H)

MS : (*m/z*) 434 (M^++1)

4-Benzhydryl-1-[*N*-(4-oxo-4*H*-pyrido[1,2-a]pyrimidin-3-yl)]carboxamido-piperazine (II-4)

The isocyanate (**6a**) (0.3 g, 0.16 mmole) was reacted with benzhydrylpiperazine (0.404 g, 0.16 mmole) as described above for compound (**I-1**). The crude product was purified by column chromatography using hexane (5%) in ethyl acetate as eluent offering the titled compound (**II-4**) (0.2 g, 42.5%), m. p. 253-55 °C.

Anal.:

TLC : R_f 0.45 (EtOAc)

IR : 3403, 3032, 1657, 1527, 1484, 1294, 1232 and 1110 cm^{-1}

^{1}H-NMR : 2.33-2.36 (t, 4H), 3.48-3.49 (t, 4H), 4.35 (s, 1H), 7.19-7.22

(m, 2H), 7.30-7.34 (m, 5H), 7.45-7.47 (d, 4H), 7.66-7.68 (d, 1H), 7.79-7.83 (m, 1H), 7.93 (s, 1H), 8.74 (s, 1H), 8.88-8.90 (d, 1H)

MS : (*m/z*) 440 (M^++1)

- **Synthesis of *N*-(8-methyl-4-oxo-4*H*-pyrido[1,2-*a*]pyrimidin-3-yl)-4-(pyridin-2-yl)piperazine-1-carboxamide derivatives**

***N*-(8-Methyl-4-oxo-4*H*-pyrido[1,2-*a*]pyrimidin-3-yl)-4-(pyridin-2-yl)piperazine-1-carboxamide (II-5)**

Compound (**6b**) (0.3 g, 0.149 mmole) was reacted with 4-(2-pyridyl)piperazine (0.243 g, 0.149 mmole) as described above for compound (**I-1**). The chromatographic purification of the crude product was done using methanol (2%) in ethyl acetate as eluent to get the product (**II-5**) (0.18 g, 33.1%), m. p. 160-61°C.

Anal.:

TLC : R_f 0.75 (1% MeOH in EtOAc)

IR : 3395, 3045, 1654, 1596, 1531, 1484, 1245, and 1192 cm^{-1}

^{1}H-NMR : 2.45 (s, 3H), 3.57 (b, 8H), 6.65-6.68 (m, 1H), 6.86-6.88 (d, 1H), 7.20-7.22 (d, 1H), 7.50 (s, 1H), 7.54-7.58 (m, 1H), 8.05 (s, 1H), 8.13-8.14 (d, 1H), 8.66 (s, 1H), 8.82-8.84 (d, 1H)

MS : (*m/z*) 365 (M^++1)

***N*-(8-Methyl-4-oxo-4*H*-pyrido[1,2-*a*]pyrimidin-3-yl)-4-[(4-methoxyphenyl)]-piperazine-1-carboxamide (II-6)**

Compound (**II-6**) was prepared by reacting compound (**6b**) (0.3 g, 0.149 mmole) with 4-(4-methoxyphenyl)piperazine (0.287 g, 0.149 mmole) as described above for compound (**I-1**). Chromatographic purification of the crude product using methanol (2%) in ethyl acetate as eluent provided the titled compound (**II-6**) (0.195 g, 33.2%), m. p. 134-35 °C.

Anal.:

TLC : R_f 0.78 (1% MeOH in EtOAc)

IR : 3393, 1648, 1530, 1483, 1241, 1188 and 1153 cm^{-1}

^{1}H-NMR : 2.44 (s, 3H), 2.97-2.99 (b, 4H), 3.58-3.61 (b, 4H), 3.80 (s, 3H), 6.87-7.00 (m, 4H), 7.19-7.22 (dd, 1H), 7.50 (s, 1H), 8.00

(s, 1H), 8.66 (s, 1H), 8.82-8.84 (d, 1H)

MS : (*m/z*) 394 (M^++1)

***N*-(8-Methyl-4-oxo-4*H*-pyrido[1,2-*a*]pyrimidin-3-yl)-4-benzhydrylpiperazine-1-carboxamide** (**II-7**)

The isocyanate derivative (**6b**) (0.3 g, 0.149 mmole) and benzhydryl piperazine (0.376 g, 0.147 mmole) were reacted together as described above for compound (**I-1**). The crude product was purified by chromatographic purification using methanol (0.5%) in ethyl acetate as eluent to obtain the compound (**II-7**) (0.2 g, 29.5%), m. p. 233-35 °C.

Anal.:

TLC : R_f 0.54 (EtOAc)

IR : 3000, 1644, 1529, 1481, 1237 and 1186 cm^{-1}

^{1}H-NMR : 2.32-2.34 (b, 4H), 2.43 (s, 3H), 3.46-3.48 (b, 4H), 4.34 (s,1H), 7.18-7.22 (m, 3H), 7.29-7.33 (m, 4H), 7.44-7.48 (m, 5H), 7.87 (s, 1H), 8.63 (s, 1H), 8.79-8.81 (d, 1H)

MS : (*m/z*) 454 (M^++1)

- **Synthesis of *N*-(7-chloro-4-oxo-4*H*-pyrido[1,2-*a*]pyrimidin-3-yl)-4-(pyridin-2-yl)piperazine-1-carboxamide derivatives**

***N*-[(7-Chloro-4-oxo-4*H*-pyrido[1,2-*a*]pyrimidin-3-yl)-4-(pyridin-2-yl)piperazine]-1-carboxamide** (**II-8**)

Compound (**II-8**) was prepared by reacting compound (**6c**) (0.3 g, 0.135 mmole) with 4-(2-pyridyl)piperazine (0.221 g, 0.135 mmole) as described above for compound (**I-1**). The chromatographic purification of the crude product was done using methanol (2%) in ethyl acetate as eluent to earn the compound (**II-8**) (0.21 g, 40.3%), m. p. 189-90 °C.

Anal.:

TLC : R_f 0.45 (10% MeOH in EtOAc)

IR : 3397, 3088, 1729, 1643, 1531, 1482, 1243 and 1124 cm^{-1}

^{1}H-NMR : 3.57-3.58 (m, 8H), 6.65-6.68 (m, 1H), 6.86-6.88 (d, 1H), 7.54-7.58 (m, 1H), 7.69-7.71 (d, 1H), 7.83-7.86 (dd, 1H), 8.13-8.14 (d, 1H), 8.16 (s, 1H), 8.82 (s, 1H), 8.89-8.90 (d, 1H)

MS : (*m/z*) 385 (M^++1)

***N*-[(7-Chloro-4-oxo-4*H*-pyrido[1,2-*a*]pyrimidin-3-yl)-4-(4-methoxyphenyl)-piperazine]-1-carboxamide (II-9)**

Compound (**6c**) (0.3 g, 0.135 mmole) was reacted with 4-(4-methoxyphenyl)piperazine (0.26 g, 0.135 mmole) as described above for compound (**I-1**). Chromatographic purification of the crude product was done using methanol (2%) in ethyl acetate as eluent yielding the titled compound (**II-9**) (0.25 g, 44.72%), m. p. 163-64 °C.

