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Synthesis, Characterisation of 2,3-Dihydroquinazolinone Derivatives and their Antimicrobial Studies

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Abstract: Twelve 2,3-Dihydroquinazolinone derivatives were synthesized and were identified by spectral analysis. All the synthesized compounds of 2,3- Dihydroquinazolinone derivatives were screened for their antibacterial activities against two gram positive bacterial strains *Staphylococcus aureus* and *Bacillus subtilis* and two gram negative bacterial strains *Escherichia coli* and *Pseudomonas aeruginosa* were used for antibacterial study . Antifungal activity was also studied against *Candida albicans* and *Aspergillus niger*.The standard antibacterial and antifungal agents used were Amikacin and ketoconalzole respectively. The antimicrobial screening studies revealed that compounds 3d,3e,3f,3k &3l showed moderately high activity against B.subtilis and P.aeruginosa and moderate activity against S. aureus. The antifungal screening studies revealed that 3a,3b,3i&3j showed mild activity against Candida albicans and Compounds 3e& 3j showed excellent activity against Asperigillus niger comparable to the standard drug Ketaconazole. The enhanced activity of 3j against Asperigillus niger may be due to the presence of two methoxyl groups at 3, 4 position which are with the electron donating behaviour.
Key words: Dihydroquinazolinone,antibacterial, antifungal activity.

Introduction

Spread of drug-resistant bacteria has badly affected the efficiency of many known antibacterial agents [1] while the emergence of antifungal infections in immune compromised population has also significantly increased over past few decades [2,3]. Therby novel antibacterial and antifungal agents with various mechanisms of action and antimicrobial activities are needed for the effective control of these clinically important infections.Nitrogen containing heterocycles are an integral moiety of many drug molecules or physiologically active natural products and/or synthetic molecules which are highly useful as a potent drug molecule. Quinazolinone analogues are used as chemotherapeutic agents for the treatment of diseases resulting from different microorganisms and now there has been a major expansion in the number of quinazolinone derivatives as drugs. DHQZ is a privileged scaffold because of its extensive pharmacological activities including anti-bacterial, anti-fertility, anti-tumor, anti-fibrilatory, vasodilatory, anti-fungal, and analgesic efficacy[4-12]. Quinazolinone derivatives are now known to have very useful biological and medicinal activities; they can be used as hypnotic, sedative, analgesic, anticonvulsant, antitussive, antibacterial, antidiabetic, anti-inflammatory, and antitumor agents.[13-16] In addition to this, some therapeutic agents containing this core structure have been on the

market or are in clinical trials for the treatment of cancer.[17] In view of the importance of these compounds,as a part of our research work,we want to synthesise many derivatives of 2,3-Dihydroquinazolinone and investigate its antimicrobial activities.

Experimental:

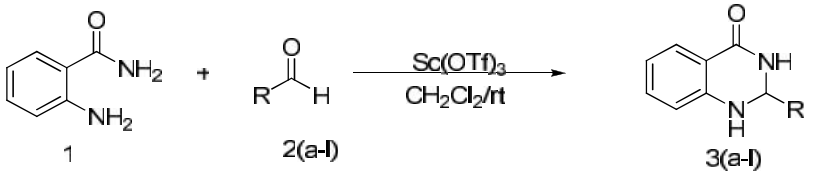
All reactions were carried out in a flame dried flask. Solvents used for reactions and column chromatography were commercial grade and distilled prior to use. Toluene and THF were dried over sodium/benzophenone, whereas CH_2Cl_2 and $CHCl_3$ were dried over CaH_2. TLC was performed on pre-coated Merck silica gel aluminium plates with 60_F254 indicator, visualised by irradiation with UV light. Column chromatography was performed using silica gel Merck 60-100 mesh. ^{1}H-NMR and ^{13}C-NMR were recorded on a Bruker AV 500 MHz using DMSO-d_6 or $CDCl_3$ as solvent and multiplicity indicated as follows: s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), dd (doublet of doublet), dt (doublet of triplet) bs (broad singlet). Coupling constants J are reported in Hz. High resolution mass spectra were obtained by ESI using Waters/Micromass Q-TOF mass spectrometer. IR spectra were recorded on a Perkin Elmer FT/IR-420 spectrometer and are reported in terms of frequency of absorption (cm^{-1}).

