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Synthesis and antimicrobial studies of some new Substituted 3-arylidene-2-methylpyrazolo[5,1-*b*]quinazolin-9(3*H*)-ones

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ABSTRACT

Synthesis of substituted 3-arylidene-2-methylpyrazolo[5,1-b]quinazolin-9(3H)-ones [4a-t] is attempted by the condensation of aromatic aldehydes [3a-d] with 2-methylpyrazolo[5,1-b]quinazolin-9(4H)-ones [2a-e] in the presence of piperdine. 2a-e were obtained by azeotropic distillation of 3-methyl-1H-pyrazol-5(4H)-one and 1H-benzo[d][1,3]oxazine-2,4-diones [1a-e]. The structures of synthesized compounds are confirmed by IR and ^{1}HNMR, ^{13}CNMR 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.

Keywords: substituted arylidene-pyrazol-quinazolinones,3-methyl-1*H*-pyrazol-5(4*H*)-one, aromatic aldehydes, antibacterial and antifungal activity.

INTRODUCTION

Compounds with biological activity are often derived from heterocyclic structures. Indeed, one of the richest sources of diversity for medicinal chemists is fused heterocyclic rings, which, in addition to often exhibiting biological activity. Quinazolines are considered to be important chemical synthons of various physiological significances and pharmaceutical utilities. They possess a variety of biological effects, including antihypertensive,[1,2] antibavterial,[3,4] antifungal,[5] antihyperlipidemic,[6,7] antiinflammatory,[8,9] and anticonvulsant[10-13] activities. Moreover, many quinazolines contributed to the quest for an ultimate antitumor chemotherapeutic agent.[14-18] Several pyrazolo-quinazolinones derivatives proved to be a potent class of PARP-1 inhibitors.[19] Derivatives of 4-(benylidiene)-3-methyl-1H-pyrazolo-5(4*H*)-ones possess anti-hypertensive, [20]anti-inflammatory, [21] anti-convulsant [22] and anti-microbial activities.[23,24] Hence, the present communication comprises the Synthesis and antimicrobial studies of some new Substituted 3-arylidene-2-methylpyrazolo[5,1-*b*]quinazolin-9(3*H*)-ones.

EXPERIMENTAL SECTION

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 ^{1}H 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 followed by TLC (Silica gel, aluminum sheets 60 F_{254}, Merck).

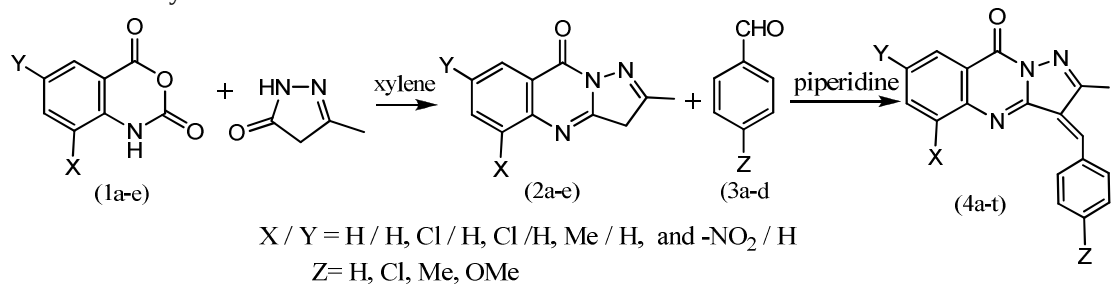
All the chemical and solvents used were of A.R. grade. All chemicals used were of E-Merck and S.D. fine Ltd. Melting points were determined in an open capillary tube and are uncorrected. The purity of the compound has been checked by TLC. IR spectra were recorded in $CHCl_3$ on a Shimadzu FTIR-8300 spectrophotometer. The ^{1}HNMR(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 δ 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 2-methylpyrazolo[5,1-*b*]quinazolin-9(4*H*)-ones (2a-e)

