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Synthesis and Antimicrobial Studies of Some New Substituted 4-arylidene-3-methyl-1H-pyrimido[6,1-b] quinazoline-1,10(4H)-diones

KEYWORDS: substituted arylidene-pyrimido-quinazolinones, 6-methyl uracil, aromatic aldehydes, antibacterial and antifungal activity

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ABSTRACT *Synthesis of substituted 4-arylidene-3-methyl-1H-pyrimido[6,1-b]quinazoline-1,10(4H)-diones [4a-t] is attempted by the condensation of aromatic aldehydes [3a-d] with 3-methyl-1H-pyrimido[6,1-b]quinazoline-1,10(4H)-diones derivatives [2a-e] in the presence of piperdine. [2a-e] were obtained by azeotropic distillation of 6-methyl uracil and deravaties of 1H-benzo[d][1,3]oxazine-2,4-diones [1a-e]. The structures of synthesized compounds are confirmed by IR and 1HNMR, 13CNMR and mass spectral studies. Further, they were screened in vitro for antibacterial activity against Escherichia coli and Salmonella typhi. Antifungal activity is evaluated against Aspergillus niger and Penicillium chrysogenum using Paper disc diffusion method. Some of the compounds were found to exhibit promising antibacterial and antifungal activities.*

Introduction

The fused heterocyclic those are important because of the wide range of their biological activity which was obtained from heterocyclic structures. Among them different nitrogen heterocycles that have been explored for their biologically important molecules. Fused heterocycles like quinazolinones are of interest as they possess potential bioactive molecules and having wide range of importance in the field of medicinal chemistry because of their biological potential. They are known to exhibiting pharmacological activities such as antitumor [1], In vitro anticancer activity [2] anticonvulsant activity [3], Parkinson's disease [4], anti-oxidant, anti-inflammatory and analgesic activities [5], antimicrobial activity, potent anti-inflammatory and analgesic activities [6], Pharmacological study shows that the these derivatives implement depressive action on the CNS and neuroleptic activity.[7] Hence, the present communication comprises the Synthesis and antimicrobial studies of some new Substituted 4-arylidene-3-methyl-1H-pyrimido[6,1-b]quinazoline-1,10(4H)-diones.

MATERIALS AND METHODS

All the reagents were of analytical reagent grade and were used without further purification. All the products were synthesized and characterized by their spectral analysis. All chemical and solvents were purchased from S.D. Fine chemicals (India).Melting points were taken in open capillary tube. IR spectra (KBr,ν, cm^{-1}) were recorded on Perkin-Elmer Spectrophotometer and ^1H NMR400 MHz ($CDCl_3$)and chemical shifts are given in δ (ppm), ^{13}C NMR 7 MHz ($CDCl_3$). The mass spectra were performed using VG 2AB-3F spectrometer (70 ev), (M^{+1}). All reactions were fowlled by TLC (Silica gel, aluminum sheets 60 F_{254}, Merck).

Experimental

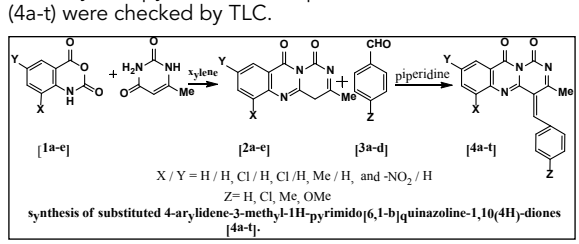
All the chemical and solvents used were of A.R. grade. All chemicals used were of E-Merck and S.D. fine Ltd. Melting points were determined in an open capillary tube and are uncorrected. The purity of the compound has been checked by TLC. IR spectra were recorded in $CHCl_3$ on a Shimadzu FTIR-8300 spectrophotometer. The ^1HNMR(300 MHz) and ^{13}C NMR (70 MHz) were run on a Bruker Avance DPX-250 spectrometer in $CDCl_3$ using tetramethylsilane as an internal standard. Chemical shift values are given in d scale. Mass spectra were recorded on VG 2AB-3F spectrometer (70 ev), (M^{+1}). The in vitro biological screenings of the investigated compounds were tested against the bacterial species by agar cup method and fungal species by the poison plate method.