General procedure for the synthesis of 2,3-dihydroquinazolinones.

In a oven dried flask $Sc(OTf)_3$ (3 µmol) was taken in 1 mL of anhydrous dichloromethane. After 3 h, Anthranilamide (300 µmol) solubilized in 1 mL of dichloromethane was added at room temperature, followed by aldehyde (360 µmol) and stirred further at the same temperature for 4-6h. Completion of the reaction was ascertained by TLC, and the product was purified by using a small pad of silica gel 60-100 mesh to afford dihydroquinazolinones as colourless solids.

Synthesis of 2,3-Dihydroquinazolinone derivatives

2,3- Dihydroquinazolinone derivatives (3a-l) were synthesised according to the route described in Schemes (1&2). The compounds were synthesised according to literature reported procedure of (Muthuraj Prakash et.al)[18].



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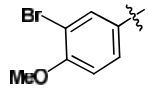
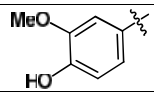
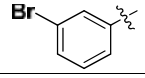
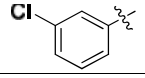
1		7	3a:89
2		7	3b:87
3		5	3c: 88
4		4	3d:86

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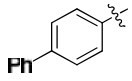
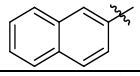
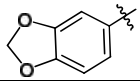
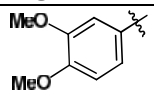
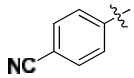
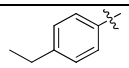
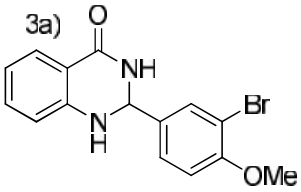
6		4	3f:91
7		4	3g:92
8		7	3h:90
9		5	3i: 86
10		7	3j: 89
11		5	3k:85
12		5	3l:91

3a)



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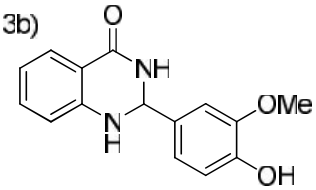

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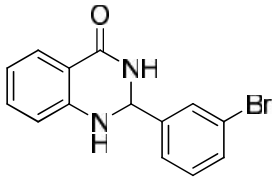

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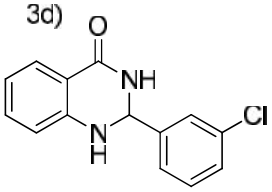

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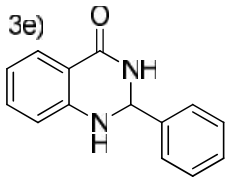
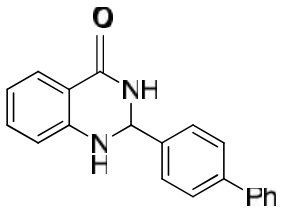
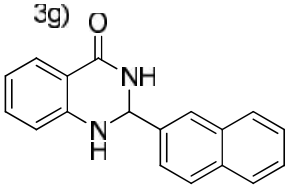


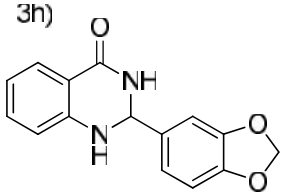
3f)



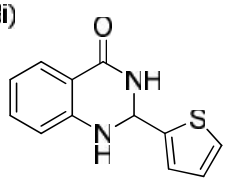
3g)



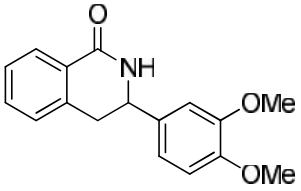
3h)



3i)



3j)



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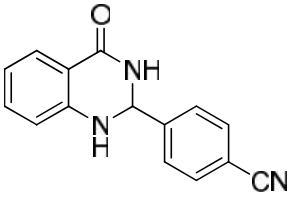
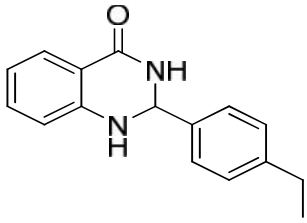


3l)



All the synthesized compounds were screened for antimicrobial activities by well diffusion technique. Compounds are screened for their *in vitro* anti-microbial activity against *Escherichia coli*(ATCC-25922) , *Pseudomonas aeruginosa*(ATCC-2853), *Bacillus subtilis*(ATCC-6051) , *Staphylococcus aureus* (ATCC-9144), *Candida albicans(ATCC2091)* and *Aspergillus niger(ATCC9029)* are compared with standard drug amikacin and ketoconalzole. The zone of inhibition formed for the compounds against bacteria and fungi were calculated.