These are synthesized by earlier known method. [25] 3-methyl-1*H*-pyrazol-5(4*H*)-one (0.05mole) is introduced in 50 ml of xylene and heated to 120-130^o C. 1*H*-benzo[*d*][1,3]oxazine-2,4-diones (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^o 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 3-arylidene-2-methylpyrazolo[5,1-*b*]quinazolin-9(3*H*)-ones (4a-t)

A mixture of 2-methylpyrazolo[5,1-*b*]quinazolin-9(4*H*)-ones (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 were poured on 200gms crushed ice. The resultant solid products**4a-4t**were filtered, washed and recrystallized by using absolute alcohol. The purity of 3-arylidene-2-methylpyrazolo[5,1-*b*]quinazolin-9(3*H*)-ones (4a-t) were checked by TLC.



synthesis of substituted 3-arylidene-2-methylpyrazolo[5,1-b]quinazolin-9(3H)-ones (4a-t)

Characterization of synthesized substituted 3-arylidene-2-methylpyrazolo[5,1-*b*]quinazolin-9(3*H*)-ones (4a-t)

3-benzylidene-2-methylpyrazolo[5,1-*b*]quinazolin-9(3*H*)-one (4a)

Colour: Yellow, **Yield** = 84%, **M.P.:** 170^{o}C, **IR (KBr, cm^{-1}):** 3033(C=C-H), 1686 (C=O), 1640 and 1624 (C=N), 1610 and 1512 (aro. C=C). **H^{1}NMR:** δ 2.41 (s,3H), 7.30-7.65 (m,5H), 7.59-8.10 (m,4H), 5.69 (s,1H). **C^{13}NMR:** δ 11.7, 116.7, 122.8, 127.3, 126.7, 127.9, 129.3, 129.3, 129.4, 129.9, 129.3, 134.2, 134.9, 138.9, 146.3, 148.1, 153.3, 163.2. **Mass Spectra [M$^+$]:** 289.09

3-benzylidene-5-chloro-2-methylpyrazolo[5,1-*b*]quinazolin-9(3*H*)-one (4b)

Colour: Yellow, **Yield** = 77%, **M.P.:** 181^{o}C, **IR (KBr, cm^{-1}):** 3038 (C=C-H), 1686 (C=O), 1642 and 1626 (C=N), 1607 and 1516 (aro. C=C). **H^{1}NMR:** δ 2.39 (s,3H), 7.35-7.69 (m,5H), 7.61- 7.91 (m,3H), 5.61 (s,1H). **C^{13}NMR:** δ 11.1, 116.3, 122.7, 125.3, 128.1, 129.4, 129.1, 129.3, 129.3, 129.4, 133.3, 133.1, 134.3, 138.4, 148.2, 153.3, 161.9, 162.8. **Mass Spectra [M$^+$]:** 322.13.

3-benzylidene-7-chloro-2-methylpyrazolo[5,1-*b*]quinazolin-9(3*H*)-one (4c)

Colour: Yellow, **Yield** = 72%, **M.P**.: 187^{o}C, **IR (KBr, cm^{-1}):** 3040 (C=C-H), 1689(C=O), 1645 and 1629 (C=N), 1609 and 1512 (aro. C=C). **H^{1}NMR:** δ 2.40 (s,3H), 7.34-7.70 (m,5H), 7.49(d,1H), 7.80 (d,1H),7.99(s,1H) and 5.78 (s,1H). **C^{13}NMR:** δ 11.3, 116.3, 123.0, 128.1, 128.1, 128.4, 129.3, 129.8, 129.9, 129.9, 133.3, 133.5, 134.7, 138.2, 144.1, 148.5, 153.4, 162.9. **Mass Spectra [M$^+$]:** 322.19

3-benzylidene-2,7-dimethylpyrazolo[5,1-*b*]quinazolin-9(3*H*)-one (4d)