Anal.:

TLC : R_f 0.75 (10% MeOH in EtOAc)

IR : 3393, 1656, 1626, 1525, 1483, 1347, 1236 and 1065 cm^{-1}

^{1}H-NMR : 2.97-2.99 (b, 4H), 3.60-3.61(b, 4H), 3.80 (s, 3H), 6.87-7.00 (m, 4H), 7.69-7.71 (d, 1H), 7.83-7.86 (m, 1H), 8.13 (s, 1H), 8.89 (s, 1H), 8.90 (s, 1H)

MS : (*m/z*) 414 (M^++1)

***N*-[(7-Chloro-4-oxo-4*H*-pyrido[1,2-*a*]pyrimidin-3-yl)-(4-*tert*-butyloxycarbony-l)-piperazine]-1-carboxamide (II-10)**

Isocyanate derivative (**6c**) (0.25 g, 11 mmole) in toluene (25 ml) was refluxed with boc-piperazine (0.209 g, 0.11 mmole) to get a solid precipitate. The solid so obtained was filtered and washed with hexane. Chromatographic purification of the crude product using hexane (10%) in ethyl acetate provided the desired compound (**II-10**) (0.2 g, 43.4%), m. p. 229-30 °C.

Anal.:

TLC : R_f 0.6 (1% MeOH in EtOAc)

IR : 3393, 1691, 1650, 1629, 1490, 1422, 1233 and 1173 cm^{-1}

^{1}HNMR : 1.42 (s, 9H), 3.39 (b, 4H), 3.44-3.45 (b, 4H), 7.68-7.71 (d, 1H), 7.83-7.85 (d, 1H), 8.13 (s, 1H), 8.78 (s, 1H), 8.88-8.89 (d, 1H)

MS : (*m/z*) 408.41, 410.39 (M^+-1)

***N*-[(7-Chloro-4-oxo-4*H*-pyrido[1,2-*a*]pyrimidin-3-yl)-4-(furan-2-carbonyl)-piperazine]-1-carboxamide (II-11)**

Isocyanate derivative (**6c**) (0.25 g, 0.11 mmole) was reacted with 1-(furan-2-carbonyl)piperazine (0.203 g, 0.11 mmole) as described above for compound (**I-1**). Chromatographic purification of the crude product using 1% methanol in ethyl acetate offered the desired compound (**II-11**) (0.19 g, 41.9%), m. p. 227-28 °C.

Anal.:

TLC : R_f 0.58 (1% MeOH in EtOAc)

IR : 3446, 3086, 1680, 1626, 1427, 1290, 1242 and 1199 cm^{-1}

^{1}HNMR : 3.57-3.58 (b, 4H), 3.74 (b, 4H), 6.65 (s, 1H), 7.04-7.05 (d, 1H), 7.69-7.71 (d, 1H), 7.83-7.86 (m, 1H), 7.87 (s, 1H), 8.18 (s, 1H), 8.80 (s, 1H), 8.89 (b, 1H)

MS : (*m/z*) 402 (M^+-1)

4.1.4 Synthesis of 4-oxo-4*H*-pyrido[1,2-*a*]pyrimidin-3-yl-carbamate derivatives (Series III)

- **Synthesis of 4-oxo-4*H*-pyrido[1,2-*a*]pyrimidin-3-yl-carbamate derivatives**

Benzyl (4-oxo-4*H*-pyrido[1,2-*a*]pyrimidin-3-yl)carbamate (III-1)

Compound (**6a**) (0.3 g, 16 mmole) and benzyl alcohol (0.173 g, 16 mmole) in toluene (25ml) were refluxed for 6 h to get a solid precipitate. The solid precipitate was filtered and washed with hexane and the crude product so obtained was purified by column chromatography using hexane (10%) in ethyl acetate as eluent to offer the titled compound (**III-1**) (0.5 g, 61.1%), m. p. 158-60 °C (Lit.[221] 153-55 °C).

Anal.:

TLC : R_f 0.6 (1% MeOH in EtOAc)

IR : 3239, 1718, 1650, 1461, 1274, 1228, 1180 and 1116 cm^{-1}

^{1}H-NMR : 5.17 (s, 2H), 7.32-7.44 (m, 6H), 7.69-7.71 (d, 1H), 7.84-7.89 (m, 1H), 8.70 (b, 1H), 8.92-8.94 (d, 1H), 9.05 (b, 1H)

MS : (*m/z*) 296 (M^++1)

Pyridin-2-ylmethyl (4-oxo-4*H*-[1,2-*a*]pyrimidin-3-yl)carbamate (III-2)

Compound (**III-2**) was prepared by reacting (**6a**) (0.5 g, 0.26 mmole) with pyridine-2-methanol (0.175 g, 0.16 mmole) as described above for compound (**III-1**). The crude product was subjected to chromatographic purification using hexane (10%) in ethyl acetate as eluent affording the titled compound (**III-2**) (0.24 g, 50.5%), m. p. 178-80 °C.

Anal.:

TLC : R_f 0.6 (1% MeOH in EtOAc)

IR : 3245, 3070, 1713, 1666, 1549, 1477, 1234 and 1125 cm^{-1}

^{1}H-NMR : 5.22 (s, 2H), 7.33-7.38 (m, 2H), 7.51-7.53 (d, 1H), 7.69-7.72 (d, 1H), 7.83-7.89 (m, 2H), 8.55-8.57 (d, 1H), 8.72 (s, 1H), 8.94-8.95 (d, 1H), 9.21 (b, 1H)

MS : (*m/z*) 297 (M^++1)

3-Fluorobenzyl (4-oxo-4*H*-pyrido[1,2-*a*]pyrimidin-3-yl)carbamate (III-3)

A mixture of isocyanate derivative (**6a**) (0.25 g, 0.13 mmole) and 3-fluorobenzyl alcohol (0.169 g, 0.13 mmole) were reacted as described above for compound (**III-1**). The crude product was purified by column chromatography using hexane (20%) in ethyl acetate to attain the titled compound (**III-3**) (0.11 g, 26.2%), m. p. 158-60 °C.

Anal.:

TLC : R_f 0.65 (EtOAc)

IR : 3416, 3264, 1716, 1659, 1480, 1441, 1403, 1234, 1200, 1184, 1134, 796 and 773 cm^{-1}

^{1}HNMR : 5.19 (s, 2H), 7.14-7.19 (m, 1H), 7.27-7.37 (m, 3H), 7.41-7.47 (m, 1H), 7.69-7.71 (d, 1H), 7.85-7.89 (m, 1H), 8.72 (s, 1H), 8.93-8.95 (d, 1H), 9.16 (b, 1H)

MS : (*m/z*) 314, (M^+-1)

3,4-Methylenedioxybenzyl(4-oxo-4*H*-pyrido[1,2-*a*]pyrimdin-3-yl)carbamate (III-4)

6a (0.5 g, 0.26 mmole) was reacted with 3,4-methylenedioxybenzyl alcohol (0.244 g, 0.106 mmole) as described above for compound (**III-1**). The chromatographic purification of the crude product using hexane (10%) in ethyl

acetate as eluent offered the titled compound (**III-4**) (0.18 g, 33%), m. p. 175-76 °C.