Synthesis of substituted 3-methyl-1H-pyrimido[6,1-b]quinazoline-1,10(4H)-dione (2a-e):

These are synthesized by earlier known method. [8] 6-methylpyrimidine-2,4(1H,3H)-dione (0.05mole) is introduced in 50 ml of xylene and heated to 120-130° C. substituted isatoic anhydride (1a-e) (0.05mole) were slowly added to the mixture with continuous stirring. After the evolution of carbon dioxide has ceased, the temperature is raised to 140-150° C with simultaneous azeotropic removal of water. The heating is continued till no further water is formed. The reacting mixture is cooled, filtered, washed with methanol and then with warm water to obtain 2a-e.

Procedure for synthesis of substituted 4-arylidene-3-methyl-1H-pyrimido[6,1-b]quinazoline-1,10(4H)-diones [4a-t].

A mixture of 3-methyl-1H-pyrimido[6,1-b]quinazoline-1,10(4H)-diones (2a-e) (0.01\mole), aromatic aldehydes (3a-d)(0.01 mole), piperidine 0.5ml and alcohol 5ml were taken in RBF. The reaction mixture is then refluxed for 6 hrs and then the content was poured on 200gms crushed ice. The resultant solid products4a-4twere filtered, washed and recrystallized by using absolute alcohol. The purity of 4-arylidene-3-methyl-1H-pyrimido[6,1-b]quinazoline-1,10(4H)-diones (4a-t) were checked by TLC.



synthesis of substituted 4-arylidene-3-methyl-1H-pyrimido[6,1-b]quinazoline-1,10(4H)-diones [4a-t].

Characterization of synthesized substituted substituted 4-arylidene-3-methyl-1H-pyrimido [6,1-b]quinazoline-1,10(4H)-dione[4a-t].

a. 4-benzylidene-3-methyl-1H-pyrimido[6,1-b]quinazoline-1,10(4H)-dione:

Colour: Faint Yellow, Yield = 75%, M.F.: $C_{19}H_{13}N_3O_2$ M.P.: 210°C, IR (KBr, cm^{-1}): 3030(C=C-H), 1680(C=O), 1638 and 1626 (C=N), 1613 and 1520 (aromatic C=C). H^1NMR: δ 2.05 (s,3H), 6.84 (s,1H), 7.31-7.63 (m,5H), 7.61-8.06 (m,4H). $C^{13}NMR$: δ 19.2, 108.3, 120.3, 126.3, 126.9, 127.5, 127.3, 128.8, 128.8, 129.3, 129.3, 132.6, 133.7, 137.3 145.8, 159.3, 162.2,

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164.8, 168.9. LCMS [M+]: 316.10.

b.4-benzylidene-6-chloro-3-methyl-1H-pyrimido[6,1-b] quinazoline-1,10(4H)-dione:
Colour: Yellow, Yield = 78%, M.F.: $C_{19}H_{12}ClN_3O_2$, M.P.: 223°C, IR (KBr, cm^{-1}): 3033 (C=C-H), 1682 (C=O), 1640 and 1629 (C=N), 1605 and 1510 (aromatic C=C). H^1NMR: δ 2.10 (s,3H), 6.91 (s,1H), 7.35-7.62 (m,5H), 7.60-7.88 (m,3H). C^{13}NMR: δ 19.5, 108.4, 122.4, 124.3, 127.6, 128.8, 128.8, 128.9, 128.9, 129.3, 132.1, 132.7, 133.8, 136.6, 158.7, 161.4, 162.8, 164.9, 168.9. LCMS [M+]: 350.10.