Colour: Yellow, **Yield** = 79%, **M.P**.: 198^{o}C, **IR (KBr, cm^{-1}):** 3037 (C=C-H), 1685(C=O), 1648 and 1622 (C=N),1607 and 1510 (aro. C=C). **H^{1}NMR:** δ 2.42 (s,3H), 2.38 (s,3H), 7.39-7.72 (m,5H), 7.41(d,1H), 7.51 (d,1H),7.81 (s,1H), 5.84 (s,1H). **C^{13}NMR:** δ 11.6, 22.5, 116.3, 121.0, 126.5, 128.1, 128.2, 129.3, 129.3, 129.7, 129.9, 133.3, 134.3, 137.7, 138.1, 142.8, 148.3, 153.7, 162.7. **Mass Spectra [M$^+$]:** 302.22.

3-benzylidene-2-methyl-7-nitropyrazolo[5,1-*b*]quinazolin-9(3*H*)-one (4e)

Colour: Yellow, **Yield** = 80, **M.P**.: 215^{o}C, **IR (KBr, cm^{-1}):** 3039 (C=C-H), 1680(C=O), 1640 and 1628 (C=N), 1609 and 1520 (aro. C=C). **H^{1}NMR:** δ 2.43 (s,3H), 7.32-74 (m,5H), 7.81 (d,1H), 8.42 (d,1H), 8.73 (s,1H), 5.93

(s,1H). **C^{13}NMR:** δ 11.7, 116.3, 122.2, 12.9, 124.2, 128.1, 129.2, 129.2, 129.4, 129.4, 129.5, 133.3, 138.4, 144.2, 148.3, 152.3, 153.5, 162.8. **Mass Spectra [M^+]:** 333.36.

3-(4-chlorobenzylidene)-2-methylpyrazolo[5,1-*b*]quinazolin-9(3*H*)-one (4f)
Colour: Yellowish green, **Yield** = 86%, **M.P**.: 212°C, **IR (KBr, cm^{-1}):** 3037 (C=C-H), 1686(C=O), 1642 and 1625 (C=N), 1608 and 1518 (aro. C=C). **H^1NMR:** δ 2.41(s,3H), 7.69-8.10 (m,4H), 7.49 and 7.71 (dd,4H), 5.62 (s,1H). **C^{13}NMR:** δ 11.8, 116.3, 122.3, 127.5, 128.3, 128.3, 129.2, 129.2, 132.0, 134.1, 134.9, 135.3, 135.5, 138.3, 146.3, 148.4, 153.3, 162.7. **Mass Spectra [M^+]:** 322.42.

5-chloro-3-(4-chlorobenzylidene)-2-methylpyrazolo[5,1-*b*]quinazolin-9(3*H*)-one (4g)
Colour: Yellowish green, **Yield** = 84%, **M.P**.: 219°C, **IR (KBr, cm^{-1}):** 3041 (C=C-H), 1688(C=O), 1644 and 1627 (C=N), 1610 and 1520 (aro. C=C). **H^1 NMR:** δ 2.42 (s,3H), 7.51 and 7.73 (dd,4H), 7.61-7.99 (m,3H), 5.64 (s,1H). **C^{13}NMR:** δ 11.9 116.1, 123.2, 125.1, 129.5, 129.5, 129.5, 131.6, 132.9, 133.8, 134.1, 135.3, 135.3, 138.3, 148.3, 153.2, 161.7, 162.6. **Mass Spectra [M^+]:** 356.23.