Detail of the organism used for the study

Grams strain	Name of the organism	Std Code
Gram-negative rod	*Pseudomonas aeruginosa*	(ATCC-2853)
Gram negative	*Escherichia coli*	(ATCC-25922)
Gram- positive bacterium	*Bacillus subtilis*	(ATCC-6051)
Gram-positive spherical bacteria	*Staphylococcus aureus*	(ATCC-9144)

Antibaterial activity:

The synthesized 2,3- Dihydroquinazolinone derivatives were screened for their antibacterial activity against two gram positive bacterial strains *Staphylococcus aureus* (ATCC 9144) and *Bacillus subtilis* (ATCC-6051) and two gram negative bacterial strains *Escherichia coli* (ATCC 25922) and *Pseudomonas aeruginosa* (ATCC 2853) .The antibacterial activities of all test compounds were carried out by Agar well diffusion assay. Muller Hinton Agar (MHA) medium was used for the study. After sterilization the nutrient agar medium was melted, cooled and inoculated with bacterial strains, poured into sterile Petri dish to get a uniform thickness. Cups were made out in the other plate using sterile cork borer (6 mm diameter). Dimethyl sulfoxide was used as a solvent to prepare the stock solution of the test compounds. The tested compounds in a concentration of 25 and 50 µg/ml were added with the sterile micro pipette into each cup. Standard drug Amikacin (25 µg/ml) was used as a standard drug to determine the sensitivity of each bacterial species tested. The plates were then incubated at 37°C for 24 h and the diameter of zone of inhibition was measured and expressed in millimetres (mm) as its anti-bacterial activity.

Antibacterial activity data of synthesized compounds (3a-l)

Table: 2

Compounds	Zone of inhibition (mm)							
	Gram-positive bacteria				Gram-negative bacteria			
	S.aureus		*B.substilis*		*E.coli*		*P.aeruginosa*	
	25µg	50µg	25µg	50µg	25µg	50µg	25µg	50µg
3a	-	2	-	-	-	-	3	7
3b	-	4	2	7	3	7	5	8
3c	1	5	4	10	2	8	5	10
3d	2	8	5	12	3	9	6	12
3e	3	7	8	15	1	5	7	14
3f	-	6	7	14	-	4	5	13
3g	4	9	5	9	4	9	3	6
3h	5	8	4	9	3	7	3	8
3i	-	-	-	-	2	6	5	9
3j	-	3	2	6	3	6	4	7
3k	1	6	7	13	1	3	4	12
3l	-	4	6	12	-	3	5	12
Amikacin (25 µg)	18		20		17		17	

The results of antibacterial activity are reported as zone of inhibition in mm. (-; indicates no activity).
Standard :Amikacin Solvent : DMSO

Anti-fungal activity

Anti-fungal activity was performed by agar diffusion method using Potato dextrose agar medium. After sterilization the medium was inoculated with *Candida albicans (ATCC2091)* and *Aspergillus niger (ATCC9029).*The standard antifungal agent ketoconalzole (10 µg/ml), solvent control (Dimethyl sulfoxide) and the tested compounds in a concentration of 25 and 50 µg/ml were then added by using sterile micro pipette. The plates were then incubated at 37°C for 48 h and the diameter of zone of inhibition was measured.

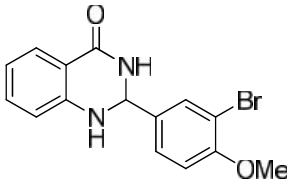
Antifungal activity data of synthesized compounds (3a-l)

Table: 3.1

Compounds	Fungi			
	C.albicans		*A.niger*	
	25µg	50µg	25µg	50µg
3a	3	6	-	3
3b	2	6	-	4
3c	-	-	2	5
3d	-	-	3	6
3e	-	-	4	11
3f	-	-	-	8
3g	-	-	3	9
3h	-	-	3	8
3i	2	7	2	6
3j	3	9	4	12
3k	-	-	3	9
3l	-	-	3	7
Ketoconazole (10 µg)	21		16	

