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A convenient synthesis of *N*-ethoxyphthalimido-3-methyl-4-substituted phenyl-pyrazolo[4',3':5,6]pyrido[2,3-*d*] pyrimido[6,1-b]quinazolin-10-one via Niementowski reaction

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Abstract: Synthesis of 5-methyl-4-substitutedbenzylidene-2,4-dihydro-3*H*-pyrazol-3-one (**3a-e**) were achieved by the condensation reaction of 5-methyl-2,4-dihydro-3*H*-pyrazol-3-one (**1**) with various arylaldehyde (**2a-e**). Further compounds (**3a-e**) were converted into (**4a-e**) by treatment with malononitrile and ammonium acetate in ethanol. Compounds (**4a-e**) refluxed with formic acid to yield 3-methyl-4-(3-nitrophenyl)-1,6-dihydro-5*H*-pyrazolo[4',3':5,6] pyrido[2,3-*d*] pyrimidin-5-one (**5a-e**). After treatment of (**5a-e**) with phthalimidoxyethyl bromide (**6**) gave 1-N,6-N-diethoxyphthalimido-3-methyl-4-(4-substitutedphenyl)-5*H*-pyrazolo[4',3':5,6]pyrido[2,3-*d*]pyrimidin-5-one (**7a-e**). In another route compounds (**8a-e**) 3-methyl-4-substitutedphenyl-pyrazolo[4',3':5,6]pyrido[2,3-*d*]pyrimido[6,1-b]quinazolin-10-one were synthesized by a Niementowski reaction involving condensation of anthranilic acid with (**5a-e**) in polyphosphoric acid media via direct fusion and classical method. Compounds (**8a-e**) were treated with (**6**) to give the final compounds N-ethoxyphthalimido-3-methyl-4-substutitedphenyl-pyrazolo[4',3':5,6]pyrido[2,3-*d*]pyrimido [6,1-b]quinazolin-10-one (**9a-e**).

Keywords: Pyrido[2,3-*d*]pyrimidin-5-one, Phthalimidoxyethyl bromide, anthranilic acid.

Introduction

Pyrazolopyridines and their related fused heterocycles are potential bioactive molecules. Pyrazolo[3,4-d] pyridines were identified as a general class of adenosine receptors [1-3] and are also important compounds as a result of their biological activity as well as structural relationship to azaindoles. A number of pyrazolo[3,4-b]pyridines are potentially biologically active compounds as new inhibitors of xanthine oxidase [4,5]. pyrazole framework plays an essential role in biologically active compounds and therefore represents an interesting template for combinatorial as well as medicinal chemistry [6-15]. Quinazolinone derivatives attract a widespread interest due to the diverse biological Activities [16] associated with them. They are pharmaceutically important as antituberculars [17] antibacterial [18] antiparkinsons [19] anticancer [20] anti-inflammatory [21] anticonvulsant [22] immunotropic [23] hypolipidemic [24] antitumor [25] antiulcer [26] analgesic [27] and antiproliferative [28] activities as well as inhibitory effects for thymidylate synthase [29] and poly(ADP-ribose) polymerase (PARP) [30]. The remarkable synthetic properties of quinazolinone derivatives have ensured long-standing studies of their utilization in organic synthesis. Rutaecarpine [31] and Luotonine A [32], the two natural quinazoline fused compounds exhibit a very potent pharmacological values. Polyfunctional pyridines are highly reactive reagents that have been used extensively in heterocyclic synthesis [33-35] and possess biological as well as pharmacological activity [36-38]. Heterocyclic rings attached to alkoxyphthalimide group have been synthesized [39] and tested for antimicrobial and antimalarial [40] activities.

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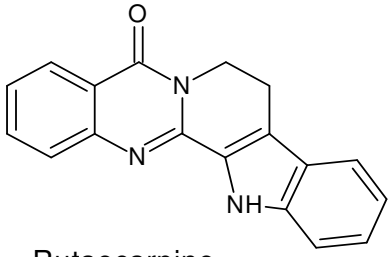
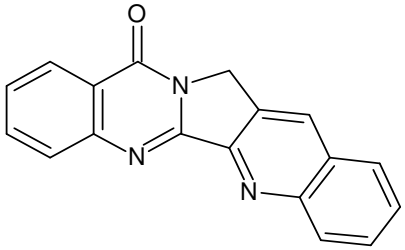
We planned to prepare 3-methyl-4-substitutedphenyl-pyrazolo [4',3':5,6]pyrido [2,3-*d*]Pyrimido [6,1-b] quinazolin-10-one,from anthranilic acids and **(5a-e)** which constitutes the Niementowski condensation [41].