Anal.:

TLC : R_f 0.5 (EtOAc)

IR : 3242, 3031, 1717, 1666, 1485, 1443, 1235 and 1137 cm^{-1}

^{1}H-NMR : 5.06 (s, 2H), 6.02 (s, 2H), 6.92 (s, 2H), 7.02 (s, 1H), 7.33-7.37 (m, 1H), 7.69-7.71 (d, 1H), 7.84-7.89 (m, 1H), 8.70 (b, 1H), 8.92-8.94 (d, 1H), 9.01 (b, 1H)

MS : (*m/z*) 340 (M^++1)

- **Synthesis of 8-methyl-4-oxo-4*H*-pyrido[1,2-*a*]pyrimidin-3-yl-carbamate derivatives**

Benzyl (8-methyl-4-oxo-4*H*-pyrido[1,2-*a*]pyrimidin-3-yl)carbamate (III-5)

Compound (**III-5**) was prepared by treating the isocyanate derivative (**6b**) (0.5 g, 0.26 mmole) with benzyl alcohol (0.161 g, 0.149 mmole) as described above for compound (**III-1**). Chromatographic purification of the crude product using hexane (10%) in ethyl acetate as eluent yielded compound (**III-5**) (0.18 g, 39%), m. p. 168-70 °C (Lit.[221] 177-79 °C).

Anal.:

TLC : R_f 0.7 (1% MeOH in EtOAc)

IR : 3242, 1717, 1635, 1546, 1465, 1224 and 1056 cm^{-1}

^{1}H-NMR : 2.45 (s, 3H), 5.15 (s, 2H), 7.21-7.23 (d, 1H), 7.31-7.44 (m, 5H), 7.52 (s, 1H), 8.60 (b, 1H), 8.83-8.85 (d, 1H), 8.97 (b, 1H)

MS : (*m/z*) 310 (M^++1)

Pyridin-2-ylmethyl (8-methyl-4-oxo-4*H*-pyrido[1,2-*a*]pyrimidin-3-yl) carbamate (III-6)

Compound (**6b**) (0.5 g, 0.26 mmole) was reacted with pyridine-2-methanol (0.163 g, 0.149 mmole) as described above for compound (**III-1**). Chromatographic purification of the crude product using hexane (10%) in ethyl acetate as eluent earned the titled compound (**III-6**) (0.19 g, 41%), m. p. 180-82 °C.

Anal.:

TLC : R_f 0.75 (1% MeOH in EtOAc)

IR : 3429, 3247, 1721, 1667, 1644, 1480, 1244 and 1117 cm^{-1}

^{1}H-NMR : 2.45 (s, 3H), 5.20 (s, 2H), 7.22-7.24 (d, 1H), 7.33-7.36 (m, 1H), 7.49-7.51 (d, 1H), 7.53 (s, 1H), 7.83-7.87 (m, 1H), 8.55-8.56 (d, 1H), 8.62 (b, 1H), 8.85-8.87 (d, 1H), 9.14 (b, 1H)

MS : (*m/z*) 311 (M^++1)

- **Synthesis of 7-chloro-4-oxo-4*H*-pyrido[1,2-*a*]pyrimidin-3-yl-carbamate derivatives**

2-Pyridinylmethyl (7-chloro-4-oxo-4*H*-pyrido[1,2-*a*]pyrimidin-3-yl)carbamate (III-7)

6c (0.25 g, 0.11 mmole) was reacted with pyridine-2-methanol (0.176 g, 0.135 mmole) as described above for compound (**III-1**). The crude product was purified by column chromatography using 2% methanol in ethyl acetate to accomplish the titled compound (**III-7**) (0.05 g, 13.4%), m. p. 196-97 °C.

Anal.:

TLC : R_f 0.62 (2% MeOH in EtOAc)

IR : 3451, 3245, 1724, 1652, 1477, 1354, 1236 and 694 cm^{-1}

^{1}HNMR : 5.23 (s, 2H), 7.33-7.36 (d, 1H), 7.51-7.53 (d, 1H), 7.71-7.73 (d, 1H), 7.83-7.87 (t, 1H), 7.88-7.91 (dd, 1H), 8.55-8.56 (d, 1H), 8.76 (s, 1H), 8.92-8.93 (d, 1H), 9.32 (s, 1H)

MS : (*m/z*) 331.37, 333.35 (M^+-1)

3-Pyridinylmethyl (7-chloro-4-oxo-4*H*-pyrido[1,2-*a*]pyrimidin-3-yl)carbamate (III-8)

6c (0.25 g, 0.11 mmole) and pyridine-3-methanol (0.123 g, 0.11 mmole) were reacted as described above for compound (**III-1**) to get solid precipitate. The solid so obtained was filtered and washed with hexane. Chromatographic purification of the crude product using hexane (5%) in ethyl acetate provided the intended compound (**III-8**) (0.15 g, 40.2%), m. p. 293-95 °C.

Anal.:

TLC : R_f 0.65 (ETOAc)

IR : 3415, 3251, 1722, 1664, 1630, 1402 and 1232 cm^{-1}

^{1}HNMR : 5.22 (s, 2H), 7.41-7.45 (m, 1H), 7.70-7.73 (d, 1H), 7.86-7.91 (m, 2H), 8.54-8.55 (d, 1H), 8.66 (b, 1H), 8.74 (b, 1H), 8.91-

8.92 (d, 1H) 9.16 (s, 1H)

MS : (*m/z*) 331.37, 333.35, (M^+-1)

3-Fluorobenzyl (7-chloro-4-oxo-4*H*-pyrido[1,2-*a*]pyrimidin-3-yl)carbamate (III-9)

Compound (**III-9**) was obtained by reaction of compound (**6c**) (0.25 g, 0.11 mmole) with 3-fluorobenzyl alcohol (0.142 g, 0.11 mmole) to get solid precipitate. The solid so obtained was filtered and washed with hexane and purified by column chromatography using hexane (10%) in ethyl acetate to give the titled compound (**III-9**) (0.06 g, 15.3%), m. p. 240-42 °C.