7-chloro-3-(4-chlorobenzylidene)-2-methylpyrazolo[5,1-*b*]quinazolin-9(3*H*)-one (4h)
Colour: Yellowish green, **Yield** = 81%, **M.P.**: 227°C, **IR (KBr,cm^{-1}):** 3045 (C=C-H), 1682(C=O), 1647 and 1624 (C=N), 1612 and 1517 (aro. C=C). **H^1NMR:** δ 2.49 (s,3H), 7.53 and 7.76 (dd,4H), 7.52 (d,1H), 7.81 (d,1H), 7.99 (s,1H), 5.84 (s,1H). **C^{13}NMR:** δ 11.3, 116.3, 122.8, 128.3, 128.3, 129.2, 129.2, 131.5, 133.3, 134.1, 134.1, 135.4, 135.4, 138.1, 143.9, 148.3, 153.3, 162.7. **Mass Spectra [M^+]:** 356.42.

3-(4-chlorobenzylidene)-2,7-dimethylpyrazolo[5,1-*b*]quinazolin-9(3*H*)-one (4i)
Colour: Yellowish green, **Yield** = 79%, **M.P**.: 215°C. **IR (KBr, cm^{-1}):** 3049 (C=C-H), 1689(C=O), 1649and 1627 (C=N), 1614 and 1519(aro. C=C). **H^1NMR:** δ 2.39 (s,3H), 7.54 and 7.78 (dd,4H), 7.43 (d,1H), 7.51 (d,1H), 7.89 (s,1H), 5.70(s,1H). **C^{13}NMR:** δ 11.3, 21.7, 115.9, 121.1, 125.9 127.9, 129.3, 129.3, 131.6, 133.9, 134.2, 135.3, 135.3, 137.7, 138.3, 142.9, 148.4, 153.1, 162.8. **Mass Spectra [M^+]:** 336.28.

3-(4-chlorobenzylidene)-2-methyl-7-nitropyrazolo[5,1-*b*]quinazolin-9(3*H*)-one (4j)
Colour: Yellowish green, **Yield** = 83%, **M.P**.: 247°C. **IR (KBr, cm^{-1}):** 3047 (C=C-H), 1688 (C=O), 1646 and 1629 (C=N), 1610 and 1515 (aro. C=C), 1490-1360 (NO_2). **H^1NMR: δ** 2.41 (s,3H), 7.57 and 7.73 (dd,4H), 7.80 (d,1H), 8.44 (d,1H), 8.63 (s,1H), 5.83 (s,1H). **C^{13}NMR:** δ 11.3, 116.3, 122.2, 124.1, 124.2, 129.4, 129.3, 129.3, 131.5, 134.3, 135.4, 135.4, 138.2, 144.2, 148.3, 151.9, 153.3, 162.8. **Mass Spectra [M^+]:** 367.18.

2-methyl-3-(4-methylbenzylidene)pyrazolo[5,1-*b*]quinazolin-9(3*H*)-one (4k)
Colour: Yellow, **Yield** = 85%, **M.P**.: 203°C. **IR (KBr, cm^{-1}):** 3058 (C=C-H), 1678 (C=O), 1648 and 1630 (C=N), 1603 and 1513 (aro. C=C). **H^1NMR: δ** 2.39 (s,3H), 7.70-8.10 (m,4H), 7.20 and7.67 (dd,4H), 5.91 (s,1H). **C^{13}NMR:** δ 11.5, 21.9, 116.3, 122.4, 126.9, 127.3, 127.9, 129.3.9, 129.3, 129.3, 133.9, 133.9, 133.9, 138.3, 138.3, 145.8, 148.2, 153.1, 162.7. **Mass Spectra [M^+]:** 302.44.

5-chloro-2-methyl-3-(4-methylbenzylidene)pyrazolo[5,1-*b*]quinazolin-9(3*H*)-one (4l)
Colour: Yellowish green, **Yield** = 80%, **M.P**.: 209°C. **IR (KBr, cm^{-1}):** 3044 (C=C-H), 1683(C=O), 1646 and 1629 (C=N), 1605 and 1511 (aro. C=C). **H^1NMR: δ** 2.41 (s,3H), 7.22 and 7.63 (dd,4H), 7.60–7.99 (m,3H), 5.62 (s,1H). **C^{13}NMR:** δ 11.7, 21.8, 116.3, 122.7, 124.9, 129.3, 129.3, 129.3, 129.5, 132.8, 134.7, 134.7, 133.9, 138.4, 138.4, 148.3, 152.9, 161.6, 162.7. **Mass Spectra [M^+]:** 336.34.