Rutaecarpine



Luotonine A3

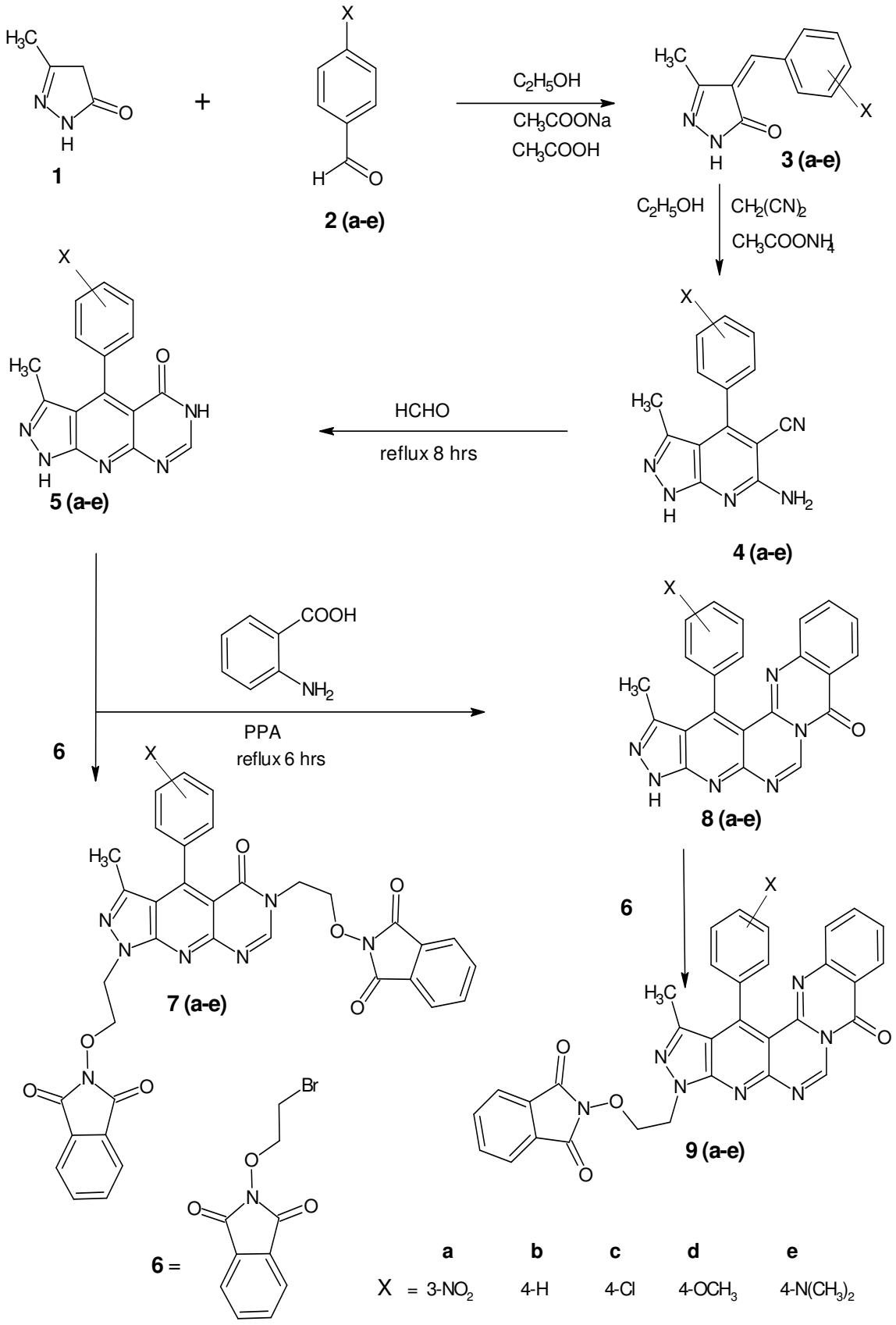
Results and discussion

Substituted benzylidene-5-methyl-2,4-dihydro-3H-pyrazol-3-one **3a-e** have been synthesized by the reaction of 5-methyl-2,4-dihydro-3H-pyrazole-3-one **1** with various substituted aryldehydes. Additionally when **3a-e** were reacted with malononitrile and ammonium acetate, it gave 6-amino-3-methyl-4-substitutedphenyl-1*H*-pyrazolo-[3,4-*b*] pyridine-5-carbonitrile **4a-e.** The IR spectrum of compound **4** shows bands 2246 cm^{-1} due to CN stretching , as expected for the formation of compound **4**, which was confirmed by ^1H NMR spectrum. In addition to it, we found a peak at δ 6.85 (singlet), which showed the presence of NH_2 group. Further the reaction involving synthesis of 3-methyl-4-substitutedphenyl-1,6-dihydro-5*H*-pyrazolo [4',3':5,6]pyrido[2,3-*d*]pyrimidin-5-one **5a-e** took place by reacting 6-amino-3-methyl-4-substitutedphenyl-1*H*-pyrazolo[3,4-*b*]pyridine-5-carbonitrile **4a-e** with formic acid. Formation of this compound was confirmed by C=O stretching at 1692 in IR region and characteristic peak at δ (7.90) in ^1H NMR for CONH group. Further compounds **5a-e** were reacted with bromoalkoxy phthalimide **6** to gave **7a-e** as shown by new four triplets peak of two (CH_2-CH_2) at δ 3.5-5.0 in NMR region and do not show any absorption band of NH group. The other route involved the reaction of anthranilic acids with 3-methyl-4-substitutedphenyl-1, 6-dihydro-5*H* pyrazolo[4',3':5,6] pyrido[2,3*d*]pyrimidine-5-one **5a-e** gave the products **8a-e** via the Niementowski condensation [41]. The reaction can be carried out either by classical stirring method using polyphosporic acid or by direct fusion method. It is assumed that formation of products **8a-e** requires an intermolecular aryl substitution between the pyrimidine nitrogen and the carboxylic acid group of the intermediate carboxylic acid. Synthesis of compounds **8a-e** was confirmed by disappearance of CONH peak and formation of new C=O peak at 1752 in IR spectrum. Further compounds **8a-e** were reacted with phthalimidoxyethyl bromide **6** to gave **9a-e** (Scheme and Table). Formation of **9a-e** compounds were confirmed by disappearance of NH peak and generation of two new triplet of (CH_2-CH_2) at δ 3.7 (N-CH_2) and δ 4.7 (O-CH_2).

Experimental

Apparatus

Melting points were taken in open capillary tubes and are therefore uncorrected. Purity of the compounds was checked on silica gel TLC plates of 2 mm thickness using n-hexane and ethyl acetate as solvent system. The visualization of spot was carried out in an iodine chamber. The IR spectra were recorded on Perkin-Elmer spectrometer. The ^1H NMR spectra were scanned on a Bruker DRX-300 MHz. spectrometer (300 MHz) in ($CDCl_3$) using TMS as internal standard and chemical shifts are expressed in δ ppm. The mass spectra were recorded on a Joel SX-102 (FAB) spectrometer. Phthalimidoxyethyl bromide [40] was synthesized by reported method.


1
2 (a-e)
C2H5OH
CH3COONa
CH3COOH
3 (a-e)
C2H5OH
CH2(CN)2
CH3COONH4
4 (a-e)
HCHO
reflux 8 hrs
5 (a-e)
6
COOH
NH2
PPA
reflux 6 hrs
8 (a-e)
7 (a-e)
6
9 (a-e)
6 =
X = 3-NO2 4-H 4-Cl 4-OCH3 4-N(CH3)2
a b c d e

Table

S.No.	Molecular formula	Reaction time (hrs.)	Molecular weight	Yield %
3a	$C_{11}H_9N_3O_3$	10	231	69
3b	$C_{11}H_{10}N_2O$	12	186	68
3c	$C_{11}N_9ClN_2O$	16	220	73
3d	$C_{12}H_{12}N_2O_2$	09	216	70
3e	$C_{13}H_{15}N_3O$	12	229	69
4a	$C_{14}H_{10}N_6O_2$	12	229	66
4b	$C_{14}H_{11}N_5$	8	249	69
4c	$C_{14}H_{10}ClN_5$	15	283	68
4d	$C_{15}H_{13}N_5O$	11	279	71
4e	$C_{16}H_{16}N_6$	13	292	64
5a	$C_{15}H_{10}N_6O_3$	5	322	60
5b	$C_{15}H_{11}N_5O$	10	277	65
5c	$C_{15}H_{10}ClN_5O$	8	311	66
5d	$C_{16}H_{13}N_5O_2$	6	307	62
5e	$C_{17}H_{16}N_6O$	5	320	61
7a	$C_{35}H_{24}N_8O_9$	12	700	74
7b	$C_{35}H_{25}N_2O_7$	10	655	78
7c	$C_{35}H_{24}ClN_7O_7$	8	690	69
7d	$C_{36}H_{27}N_7O_8$	10	685	75
7e	$C_{37}H_{30}N_8O_7$	9	698	77
9a	$C_{32}H_{20}N_8O_6$	8	612	81
9b	$C_{32}H_{21}N_7O_4$	9	567	84
9c	$C_{32}H_{20}ClN_7O_{4,}$	8	601	79
9d	$C_{33}H_{23}N_7O_5$	7	597	79
9e	$C_{34}H_{26}N_8O_4$	10	610	88

Synthesis of 4-(3-nitrobenzylidene)-5-methyl-2,4-dihydro-3H-pyrazol-3-one (3a):

A mixture of 3-methyl-2, 4-dihydro-3H-pyrazol-3-one (0.01mole) m-nitrobenzaldehyde and anhydrous sodium acetate (0.01 mole) were suspended in acetic acid (30 ml) and refluxed for 10 hrs. The mixture was filtrate and the filtrate was poured on cursed ice. The solid obtained, was crystallized from ethanol. Compounds 3b-e were also synthesized the similar method using appropriate reactants with required change in reflux time. Yield (69%), m.p 169 ºC. IR (KBr) cm^{-1}: 3418 (N-H str.), 3090 (C-H str., Ar-H), 2958 (C-H str., CH_3), 1725 (C=O str.), 1618 (C=N str.), 1355-1466 (NO_2). ^{1}H NMR ($CDCl_3$) δ : δ 8.22 (s, 1H, NH), 7.25-7.79 (m, 4H, Ar-H), 6.39 (s, 1H, =CH-Ar), 1.88 (s, 3H, CH_3). ^{13}C-NMR ($CDCl_3$): δ 21, 123.1, 124.4, 128.4, 131.7. 133.1, 137.2, 143.5, 148.3, 156.3, 169.7. MS: (*m/z*) $[M]^{+.}$ 231, Anal. calcd for $C_{11}H_9N_3O_3$:

C, 57.14; H, 3.92; N, 18.17%. Found: C, 74.54; H, 3.78; N, 18.70%.