Anal.:

TLC : R_f 0.62 (1% MeOH in EtOAc)

IR : 3431, 3276, 1726, 1660, 1546, 1229 and 1127 cm^{-1}

^{1}HNMR : 5.15 (s, 2H), 7.20-7.24 (m, 2H), 7.48-7.51 (m, 2H), 7.70-7.72 (d, 1H), 7.88-7.90 (d, 1H), 8.74 (s, 1H), 8.91 (s, 1H), 9.18 (s, 1H)

MS : (*m/z*) 350 (M^+-1), 348 (M^+-3)

4.1.5 Synthesis of 4-oxo-4*H*-pyrido[1,2-*a*]pyrimidin-3-yl-carboxamide derivatives (Series IV)

- **Synthesis of 4-oxo-4*H*-pyrido[1,2-*a*]pyrimidin-3-yl-carboxamide derivatives**

***N*-(4-Methoxybenzyl)-4-oxo-4*H*-pyrido[1,2-*a*]pyrimidine-3-carboxamide (IV-1)**

In a two neck round bottom flask (100 ml) equipped with calcium chloride guard tube, the acid (**4a**) (0.5 g, 0.26 mmole) was dissolved in dichloromethane (50 ml) and the solution was cooled to 0 °C. 1-Hydroxybenzotriazole hydrate (0.355 g, 0.26 mmole), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide (0.603 g, 0.31 mmole) and *N,N*-diisopropylethylamine (0.679 g, 0.52 mmole) were added to the above solution. After 20 min 4-methoxybenzylamine (0.397 g, 0.26 mmole) was added and the reaction mixture was stirred for 1 h at 0 °C and for another 8 h at room

temperature. The reaction mass was quenched by adding cold water (20 ml) and the medium was neutralized using dilute hydrochloric acid, extracted using ethyl acetate (3x100 ml), dried over anhydrous sodium sulfate and concentrated to get a dark brown product. The crude product was purified by column chromatography using methanol (2%) in ethyl acetate to offer the compound (**IV-1**) (0.24 g, 28.2%), m. p. 192-94 °C.

Anal.:

TLC : R_f 0.51 (EtOAc)

IR : 3336, 1679, 1489, 1334, 1297, 1243 and 1030 cm^{-1}

^{1}H-NMR : 3.80 (s, 3H), 4.62-4.64 (d, 2H), 6.86-6.90 (m, 2H), 7.31-7.33 (d, 2H), 7.34-7.38 (m, 1H), 7.84-7.86 (d, 1H), 7.92-7.97 (m, 1H), 9.19-9.21 (d, 1H), 9.30 (b, 1H), 9.38 (s, 1H)

MS : (*m/z*) 310 (M^++1)

***N*-(3-Fluorobenzyl)-4-oxo-4*H*-pyrido[1,2-*a*]pyrimidine-3-carboxamide (IV-2)**

Compound (**IV-1**) was prepared by reacting compound (**4a**) (0.5 g, 0.26 mmole) with 3-fluorobenzylamine (0.329 g, 0.26 mmole) as described above for compound (**IV-1**). The crude product was purified by column chromatography using hexane (5%) in ethyl acetate as eluent offering the compound (**IV-2**) (0.32 g, 40.9%), m. p. 168-70 °C.

Anal.:

TLC : R_f 0.64 (EtOAc)

IR : 3327, 3122, 1662, 1623, 1569, 1533, 1500 and 1240 cm^{-1}

^{1}H-NMR : 4.59-4.61 (d, 2H), 7.06-7.11 (m, 1H), 7.15-7.21 (m, 2H), 7.36-7.41 (m, 1H), 7.59-7.63 (m, 1H), 7.90-7.92 (d, 1H), 8.19-8.23 (m, 1H), 9.05 (s, 1H), 9.19-9.21 (d, 1H), 9.43-9.46 (t, 1H)

MS : (*m/z*) 298 (M^++1)

4-Oxo-*N*-[2-(trifluoromethyl)benzyl]-4*H*-pyrido[1,2-*a*]pyrimidin-3-carboxamide (IV-3)

Compound (**IV-3**) was prepared by treating compound (**4a**) (0.5 g, 0.26 mmole) with 2-trifluoromethylbenzylamine (0.461 g, 0.26 mmole) as described above for compound (**IV-1**). Chromatographic purification of the crude product

using hexane (5%) in ethyl acetate as eluent yielded compound (**IV-3**) (0.32 g, 35%), m. p. 158-60 °C.

Anal.:

TLC : R_f 0.6 (EtOAc)

IR : 3299, 3079, 1695, 1630, 1476, 1315, 1167 and 1094 cm^{-1}

^{1}H-NMR : 4.76-4.78 (d, 2H), 7.48-7.52 (m, 1H), 7.59-7.69 (m, 3H), 7.75-7.77 (d, 1H), 7.91-7.93 (d, 1H), 8.20-8.24 (m, 1H), 9.05 (s, 1H), 9.21-9.23 (d, 1H), 9.48-9.51 (t, 1H)

MS : (*m/z*) 348 (M^++1)

4-Oxo-*N*-[3-(trifluoromethyl)benzyl]-4*H*-pyrido[1,2-*a*]pyrimidin-3-carboxamide (IV-4)

Compound (**4a**) (0.5 g, 0.26 mmole) was reacted with 3-trifluoromethylbenzylamine (0.461 g, 0.26 mmole) as described above for compound (**IV-1**). The chromatographic purification of the crude product using hexane (5%) in ethyl acetate as eluent furnished the compound (**IV-4**) (0.33 g, 36.1%), m. p. 139-40 °C.

Anal.:

TLC : R_f 0.63 (EtOAc)

IR : 3328, 3113, 1691, 1645, 1532, 1490, 1415 and 1335 cm^{-1}

^{1}H-NMR : 4.66-4.67 (d, 2H), 7.56-7.63 (m, 3H), 7.66-7.68 (d, 1H), 7.72 (s, 1H), 7.90-7.92 (d, 1H), 8.18-8.23 (m, 1H), 9.05 (s, 1H), 9.20-9.21 (d, 1H), 9.50-9.53 (t, 1H)

MS : (*m/z*) 348 (M^++1)

4-Oxo-*N*-[4-(trifluoromethyl)benzyl]-4*H*-pyrido[1,2-*a*]pyrimidin-3-carboxamide (IV-5)

Compound (**IV-5**) was prepared by reacting (**4a**) (0.5 g, 0.26 mmole) with 4-trifluoromethylbenzylamine (0.461 g, 0.26 mmole) as described above for compound (**IV-1**). The chromatographic purification of the crude product using hexane (5%) in ethyl acetate as eluent yielded compound (**IV-5**) (0.25 g, 26.2%), m. p. 167-69 °C.

Anal.:

TLC : R_f 0.6 (EtOAc)

IR : 3336, 3115, 1663, 1600, 1570, 1500, 1325 and 1123 cm^{-1}

^{1}H-NMR : 4.75-4.76 (d, 2H), 7.38-7.41 (m, 1H), 7.49-7.51 (d, 2H), 7.58-7.60 (d, 2H), 7.86-7.88 (d, 1H), 7.96-8.00 (m, 1H), 9.21-9.23 (d, 1H), 9.37-9.38 (d, 1H), 9.47 (b, 1H)

MS : (*m/z*) 348 (M^++1)

***N*-(2,4-Difluorobenzyl)-4-oxo-4*H*-pyrido[1,2-*a*]pyrimidin-3-carboxamide (IV-6)**

Compound (**IV-6**) was prepared by reacting (**4a**) (0.5 g, 0.26 mmole) with 2,4-difluoromethylbenzylamine (0.376 g, 0.26 mmole) as described above for compound (**IV-1**). The chromatographic purification of the crude product using hexane (20%) in ethyl acetate as eluent afforded the desired product (**IV-6**) (0.21 g, 25.3%), m. p. 172-75 °C.