c.4-benzylidene-8-chloro-3-methyl-1H-pyrimido[6,1-b] quinazoline-1,10(4H)-dione:
Colour: Yellow, Yield = 74%, M.F.: $C_{19}H_{12}ClN_3O_2$, M.P.: 227°C, IR (KBr, cm^{-1}): 3036 (C=C-H), 1685(C=O), 1644 and 1620 (C=N), 1611 and 1517 (aromatic C=C). H^1NMR: δ 2.14 (s,3H), 6.93 (s,1H), 7.38-7.65 (m,5H), 7.47 (d,1H), 7.77 (d,1H), 7.97 (s,1H). C^{13}NMR: δ 19.7, 108.7, 122.5, 127.2, 127.2, 127.7, 128.8, 128.8, 129.3, 129.3, 133.3, 133.3, 134.2, 136.4, 143.2, 158.5, 162.8, 164.8, 168.9. LCMS [M+]: 350.13.

d.4-benzylidene-3,8-dimethyl-1H-pyrimido[6,1-b]quinazoline-1,10(4H)-dione :
Colour: Yellow, Yield = 81%, M.F.: $C_{20}H_{15}N_3O_2$, M.P.: 231°C, IR (KBr, cm^{-1}): 3040 (C=C-H), 1683(C=O), 1650 and 1625 (C=N),1606 and 1513 (aromatic C=C). H^1NMR: δ 2.17 (s,3H), 2.37 (s,3H), 6.96 (s,1H), 7.40-7.67 (m,5H),7.41 (d,1H), 7.52 (d,1H), 7.99 (s,1H). C^{13}NMR: δ 19.9, 20.3, 108.5, 120.3, 125.5, 127.6, 127.7, 128.8, 128.8, 129.1, 129.1, 132.6, 133.3, 136.4, 137.3, 142.7, 158.3, 162.1, 164.2, 168.3. LCMS [M+]: 330.17.

e.4-benzylidene-3-methyl-8-nitro-1H-pyrimido[6,1-b] quinazoline-1,10(4H)-dione:
Colour: Yellow, Yield = 75%, M.F.: $C_{19}H_{12}N_4O_4$, M.P.: 237°C, IR (KBr, cm^{-1}): 3036 (C=C-H), 1688(C=O), 1645 and 1630 (C=N), 1605 and 1509 (aromatic C=C). H^1NMR: δ 2.19 (s,3H), 6.99 (s,1H), 7.31-7.59 (m,5H),7.79 (d,1H), 8.39 (d,1H), 8.52 (s,1H). C^{13}NMR: δ 20.2, 108.3, 121.4, 123.1, 123.9, 127.4, 128.7, 128.7, 128.9, 128.9, 129.4, 132.5, 136.5, 143.5, 151.3, 158.4, 162.1, 164.1, 168.3. LCMS [M+]: 361.09.

f.4-(4-chlorobenzylidene)-3-methyl-1H-pyrimido[6,1-b] quinazoline-1,10(4H)-dione:
Colour: Yellowish green, Yield = 83%, M.F.: $C_{19}H_{12}N_4O_4$ M.P.: 241°C, IR (KBr, cm^{-1}): 3035 (C=C-H), 1682(C=O), 1640 and 1620 (C=N), 1602 and 1510(aromatic C=C). H^1NMR: δ 2.11 (s,3H), 6.89 (s,3H), 7.47 and7.64 (dd,4H), 7.66-8.08 (m,4H). C^{13}NMR: δ 19.6, 108.4, 120.2, 126.3, 126.1, 127.9, 128.9, 128.9, 131.2, 133.1, 133.7, 134.5, 134.5, 136.3, 145.1, 158.2, 162.2, 164.3, 168.2. LCMS [M+]: 350.02.

g.6-chloro-4-(4-chlorobenzylidene)-3-methyl-1H-pyrimido[6,1-b]quinazoline-1,10(4H)-dione:
Colour: Yellowish green, Yield = 84%, M.F.: $C_{19}H_{11}Cl_2N_3O_2$, M.P.: 236°C, IR (KBr, cm^{-1}): 3035 (C=C-H), 1685(C=O), 1643 and 1624 (C=N), 166 and 1503(aromatic C=C). H^1 NMR: δ 2.13 (s, 3H), 6.93 (s, 1H), 7.50 and 7.65 (dd, 4H), 7.61-7.93 (m, 3H). C^{13}NMR: δ 19.7, 108.6, 122.5, 124.3, 128.3, 128.3, 128.3, 131.3, 132.7, 133.8, 133.8, 134.6, 134.7, 136.3, 158.5, 161.3, 162.8, 164.8, 168.9. LCMS [M+]: 384.05.