4-(benzylidene)-5-methyl-2,4-dihydro-3H-pyrazol-3-one (3b):
Yield 68 %, m.p 171ºC. IR (KBr) cm^{-1}: 3395 (N-H str.), 3066 (C-H str., Ar-H), 2949 (C-H str., CH_3), 1710 (C=O str.), 1596 (C=N str.). ^{1}H NMR ($CDCl_3$) δ: 8.12 (s, 1H, NH), 7.18-7.68 (m, 5H, Ar-H), 6.28 (s, 1H, =CH-Ar), 1.82 (s, 3H, CH_3). ^{13}C-NMR ($CDCl_3$): 20.5, 128.2, 128.7, 129.3, 130.5, 130.5, 137.6, 143.4, 156.2, 169.6. MS: (*m/z*) $M^{+\cdot}$ 186, Anal. calcd for $C_{11}H_{10}N_2O$: C, 70.95; H, 5.41; N, 15.04%. Found: C, 70.78; H, 5.43; N, 15.01%.

4-(4-chlorobenzylidene)-5-methyl-2,4-dihydro-3H-pyrazol-3-one (3c):
Yield 73%, m.p 168ºC. IR (KBr) cm^{-1}: 3412 (N-H str.), 3075 (C-H str., Ar-H), 2954 (C-H str., CH_3), 1720 (C=O str.), 1612 (C=N str.), 735 (C-Cl str.). ^{1}H NMR($CDCl_3$) δ : 8.14 (s, 1H, NH),7.20-7.70 (m, 4H, Ar-H), 6.38 (s, 1H, =CH-Ar),1.86 (s, 3H, CH_3). ^{13}CNMR ($CDCl_3$): 20.5, 127.5, 127.6, 128.2, 129.3, 129.9, 134.1, 134.3, 143.5, 156.3, 169.7. MS : (*m/z*) $[M]^{+\cdot}$ 220, [M+2] 222. Anal. calcd for $C_{11}N_9ClN_2O$: C, 59.88; H, 4.11; N, 12.70 %. Found: C, 59.12; H, 4.10; N,12.74%.

4-(4-methoxybenzylidene)-5-methyl-2,4-dihydro-3H-pyrazol-3-one (3d):
Yield 70%, m.p 167ºC. IR (KBr) cm^{-1}: 3435 (N-H str.), 3081 (C-H str., Ar-H), 2960 (C-H str., CH_3), 1722 (C=O str.), 1616 (C=N str.), 1096 (C-O str.). ^{1}H NMR ($CDCl_3$) δ : 8.21 (s, 1H, NH), 7.18-7.73 (m, 4H, Ar-H), 6.32 (s, 1H, =CH-Ar), 3.70 (s, 3H, OCH_3),1.82 (s, 3H, CH_3). ^{13}C-NMR ($CDCl_3$): 20.7, 54.5, 116.2, 128.4, 128.5, 128.6, 129.8, 143.58, 156.2, 169.6. MS: (*m/z*) $[M]^{+\cdot}$ 216, Anal. calcd for $C_{12}H_{12}N_2O_2$: C, 66.65; H, 5.59; N, 12.96 %. Found: C, 65.89; H, 5.62; N, 13.00 %.

4-(4-N,N-Dimethylaminobenzylidene)-5-methyl-2,4-dihydro-3H-pyrazol-3-one (3e):
Yield (69%), m.p 175ºC. IR (KBr) cm^{-1}: 3400 (N-H str.), 3062 (C-H str., Ar-H), 2949 (C-H str., CH_3), 1712 (C=O str.), 1598 (C=N str.), 1360 (N-C str., N-CH_3). ^{1}H NMR ($CDCl_3$) δ : 8.13 (s, 1H, NH), 7.19-7.70 (m, 4H, Ar-H), 6.29 (s, 1H, =CH-Ar), 1.83 (s, 3H, C-CH_3), 3.27 (s, 6H, N-$(CH_3)_2$). ^{13}C-NMR ($CDCl^3$): 20.6, 43.3, 115.1, 123.4, 125.2, 143.5, 145.2, 156.1, 169.5. MS : (*m/z*) $[M]^{+\cdot}$ 229, Anal. calcd for $C_{13}H_{15}N_3O$: C, 68.10; H, 6.59; N, 18.33%. Found: C, 68.15; H, 6.65; N, 18.29%.

Synthesis of 6-amino-3-methyl-4-(3-nitrophenyl)-1H-pyrazolo[3,4-b]pyridine-5- carbonitrile (4a)
A mixture of compound **3a** (0.01 mole), malononitrile (0.01mole) and ammonium acetate (0.08 mole) were dissolved in ethanol (30 ml) and refluxed for 12 hrs. The mixture was cooled and poured over crushed ice. Solid was filtered, dried and recrystallised from ethanol. Similarly, compounds 4b-e also synthesized by changing reflux time. Yield (66%), m.p 268 ºC. IR (KBr) cm^{-1}: 3264 (str. NH), 3452-3338 (NH_2 str.), 1353-1468 (NO_2); 3092 (C-H str., Ar-H), 2964 (C-H str., CH_3), 1620-1430 (C=N, C=C str.), 1178 (N-N str.) 1358-1466 (NO_2).^{1}HNMR ($CDCl_3$) δ : 8.25 (s, 1H, NH), 7.28-7.83 (m, 4H, Ar-H), 6.85 (s, 2H, NH_2), 1.90 (s, 3H, CH_3). ^{13}C-NMR ($CDCl_3$): 20.9, 108.1, 118.5, 121.8, 125.3, 126.2, 128.4, 131.1, 137.6, 140.9, 150.2, 155.4, 163.6. MS : (*m/z*) $[M]^{+\cdot}$ 229, Anal. calcd for $C_{14}H_{10}N_6O_2$: C,57.14 ; H,3.43; N, 28.56 %. Found: C, 57.10; H, 3.50; N, 28.49%.

6-amino-3-methyl-4-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-5-carbonitrile (4b):
Yield 69%, m.p 271°C. IR (KBr) cm^{-1} 3261 (str. NH), 3450-3331(NH_2), 3076 (C-H str., Ar-H), 2239 (C≡N), 2958 (C-H str., CH_3), 1616-1425 (C=N,C=C str.), 1172 (N-N str.). ^{1}HNMR ($CDCl_3$) δ : 8.20 (s, 1H, NH), 7.19-7.70 (m, 5H, Ar-H), 6.79 (s, 2H, NH_2) 1.84 (s, 3H, CH_3). ^{13}C-NMR ($CDCl_3$): 20.1, 108.6, 118.4, 121.7, 125.2, 130.1, 130.6, 130.9, 137.5, 141.4, 143.4, 155.3, 163.5. MS: (*m/z*) $[M]^{+\cdot}$ 249. Anal. calcd for $C_{14}H_{11}N_5$: C, 67.46; H,4.45 ; N,28.10%. Found: C, 67.40; H, 4.51; N, 28.17%.

6-amino-3-methyl-4-(4-chlorophenyl)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carbonitrile(4c):
Yield 68%. m.p 260°C. IR (KBr) cm^{-1} 3456-3335 (NH_2), 3262 (str. NH), 3080 (C-H str., Ar-H), 2244 (C≡N), 2960 (C-H str., CH_3), 1617-1425 (C=N,C=C str.), 1176 (N-N str.) , 732 (C-Cl str.). ^{1}HNMR ($CDCl_3$) δ : 8.23 (s, 1H, NH), 7.22-7.80 (m, 4H, Ar-H), 6.84 (s, 2H, NH_2) 1.87(s, 3H,CH_3). ^{13}C-NMR ($CDCl_3$) : 20.7, 108.7, 118.4, 121.6, 130.2, 130.1, 131.4, 131.7, 136.3, 137.5, 137.7, 143.4, 155.3, 163.6. MS : (*m/z*) $[M]^{+\cdot}$ 283, [M+2] 285. Anal. calcd for $C_{14}H_{10}ClN_5$ C, 59,27; H, 3.55; N, 24.68 %. Found: C, 59.22; H, 3.59; N, 24.90%.