7-chloro-2-methyl-3-(4-methylbenzylidene)pyrazolo[5,1-*b*]quinazolin-9(3*H*)-one (4m)
Colour: Yellowish green, **Yield** = 82%, **M.P**.: 221°C. **IR (KBr,cm^{-1}):** 3048 (C=C-H), 1688(C=O), 1646 and 1623 (C=N), 1603 and 1519 (aro. C=C). **H^1NMR: δ** 2.41 (s,3H), 7.22 and 7.63 (dd,4H), 7.54(d,1H), 7.80 (d,1H), 8.1 (s,1H), 5.72 (s,1H). **C^{13}NMR:** δ 11.7, 21.8, 116.3, 122.7, 127.9, 127.9, 129.3, 129.3, 130.2, 133.1, 133.8, 134.7, 134.7, 137.9, 138.1, 138.1, 143.8, 148.3, 152.9, 162.8.**Mass Spectra [M^+]:** 336.24.

2,7-dimethyl-3-(4-methylbenzylidene)pyrazolo[5,1-*b*]quinazolin-9(3*H*)-one (4n)
Colour: Yellow, **Yield** = 78%, **M.P**.: 204°C. **IR (KBr, cm^{-1}):** 3050(C=C-H), 1682 (C=O), 1645 and 1631 (C=N), 1609and 1520 (aro. C=C). **H^1 NMR: δ** 2.43 (s,3H), 7.20 and 7.62 (dd,4H), 7.41 (d,1H), 7.49 (d,1H), 7.82 (s,1H), 5.84 (s,1H). **C^{13}NMR:** δ 11.7, 21.9, 21.9, 115.8, 121.1, 125.8, 127.9, 129.3, 129.3, 130.1, 133.9, 134.7, 134.7, 137.3, 137.9, 137.9, 142.8, 148.3, 152.9, 162.7. **Mass Spectra [M^+]:** 316.18.

2-methyl-3-(4-methylbenzylidene)-7-nitropyrazolo[5,1-*b*]quinazolin-9(3*H*)-one (4o)
Colour: Yellow, **Yield** = 76%, **M.P**.: 235°C. **IR (KBr, cm^{-1}):** 3052(C=C-H), 1688 (C=O), 1649and 1630 (C=N), 1607 and 1522 (aro. C=C), 1492-1360(-NO_2). **H^1NMR:** δ 2.47 (s,3H), 7.22 and 7.64 (dd,4H), 7.80 (d,1H), 8.40

(d,1H), 8.63 (s,1H), 5.91 (s,1H). **C^{13}NMR:** δ 11.3, 21.7, 115.9, 121.9, 123.8, 124.3, 128.9, 129.3, 129.3, 130.2, 134.7, 134.7, 137.9, 137.9, 144.4, 148.2, 151.9, 152.9, 162.6. **Mass Spectra [M^+]:** 347.16.

3-(4-methoxybenzylidene)-2-methylpyrazolo[5,1-*b*]quinazolin-9(3*H*)-one (4p)
Colour: Green, **Yield** = 84%, **M.P**.: 223°C. **IR (KBr, cm^{-1}):** 3048 (C=C-H), 1685 (C=O), 1648 and 1628 (C=N), 1601 and 1518 (aro. C=C),1252(aro-OCH_3).**H^1 NMR: δ** 2.43 (s,3H), 3.94 (s, 3H –OCH_3), 6.99 and 8.41 (dd,4H), 7.69–8.40 (m,4H), 5.68 (s,1H).**C^{13}NMR:** δ 10.9, 56.3, 114.6, 114.6, 115.6, 122.3, 125.5, 126.9, 126.9, 127.6 130.5, 130.5, 133.7 137.9, 145.8, 148.2, 152.9, 160.2, 162.3. **Mass Spectra [M^+]:** 318.34.