h.8-chloro-4-(4-chlorobenzylidene)-3-methyl-1H-pyrimido[6,1-b]quinazoline-1,10(4H)-dione:
Colour: Yellowish green, Yield = 81%, M.F.: $C_{19}H_{11}Cl_2N_3O_2$, M.P.: 245°C, IR (KBr,cm^{-1}): 3038 (C=C-H), 1688(C=O), 1646 and 1629 (C=N), 1610 and 1515 (aromatic C=C). H^1NMR: δ 2.14 (s,3H), 6.93 (s,1H), 7.52 and 7.67 (dd,4H),7.47 (d,1H), 7.77 (d,1H), 7.97 (s,1H). C^{13}NMR: δ 19.9, 108.3, 122.5, 127.3, 127.3, 128.5, 128.5, 131.3, 132.5, 133.6, 133.6, 134.5, 134.5, 136.2, 143.3, 158.4, 162.1, 164.7, 168.8. LCMS [M+]: 384.07.

i.4-(4-chlorobenzylidene)-3,8-dimethyl-1H-pyrimido[6,1-b] quinazoline-1,10(4H)-dione:
Colour: Yellowish green, Yield = 79%, M.F.: $C_{20}H_{14}ClN_3O_2$, M.P.: 249°C. IR (KBr, cm^{-1}): 3041(C=C-H), 1690(C=O), 1650and 1622 (C=N), 1610 and 1517(aromatic C=C). H^1NMR: δ 2.14 (s,3H), 2.42 (s,3H), 6.91 (s,1H), 7.47 and 7.73 (dd,4H),7.43 (d,1H), 7.50 (d,1H), 7.78 (s,1H). C^{13}NMR: δ 19.3, 20.5, 108.5, 120.3, 125.4, 127.1, 128.3, 128.3, 131.6, 133.7, 133.9, 134.5, 134.5, 136.3, 137.3, 142.8, 158.2, 162.4, 164.9, 168.9. LCMS [M+]: 364.02.

j.4-(4-chlorobenzylidene)-3-methyl-8-nitro-1H-pyrimido[6,1-b]quinazoline-1,10(4H)-dione:
Colour: Yellowish green, Yield = 82%, M.F.: $C_{19}H_{11}ClN_4O_4$, M.P.: 250°C. IR (KBr, cm^{-1}): 3044 (C=C-H), 1686 (C=O), 1648 and 1626 (C=N), 1613 and 1512 (aromatic C=C), 1492-1358 (NO_2). H^1NMR: δ 2.20 (s,3H), 6.99 (s,1H), 7.46 and 7.72 (dd,4H), 7.81 (d,1H), 8.39 (d,1H), 8.55 (s,1H). C^{13}NMR: δ 19.5, 108.3, 121.2, 123.1, 123.4, 128.0, 128.9, 128.9, 131.3, 133.2, 134.5, 134.5, 136.4, 143.4, 151.2, 159.2, 162.7, 164.9, 168.7. LCMS [M+]: 395.55.

k.3-methyl-4-(4-methylbenzylidene)-1H-pyrimido[6,1-b] quinazoline-1,10(4H)-dione:
Colour: Yellow, Yield = 88%, M.F.: $C_{20}H_{15}N_3O_2$, M.P.: 256°C. IR (KBr, cm^{-1}): 3040 (C=C-H), 1670 (C=O), 1640 and 1622 (C=N), 1600 and 1509 (aromatic C=C). H^1NMR: δ 2.12 (s,3H), 2.37 (s,3H), 6.90 (s,3H), 7.13 and 7.61 (dd,4H), 7.66-8.08 (m,4H). C^{13}NMR: δ 19.3, 21.6, 108.7, 121.3, 126.2, 126.9, 127.9, 128.7, 128.7, 129.5, 133.7, 134.7, 134.7, 136.4, 137.9, 145.7, 158.2, 162.7, 164.9, 168.5. LCMS [M+]: 330.20.