6-amino-3-methyl-4-(4-methoxyphenyl)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carbonitrile (4d):

Yield 71%. m.p 266°C. IR (KBr) cm^{-1} 3455-3330 (str. NH_2), 3254 (str. NH), 3081 (C-H str., Ar-H), 2242 (C≡N), 2959 (C-H str., CH_3), 1616-1421 (C=N,C=C str.), 1176 (N-N str.); 1095 (C-O-C). ^{1}HNMR ($CDCl_3$) δ: 8.22 (s, 1H, NH), 7.20-7.79 (m, 4H, Ar-H), 6.85 (s, 2H, NH_2) 1.85 (s, 3H, CH_3), 1.93 (OCH_3). ^{13}C-NMR ($CDCl_3$): 20.8, 56.2, 108.7, 118.4,118.5, 118.8, 121.6, 132.1, 132.5, 135.4, 135.3, 137.5, 143.4, 155.3, 163.1, 165.6. MS: (*m/z*) $[M]^{+\cdot}$ 279. Anal. calcd for $C_{15}H_{13}N_5O$: C, 64.50; H, 4.69; N, 25.07%. Found: C, 64.54; H, 4.78; N, 24.96%.

6-amino-3-methyl-4-(4-N,N-Dimethylaminobenzylidene)-1*H*-pyrazolo[3,4-*b*]pyridine-5-carbonitrile (4e):
Yield 64%. m.p.: 263°C. IR (KBr) cm^{-1} 3459-3331(NH_2), 3250 (str. NH), 3076 (C-H str., Ar-H) ,2239 (C≡N), 2958 (C-H str., CH_3), 1616-1425 (C=N,C=C str.), 1172 (N-N str.). ^{1}HNMR ($CDCl_3$) δ : 8.20 (s, 1H, NH), 7.19-7.70 (m, 4H, Ar-H), 6.79(s, 2H, NH_2) 1.84 (s, 3H, CH_3), 3.33 (s, 6H, $N(CH_3)_2$). ^{13}C-NMR ($CDCl_3$) 20.7, 42.1, 108.4, 115.6, 118.4, 129.5, 130.5, 130.8, 137.3, 143.4, 155.3, 163.6. MS: (*m/z*) $[M]^{+\cdot}$ 292. Anal. calcd for $C_{16}H_{16}N_6$: C, 65.74; H, 5.52; N, 28.57 %. Found: C, 65.81; H, 5.47; N, 28.63%.

Synthesisof3-methyl-4-(3-nitrophenyl)-1,6-dihydro-5*H*-pyrazolo[4',3':5,6]pyrido[2,3-*d*]pyrimidin-5-one (5a):
The appropriate compound **4a** (0.01 mole) in formic acid (25 ml) was refluxed for 5 hrs, cooled poured into in ice-water to give precipitate, which was filtered off, dried and recrystallised from ethanol. Yield. (60%).. Compounds **(5b-e)** also synthesized by change reflux time. m.p.: 298 °C. IR (KBr) cm^{-1}, 3248 (str. NH Pyrazole ring), 3222 (str. NH), 3092 (C-H str., Ar-H), 2964 (C-H str.,CH_3), 1351-1469 (NO_2), 1636-1438 (C=N, C=C str.) 1692 (C=O). ^{1}HNMR ($CDCl_3$) δ : 8.51 (s, 1H, NH), 7.35-7.87 (m, 4H, Ar-H), 1.97 (s, 3H, CH_3), 7.90 (s, CONH) , 7.51 (s, N=CH). ^{13}C-NMR ($CDCl_3$): 26.0, 105.56, 121.34, 124.80, 125.33, 128.21, 130.0, 138.43, 143.50, 149.41, 147.33, 151.44, 165.52, 171.77. MS: (*m/z*) $[M]^{+\cdot}$322. Anal. calcd for $C_{15}H_{10}N_6O_3$: C, 55.90; H, 3.13; N, 26.08 %. Found: C, 55.84; H, 3.21; N, 26.16%.

3-methyl-4-phenyl-1,6-dihydro-5*H*-pyrazolo[4',3':5,6]pyrido[2,3-*d*]pyrimidin-5-one (5b):
Yield 65%. m.p.>300°C. IR (KBr) cm^{-1} 3232 (str. NH pyrazole ring), 3211 (str. NH), 3078 (C-H str., Ar-H), 2960 (C-H str., CH_3), 1628-1433 (C=N, C=C str.) 1684 (C=O, str.). ^{1}HNMR ($CDCl_3$) δ: 8.42 (s, 1H, NH), 7.28-7.72 (m, 5H, Ar-H), 1.94 (s, 3H, CH_3), 7.85 (s, CONH) , 7.48 (s, N=CH). ^{13}C-NMR ($CDCl_3$) (δ ppm) 25.8, 105.5, 122.2, 129.4, 129.7, 138.4, 143.2, 147.2 151.3, 165.4, 171.4. MS : (*m/z*) $[M]^{+\cdot}$ 277. Anal. calcd for $C_{15}H_{11}N_5O$, C, 64.97; H, 4.00; N, 25.26%. Found: C, 65.01; H, 3.92; N, 25.56%.

4-(4-chlorophenyl)-3-methyl-1,6-dihydro-5*H*-pyrazolo[4',3':5,6]pyrido[2,3-*d*]pyrimidin-5-one (5c):
Yield 66 %. m.p 295°C. IR (KBr) cm^{-1}. 3239 (str. NH pyrazole ring), 3225 (str. NH), 3087 (C-H str., Ar-H), 2963 (C-H str., CH_3), 1633-1437 (C=N, C=C str.) 1689 (C=O), 733 (C-Cl). ^{1}HNMR($CDCl_3$) δ : 8.47 (s, 1H, NH), 7.30-7.82 (m, 4H, Ar-H), 1.95 (s, 3H, CH_3), 7.87 (s, CONH), 7.49 (s, N=CH). ^{13}C-NMR ($CDCl_3$): 25.34, 105.6, 121.1, 132.6, 132.5, 134.2, 134.4, 138.1, 138.3, 138.6,147.6, 151.5, 165.3, 171.5. MS: (*m/z*) $[M]^{+\cdot}$ 311, [M+2] 313. Anal. calcd for $C_{15}H_{10}ClN_5O$, C, 57.69; H, 3.23; N, 22.47 %. Found: C, 57.62 ; H, 328; N, 22.53%.

4-(4-methoxyphenyl)-3-methyl-1,6-dihydro-5*H*-pyrazolo[4',3':5,6]pyrido[2,3*d*] pyrimidin-5-one (5d):
Yield 62%. m.p>300°C. IR (KBr) cm^{-1} . 3241 (str. NH pyrazole ring), 3216 (str. NH), 3090 (C-H str., Ar-H), 2963 (C-H str., CH_3), 1634-1437 (C=N, C=C str.) 1686 (C=O), 1097 (C-O-CH_3). ^{1}H NMR ($CDCl_3$) δ : 8.46 (s, 1H, NH), 7.33-7.85 (m, 4H, Ar-H), 1.95 (s, 3H, CH_3), 7.88 (s, CONH), 7.49 (s, N=CH), 3.22 (OCH_3). ^{13}C-NMR ($CDCl_3$) : 25.3, 58.1, 105.5, 114.3, 121.1, 128.4, 131.5, 141.6, 161.3, 165.4, 167.1, 171.3. MS: (*m/z*) 307. Anal. calcd for $C_{16}H_{13}N_5O_2$ C, 62.53 ; H, 4.26 ; N, 22.79 %. Found: C, 62.48; H, 4.20; N, 22.86%.