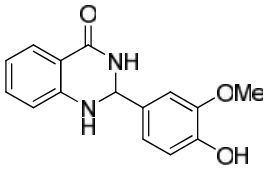
The results of antifungall activity are reported as zone of inhibition in mm.
(-; indicates no activity). Standard : Ketoconazole Solvent : DMSO

1)2-(3-Bromo-4-methoxyphenyl)-2,3-dihydroquinazolin-4(*1H*)-one



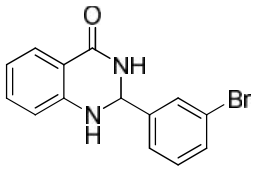
^{1}H NMR (500 MHz, DMSO-d_6): δ = 8.29 (bs, 1H), 7.69 (d, *J* = 2.0 Hz, 1H), 7.61(dd, *J* = 7.8 and 1,5 Hz, 1H), 7.42 (dd, *J* = 8.5 and 2.3 Hz, 1H), 7.32 – 7.20 (m, 1H), 7.18 – 7.04 (m, 2H), 6.82 – 6.58 (m, 2H), 5.73 (bs, 1H), 3.84 (s, 3H); ^{13}C NMR (125 MHz, DMSO-d_6): δ = 163.4, 155.2, 147.5, 135.2, 133.2, 131.2, 127.3, 127.2, 117.1, 114.8, 114.3, 112.2, 110.2, 65.2, 56.2; IR (KBr): $\bar{\nu}$ = 3281, 3180, 2836, 1644, 1612, 1496, 1438, 1386, 1298, 1266, 1158, 1054, 890, 808, 747, 675, 623 cm^{-1}.

2) 2-(4-hydroxy-3-methoxyphenyl)-2,3-dihydroquinazolin-4(1H)-one



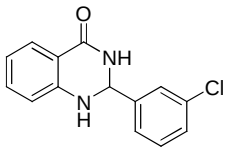
^{1}H NMR (500 MHz, DMSO-D_6): δ = 9.15 (bs, 1H), 8.09 (bs, 1H), 7.62 3 (d, *J* = 7.5 Hz, 1H), 7.24 (t, *J* = 7.5 Hz, 1H), 7.09 (bs, 1H), 6.95 (s,1H), 6.89 (d, *J* = 7.5 Hz, 1H), 6.77 – 6.74 (m, 2H), 6.82 (t, *J* = 7.5 Hz, 1H), 5.66 (bs, 1H), 3.77 (s, 3H); ^{13}C NMR (125 MHz, DMSO-D_6): δ = 164.2, 148.6, 147.8, 147.6, 133.5, 132.3, 127.8, 120.1, 117.5, 115.5, 115.3, 114.6, 111.4, 67.3, 55.9; IR (KBr): $\bar{\nu}$ = 3388, 3354, 3058, 2969, 2935, 2841, 1646, 1610, 1499, 1427, 1357, 1270, 1125, 1021, 766cm^{-1}.

3) 2-(3-bromophenyl)-2,3-dihydroquinazolin-4(1H)-one



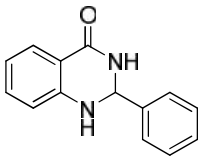
^{1}H NMR (500 MHz, DMSO-d_6): δ = 8.40 (bs, 1H), 7.68 (t, *J* = 1.8 Hz, 1H), 7.62-7.60 (dd, *J* = 7.5 and 1.5 Hz, 1H), 7.55-7.53 (m, 1H), 7.50-7.48 (m, 1H), 7.36 (t, *J* = 7.5Hz), 7.28-7.24 (m, 1H), 7.22 (bs, 1H), 6.76 (d, *J* = 7.5 Hz, 1H), 6.70 –6.67 (m, 1H), 5.79 (t, *J* = 2Hz, 1H); ^{13}C NMR (125 MHz, DMSO-d_6): δ =163.8, 147.9, 145.0, 133.9, 131.6, 131.0, 130.1, 127.8, 126.2, 122.0, 117.7, 115.3, 114.9, 65.9; IR (KBr): $\bar{\nu}$ = 3289, 3198, 3062, 1645, 1613, 1515, 1429, 1299, 1157, 865, 791, 757, 698 cm^{-1}.