l.6-chloro-3-methyl-4-(4-methylbenzylidene)-1H-pyrimido[6,1-b]quinazoline-1,10(4H)-dione:
Colour: Yellowish green, Yield = 77%, M.F.: $C_{20}H_{14}ClN_3O_2$, M.P.: 244°C. IR (KBr, cm^{-1}): 3044 (C=C-H), 1680(C=O), 1644 and 1624 (C=N), 1605 and 1507 (aromatic C=C). H^1NMR: δ 2.15 (s,3H), 2.39 (s,3H), 6.93 (s,1H), 7.20 and 7.63 (dd,4H), 7.69-7.96 (m,3H). C^{13}NMR: δ 19.3, 21.6, 109.3, 122.5, 124.3, 128.0, 129.3, 129.3, 129.3, 132.3, 133.7, 134.6, 134.6, 136.3, 137.9, 158.4, 161.3, 162.7, 164.3, 168.4. LCMS [M+]: 364.55.

m.8-chloro-3-methyl-4-(4-methylbenzylidene)-1H-pyrimido[6,1-b]quinazoline-1,10(4H)-dione:
Colour: Yellowish green, Yield = 85%, M.F.: $C_{20}H_{14}ClN_3O_2$, M.P.: 248°C. IR (KBr,cm^{-1}): 3047 (C=C-H), 1678(C=O), 1647 and 1627 (C=N), 1608 and 1515 (aromatic C=C). H^1NMR: δ 2.17 (s,3H), 2.41 (s,3H), 6.95 (s,1H), 7.23 and 7.65 (dd,4H), 7.49 (d,1H), 7.79 (d,1H), 8.01 (s,1H). C^{13}NMR: δ 19.5, 21.7, 108.3, 122.5, 127.3, 127.3, 128.5, 128.5, 129.5, 132.7, 133.3, 134.7, 134.7, 136.3, 137.9, 143.3, 158.4, 162.7, 164.6, 169.1. LCMS [M+]: 364.67.

n. 3,8-dimethyl-4-(4-methylbenzylidene)-1H-pyrimido[6,1-b]quinazoline-1,10(4H)-dione:
Colour: Yellow, Yield = 72%, M.F.: $C_{21}H_{17}N_3O_2$, M.P.: 257°C. IR (KBr, cm^{-1}): 3050(C=C-H), 1680 (C=O), 1645 and 1637 (C=N), 1605and 1516 (aromatic C=C). H^1 NMR: δ 2.19 (s,3H), 2.43 (s,3H), 2.45 (s,3H), 6.97 (s,1H), 7.29 and 7.69 (dd,4H), 7.43 (s,1H), 7.50 (d,1H), 7.78 (s,1H). C^{13}NMR: δ 19.5, 20.6, 21.7, 108.5, 120.3, 125.1, 127.1, 128.4, 128.3, 129.5, 133.6, 134.2, 134.3, 136.3, 137.4, 137.3, 142.2, 158.3, 162.4, 164.4, 168.2. LCMS [M+]: 344.41.

o.3-methyl-4-(4-methylbenzylidene)-8-nitro-1H-pyrimido[6,1-b]quinazoline-1,10(4H)-dione:
Colour: Yellow, Yield = 78%, M.F.: $C_{20}H_{14}N_4O_4$, M.P.: 261°C. IR (KBr, cm^{-1}): 3056(C=C-H), 1689 (C=O), 1649and 1630 (C=N), 1607 and 1522 (aromatic C=C), 1490-1361(-NO_2). H^1NMR: δ 2.21 (s, 3H), 2.45 (s, 3H), 6.99 (s, 1H), 7.20 and 7.63 (dd, 4H), 7.73 (d, 1H), 8.43 (d, 1H), 8.55 (s, 1H). C^{13}NMR: δ 19.6, 21.7, 108.7, 121.5, 123.6, 123.4, 128.3, 128.5, 128.5, 129.3, 134.7, 134.7, 136.6, 137.9, 143.6, 151.4, 158.5, 162.6, 164.8, 168.9. LCMS [M+]: 375.16.

p. 4-(4-methoxybenzylidene)-3-methyl-1H-pyrimido[6,1-b] quinazoline-1,10(4H)-dione:
Colour: Green, Yield = 80%, M.F.: $C_{20}H_{15}N_3O_3$, M.P.: 248°C.