4-[4-(dimethylamino)phenyl]-3-methyl-1,6dihydro5*H*pyrazolo[4',3':5,6]pyrido[2,3*d*] pyrimidin-5-one (5e):
Yield 61%. m.p 291°C. IR (KBr) cm^{-1}. 3246 (str. NH pyrazole ring), 3228 (str. NH), 3085 (C-H str., Ar-H), 2962 (C-H str., CH_3), 1634-1435 (C=N, C=C str.) 1688 (C=O). ^{1}HNMR ($CDCl_3$) δ: 8.45 (s, 1H, NH), 7.30-7.80 (m, 4H, Ar-H), 1.95 (s, 3H, CH_3), 7.85 (s, CONH), 7.48 (s, N=CH), 3.35 (s, 6H, $N(CH_3)_2$). ^{13}C-NMR ($CDCl_3$) : 13.3, 43.1, 105.3, 118.1, 118.1, 128.6, 130.2, 130.3, 138.4, 143.2, 146.5, 165.6, 171.2. $[M]^{+\cdot}$: (*m/z*) 320. Anal. calcd for $C_{17}H_{16}N_6O$, C, 63.74; H, 5.03; N, 26.23 %. Found: C, 63.79; H, 5.0; N, 26.29%.

Synthesis of 1N-6N-diethoxyphthalimido-3-methyl-4-(3-nitrophenyl)-5*H*-pyrazolo [4',3':5,6]pyrido[2,3-*d*]pyrimidin-5-one (7a):
A mixture of compounds **5a** (0.01 mole) phthlimidoxy ethyl bromide (0.02 mole) and pyridine (0.02 mole) were suspended in mathanol, and refluxed for 12 hrs. The mixture was filtered and filterate was poured on crused ice . the solid obtained, recystallized from ethanol. Compounds **7b-e** were also synthesized by the similar method with required change in reflux time. Yield 74%. m.p.:122°C. IR (KBr) cm^{-1} 3098 (C-H str., Ar-H), 2968 (C-H str., CH_3), 1350-1471 (NO_2), 1638-1441 (C=N, C=C str.), 1745 (C=O), 1748 (CO-N-CO). ^{1}HNMR ($CDCl_3$) δ: 7.3-8.1 (m, Ar-H), 2.35 (s, 3H, CH_3), 7.41 (s, N=CH), 3.5 (*J* = 6.3 Hz, t, N-CH_2, pyrazole ring), 4.68 (*J* = 6.3 Hz, t, O-CH_2, pyrazole ring), 3.8 (*J* = 6.8 Hz, t, N-CH_2), 4.85 (*J* = 6.8 Hz, t, O-CH_2).^{13}C-NMR ($CDCl_3$) 29.0, 40.0, 64.8, 77.0, 79.8, 116.2, 123.2, 123.4, 128.6, 129.2, 130.5, 131.7, 134.7, 135.2, 136.6, 142.0, 147.6, 150.3, 157.4, 160.9, 163.2. MS: (*m/z*) $[M]^{+\cdot}$ 700. Anal. calcd for $C_{35}H_{24}N_8O_9$, C, 61.53; H, 4.46; N, 22.83 %. Found: C, 61.59; H, 4.50; N, 22.79%.

1N-6N-diethoxyphthalimido-3-methyl-4-phenyl-5*H*-pyrazolo[4',3':5,6]pyrido[2,3-*d*] pyrimidin-5-one (7b):
Yield 78%. m.p.: 106°C. IR (KBr) cm^{-1} 3092 (C-H str., Ar-H), 2964 (C-H str., CH_3), 1636-1438 (C=N, C=C str.), 1741 (C=O), 1745, 1661 (CO-N-CO). ^{1}HNMR ($CDCl_3$) δ: 7.0-7.9 (m, Ar-H), 2.31 (s, 3H, CH_3), 7.35 (s, N=CH), 3.1 (*J* = 5.9 Hz, t, N-CH_2, pyrazole ring), 4.54 (*J* = 5.9 Hz, t, O-CH_2, pyrazole ring), 3.5 (*J* = 6.5 Hz, t, N-CH_2), 4.7 (*J* = 6.5 Hz, t, O-CH_2). ^{13}C-NMR ($CDCl_3$): 28.9, 40.0, 64.7, 77.0, 79.7, 116.1, 123.1, 123.0, 124.6, 128.5, 129.1, 130.4, 131.6, 134.6, 135.0, 136.5, 141.9, 146.9, 150.2, 157.4, 160.8, 163.1. MS : (*m/z*) $[M]^{+\cdot}$655. Anal. calcd for $C_{35}H_{25}N_2O_7$, C, 68.73; H, 5.24; N, 21.86 %. Found: C, 68.69; H, 5.27; N, 21.89%.

1N-6N-diethoxyphthalimido-3-methyl-4-(4-chlorophenyl)-5*H*-pyrazolo[4',3':5,6]pyrido [2,3-*d*]pyrimidin-5-one (7c):
Yield 69%. m.p 145°C. IR (KBr) cm^{-1} 3097 (C-H str., Ar-H), 2968 (C-H str., CH_3), 1638-1439 (C=N, C=C str.) 1743 (C=O), 736 (C-Cl), 1748,1669 (CO-N-CO). ^{1}HNMR ($CDCl_3$) δ : 7.23-8.15 (m, Ar-H), 2.31 (s, 3H, CH_3), 7.38 (s, N=CH), 3.4 (*J* = 6.2 Hz, t, N-CH_2, pyrazole ring), 4.69 (*J* = 6.2 Hz, t, O-CH_2, pyrazole ring), 3.72 (*J* = 6.7 Hz, t, N-CH_2), 4.81 (*J* = 6.7 Hz, t, O-CH_2). ^{13}C-NMR ($CDCl_3$) 28.9, 40.0, 64.8, 77.0, 79.7, 116.2, 123.0, 123.2, 124.6, 128.6, 129.2, 130.7, 131.6, 134.7, 135.2, 136.5, 142.0, 147.5, 150.2, 157.4, 160.9, 163.0. MS: (*m/z*) $[M]^{+\cdot}$ 690, [M+2] 692. Anal. calcd for $C_{35}H_{24}ClN_7O_7$, C, 63.08; H, 4.57; N, 20.06 %. Found: C, 63.12; H, 4.59; N, 20.19%.

1N-6N-diethoxyphthalimido-3-methyl-4-(4-methoxyphenyl)-5*H*-pyrazolo[4',3':5,6]pyrido [2,3-*d*]pyrimidin-5-one (7d):
Yield 75%. m.p.: 134°C. IR (KBr) cm^{-1}, 3095 (C-H str., Ar-H), 2968 (C-H str., CH_3), 1635-1440 (C=N, C=C str.) 1741 (C=O), 1099 (C-O-CH_3), 1746 (CO-N-CO). ^{1}HNMR($CDCl_3$) δ: 7.29-8.0 (m, Ar-H), 2.29 (s, 3H, CH_3), 7.36 (s, N=CH), 3.85 (*J* = 6.4 Hz, t, N-CH_2, pyrazole ring), 4.69 (*J* = 6.4 Hz, t, O-CH_2, pyrazole ring), 3.69 (*J* = 6.3 Hz, t, N-CH_2), 4.80 (*J* = 6.3 Hz, t, O-CH_2). ^{13}C-NMR ($CDCl_3$): 29.0, 40.0, 56.1, 64.8, 76.9, 79.8, 114.0, 116.2, 123.3, 128.6, 128.7, 130.5, 130.6, 130.9, 131.7, 135.2, 142.0, 147.6, 150.3, 157.4, 160.9, 163.2. MS: (*m/z*) $[M]^{+\cdot}$ 685. Anal. calcd for $C_{36}H_{27}N_7O_8$, C, 66.65; H, 5.35; N, 20.28 %. Found: C, 66.61; H, 5.38; N, 20.32%.