Anal.:

TLC : R_f 0.62 (EtOAc)

IR : 3328, 3125, 1664, 1500, 1430, 1184 and 1072 cm^{-1}

^{1}H-NMR : 4.60-4.62 (d, 2H), 7.14-7.21 (m, 2H), 7.24-7.29 (m, 1H), 7.59-7.63 (m, 1H), 7.89-7.92 (d, 1H), 8.19-8.23 (m, 1H), 9.03 (s, 1H), 9.20-9.23 (d, 1H), 9.42-9.45 (t, 1H)

MS : (*m/z*) 316 (M^++1)

***N*-[2-(Morpholin-4-yl)ethyl]-4-oxo-4*H*-pyrido[1,2-*a*]pyrimidin-3-carboxamide (IV-7)**

Reaction of compound (**4a**) (0.5 g, 0.26 mmole) with 2-(4-morpholinyl)ethylamine (0.342 g, 0.26 mmole) was effected as described above for compound (**IV-1**). The chromatographic purification of the crude product using methanol (0.2%) in ethyl acetate as eluent offered the titled compound (**IV-7**) (0.18 g, 22.6%), m. p. 193-95 °C.

Anal.:

TLC : R_f 0.3 (1% MeOH in EtOAc)

IR : 3123, 1690, 1631, 1483, 1400, 1251 and 1115 cm^{-1}

^{1}H-NMR : 2.43 (b, 4H), 2.50-2.51 (m, 2H), 3.45-3.50 (m, 2H), 3.59-3.61 (t, 4H), 7.57-7.61 (m, 1H), 7.84-7.90 (d, 1H), 8.17-8.21 (m, 1H), 9.02 (s, 1H), 9.15-9.16 (t, 1H), 9.20-9.22 (d, 1H)

MS : (*m/z*) 303 (M^++1)

4-Oxo-*N*-[3-(*n*.pentyloxy)pyridin-2-yl]-4*H*-pyrido[1,2-*a*]pyrimidin-3-carboxami-de (IV-8)

Compound (**IV-8**) was prepared by reacting (**4a**) (0.5 g, 0.26 mmole) with 2-amino-3-*n*.pentyloxypyridine (0.474 g, 0.26 mmole) as described above for compound (**IV-1**). The chromatographic purification of the crude product using methanol (2.5%) in ethyl acetate as eluent produced the titled product (**IV-8**) (0.3 g, 32.3%), m. p. 159-60 °C.

Anal.:

TLC : R_f 0.3 (EtOAc)

IR : 3292, 3237, 1693, 1595, 1470, 1333 and 1218 cm^{-1}

^{1}H-NMR : 0.89-0.93 (t, 3H), 1.36-1.43 (m, 2H), 1.49-1.57 (m, 2H), 1.78-1.84 (m, 2H), 4.09-4.13 (t, 2H), 6.55 (s, 1H), 7.13-7.16 (m, 1H), 7.46-7.48 (d, 1H), 7.66-7.70 (m, 1H), 7.95-7.97 (d, 1H), 8.24-8.28 (m, 1H), 9.13 (s, 1 H), 9.21-9.24 (d, 1H), 11.51 (s, 1H)

MS : (*m/z*) 353 (M^++1)

***N*-[3-(Benzyloxy)pyridin-2-yl]-4-oxo-4*H*-pyrido[1,2-*a*]pyrimidin-3-carboxam-ide (IV-9)**

Compound (**4a**) (0.5 g, 0.26 mmole) and 2-amino-3-benzyloxypyridine (0.526 g, 0.26 mmole) were reacted together as described above for compound (**IV-1**). The chromatographic purification of the crude product using methanol (1%) in ethyl acetate as eluent offered compound (**IV-9**) (0.23 g, 23.4%), m. p. 193-95 °C.

Anal.:

TLC : R_f 0.55 (EtOAc)

IR : 3480, 3106, 1699, 1598, 1482, 1285 and 1012 cm^{-1}

^{1}H-NMR : 5.28 (s, 2H), 7.00-7.04 (dd, 1H), 7.23-7.26 (dd, 1H), 7.34-7.38 (m, 1H), 7.41-7.44 (m, 2H), 7.53-7.55 (m, 1H), 7.58-7.60 (d, 2H), 7.88-7.91 (d, 1H), 7.98-8.02 (m, 1H), 8.10-8.14 (m, 1H), 8.16-8.18 (dd, 1H), 9.27-9.31 (m, 1H), 9.49 (s, 1H), 11.76 (s, 1H)

MS **:** (*m/z*) 373 (M^++1)

***N*-[(2,5-Diethoxy)-4-(morpholin-4-yl)phenyl]-4-oxo-4*H*-pyrido[1,2-*a*]pyrimidine-3-carboxamide (IV-10)**

Compound (**IV-10**) was prepared by treating compound (**4a**) (0.5 g, 0.26 mmole) with 2,5-diethoxy-4-morpholin-4-yl-phenylamine (0.7 g, 0.26 mmole) as described above for compound (**IV-1**). The chromatographic purification of the crude product using methanol (1%) in ethyl acetate as eluent provided compound (**IV-10**) (0.35 g, 30.3%), m. p. 166-67 °C.

Anal.:

TLC **:** R_f 0.7 (EtOAc)

IR **:** 3263, 1685, 1487, 1260, 1199, 1113, 1043 cm^{-1}

^{1}H-NMR **:** 1.44-1.47 (t, 3H), 1.54-1.58 (t, 3H), 3.09-3.10 (t, 4H), 3.89-3.91 (t, 4H), 4.12-4.17 (m, 4H), 6.60 (s, 1H), 7.37-7.41 (m, 1H), 7.85-7.87 (d, 1H), 7.95-7.99 (m, 1H), 8.40 (s, 1H), 9.33-9.34 (d, 1H), 9.42 (s, 1H), 11.49 (s, 1H)

MS **:** (*m/z*) 439 (M^++1)

***N*-(3,5-Dimethyl-1,2-oxazol-4-yl)-4-oxo-4*H*-pyrido[1,2-*a*]pyrimidin-3-carboxamide (IV-11)**

Compound (**IV-11**) was prepared by reacting (**4a**) (0.5 g, 0.26 mmole) with 3,5-dimethyl-1,2-oxazol-4yl-amine (0.295 g, 0.26 mmole) as described above for compound (**IV-1**). The chromatographic purification of the crude product using hexane (10%) in ethyl acetate as eluent offered compound (**IV-11**) (0.34 g, 45.4%), m. p. 243-45 °C.