Volume : 3 | Issue : 8 | Aug 2013 | ISSN - 2249-555X

IR (KBr, cm^{-1}): 3052 (C=C-H), 1688(C=O), 1649 and 1625 (C=N), 1605 and 1512 (aromatic C=C),1250(aro-OCH_3).H^1 NMR: δ 2.15 (s,3H), 3.75 (s,3H -OCH_3), 6.81 (s,1H), 7.05 and 8. 41 (dd,4H), 7.70 -8.09 (m,4H). C^{13}NMR: δ 19.2, 55.6, 108.5, 114.3, 114.3, 120.6, 125.5, 126.9, 126.3, 127.6, 130.6, 130.6, 133.6, 136.8, 145.7, 158.5, 159.6, 162.3, 164.2, 168.1. LCMS [M^+]: 345.06.

q.6-chloro-4-(4-methoxybenzylidene)-3-methyl-1H-pyrimido[6,1-b]quinazoline-1,10(4H)-dione:
Colour: Green, Yield = 80%, M.F.: $C_{20}H_{14}ClN_3O_3$, M.P.: 266°C. IR (KBr, cm^{-1}): 3056 (C=C-H), 1691 (C=O), 1643and 1620 (C=N), 1610and 1513 (aromatic C=C), 1253 (aromatic -OCH_3). H^1 NMR: δ 2.19 (s, 3H), 3.81 (s, 3H -OCH_3), 6.83 (s, 1H), 7.11 and 8. 48 (dd,4H), 7.61 -7.95 (m,3H). C^{13}NMR: δ 19.4, 55.9, 108.6, 114.5, 114.5, 122.6, 124.3, 125.5, 128.6, 130.5, 130.5, 132.7, 133.8, 136.5, 158.3, 159.7, 161.4, 162.8, 164.8, 168.9. LCMS [M^+]: 379.33.

r.8-chloro-4-(4-methoxybenzylidene)-3-methyl-1H-pyrimido[6,1-b]quinazoline-1,10(4H)-dione:
Colour: Green,Yield = 85%, M.F.: $C_{20}H_{14}ClN_3O_3$, M.P.: 271°C. IR (KBr, cm^{-1}): 3050 (C=C-H), 16888 (C=O), 1644 and 1620 (C=N), 1610and 1513 (aromatic C=C), 1256 (aro-OCH_3). H^1NMR: δ 2.21(s, 3H), 3.86 (s, 3H -OCH_3), 6.85 (s, 1H), 7.13 and 8. 51 (dd,4H), 7.45 (d,1H), 7.77 (d,1H), 7.95 (s,1H). . C^{13}NMR: δ 19.6, 56.3, 108.3, 114.7, 114.7, 122.5, 125.5, 127.9, 127.9, 130.5, 130.5, 133.3, 134.6, 136.6, 143.3, 159.3, 160.2, 162.1, 164.2, 168.4. LCMS [M^+]: 379.41.

s.4-(4-methoxybenzylidene)-3,8-dimethyl-1H-pyrimido[6,1-b]quinazoline-1,10(4H)-dione:
Colour: Green, Yield = 72%, M.F.: $C_{21}H_{17}N_3O_3$, M.P.: 248°C. IR (KBr, cm^{-1}): 3050 (C=C-H), 1682(C=O), 1641 and 1620 (C=N), 1610and 1515 (aromatic C=C), 1258 (aromatic -OCH_3). H^1NMR: δ 2.24 (s, 3H), 2.39 (s, 3H) 3.89 (s, 3H -OCH_3), 6.90 (s,1H), 7.17 and 8. 42 (dd,4H), 7.48 (d,1H), 7.50 (d,1H), 7.80 (s,1H). C^{13}NMR: δ 19.6, 56.3, 108.3, 114.7, 114.7, 122.5, 125.5, 127.9, 127.9, 130.5, 130.5, 133.3, 134.6,136.6, 143.3, 159.3, 160.2, 162.1, 164.2, 168.4. LCMS [M^+]: 360.09.