4) 2-(3-chlorophenyl)-2,3-dihydroquinazolin-4(1H)-one



^{1}H NMR (DMSO-d_6, 500 MHz): δ = 1.64 (s, 3H, CH_3), 6.61 (t, J =7.6 Hz, 1H, ArH), 6.80 (d, J = 8.0 Hz, 1H, ArH), 7.21~7.27 (m, 2H, ArH), 7.33 (t, J =8.0 Hz, 1H, ArH), 7.45~7.47 (m, 1H, ArH), 7.51 (dd, J = 8.0 Hz, J' = 1.6 Hz, 1H,ArH), 7.56 (t, J = 1.6 Hz, 1H, ArH), 7.71 (s, 1H, NH), 8.84 (s, 1H, NH). ^{13}C NMR (125 Hz, DMSO-d_6): δ = 163.7, 150.4, 146.9, 133.5, 132.9, 130.0, 127.1, 125.3, 123.9, 117.1, 114.9, 114.3, 69.9, 30.4. IR (KBr): 3174, 3040, 2932, 1664, 1614, 1593, 1526, 1485, 1439, 1412, 1385, 1205, 1152, 1097, 825, 784, 757, 715 cm^{-1}.

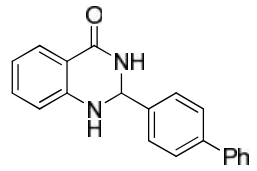
5) 2-phenyl-2,3-dihydroquinazolin-4(1H)-one



^{1}H NMR (500 MHz, DMSO-d_6): δ = 8.29 (bs, 1H), 7.63 (dd, *J* = 7.8 and 1.5 Hz, 1H), 7.51 – 7.40 (m, 2H), 7.44 – 7.30 (m, 3H), 7.28 – 7.17 (m, 1H), 7.11 (bs, 1H), 6.77 (d, *J* = 8 Hz, 1H), 6.68 (m, 1H), 5.75 (t, *J* = 1.5 Hz, 1H); ^{13}C NMR (125 MHz, DMSO-d_6): δ = 164.0,

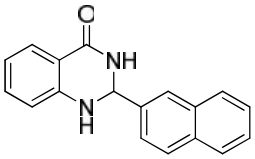
148.3, 142.1, 133.7, 128.9, 128.7, 127.8, 127.3, 117.5, 115.4, 114.8, 67.0; IR (KBr): $\bar{\nu}$ = 3303, 3186, 3062, 1652, 1613, 1511, 1391, 1300, 1148, 809, 748, 699 cm^{-1}.

6) 2-(Biphenyl-4-yl)-2,3-dihydroquinazolin-4(*1H*)-one



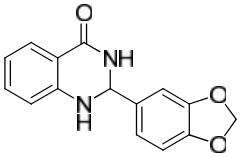
^{1}H NMR (500 MHz, DMSO-d_6): δ = 8.35 (bs, 1H), 7.70 – 7.58 (m, 7H), 7.48 – 7.45 (m,2H), 7.39 – 7.36 (m, 1H), 7.28 – 7.25 (m, 1H), 7.18 (bs, 1H), 6.78 (d, *J* = 8 Hz, 1H), 6.71 – 6.68 (m, 1H), 5.81 (bs, 1H); ^{13}C NMR (125 MHz, DMSO-d_6): δ = 164.1, 148.3, 141.3, 140.8, 140.1, 133.8, 129.4, 128.0, 127.9, 127.8, 127.1,127.1, 117.6, 115.4, 114.9, 66.6; IR (KBr): $\bar{\nu}$ = 3290, 3183, 3057, 1652, 1611, 1508,1386, 1297, 1153, 750, 689 cm^{-1}.