Anal.:

TLC **:** R_f 0.6 (EtOAc)

IR **:** 3253, 3209, 1694, 1486, 1332, 1235 and 1067 cm^{-1}

^{1}H-NMR **:** 2.15 (s, 3H), 2.33 (s, 3H), 7.65-7.69 (m, 1H), 7.95-7.97 (d, 1H), 8.24-8.29 (m, 1H), 9.09 (s, 1H), 9.26-9.27 (d, 1H), 10.20 (s, 1H)

MS **:** (*m/z*) 285 (M^++1)

***N*-[1-(4-Methoxyphenyl)ethyl]-4-oxo-4*H*-pyrido[1,2-*a*]pyrimidin-3-carboxamide (IV-12)**

Compound (**4a**) (0.5 g, 0.26 mmole) was reacted with α-methyl-4-methoxybenzylamine (0.397 g, 0.26 mmole) as described above for compound (**IV-1**) Chromatographic purification of the crude product using methanol (0.2%) in ethyl acetate as eluent afforded compound (**IV-12**) (0.24 g, 28.2%), m. p. 173-75 °C.

Anal.:

TLC : R_f 0.6 (EtOAc)

IR : 3315, 3128, 1667, 1630, 1506, 1240 and 1025 cm^{-1}

^{1}H-NMR : 1.61-1.66 (d, 3H), 3.79 (s, 3H), 5.28-5.35 (m, 1H), 6.87-6.91 (d, 2H), 7.34-7.38 (m, 3H), 7.83-7.86 (d, 1H), 7.92-7.97 (m, 1H), 9.20-9.22 (d, 1H), 9.33-9.36 (m, 2H)

MS : (*m/z*) 324 (M^++1)

***N*-(1-Benzylpiperidin-4-yl)-4-oxo-4*H*-pyrido[1,2-*a*]pyrimidin-3-carboxamide (IV-13)**

Compound (**IV-13**) was obtained by reaction of compound (**4a**) (0.5 g, 0.26 mmole) with 4-amino-1-benzylpiperidine (0.5 g, 0.26 mmole) as described above for compound (**IV-1**). The chromatographic purification of the crude product using hexane (10%) in ethyl acetate as eluent earned the titled compound (**IV-13**) (0.25 g, 5%), m. p. 180-83 °C.

Anal.:

TLC : R_f 0.56 (EtOAc)

IR : 3288, 1695, 1544, 1479, 1335 and 1061 cm^{-1}

^{1}H-NMR : 1.52-1.58 (m, 2H), 1.89-1.92 (d, 2H), 2.18-2.22 (t, 2H), 2.70 (b, 2H), 3.50 (s, 2H), 3.88 (b, 1H), 7.26 (b, 1H), 7.33 (b, 4H), 7.60-7.64 (t, 1H), 7.90-7.92 (d, 1H), 8.19-8.23 (t, 1H), 9.04 (b, 2H), 9.20-9.22 (d, 1H)

MS : (*m/z*) 363 (M^++1)

***N*-(3,4-Methylenedioxybenzyl)-4-oxo-4*H*-pyrido[1,2-*a*]pyrimidine-3-carboxamide (IV-14)**

The reaction of compound (**4a**) (0.5 g, 0.26 mmole) with 3,4-methylenedioxybenzyl amine (0.397 g, 0.26 mmole) was performed as described above for compound (**IV-1**). The chromatographic purification of the crude product using hexane (20%) in ethyl acetate as eluent produced compound (**IV-14**) (0.3 g, 35.2%), m. p. 193-95 °C.

Anal.:

TLC : R_f 0.6 (EtOAc)66

IR : 3260, 3071, 1665, 1627, 1490, 1434, 1246 and 1224 cm^{-1}

^{1}H-NMR : 4.46-4.48 (d, 2H), 5.98 (s, 2H), 6.82-6.88 (m, 2H), 6.93 (s, 1H), 7.58-7.62 (m, 1H), 7.89-7.91 (d, 1H), 8.17-8.22 (m, 1H), 9.05 (s, 1H), 9.17-9.19 (d, 1H), 9.27-9.33 (t, 1H)

MS : (*m/z*) 324 (M^++1)

***N*-Cyclopropyl-*N*-(2-fluorobenzyl)-4-oxo-4*H*-pyrido[1,2-*a*]pyrimidin-3-carboxamide (IV-15)**

The reaction of (**4a**) (0.5 g, 0.26 mmole) with N-cyclopropyl-2-fluoro benzylamine (0.434 g, 0.26 mmole) was performed as described above for compound (**IV-1**). The chromatographic purification of the crude product using hexane (5%) in ethyl acetate as eluent yielded the desired compound (**IV-15**) (0.24 g, 27%), m. p. 137-40 °C.

Anal.:

TLC : R_f 0.55 (EtOAc)

IR : 3110, 1669, 1492, 1404, 1090 and 1031cm^{-1}

^{1}H-NMR : 0.58-0.61 (d, 4H), 3.06 (b, 1H), 4.93 (s, 2H), 7.11-7.13 (m, 1H), 7.23-7.25 (m, 1H), 7.32-7.34 (m, 2H), 7.67 (b, 1H), 7.80-7.82 (d, 1H), 7.90-7.94 (m, 1H), 8.60 (s, 1H), 9.21-9.23 (d, 1H)

MS : (*m/z*) 338 (M^++1)

- **Synthesis of 8-methyl-4-oxo-4*H*-pyrido[1,2-*a*]pyrimidine-3-carboxamide derivatives**

***N*-(4-Fluorobenzyl)-8-methyl-4-oxo-4*H*-pyrido[1,2-*a*]pyrimidin-3-carbox-amide (IV-16)**

Compound (**IV-16**) was prepared by coupling reaction of (**4b**) (0.5 g, 0.26 mmole) with 4-fluorobenzylamine (0.306 g, 0.24 mmole) as described above for compound (**IV-1**). Chromatographic purification of the crude product using hexane (10%) in ethyl acetate as eluent furnished the titled product (**IV-16**) (0.15 g, 51.9%), m. p. 185-87 °C.

Anal.:

TLC : R_f 0.68 (1% MeOH in EtOAc)

IR : 3287, 3014, 1677, 1633, 1481, 1279, 1222 and 1146 cm^{-1}

^{1}H-NMR : 2.58 (s, 3H), 4.65-4.66 (d, 2H), 7.00-7.04 (m, 2H), 7.18-7.21 (m, 1H), 7.34-7.37 (m, 2H), 7.63 (s, 1H), 9.08-9.09 (d, 1H), 9.33 (s, 1H), 9.35 (b, 1H)

MS : (*m/z*) 312 (M^++1)

***N*-(4-Trifluorobenzyl)-8-methyl-4-oxo-4*H*-pyrido[1,2-*a*]pyrimidin-3-carbox-amide (IV-17)**

Compound (**IV-17**) was prepared by reacting (**4b**) (0.4 g, 0.19 mmole) with 4-trifluoromethylbenzylamine (0.343 g, 0.19 mmole) as described above for compound (**IV-1**). Chromatographic purification of the crude product using methanol (5%) in methylene chloride as eluent yielded the titled product (**IV-17**) (0.15 g, 21.2%), m. p. 175-77 °C.

