*Available online at* www.joac.info

ISSN: 2278-1862

***Journal of Applicable Chemistry***

**2015, 4 (6): 1828-1835**

(International Peer Reviewed Journal)

# Synthesis and Antimicrobial Activities of Novel 6-Benzyloxy-7-Methoxyquinazolin-4(3h)-Ones

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Accepted on 21st November 2015

## ABSTRACT

*Novel 6-benzyloxy-7- methoxyquinazolin-4(3H)-ones* ***(8a-j)*** *synthesized from 4-(benzyloxy)-5-methoxy-2-nitrobenzamide* ***(6)*** *using tin chloride, where in reduction followed by cyclization took place in methanol. 4-benzyloxy-5-methoxy-2-nitrobenzamide* ***(6)*** *prepared from 4-benzyloxy-5-methoxy-2-nitrobenzoic acid (5) in the presence of Tetrahydrofuran- water combination and sodium hydroxide. All the synthesized compounds were characterized basing on their spectral and analytical data. These molecules synthesized were tested for their antimicrobial activities in two Gram-positive bacteria (Staphylococcus aureus, Bacillus subtillis) and two Gram-negative bacteria (Echerichia coli and Pseudomonas aeuroginosa), two fungi (Aspergillus Niger and Aspergillus fumigatus) strains using Cup plate method.*

**Keywords:** Antimicrobial activity, 4-benzyloxy-5-methoxy-2-nitrobenzamide, tin chloride, aliphatic aldehydes.

## INTRODUCTION

Quinazolinone is a building block for quite a good number of naturally occurring alkaloids isolated from time to time, sourced from a number of families of the plant kingdom, animals and microorganisms. The quinazolinone was first synthesized [1] from anthranilic acid and cyanogens to give 2-cyanoquinazolinone. Interest in the medicinal chemistry of quinazolinone derivatives was stimulated in the early 1950's with the elucidation of a quinazolinone alkaloid, 3-[b-keto-g-(3-hydroxy-2-piperidyl)- propyl]-4-quinazolone febri fugine [2] from an Asian plant Dichroa febrifuga, which is an ingredient of a traditional Chinese herbal remedy, effective against malaria.

In a quest to find additional potential quinazolinone-based drugs, various substituted quinazolinones have been synthesized and exploited for their biological profiles, which led to the synthesis of the derivative like 2-methyl-3-o-tolyl-4-(3H)-quinazolinonemethaqualone. Methaqualone was synthesized [3] in 1951 and it is the most well-known synthetic quinazolinone drug, well known for its sedative-hypnotic effects [4]. The identification and introduction of methaqualone as one of the potential molecule as a hypnotic triggered the research activities toward the isolation, synthesis, and studies on the pharmacological properties of the

quinazolinones and related compounds. Quinazolinones and their derivatives are now established as molecules with a wide range of useful biological properties, such as hypnotic, sedative, analgesic, anti-convulsant, anti-tussive, anti-bacterial, anti-diabetic, anti-inflammatory, anti-tumor, and several others [5,6]. Quinazolinone derivatives are of special interest because of their pharmacological properties [6,7], Anti-microbial, anticonvulsant, sedative, hypotensive, anti-depressant, antimflammatory, and anti-allergy properties. Some of the compounds having quinazolinone skeleton also pronounced biological properties [7-10] such as anti-malarial activity, biofungicide, and diuretic properties.

In view of their biological activity, 2-substituted-3H-quinazoline-4-ones represent one of the most interesting groups of alkaloids. In particular, quinazoline-4-one alkaloids such as sedative hypnotic drug Methaqualone. The development of new methods for the expeditious synthesis of biologically relevant heterocyclic compounds, we became interested in developing a one pot analogue of the Quinazolinones. Most of the methods reported in the literature for constructing Quinazolinone ring system, containing ortho-amino benzanilides as starting materials, which involves the reduction of nitro group of ortho-nitro benzanilide, We are successful in minimizing the number of steps, in which the intermediate o-aminobenzanilide was used without purification, but rather immediately utilized without isolation by converting in situ to a Quinazolinone derivatives, we have developed novel one-pot intermolecular reductive cyclization of *o*-nitrobenzamides and aromatic or aliphatic aldehydes to Quinazolinones derivatives.