1N-6N-diethoxyphthalimido-3-methyl-4-(4-{dimethylamino}phenyl)-5*H*-pyrazolo [4',3':5,6]pyrido[2,3-*d*]pyrimidin-5-one (7e):
Yield 77 %. m.p 128 °C. IR (KBr) cm^{-1} 3093 (C-H str., Ar-H), 2969 (C-H str., CH_3), 1637-1442 (C=N, C=C str.) 1744 (C=O), 1746, (CO-N-CO). ^{1}HNMR ($CDCl_3$) δ : 7.21-7.95 (m, Ar-H), 2.31 (s, 3H, CH_3), 7.39 (s, N=CH), 3.37 (s, 6H, $N(CH_3)_2$), 4.0 (*J* = 6.0 Hz, t, N-CH_2, pyrazole ring), 4.64 (*J* = 6.0 Hz, t, O-CH_2, pyrazole ring), 3.72 (*J* = 6.7 Hz, t, N-CH_2), 4.79 (*J* = 6.7 Hz, t, O-CH_2). ^{13}CNMR ($CDCl_3$): 29.0, 40.5, 40.3, 58.1, 64.8, 76.9, 79.8, 114.3, 116.2, 123.2, 127.2, 128.2, 128.6, 130.9, 131.7, 135.2, 142.2, 147.6, 150.3, 150.8, 157.4, 160.8, 163.1. MS : (*m/z*) $[M]^{+\cdot}$ 698. Anal. calcd for $C_{37}H_{30}N_8O_7$, C, 67.43; H, 5.89; N, 22.93 %. Found: C, 67.45; H, 5.86; N, 22.87%.

Synthesis of 3-methyl-4-(3-{nitrophenyl}-pyrazolo)[4',3':5,6]pyrido[2,3-*d*]pyrimido[6,1-b]: quinazolin-10-one (8a). Method a (classical) Take mixture of compounds **5a** (0.61 mole) and anthranilic acid (3.4 mole) in polyphosphoric acid (5 ml) were stirred and heated at 170°C for 5 hrs. The reaction mixture was cooled and added to ice cooled water and neutralized with aqueous ammonia and solid was filtered, separated, washed with water, dried and recrystallised from ethanol. Yield 78%.

Method b (direct fusion method):
In a round bottom flask, a mixture of the appropriate compound **5a** (0.61 mole) and anthranilic acid (3.4 mole) were ground thoroughly and the mixture was heated above its melting point (+10ºC). The reaction mixture was kept in molten state for 8-15 minutes and then was cooled gradually. The residue obtained on cooling was triturated with petroleum ether, filtered and recrystallised ethanol to yield the corresponding pure compound. Compounds 8b-e also synthesized by changing fusion time. Yield 38%. m.p 291°C. IR (KBr) cm^{-1} 3228 (NH), 3095 (C-H str., Ar-H), 2970 (C-H str. CH_3), 1640-1436 (C=N, C=C str.), 1752 (C=O, str.), 1355-1468 (NO_2 str.). ^{1}H NMR ($CDCl_3$) δ: 9.4 (s, 1H, NH), 7.41-8.39 (m, 8H, Ar-H), 1.99 (s, 3H, CH_3), 7.54 (s, N=CH). ^{13}CNMR ($CDCl_3$): 22.8, 103.5, 116.3, 120.7, 126.1, 126.8, 127.2, 129.4, 130.2, 132.4, 133.8, 138.4, 145.5, 148.3, 151.5, 163.7, 168.3, 170.6. MS: (*m/z*) $[M]^{+\cdot}$ 423. Anal. calcd for $C_{22}H_{13}N_7O_3$, C, 61.53; H, 4.46; N, 22.83 %. Found: C,61.63; H, 4.51; N, 22.78%.

3-methyl-4-(4-{phenyl}-pyrazolo)[4',3':5,6]pyrido[2,3-*d*]pyrimido[6,1-b]quinazolin-10-one (8b):
Yield. 61%. m.p 284°C. IR (KBr) cm^{-1} 3220 (NH), 3089 (C-H str., Ar-H), 2962 (C-H str., CH_3), 1635-1430 (C=N, C=C str.) 1743 (C=O, str.). ^{1}HNMR ($CDCl_3$) δ: 9.1 (s, 1H, NH), 7.32-8.31 (m, 9H, Ar-H), 1.97 (s, 3H, CH_3), 7.50 (s, N=CH). ^{13}CNMR ($CDCl_3$) : 22.3, 116.1, 120.5, 126.3, 126.7, 127.3, 130.2, 130.3, 130.5, 133.5, 135.2, 145.7, 146.2, 146.7, 148.5, 157.7, 163.2, 168.4, 170.2. MS: *m/z*, $[M]^{+\cdot}$ 378. Anal. calcd for $C_{22}H_{14}N_6O$, C, 68.73; H, 5.24; N, 21.86 %. Found: C, 68.66; H, 5.21; N, 21.94%.

3-methyl-4-(4-{chlorophenyl}-pyrazolo)[4',3':5,6]pyrido[2,3-*d*]Pyrimido[6,1-b]quinazolin:
-10-one (8c). Yield.61%. m.p 291°C. IR (KBr) cm^{-1} 3226 (NH), 3093 (C-H str., Ar-H), 2967 (C-H str., CH_3), 1637-1436 (C=N, C=C str.), 1749 (C=O, str.), 1749 (C-Cl). ^{1}H NMR ($CDCl_3$) δ : 9.3 (s, 1H, NH), 7.38-7.36 (m, 8H, Ar-H), 1.99 (s, 3H, CH_3),7.54 (s, N=CH). ^{13}C-NMR ($CDCl_3$) : 22.4, 103.3, 116.7, 120.2, 126.2, 126.6, 127.2, 128.5, 128.4, 130.3, 130.4, 133.9, 134.3, 135.6, 138.2, 145.6, 146.8, 157.6, 163.3, 168.4, 170.6. MS: (*m/z*) 412, $[M+2]^{+\cdot}$ 412. Anal. calcd for $C_{22}H_{13}ClN_6O$, C, 63.08; H, 4.57; N, 20.06 %. Found: C, 63.15; H, 4.60; N, 20.01 %.

3-methyl-4-(4-{methoxyphenyl}-pyrazolo)[4',3':5,6]pyrido[2,3*d*]pyrimido[6,1-b] quinazolin-10-one (8d):
Yield. 61% m.p 291°C. IR (KBr) cm^{-1} 3225 (NH), 3092 (C-H str., Ar-H), 2966 (C-H str., CH_3), 1635-1434 (C=N, C=C str.) 1746 (C=O, str.), 1100 (C-O-C). ^{1}HNMR ($CDCl_3$) δ: 9.3 (s, 1H, NH), 7.35-8.33 (m, 8H, Ar-H), 1.97 (s, 3H, CH_3), 7.53 (s, N=CH), 3.22 (OCH_3), 1145 str. (C-O-C). ^{13}CNMR ($CDCl_3$) 22.3, 59.2, 103.5, 113.3, 113.8, 116.2, 120.5, 126.1, 126.3, 126.5, 126.7, 127.3, 132.4, 133.7, 138.4, 145.5, 146.2, 148.6, 163.3, 168.6, 170.4. MS: (*m/z*) $[M]^{+\cdot}$ 408. Anal. calcd for $C_{23}H_{16}N_6O_2$, C, 66.65; H, 4.57; N,20.93 %. Found: C, 66.68; H, 4.62; N, 20.98%.