Anal.:

TLC : R_f 0.4 (EtOAc)

IR : 3414, 3294, 1695, 1634, 1545, 1330, 1117, 1015 and 793 cm^{-1}

^{1}H-NMR : 2.55 (s, 3H), 4.65-4.67 (d, 2H), 7.46-7.49 (dd, 1H), 7.55-7.57 (d, 2H), 7.69-7.73 (m, 3H), 9.00 (s, 1H), 9.08-9.10 (d, 1H), 9.45-9.48 (t, 1H)

MS : (*m/z*) 362 (M^++1)

- **Synthesis of 7-chloro-4-oxo-4*H*-pyrido[1,2-*a*]pyrimidine-3-carbox-amide derivatives**

***N*-(3,4-Methylenedioxybenzyl)-7-chloro-4-oxo-4*H*-pyrido[1,2-*a*]pyrimidine-3-carboxamide (IV-18)**

Compound (**4c**) (0.5 g, 0.22 mmole) was coupled with 3,4-methylenedioxybenzylamine (0.336 g, 0.22 mmole) as described above for compound (**IV-1**). Chromatographic purification of the crude product using hexane (10%) in ethyl acetate as eluent yielded the desired product (**IV-18**) (0.4 g, 50.2%), m. p. 200-01 °C.

Anal.:

TLC : R_f 0.4 (EtOAc)

IR : 3500, 3300, 1672, 1490, 1434, 1248 and 1066 cm^{-1}

^{1}H-NMR : 4.46-4.48 (d, 2H), 5.98 (s, 2H), 6.81-6.87 (m, 2H), 6.92 (s, 1H), 7.90-7.93 (d, 1H), 8.24-8.26 (dd, 1H), 9.04 (s, 1H), 9.15-9.16 (d, 1H), 9.23-9.26 (t, 1H)

MS : (*m/z*) 358.3 (M^++1), 360.4 (M^++2)

7-Chloro-4-oxo-*N*-[4-(trifluoromethyl)benzyl]-4*H*-pyrido[1,2-*a*]pyrimidine-3-carboxamide (IV-19)

Compound (**IV-19**) was prepared by reacting the acid (**4c**) (0.5 g, 0.22 mmole) with 4-trifluoromethylbenzylamine (0.39 g, 0.22 mmole) as described above for compound (**IV-1**). Chromatographic purification of the crude product using hexane (10%) in ethyl acetate as eluent offered compound (**IV-19**) (0.2 g, 23.5%), m. p. 212-14 °C.

Anal.:

TLC : R_f 0.51 (EtOAc)

IR : 3315, 3091, 1674, 1620, 1532, 1498, 1323 and 1134 cm^{-1}

^{1}H-NMR : 4.67-4.68 (d, 2H), 7.55-7.57 (d, 2H), 7.70-7.72 (d, 2H), 7.92-7.95 (d, 1H), 8.26 -8.29 (dd, 1H), 9.04 (s, 1H), 9.17-9.18 (d, 1H), 9.43-9.46 (t, 1H)

MS : (*m/z*) 382.2 (M^++1), 384.2 (M^++2)

7-Chloro-[*N*-cyclopropyl-*N*-(2-fluorobenzyl)]-4-oxo-4*H*-pyrido[1,2-*a*]pyrimidine-3-carboxamide (IV-20)

Compound (**IV-20**) was prepared by reacting the acid (**4c**) (0.5 g, 0.22 mmole) with N-cyclopropyl-2-fluorobenzylamine (0.367 g, 0.22 mmole) as

described above for compound (**IV-1**). The chromatographic purification of the crude product using hexane (10%) in ethyl acetate as eluent provided compound (**IV-20**) (0.28 g, 33.8%), m. p. 209-10 °C.

Anal.:

TLC : R_f 0.48 (EtOAc)

IR : 3068, 3019, 1688, 1630, 1481, 1344, 1223 and 1030 cm^{-1}

^{1}H-NMR : 0.51-0.55 (d, 4H), 2.87 (b, 1H), 4.75 (b, 2H), 7.21-7.24 (m, 2H), 7.33-7.36 (m, 1H), 7.63 (b, 1H), 7.84-7.87 (d, 1H), 8.14-8.17 (dd, 1H), 8.47 (s, 1H), 9.14 (s, 1H)

MS : (*m/z*) 372.4 (M^++1), 374.3 (M^++2)

• 7-(4-Methoxyphenyl)-4-oxo-4*H*-pyrido[1,2-*a*]pyrimidine-3-carboxylic acid intermediates

Ethyl 7-(4-methoxyphenyl)-4-oxo-4*H*-pyrido[1,2-*a*]pyrimidine-3-carboxylate (7)

Ethyl 7-chloro-4-oxo-4H-pyrido[1,2a]pyrimidine-3-carboxylate (**4c**) (10 gm, 39.6 mmole) was dissolved in dimethoxyethane (300 ml) and 4-methoxyphenylboronic acid (6 g, 39.6 mmole), potassium carbonate (8.194 gm, 59.4 mmole) and tetrakis(triphenylphosphene)palladium(0) (0.046 gm, 0.039 mmole) were added to the above reaction mixture under N_2 atmosphere. The reaction mixture was refluxed for 36 h at 90 °C. The reaction mass was filtered and the filtrate was washed with water and extracted using methylene chloride (3 x100 ml), dried over anhydrous sodium sulfate and concentrated to get a dark brown product. Chromatographic purification of the crude product using ethyl acetate (15%) in hexane as eluent offered the titled compound (**7**) (3.5 g, 27.3%), m. p. 166-67 °C.

Anal.:

TLC : R_f 0.7 (50% EtOAc in hexane)

IR : 3087, 1744, 1609, 1569, 1487, 1296, 1188, 1113, 1045, 826 and 795 cm^{-1}

MS : (*m/z*) 325, (M^+-1)

7-(4-Methoxyphenyl)-4-oxo-4*H*-pyrido[1,2-*a*]pyrimidine-3-carboxylic acid (8)

A solution of **7** (5 g, 4.3 mmole) in conc. HCl (15 ml) was refluxed for 2 h. The reaction mixture was cooled to RT to get a solid precipitate. The solid so obtained was filtered, washed with ether (100 ml) and dried to obtain 7-(4-methoxyphenyl)-4-oxo-4*H*-pyrido[1,2-*a*]pyrimidine-3-carboxylic acid (**8**) (3.1 g, 99.8%), m. p. 211-12 °C.