5-chloro-3-(4-methoxybenzylidene)-2-methylpyrazolo[5,1-*b*]quinazolin-9(3*H*)-one (4q)
Colour: Green, **Yield** = 86%, **M.P**.: 239°C. **IR (KBr, cm^{-1}):** 3048 (C=C-H), 1690 (C=O), 1642and 1622 (C=N), 1607and 1518 (aro. C=C),1255 (aro. -OCH_3). **H^1 NMR:** δ 2.46(s,3H), 3.96 (s, 3H –OCH_3),7.10 and 8.42 (dd,4H), 7.60–7.989 (m,3H), 5.94 (s,1H). **C^{13}NMR:** δ 11.3, 56.2, 114.5, 114.5 115.9, 122.6, 124.9, 125.5, 128.9, 130.6 130.6, 132.8, 133.8, 137.9, 148.2, 152.9, 159.9, 161.4, 162.6. **Mass Spectra [M^+]:** 352.26.

7-chloro-3-(4-methoxybenzylidene)-2-methylpyrazolo[5,1-*b*]quinazolin-9(3*H*)-one (4r)
Colour: Green,**Yield** = 81%, **M.P**.: 242°C. **IR (KBr, cm^{-1}):** 3048 (C=C-H), 1687 (C=O), 1644 and 1622 (C=N), 1607and 1518 (aro. C=C),1253 (aro-OCH_3). **H^1NMR: δ** 2.48(s,3H), 3.95 (s, 3H –OCH_3),7.10 and 8.42 (dd,4H), 7.51 (d,1H), 7. 83 (d,1H), 8.09 (s,1H) , 5.78 (s,1H). **C^{13}NMR:** δ 11.5, 56.3, 114.5 114.5, 115.9, 122.5, 125.5, 127.7, 127.9, 130.5, 130.5, 133.2, 133.8, 137.9, 143.9, 148.2, 152.8, 160.1, 162.5. **Mass Spectra [M^+]:** 352.54.

3-(4-methoxybenzylidene)-2,7-dimethylpyrazolo[5,1-*b*]quinazolin-9(3*H*)-one (4s)
Colour: Green, **Yield** = 77%, **M.P**.: 220°C. **IR (KBr, cm^{-1}):** 3048 (C=C-H), 1684 (C=O), 1641 and 1622 (C=N), 1607and 1518 (aro. C=C),1258 (aro. -OCH_3). **H^1NMR: δ** 2.49 (s,3H), 2.46 (s,3H), 3.97 (s, 3H –OCH_3),7.10 and 8.42 (dd,4H), 7.43 (d, 1H) 7.49 (d, 1H), 7.81 (s, 1H), 5.87 (s, 1H).

C^{13}NMR: δ 11.4, 21.6, 56.1, 114.5, 114.5, 115.9, 121.1, 125.5, 125.6, 127.6, 130.5, 130.5, 133.9, 137.3, 137.8, 142.7, 148.1, 152.9, 160.2, 162.9. **Mass Spectra [M^+]:** 332.22.

3-(4-methoxybenzylidene)-2-methyl-7-nitropyrazolo[5,1-*b*]quinazolin-9(3*H*)-one (4t)
Colour: Green, **Yield** = 82%, **M.P**.: 257°C. **IR (KBr, cm^{-1}):** 3048 (C=C-H), 2909 (aro.C-H) 1683 (C=O), 1645 and 1622 (C=N), 1607and 1518 (aro. C=C), 1258 (aro-OCH_3), 1492-1360 (-NO_2)**. H^1NMR: δ** 2.51 (s,3H), 3.96 (s, 3H –OCH_3),7.13 and 8.45 (dd,4H), 7.81 (d, 1H), 8.41 (d, 1H), 8.67 (s, 1H), 5.95 (s, 1H). **C^{13}NMR:** δ 11.6, 56.4, 114.5, 114.5, 115.6, 121.9, 123.6, 123.5, 125.5, 128.3, 130.5, 130.5, 137.9, 143.3, 147.5, 151.9, 152.9, 159.5, 162.8. **Mass Spectra [M^+]:** 363.10.