## MATERIALS AND METHODS

**General conditions:** Vanillic acid and all aliphatic aldehydes were purified before use. All the other reactants, reagents and solvents were used with purification just before use. Melting points were determined by open capillary method. IR-spectra were recorded on Perkin-Elmer Infrared-683 spectrophotometer with KBr optics. $^1$H NMR (300MHz, DMSO-$d_6$, TMS) and $^{13}$C NMR (300 MHz, DMSO-$d_6$, TMS) were recorded on spectrometer TMS as internal standard (chemical shifts and ppm). Mass spectra were recorded on a VG micromass70-70H instrument.

**Synthesis of Methyl 4-hydroxy-3-methoxybenzoate (2):** Conc.$H_2SO_4$ was added to a solution of vanillic acid **1** in methanol at 0°C and was heated under reflux condition for 4 h monitored by thin layer chromatography. After the completion of reaction, the reaction mixture was extracted with ethyl acetate and washed aqueous solution of sodium bicarbonate solution to remove unreacted acid **1** followed by water. The organic layer was separated and the reaction mixture was concentrated by removing solvent under reduced pressure to give the liquid compound **2** in 90 % yields.

**Synthesis of Methyl-4-benzyloxy-3-methoxybenzoate (3):** To a solution of ester **2** (182 mg, 1 mmol) in acetone (30 mL) was added, anhydrous $KaCO_3$ (553 mg, 4 mmol) and benzyl bromide (256 mg, 1.5 mmol), the mixture was re fluxed in an oil bath for 24 h. The reaction was monitored by TLC using EtOAc-hexane (2:8) and $K_2CO_3$ was removed by filtration and the solvent was evaporated under reduced pressure and was purified by column chromatography (10% EtOAc-hexane) to afford compound **3** (250 mg) as white solid in 92 % yield, mp: 116-118° C. $^1$H NMR (300 MHz, DMSO-$d_6$, TMS): δ 7.65 (d, 1H, *J*= 8.8 Hz,), 7.50-7.20 (m, 6H), 6.88 (d, 1H, *J*= 8.2 Hz,), 5.20 (s, 2H), 3.98 (s, 3H), 3.94 (s, 3H); MS (El): m/z 212 $[M]^+$.

**Synthesis of methyl 4-(benzyloxy)-5-methoxy-2-nitrobenzoate (4) :** A freshly prepared mixture of stannic chloride (301 mg, 1.156 mmol) and fuming nitric acid (98 mg, 1.56 mmol) in dichloromethane was added drop wise over a period of 5 min with continuous stirring to a solution of methyl-4-benzyloxy-3-methoxybenzoate **3** (272mg, 1mmol) in dichloromethane (30mL) at -78°C(dry ice/acetone). The mixture was stirred at -78°C for a further 5 minutes, quenched with water (20 mL) and then allowed to return room temperature. The organic layer was separated and the aqueous layer was extracted with dichloromethane (2 x 20 mL). The combined organic extracts were passed through anhydrous sodium sulphate, concentrated in

vacuum and it was purified by column chromatography using (20 EtOAc: 80 Hexane) to yield **4** as a yellow solid, which is confirmed by its spectral and analytical data. $^1$H NMR (300 MHz, DMSO-$d_6$, TMS), δ 3.88 (s, 3H, $OCH_3$), 3.97 (s,a 3H, $OCH_3$), 5.17 (s, 2H, $OCH_2$), 7.04 (s, 1H, Ar-H), 7.24-7.44 (m, 5H, Ar-H), 7.46 (s, 1H, Ar-H).

**Synthesis of 4-(benzyloxy)-5-methoxy-2-nitrobenzoic acid (5):** A solution of 5 % sodium hydroxide was stirred with **4** in THF: $H_2O$ (1:1) at room temperature and was heated for 4 h, monitored by TLC. After the completion of the reaction, the reaction mixture was concentrated and the residue obtained was acidified with HC1 (1 M). The reaction mixture was extracted with ethyl acetate (3X100mL) and the combined organic extracts were washed with water (3X50mL). The extracts was dried over anhydrous sodium sulphate, solvent was removed under reduced pressure in vacuo to afford crude product. Recrystalization of the resulting crude product yields nitro acid **5** in 90 % yields, which is characterized by its spectral and analytical data. M.p: 180-182°C. $^1$H NMR (300 MHz, DMSO-$d_6$, TMS), δ 3.97 (s,3H, OCH3), 5.18 (s,2H, OCH2), 7.19 (s,1H, Ar-H), 7.24-7.56 (m,6H, Ar-H).