7) 2-(naphthalen-2-yl)-2,3-dihydroquinazolin-4(1H)-one



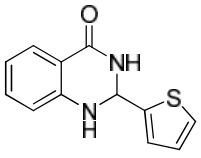
^{1}H NMR (500 MHz, DMSO-d_6): δ = 8.37 (bs, 1H), 7.96 – 7.92 (m, 4H), 7.70 (d, *J* = 7.5 Hz, 1H), 7.64 (d, *J* = 7.5 Hz, 1H), 7.55 – 7.53 (m, 2H), 7.25 (t, *J* = 8 Hz, 1H), 7.19 (bs, 1H), 6.73 (d, *J* = 8 Hz, 1H), 6.69 (t, *J* = 7.5 Hz, 1H), 5.96 (bs, 1H); ^{13}C NMR (125 MHz, DMSO-d_6): δ = 164.0, 148.3, 139.3, 133.8, 133.4, 132.9, 128.5, 128.4, 128.0, 127.8, 126.8, 126.8, 126.3, 125.3, 117.6, 115.4, 114.4, 67.3; IR (KBr): $\bar{\nu}$ = 3447, 3281, 3187, 3052, 1660, 1610, 1513, 1387, 1297, 1157, 809, 744, 689 cm^{-1}; HRMS (ESI): *m/z* calculated for $C_{18}H_{15}N_2O$ [M^++H] 275.1184, found: 275.1172.

8) 2-(Benzo[*d*][1,3]dioxol-5-yl)-2,3-dihydroquinazolin-4(*1H*)-one



^{1}H NMR (500 MHz, DMSO-d_6): δ = 8.24 (bs, 1H), 7.52 (d, *J* = 7.5 Hz, 1H), 7.25 (t, *J* = 7.3 Hz, 1H), 7.11 – 7.03 (m, 2H), 7.01 – 6.87 (m, 2H), 6.81 – 6.61 (m, 2H), 6.02 (bs, 2H), 5.68 (bs, 1H); ^{13}C NMR (125 MHz, DMSO-d_6): δ = 163.5, 147.8, 147.2, 147.1, 135.5, 133.2, 127.3, 120.4, 117.1, 114.9, 114.4, 107.8, 107.1, 101.0, 66.2; IR (KBr): $\bar{\nu}$ = 3282, 3186, 3127, 2903, 1653, 1611, 1486, 1445, 1383, 1248, 1036, 755 cm^{-1}.

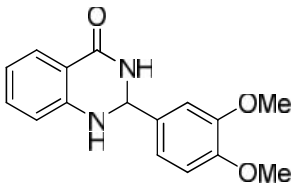
9) 2-(thiophen-2-yl)-2,3-dihydroquinazolin-4(1H)-one



^{1}H NMR (500 MHz, DMSO-d_6): δ = 8.44 (1H, br s), 7.61 (1H, dd, *J* = 7.6 1.6 Hz), 7.45 (1H, dd, *J* = 4.8 1.2 Hz), 7.24-7.28 (2H, m), 7.12 (1H, d, *J* = 3.2 Hz), 6.98 (1H, dd, *J* = 4.8 3.6 Hz), 6.76 (1H, d, J = 8 Hz), 6.70 (1H, ddd, *J* = 7.6 7.2 0.8 Hz), 6.01 (1H, t, *J* = 2.4 Hz); ^{13}C NMR (125 MHz, DMSO-d_6): δ = 163.0, 147.1, 146.3,

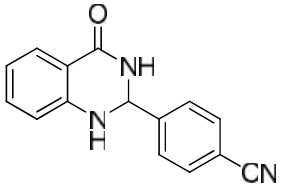
133.3, 127.2, 126.4, 125.8, 125.6,117.4, 115.0, 114.6, 62.5; IR (KBr): $\bar{\nu}$ = 3290, 1652, 1609, 1517, 1439, 764, 711, 684.

10) 2-(3,4-Dimethoxyphenyl)-2,3-dihydroquinazolin-4(*1H*)-one



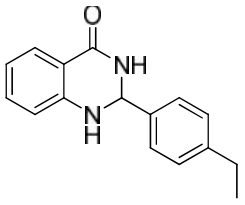
^{1}H NMR (500 MHz, DMSO-d_6): δ = 8.16 (bs, 1H), 7.61 (dd, *J* = 7.8 and 1,5 Hz,1H), 7.29 – 7.18 (m, 1H), 7.12 (d, *J* = 1,8 Hz, 1H), 7.05 – 6.87 (m, 3H), 6.75 (d, *J* = 7.8 Hz, 1H), 6.71 – 6.62 (m, 1H), 5.71 (bs, 1H), 3.81 – 3.72 (2 x s, 6H); ^{13}C NMR (125 MHz, DMSO-d_6): δ = 164.18, 149.47, 149.06, 148.50, 134.11, 133.68, 127.81, 119.65, 117.61, 114.91, 114.91, 111.81, 111.12, 66.97, 56.05, 55.95; IR (KBr): $\bar{\nu}$ = 3355, 3332, 2967, 2834, 1669, 1608, 1496, 1414, 1364, 1270, 1227, 1144, 1014, 769 cm^{-1}