BIOLOGICAL ACTIVITY
Antibacterial Activity
Procedure:
The antibacterial activity was measured by agar cup method.[26] 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 turbid suspension 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 poured separately 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 prepared in ethanol (0.1%) was added in the cups under aseptic condition with the help of micropipette. 100ml of ethanol was placed in separate cups as blank (negative control). 100 ml of solution of penicillin in ethanol (0.1%) was also placed on 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 the medium. 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.[26] 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 to be tested is added to the sterile medium in aseptic condition so as to get final concentration as 1%. A plate with ethanol

was prepared as blank (negative control) similarly a plate with 1% Gresiofulvin was prepared as standard reference plate (positive control).

Aspergillus niger and *Penicillium chrysogenum* were selected as test fungal cultures. They were allowed to grow on slant for 48 hours so as to get profuse sporulation. 5ml of 1:100 aqueous solution of Tween 80 was added to the slant and spores were scraped with the help of nichrome wire loop to form suspension. 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**) as moderate growth of fungi (++), reduced growth of fungi (+) and no growth of inoculated fungi (-) antifungal activity.

Table-1 Anti Microbial activity

Compound	Zone of Inhibition (diameter in mm)		Growth of Fungi	
	E. coli	*S. typhi*	*A. niger*	*P.chrysogenum*
Penicillin	24	18	-	-
(3a)	11	-	+	++
(3b)	16	8	-	-
(3c)	16	8	-	-
(3d)	11	-	+	++
(3e)	19	9	-	-
(3f)	13	-	+	++
(3g)	19	9	-	-
(3h)	19	9	-	-
(3i)	12	-	+	++
(3j)	21	10	-	-
(3k)	12	-	+	++
(3l)	17	6	-	-
(3m)	17	6	-	-
(3n)	13	-	+	++
(3o)	20	8	-	-
(3p)	14	-	+	++
(3q)	18	7	-	-
(3r)	18	7	-	-
(3s)	13	-	+	++
(3t)	20	11	-	-

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 2-methylpyrazolo[5,1-*b*]quinazolin-9(4*H*)-ones (2a-e) were synthesized by reported procedure [24]. 2-methylpyrazolo[5,1-*b*]quinazolin-9(4*H*)-ones **(2a-2e)** was prepared from 1*H*-benzo[*d*][1,3]oxazine-2,4-diones (1a-e) and of 3-methyl-1*H*-pyrazol-5(4*H*)-one in xylene. By refluxing 2-methylpyrazolo[5,1-*b*]quinazolin-9(4*H*)-ones **(2a-2e)** and aryl aldehyde **(3a-3d)** with piperidine in ethanol for 6 hrs yielded 3-arylidene-2-methylpyrazolo[5,1-*b*]quinazolin-9(3*H*)-ones (**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 1649-1640 and 1632-1626 cm^{-1} is assigned to ν(C=N) vibration [27] also in the region 1690-1778 cm^{-1} for carbonyl group.[28] The band around 1610-1510 cm^{-1} is assigned to the combination of ν(C=C) of the aromatic ring. Compounds **4p-4t** show peak in the rage 1258-1252 cm^{-1} assigned to aromatic C–OCH_3.

Each one of the ^{1}HNMR spectra of **4a-4t** revealed singlet for 3H between 2.39-2.51 ppm assigned to 2-methyl group, Peaks around 8.8-7.5 ppm are assigned to aromatic protons and singlet for 1H between 5.95-5.61 ppm assigned to (H−C(Ar)=C<).[29] ^{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 3.97-3.94 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 activity against *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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