t.4-(4-methoxybenzylidene)-3-methyl-8-nitro-1H-pyrimido[6,1-b]quinazoline-1,10(4H)-dione:
Colour: Green, Yield = 82%, M.F.: $C_{20}H_{14}N_4O_5$, M.P.: 282°C. IR (KBr, cm^{-1}): 3050 (C=C-H), 2910 (aromatic C-H) 1680 (C=O), 1644 and 1620 (C=N), 1610and 1517 (aromatic C=C), 1260 (aro-OCH_3), 1490-1358 (-NO_2). H^1NMR: δ 2.27 (s, 3H), 3.93 (s, 3H -OCH_3), 6.97 (s, 1H), 7.20 and 8. 46 (dd,4H), 7.80 (d,1H), 8.39 (d,1H), 8.63 (s,1H). C^{13}NMR: δ 19.9, 55.3, 109.2, 114.6, 114.6, 121.5, 123.1, 123.9, 125.5, 128.8, 130.6, 130.6, 136.4, 143.6, 151.3, 160.3, 161.3, 162.9, 164.9, 168.4. LCMS [M^+]: 391.17.

BIOLOGICAL ACTIVITY

Antibacterial Activity

Procedure:
The antibacterial activity was measured by agar cup method. Nutrient agar (Himedia) was prepared and sterilized at 15 Psi for 15 minutes in the autoclave. It was allowed to cool below 45°C and seeded with turbidsuspension of test bacteria separately, prepared from 24 hours old slant cultures. 3% inoculate were used every time. The bacterial cultures selected were, two gram negative cultures viz. Escherichia coli and Salmonella typhi. This seeded preparation was then pouredseparately in sterile petri plate under aseptic condition and allowed it to solidify.

Cups of 10 mm diameter were made in the agar plate with sterile cork borer. 100 ml of compound solution preparedin ethanol (0.1%) was added in the cups under aseptic condition with the help of micropipette. 100ml of ethanol waspllaced in separate cups as blank (negative control). 100 ml of solution of penicillin in ethanol (0.1%) was also placedon the seeded nutrient agar surface as standard reference antibiotic (positive control).

The plates were kept in refrigerator for 15 minutes to allow diffusion of the compound from agar cup into themedium. Then the plates were shifted to incubator at 37°C and incubated for 24 hours.After incubation plates were observed for the zone of inhibition of bacterial growth around the agar cup. Results were recorded by measuring the zone of inhibition in millimeter (mm) using zone reader (Table-1).

Antifungal Activity

Procedure:
Antifungal activity was performed by Poison plate method.[9] The medium used was Potato Dextrose Agar (Himedia). The medium was prepared and sterilized at 10 Psi in autoclave for 15 minutes. Then the compound tobe tested is added to the sterile medium in aseptic condition so as to get final concentration as 1%. A plate withethanol was prepared as blank (negative control) similarly a plate with 1% Gresiofulvin was prepared as standardreference plate (positive control).

Aspergillus niger and Penicillium chrysogenum were selected as test fungalcultures. They were allowed to grow on slant for 48 hours so as to get profuse sporulation. 5ml of 1:100 aqueoussolution of Tween 80 was added to the slant and spores were scraped with the help of nichrome wire loop to formsuspension. The fungal suspension was inoculated on the plates prepared using compound with the help of nicrome wire loop. The plates were incubated at room temperature for 48 hours.After incubation plates were observed for the growth of inoculated fungi. Results were recorded (Table-1) asmoderate growth of fungi (++), reduced growth of fungi (+) and no growth of inoculated fungi (-) antifungal activity.