11) 4-(4-oxo-1,2,3,4-tetrahydroquinazolin-2-yl)benzonitrile



^{1}H NMR (500 MHz, DMSO-d_6): δ = 8.46 (s, 1H), 7.74(d, *J* = 8Hz, 2H), 7.65 (d, *J* = 8 Hz, 2H), 7.61 (d, *J* = 7.5 Hz, 1H), 7.27-7.22 (m, 2H), 6.75 (d, *J* = 7 Hz, 1H), 6.68 (t, *J* = 7.5 Hz, 1H), 5.83 (s, 1H); ^{13}C NMR (125 MHz, DMSO-d_6): δ = 163.75, 147.81, 147.77, 134.00, 133.00, 132.85, 128.12, 127.83, 119.10, 117.86, 115.35, 114.96, 111.50, 65.95; IR (KBr): $\bar{\nu}$ = 3451, 3354, 3334, 2226, 1666, 1610, 1485, 1373, 1151, 837, 798, 771, 616 cm^{-1}.

12) 2-(4-ethylphenyl)-2,3-dihydroquinazolin-4(1H)-one



Melting Point : 197 C ^{1}H NMR (500 MHz, DMSO-d_6): δ = 8.25 (s, 1H), 7.60 (d, *J* = 8 Hz, 1H), 7.41 (d, *J* = 8 Hz, 2H), 7.22 – 7.20 (m, 3H), 7.054 (bs, 1H), 6.73 (d, *J* = 8.0 Hz, 1H), 6.65 (t, *J* = 8Hz, 1H), 5.71 (s, 1H), 2.05 (q, *J* = 7.5 Hz, 2H), 1.15 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (125 MHz, DMSO-d_6): δ = 164.18, 148.35, 144.67, 139.50, 133.82, 128.34,127.73, 127.28, 117.56, 115.32, 114,83, 67.10, 28.36, 16.11; IR (KBr): $\bar{\nu}$ = 3445, 3301, 3190, 3061, 1654, 1611, 1511, 1387, 1295, 1155, 807, 742, 688 cm^{-1}; HRMS (ESI): *m/z* calculated for $C_{16}H_{16}N_2O$ [M^++Na] 275.1160, found: 275.1161.

Result and Discussion

In the present research work, 12 new compounds (3a-l) were synthesized. The structures of the obtained compounds were elucidated by spectral data. Synthesizing these different derivatives of 2,3-Dihydro quinazolinone lies in the prospect of obtaining new biologically active substances having potential to act as future antibiotics. All the synthesized compounds (3a-l) were screened for their in vitro antibacterial activity against Gram +ve (S. aureus(ATCC-9144) and B. subtilis (ATCC-6051)) and Gram -ve (E. coli(ATCC-25922)and P.aeruginosa (ATCC-2853)) bacterial strains. The antimicrobial screening studies revealed that compounds 3d, 3e,3f,3k &3l showed moderately high activity against B.subtilis and P.aeruginosa and moderate activity against S. aureus (bacteria that acquired resistance against many well-known antibiotics and are responsible for a range of difficult-to- treat infections in humans) and thus showed their strong potential to be part of one of the future antibiotics against drug-resistant bacteria. and E. coli. Compounds 3a and 3i show no activity against gram +ve bacterial strains S. aureus and B. subtilis, but 3i shows mild activity against Gram -ve (E. coli and P.aeruginosa). All other compounds 3b,3c,3g,3h and 3j showed only lowered activity against both+ve (S. aureus and B. subtilis) and Gram -ve (E. coli and P.aeruginosa) bacterial strains.

The antifungal screening studies revealed that 3a,3b,3i&3j showed mild activity against Candida albicans,a fungi responsible for genital and oral infections in humans remaining all the compounds showed no activity against Candida albicans. Compounds 3e& 3j showed excellent activity against Asperigillus niger comparable to the standard drug Ketaconazole. All other compounds showed only mild to moderate activity against A.niger. The enhanced activity of 3j against Asperigillus niger may be due to the presence of two electron donating methoxyl group at 3, 4 position.

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