**Synthesis of 4-(benzyloxy)-5-methoxy-2-nitrobenzamide (6):** To a stirred solution of equimolar quantities of nitro acid **5** in benzene and thionyl chloride in 5mL DMF and refluxed for 1-2 h. Then, the benzene solvent was evaporated under reduced pressure to give acid chloride. This acid chloride was dissolved in tetrahydrofuran and solution of aqueous Ammonia was added to it then the reaction mixture was stirred for 4-5 h monitored by thin layer chromatography. Then, the solvent was evaporated and washed with water. The resulting residue was filtered off to obtain amide compound **6** in 87 % yield, which is characterized by its spectral and analytical data; m.p: 202-203°C. $^1$H NMR (300 MHz, DMSO-$d_6$, TMS) δ 3.91 (s, 3H, $OCH_3$), 5.24 (s, 2H, $OCH_2$), 7.11 (s, 1H, Ar-H), 7.31-7.50 (m, 5H, Ar-H), 7.60 (broad singlet, 1H, NH), 7.68 (s, 1H, Ar-H), 7.99 (broad singlet, 1H, NH). $^{13}$C NMR (300 MHz, DMSO-$d_6$, TMS) δ 56.39, 70.29, 108.69, 110.93, 127.20, 127.85, 128.09, 128.45, 135.99, 139.23, 147.46, 152.51, 167.10. IR (KBr) v 3395.39, 3178.63, 1649.98, 1618.63, 1574.99, 1518.48, 1456.62, 1414.54, 1373.97, 1337.26, 1279.20, 1213.31, 1118.11, 1041.91, 1001.05, 959.48, 700.25, 672.59, 634.55, 487.65 $cm^{-1}$.

**General procedure for the synthesis of title compound 6-benzyloxy- 7-methoxyquinazolin-4(3H)-ones (8a-j):**A solution of 4-(benzyloxy)-5-methoxy-2-nitrobenzamide **6** (1g, 3.311mmol, 1 equiv.), anisaldehyde (0.450gm, 3.308 mmol, 1 equiv) and $SnCl_2.2H_2O$ (2.98 gm, 13.24 mmol, 4 equiv) in Methanol. The mixture was heated at reflux temperature for 3-4 h. After the completion of reaction, monitored by TLC, the solvent was removed by evaporation in vacuo and the residue was extracted with ethyl acetate (2X 20 mL) and the resulting residue was treated with saturated solution of $NaHCO_3$ to adjust pH upto 12. The resulting mixture was filtered through a bed of Celite. Then, the two layers i.e. organic and aqueous layers were separated and the organic layer was evaporated in vacuo to give a solid product. Recrystalization of this crude product with Methanol afforded pure colorless compound (**8a-j)**. Characterization data of **8a-j** are given below.

**6-(benzyloxy)-7-methoxy-2-(4-methoxyphenyl) quinazolin-4(3H)-one (8a):** 70% yield, mp: 220-221°C. IR (KBr) 3423, 2923, 1636, 1609, 1500, 1441, 1388, 1267, 1220, 1182, 1102, 1031,948,858, 732, 694, 524 $cm^{-1}$. $^1$H NMR (300MHz, DMSO-$d_6$, TMS) δ 3.86 (s, 3H, $OCH_3$), 3.96 (s, 3H, $OCH_3$), 5.25 (s, 2H, $OCH_2$), 6.96 (d, 2H, *J*= 9.44 Hz, Ar-H), 7.17 (s, 1H, Ar-H), 7.37 (s, 1H, Ar-H), 7.27-7.42 (m, 5H, Ar-H), 8.16 (d, 2H, *J* = 8.39 Hz, Ar-H). $^{13}$C NMR (300 MHz, DMSO-$d_6$, TMS) δ 55.39, 55.71, 69.99, 105.05, 105.13, 109.23, 113.72, 113.92, 124.91, 127.19, 127.88, 128.06, 128.49, 129.05, 136.32, 148.42, 150.46, 153.60, 161.51. ESI-MS: m/z 389 $(M+H)^+$.