Table-1 Anti Microbial activity

Comp. No.	Zone of Inhibition (mm)		Growth of Fungi	
	E. coli	S. typhi	A. niger	P.chrysogenum
Penicillin	24	18	-	-
(3a)	10	-	+	++
(3b)	14	7	-	-
(3c)	14	7	-	-
(3d)	10	-	+	++
(3e)	20	8	-	-
(3f)	14	-	+	++
(3g)	20	8	-	-
(3h)	20	8	-	-
(3i)	10	-	+	++
(3j)	19	11	-	-
(3k)	13	-	+	++
(3l)	16	7	-	-
(3m)	16	7	-	-
(3n)	12	-	+	++
(3o)	21	8	-	-
(3p)	12	-	+	++
(3q)	16	8	-	-
(3r)	16	8	-	-
(3s)	12	-	+	++
(3t)	18	10	-	-

Moderate growth (++), Reduced growth (+) and No growth (-) of fungi

RESULTS AND DISCUSSION

All the reactions were carried out by conventional methods. Intermediate 1H-benzo[d][1,3]oxazine-2,4-diones (1a-e) and 3-methyl-1H-pyrimido[6,1-b]quinazoline-1,10(4H)-diones (2a-e) were synthesized by reported procedure [8]. 3-methyl-1H-pyrimido[6,1-b]quinazoline-1,10(4H)-diones (2a-2e) was prepared from 1H-benzo[d][1,3]oxazine-2,4-diones (1a-e) and of 6-methyl uracil in xylene. By refluxing 3-methyl-1H-

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pyrimido[6,1-b]quinazoline-1,10(4H)-diones (2a-2e) and aryl aldehyde (3a-3d) with piperidine in ethanol for 6 hrs yielded 4-arylidene-3-methyl-1H-pyrimido[6,1-b]quinazoline-1,10(4H)-diones (4a-4t). Increase in the time of refluxing did not improve the yield of product.

Assignment of significant peaks observed in IR, ^{1}HNMR, ^{13}CNMR spectra of the compounds 4a-4t is clarified in the analytical data. The IR spectra of compound 4a-4t showed high intensity band observed at 1650-1646 and 1630-1622 cm^{-1} is assigned to ν(C=N) vibration [10] also in the region 1600-1778 cm^{-1} for carbonyl group.[11] The band around 1600-1520 cm^{-1} is assigned to the combination of ν(C=C) of the aromatic ring. Compounds 4p-4t show peak in the rage 1260-1250 cm^{-1} assigned to aromatic C–OCH_3.

Each one of the ^{1}HNMR spectra of 4a-4t revealed singlet for 3H between 2.05-2.27 ppm assigned to 2-methyl group, Peaks around 8.2-7.9 ppm are assigned to aromatic protons and singlet for 1H between 6.99-6.81 ppm assigned to (H−C(Ar)=C<).[12] ^{1}HNMR spectra of compounds 4f-4t showed double doublet confirming para substitution at 3-arylidene moiety. Compounds 4a-4e lacks this double doublet peak. Compound 4p-4t revealed a peak at 3.75-3.93 ppm assigned to methyl proton of –OCH_3. The absence of peak due to C^2 methylene proton observed in 2a-2e supports condensation of aryl aldehydes 3a-3d. ^{13}CNMR showed peaks around 163 ppm for carbonyl carbon. Assignment given to peaks observed in IR, ^{1}HNMR, ^{13}CNMR spectra and also molecular ion peaks in mass spectra justifies the structures of compounds 4a-4t.

The synthesized compounds were evaluated for anti-bacterial and anti-fungal activity with different strains of bacteria and fungi. Results are shown in Table-1. All have shown lesser activityagainst E. coli and B. typhi compared with penicillin taken as standard. The activity of few compounds was satisfactory and has also shown activity against S. typhi. Antifungal activity observed against Aspergillus species was encouraging in comparison with Penicillium chrysogenum. Therefore it may be concluded from results that antibacterial activity may be due to the presence of halogen and methoxy group in the molecule.

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