3-methyl-4-(4-{dimethylamino}-pyrazolo)[4',3':5,6]pyrido[2,3-*d*]pyrimido[6,1-b] quinazolin-10-one (8e):
Yield. 61% m.p 291°C. IR (KBr) cm^{-1} 3222 (NH), 3090 (C-H str., Ar-H), 2963 (C-H str., CH_3), 1636-1432 (C=N, C=C str.), 1745 (C=O, str.). ^{1}H NMR ($CDCl_3$) δ: 9.2 (s, 1H, NH), 7.32-8.31 (m, 8H, Ar-H), 1.96 (s, 3H, CH_3), 7.51 (s, N=CH), 3.37 (s, 6H, $N(CH_3)_2$). ^{13}CNMR ($CDCl_3$): 22.1, 45.1, 45.1, 103.6, 116.3, 117.5, 117.7, 120.2, 126.0, 126.7, 127.3, 130.4, 130.8, 133.0 138.2, 138.6, 145.4, 146.8, 148.2, 163.5, 168.1, 170.7. MS: (*m/z*) $[M]^{+\cdot}$ 421. Anal. calcd for $C_{24}H_{19}N_7O$, C, 67.43; H, 5.89; N, 22.93 %. Found: C, 67.38; H,5.94; N, 22.98 %.

Synthesis of N-ethoxyphthalimido-3-methyl-4-{3-nitrophenyl}pyrazolo[4',3':5,6]pyrido [2,3-*d*]pyrimido[6,1-b]quinazolin-10-one (9a):
A mixture of compounds **8a** (0.01 mole), phthalimidoxy ethyl bromide (6) (0.01 mole) and K_2CO_3 (0.01 mole) were dissolved in ethanol, refluxed for 8 hrs. The reaction mixture cooled and poured in ice cold water, filtered, dried and recrystallized from ethanol. Yield. 81% m.p 228 °C. IR (KBr cm^{-1}): 3099 (C-H str., Ar-H), 2985 (C-H str., CH_3), 1353-1467 (NO_2), 1641-1452 (C=N, C=C str.) 1735 (C=O), 1741, 1694 (CO-N-CO). ^{1}HNMR ($CDCl_3$) δ : 7.1-8.2 (m, Ar-H), 2.3 (s, 3H, CH_3), 7.39 (s, N=CH), 4.7 (*J* = 6.7 Hz, t, OCH_2), 3.8 (*J* = 6.7 Hz, t, NCH_2).^{13}C-NMR ($CDCl_3$) 29.6, 65.5, 80.0, 109.8, 119.38, 123.0, 123.5, 124.9, 127.6, 129.4, 130.6, 131.4, 132.7, 133.9, 134.8, 135.3, 136.7, 147.8, 148.5, 151.7, 157.5, 161.1, 169.8. MS: (*m/z*) $[M]^{+\cdot}$ 612. Anal. calcd for $C_{32}H_{20}N_8O_6$, C, 62.13; H, 4.24; N, 18.11%. Found: C, 62.19; H, 4.28; N, 18.04%.

N-ethoxyphthalimido-3-methyl-4-(4-{phenyl}-pyrazolo)[4',3':5,6]pyrido[2,3-*d*]pyrimido [6,1-b]quinazolin-10-one (9b):
Yield. 84% m.p 247°C. IR (KBr) cm^{-1} 3092 (C-H str., Ar-H), 2968 (C-H str., CH_3), 1638-1463 (C=N, C=C str.) 1732 (C=O, str.), 1734, 1687 (CO-N-CO). ^{1}H NMR($CDCl_3$) δ: 7.1-7.9 (m, Ar-H), 2.1 (s, 3H, CH_3), 7.34 (s, N=CH), 4.3 (J = 5.9 Hz, t, OCH_2), 3.4 (J = 5.9 Hz, t, NCH_2). ^{13}C-NMR ($CDCl_3$): 29.5, 65.4, 79.8, 109.7, 119.2, 123.0, 123.3, 124.7, 127.3, 127.5, 129.4, 129.8, 131.3, 132.6, 133.8, 134.7, 136.6, 147.7, 148.4, 151.6, 157.5, 161.0, 169.8. MS: (*m/z*) $[M]^{+\cdot}$ 567. Anal. calcd for $C_{32}H_{21}N_7O_4$ C, 67.01; H, 4.74; N,17.09 %. Found: C, 67.18; H, 4.68; N, 17.14%.

N-ethoxyphthalimido-3-methyl-4-(4-{chlorophenyl}-pyrazolo)[4',3':5,6]pyrido[2,3-*d*] pyrimido[6,1-b]quinazolin-10-one (9c):
Yield. 79% m.p 235°C. IR (KBr) cm^{-1} 3095 (C-H str., Ar-H), 2994 (C-H str., CH_3), 1641-1468 (C=N, C=C str.) 1730 (C=O, str.), 751 (C-Cl), 1736,1691 (CO-N-CO). 7.2-8.36 (m, Ar-H), 2.3 (s, 3H, CH_3), 7.38 (s, N=CH), 4.4 (J = 6.1 t, OCH_2), 3.3 (J = 6.1 Hz, t, NCH_2). ^{13}CNMR ($CDCl_3$): 29.5, 65.5, 80.0, 109.7, 119.2, 123.0, 124.8, 127.5, 129.3, 129.8, 130.6, 131.4, 132.7, 133.9, 134.2, 134.7, 135.3, 136.6, 147.7, 148.5, 151.6, 157.5, 161.1, 169.7. MS: (*m/z*) $[M]^{+\cdot}$ 601, $[M+2]^{+\cdot}$ 603. Anal. calcd for $C_{32}H_{20}ClN_7O_4$, C, 63.21 ; H, 4.31; N, 16.12%. Found: C, 63.20; H, 4.22; N, 16.20%.

N-ethoxyphthalimido-3-methyl-4-(4-{methoxyphenyl}-pyrazolo)[4',3':5,6]pyrido[2,3-*d*] pyrimido[6,1-b]quinazolin-10-one (9d):
Yield. 79 % m.p 218°C. IR (KBr) cm^{-1} 3094 (C-H str., Ar-H), 2970 (C-H str., CH_3), 1640-1462 (C=N, C=C str.) 1733 (C=O, str.), 1105 (C-O-C), 1735,1689 (CO-N-CO). ^{1}HNMR($CDCl_3$) δ: 7.1-8.4 (m, Ar-H), 2.2 (s, 3H, CH_3), 7.36 (s, N=CH), 3.26 (s, 3H, OCH_3), 4.6 (J = 6.7 Hz, t, OCH_2), 3.7 (J = 6.7 Hz, t, NCH_2), 3.3 (s, 3H, OCH_3). ^{13}CNMR ($CDCl_3$): 29.5, 55.9, 65.5, 80.0, 109.7, 114.0, 119.3, 123.4, 124.8, 127.6, 129.3, 130.6, 131.4, 132.7, 133.9, 134.8, 136.7, 147.7, 148.5, 151.6, 157.5, 161.1, 161.6, 169.8. MS : (*m/z*) $[M]^{+\cdot}$ 597. Anal. calcd for $C_{33}H_{23}N_7O_5$, C,65.66; H, 4.84 ; N, 16.24%. Found: C, 65.71; H, 4.96; N, 16.14%.

N-ethoxyphthalimido-3-methyl-4-(4-{dimethylamino}-pyrazolo)[4',3':5,6]pyrido[2,3-*d*] pyrimido[6,1-b]quinazolin-10-one (9e):
Yield. 88% m.p 241°C. IR (KBr) cm^{-1} 3093 (C-H str., Ar-H), 2971 (C-H str., CH_3), 1641-1469 (C=N, C=C str.) 1732 (C=O, str.), 1736, 1687 (CO-N-CO). ^{1}HNMR($CDCl_3$) δ: 7.2-8.6 (m, Ar-H), 2.34 (s, 3H, CH_3), 7.38 (s, N=CH), 3.41 (s, 6H, $N(CH_3)_2$), 4.9 (J = 6.4 Hz, t, OCH_2), 3.5 (J = 6.4 Hz, t, NCH_2). ^{13}CNMR ($CDCl_3$): 29.5, 41.0, 65.5, 80.0, 109.8, 115.1, 119.3, 123.4, 124.9, 127.6, 127.7, 128.0, 128.6, 129.4, 130.6, 131.3, 132.7, 133.9, 134.7, 135.3, 148.6, 151.7, 157.5, 161.1, 169.7. MS: (*m/z*) $[M]^{+\cdot}$ 610. Anal. calcd for $C_{34}H_{26}N_8O_4$, C, 66.22; H, 5.23; N, 18.17%. Found: C, 66.28; H, 5.28 N, 18.21%.