Anal.:

TLC : R_f 0.17 (EtOAc)

IR : 3317, 3087, 2474, 1791, 1772, 1606, 1289 and 1187 cm^{-1}

MS : (*m/z*) 297, (M^+-1)

***N*-(3-Fluorobenzyl)-7-(4-methoxyphenyl)-4-oxo-4*H*-pyrido[1,2-*a*]pyrimidine-3-carboxamide (IV-21)**

Compound (**8**) (0.25 gm, 0.08 mmole) and 3-fluorobenzylamine (0.105 g, 0.08 mmole) were reacted as described above for compound (**IV-1**). Chromatographic purification of the crude product using hexane (15%) in ethyl acetate as eluent afforded the titled compound (**IV-21**) (0.16 g, 47.0%), m. p. 171-73 °C.

Anal.:

TLC : R_f 0.55 (1% MeOH in EtOAc)

IR : 3445, 3319, 3072, 1688, 1611, 1533, 1482, 1336, 1290, 1264, 1184, 1143, 1060, 941, 832, 793, 691, 649 and 556 cm^{-1}

^{1}HNMR : 3.83 (s, 3H), 4.60-4.62 (d, 2H), 7.07-7.16 (m, 3H), 7.20-7.22 (d, 2H), 7.37-7.42 (d, 1H), 7.79-7.81(d, 2H), 7.95-7.98 (d, 1H), 8.54-8.57 (dd, 1H), 9.04 (s, 1H), 9.27-9.28 (d, 1H), 9.45-9.48 (t, 1H)

MS : (*m/z*) 404, (M^+-1)

- **Synthesis of 7-(4-methoxyphenyl)-4-oxo-4*H*-pyrido[1,2-*a*]pyrimidine-3-carboxamide derivatives**

***N*-(3-Trifluoromethylbenzyl)-7-(4-methoxyphenyl)-4-oxo-4*H*-pyrido[1,2-*a*]pyrimidine-3-carboxamide (IV-22)**

Compound (**8**) (0.3 gm, 0.10 mmole) was reacted with 3-trifluoromethylbenzylamine (0.177 g, 0.10 mmole) as described above for compound (**IV-1**). Chromatographic purification of the crude product using

hexane (5%) in ethyl acetate as eluent offered the desired compound (**IV-22**) (0.14 g, 30.49%), m. p. 197-98 °C.

Anal.:

TLC : R_f 0.54 (EtOAc)

IR : 3414, 3290, 3110, 1692, 1563, 1478, 1333, 1262, 1163, 1112, 1066, 828 and 704 cm^{-1}

^{1}HNMR : 3.84 (s, 3H), 4.68-4.69 (d, 2H), 7.13-7.15 (d, 2H), 7.57-7.59 (d, 2H), 7.71-7.73 (d, 2H), 7.80-7.82 (d, 2H), 7.96- 7.99 (d, 1H), 8.55-8.58 (dd, 1H), 9.04 (s, 1H), 9.28-9.29 (d, 1H), 9.52-9.55 (t, 1H)

MS : (*m/z*) 454, (M^+-1)

***N*-(4-Trifluoromethylbenzyl)-7-(4-methoxyphenyl)-4-oxo-4*H*-pyrido[1,2-*a*]pyrimidine-3-carboxamide (IV-23)**

Compound (**IV-23**) was obtained by reacting (**8**) (0.3 gm, 0.10 mmole) with 4-trifluoromethylbenzylamine (0.177 g, 0.10 mmole) as described above for compound (**IV-1**). Chromatographic purification of the crude product using hexane (5%) in ethyl acetate as eluent yielded the titled compound (**IV-23**) (0.16 g, 45.9%), m. p. 209-10 °C.

Anal.:

TLC : R_f 0.58 (EtOAc)

IR : 3425, 3293, 1689, 1623, 1333, 1263, 792, 583 and 558 cm^{-1}

^{1}HNMR : 3.83 (s, 3H), 4.67-4.68 (d, 2H), 7.11-7.14 (d, 2H), 7.57-7.64 (m, 2H), 7.67-7.69 (m, 1H), 7.72 (b, 1H), 7.78-7.81 (d, 2H), 7.95-7.97 (d, 1H), 8.53-8.56 (dd, 1H), 9.04 (s, 1H), 9.26 (s, 1H), 9.51-9.54 (t, 1H)

MS : (*m/z*) 454, (M^1-1)

***N*-(Tetrahydrofuran-2-ylmethyl)-7-(4-methoxyphenyl)-4-oxo-4*H*-pyrido[1,2-*a*]pyrimidine-3-carboxamide (IV-24)**

Compound (**IV-24**) (0.25 gm, 0.08 mmole) was reacted with 2-tetrahydrofuranyl methylamine (0.085 g, 0.08 mmole) as described above for compound (**IV-1**). Chromatographic purification of the crude product using

hexane (20%) in ethyl acetate as eluent provided compound (**IV-24**) (0.1 g, 31.2%), m. p. 176-77 °C.

Anal.:

TLC : R_f 0.61(1% MeOH in EtOAc)

IR : 3453, 3306, 1689, 1611, 1545, 1337, 1264 and 1180 cm^{-1}

^{1}HNMR : 1.54-1.61 (m, 1H), 1.80-1.89 (m, 2H), 1.90-1.99 (m, 1H), 3.38-3.39 (d, 1H), 3.52-3.57 (m, 1H), 3.66-3.69 (m, 1H), 3.80-3.81 (d, 1H), 3.84 (s, 3H), 3.96-3.99 (m, 1H), 7.12-7.15 (d, 2H), 7.79-7.84 (d, 2H), 7.91-7.97 (d, 1H), 8.54-8.56 (dd, 1H), 9.03 (s, 1H), 9.17-9.19 (t, 1H), 9.29-9.30 (d, 1H)

MS : (*m/z*) 380, (M^+-1)

4.2 Biological work

4.2.1 Falcipain-2 enzyme inhibition assay

The diluted soluble *Plasmodium falciparum* FP-2 (30 nM) was incubated for 10 min at room temperature in 100 mM sodium acetate, *p*H 5.5, 10 mM DTT, with a fixed/different concentration of the compounds to be tested or the standard (E64). Compound solutions were prepared from stock in DMSO. After 10 min incubation, the substrate Z-Phe-Arg-AMC was added to a final concentration of 25 μM. The fluorescence intensity was monitored (excitation 355 nm; emission 460 nm) for 10 min at room temperature with a Synergy^{TM} 4 Multi-Mode Microplate Reader (BioTek). The inhibition rate (%) is calculated using the given equation:

$$\% \text{ Inhibition} = [1 - (F \text{ test} / F \text{ stand.})] \times 100$$

where, *F test* is the fluorescence intensity of the test compound, *F* control is the fluorescence intensity of the standard (**E64**). All values are the means of three independent determinations and the deviations are <10 % of the mean value. The IC_{50} values were determined for those compounds only which showed 40 % or more of enzyme inhibition at 10 μM.