References

[1] Hamilton, H. W.; Ortwine, D. F.; Worth, D. F.; Bristol, J. A. *J. Med. Chem.* **1987**, *30*, 91.

[2] Poulsen, S. A.; Quinn, R. J. *J. Med. Chem.* **1996**, *39*, 4156.

[3] Harden, F. A.; Quinn, R. J.; Scammells, P. J. *J. Med. Chem*. **1991**, *34*, 2892.

[4] Lynck, B. M.; Khan, M. A.; Teo, H. C.; Pedrotti, F. *J. Chem*. **1988**, *66* , 420.

[5] Salaheldin, A. M.; Campos, A. M.; Rodrigues, L. M . *Tetrahedron. Lett.* **2007,** *48*, 8819.

[6] Alessandro, B.; Maria, A.; Mauro, M.; Mariangela, M.; Maria, B.; Luciano, O.; Franco, D. *Bioorg. Med. Chem.* **2006,** *14,* 5251.

[7] John, M. F.; Joseph, C.; Joseph, B. J.; Karen, A. R.; Robert, K. M.; Joseph, M. L.; Pancras, C. W.; Stephen, A. B.; Ruth, R. W. *Bioorg. Med. Chem. Lett*. **2006**, *16*, 3755.

[8] Michael, G. C.; Kahn, K. E.; Francis, D. D.; Labaree, R. B.; Robert, M. H. *Bioorg. Med. Chem. Lett*. **2006**, *16*, 3454.

[9] Thomas, D. P.; Albert, K.; Barbara, B. C.; Mark, A. R.; L. B.; Mark, W.; Yaping D. V.; Tiffany, E.; Wayne, B. F.; Mary, K. F. *Bioorg. Med. Chem. Lett*. **2006,** *16*, 3156.

[10] Manuela, V.; Valeria, P.; Paola, V.; Alexander, C.; Marina, C.; Ciro, M. *Bioorg. Med. Chem. Lett*. **2006**, *16*, 1084.

[11] Bhat, B. A.; Dhar, K. L.; Puri, S. C.; Saxena, A. K.; Shanmugavel, M.; Qazi, G. N.; *Bioorg. Med. Chem. Lett*. **2005**, *15*, 3177.

[12] Petra, C.; Giang, V. T.; Viktor, M. L.; André, J.; Soña, T. *Tetrahedron* **2005**, *61,* 537.

[13] Gabriele, M.; Stefania, R.; Jean-Mario, M.; Giovanni, L.; Giuseppe, E. G.; Mauro, A. M.; Paolo, L.; Luca Pani, P.; Gérard, A. P. *Bioorg. Med. Chem. Lett.* **2005**, *19*, 3309.

[14] Selvam, C.; Sanjay, M. M. J.; Ramasamy, T.; Asit. K. C. *Bioorg. Med. Chem. Lett.* **2005**, *15*, 1793.

[15] Laxminarayan, B.; Bernd, J.; Tracy, M. D.; Tristen, L. M.; Moors, L.; Mark, A. G. *Bioorg. Med. Chem. Lett.* **2005**, *15*, 85.
[16] Satsangi, R. K. *Indian Drugs.* **1979**, *17*, 79.
[17] Joshi, V.; Chaudhari, R. P. *Indian J. Chem.* **1987**, *26B*, 602.
[18] Srivastava,V. K.; Gulati, S. S.; Shanker, K. *Indian J. Chem.* **1987**, *26B*, 652.
[19] Gupta, D. P.; Ahmad, S.; Kumar, A.; Shanker, K. *Indian J. Chem.* **1988**, *27B* , 1060.
[20] Abdel-Hamid, S. G. *J. Indian Chem. Soc.* **1997**, *74*, 613.
[21] Barker, A. J. *Chem. Abstr.* **1995**, *122*, 214099.
[22] Yang, L. M.; Chen, C. F.; Lee, K. H. *Bioorg. Med. Chem. Lett.* **1995**, *5*, 465,
[23] Ma, Z. Z.; Hano, Y.; Nomura, T. Chen, *J. Heterocycles* **1997**, *46*, 541.
[24] Bekhit, A. A.; Khalil, M. A. *Pharmazie* **1998**, *53*, 539.
[25] Gursoy, A.; Karali, N. *Farmaco*. **1995**, *50*, 857.
[26] Nawrocka, W.; Ziemecki, M. *Arch. Pharm.* **1997**, *330*, 339.
[27] Kurogi,Y.; Inoue, Y.; Tsutsumi, K.; Nakamura, S.; Nagae, K.; Yoshitsugu, H.; Tsuda, Y. *J. Med. Chem.* **1996**, *39*, 143.
[28] Hamel, E.; Lin, C. M.; Plowman, J.; Wang, H. K.; Lee, K. H.; Paull, D. K. *Bioorg Pharm.* **1996**, *51*, 53.
[29] Terashima, K.; Shimamura, H.; Kawase, A.; Tanaka, Y.; Tanimura, T.; Kamisaki, T.; Ishizuka, Y.; Sato, M. *Chem. Pharm. Bull.* **1995**, *43*, 2021.
[30] Raffa, D.; Dailone, G.; Maggio, B.; Sehillaci, D.; Plescia, F. *Arch Pharm.* **1999,** *332*, 317.
[31] Baek, D. J.; Park, Y. K.; Heo, H. I.; Lee, M. H.; Yang, Z. Y.; Chio, M. H. *Bioorg Med. Chem. Lett.* **1998**, *8*, 3287.
[32] Griffin, R. J.; Srinivasan, S.; Bowman, K.; Calvert, A. H.; Curtin, N. J.; Neweli, D. R.; Pemberton, L. C.; Golding, B. T. *J. Med .Chem.* **1998**, *41*, 5256.
[33] lnagdi, M. H.; Ghozlan, S. A.; Abdel-Razik, F. M.; Maghraby, A. S. *Chem. Synop* **1991**, *5* ,116.
[34] Taby, F. A.; Eldin, S. M.; Abdel-Razik, F. M. *Phosphorus, Sulfur, Silicon Relat. Elem.* **1995**, *21*, 106.
[35] Sadov, Kh. A.; Burangulova, R. N.; Guseninov, F. H.; Gilmanov, R. Z.; Phaljachov, I. Ph. *Chem. Heterocycl. Compounds* **2003**, *39*, 392.
[36] Miletin, M.; Hartl , J.; Odlerova, M. Z.; Kralova , K.; Machacek, M. *Molecules* **2000**, *5,* 208.
[37] Abdel-Rahman, A.; Bakhite, E. A.; Al Laifi, E. A. *J Chin. Chem. Soc.* **2002**, *49*, 223.
[38] Rao, C. S.; Venkaleswarlu, V. *Bioorg Med. Chem. Lett.* **2006**, *16*, 2134.
[39] Banu,T.; Rajora, S.; Khatri, D.; Talesara, G. L. *J. Ind. Soc, Chem.* **2000**, *77*, 300.
[40] Bauer, L.; Suresh, K. S. *J. Org. Chem.* **1963**, *28*, 1604.
[41] Niementowski, Von.; S. Prakt. *J. Chem.* **1895**, *51*, 564.
[42] Simmons. A.; *Practical Medical Microbiology*, 14th Edn, Churchill Livingston, Edinberg, **1996**, *11*, 163.