**6-(benzyloxy)-2-(lH-indol-3-yl)-7-methoxyquinazolin-4(3H)-one (8b):** Yield 72%, m.p: 235-237 °C. IR (KBr): 3443, 3112, 2921, 1665, 1596, 1483, 1430, 1392, 1363, 1282, 1228, 1193, 1134, 1101, 1039, 917, 846, 746, 697, 610, 581, 543, 486, 425 $cm^{-1}$. $^1$H NMR (300 MHz, DMSO-$d_6$, TMS) δ 3.94 (s, 3H, $OCH_3$), 5.27 (s, 2H, $OCH_2$), 7.12- 7.21 (m, 2H, Ar-H), 7.25 (s, 1H, Ar-H), 7.41 (s, 1H, Ar-H), 7.01-7.42 (m, 6H,

Ar-H), 8.41 (s, 1H, Ar-H), 8.64- 8.72 (m, 1H, Ar-H), 11.40 (bs, 1H, NH), 11.88 (bs, 1H, NH). $^{13}$C NMR (300 MHz, DMSO-$d_6$, TMS) δ 55.81, 70.30, 78.43, 78.86, 79.31, 95.73, 105.52, 108.84, 108.96, 112, 113.51, 120.76,122.52, 125.56,127.94, 128.17,128.44, 128.57, 136.31, 136.96, 145.74, 147.98, 149.24, 153.80, 161.89. ESI-MS: m/z 398 $(M+H)^+$.

**2-benzyl-6-(benzyloxy)-7-methoxyquinazolin-4(3H)-one** (**8c):** Yield 70%, mp: 244-246 °C. IR (KBr): 3409, 3004, 2921, 1666, 1610, 1492, 1442, 1390, 1274, 1222, 1177, 1099, 1009, 904, 863, 732, 696, 593, 555, 464 cm$^{-1}$. $^1$H NMR (300 MHz, DMSO-$d_6$, TMS) δ 3.87 (s, 2H, $CH_2$), 3.88 (s, 3H, $OCH_3$), 5.21 (s, 2H, $OCH_2$), 7.14 (s, 1H, Ar-H), 7.42 (s, 1H, Ar-H), 7.17- 7.50 (m, 10H, Ar-H). $^{13}$C NMR (300 MHz, DMSO-$d_6$, TMS) δ 56.17, 56.55, 70.45, 105.45, 109.46, 114.18, 127.22, 128.35, 128.52, 128.96, 129.31, 129.54, 136.78, 145.34, 153.95, 154.88, 161.69. ESI-MS: m/z 373 $(M+H)^+$.

**2-(benzo[d][l,3]dioxol-5-yl)- 6-(benzyloxy)-7-methoxyquinazolin-4(3H)-one (8d) :** Yield 74%, m.p: 265-267 °C. IR (KBr) v 3086, 2926, 1650, 1612, 1587, 1495, 1463, 1446, 1391, 1351, 1282, 1219, 1196, 1180, 1105, 1040, 993, 969, 930, 878, 846, 781, 745, 698, 674, 593, 561, 497, cm$^{-1}$ $^1$H NMR (300 MHz, DMSO-$d_6$,, TMS) δ 3.90 (s, 3H, $OCH_3$), 5.28 (s, 2H, $OCH_2$), 6.14 (s, 2H, O-$CH_2$-O), 7.06 (d, 1H, $J$ = 8.30 Hz, Ar-H), 7.28 (s, 1H, Ar-H), 7.44 (s, 1H, Ar-H), 7.34-7.54 (m, 5H, Ar-H), 7.71 (d, 1H, $J$= 1.51 Hz, Ar-H), 7.77 (d, 1H, $J$= 8.12 Hz, Ar-H), 12.26 (broad singlet, 1H, NH). $^{13}$C NMR (300 MHz, DMSO-$d_6$, TMS) δ 56.19, 70.49, 102.25, 105.60, 107.72, 108.74, 109.79, 114.30, 122.82, 127.09, 128.41, 128.55, 128.99, 136.79, 145.14, 148.10, 149.03, 150.20, 150.63, 154.12, 162.01. ESI-MS: m/z 403 $(M+H)^+$.

**6-(benzyloxy)-2-(2, 4-dimethoxyphenyl)-7-methoxyquinazolin-4(3H)-one (8e):** Yield 71%, m.p: 208-210 °C. IR (KBr): 3448, 3323, 2933, 2835, 1665, 1614, 1588, 1494, 1463, 1434, 1383, 1271, 1210, 1161, 1130, 1088, 1021, 912, 860, 782, 742, 695, 576, 534 cm$^{-1}$. $^1$H NMR (300 MHz, DMSO-$d_6$, TMS) δ 3.85 (s, 3H, $OCH_3$), 3.89 (s, 6H, $OCH_3$), 5.27 (s, 2H, $OCH_2$), 6.68 (dd, 2H, $J_1$ = 8.49 Hz & $J_2$= 3.02 Hz, Ar-H), 7.26 (s, 1H, Ar-H), 7.43 (s, 1H, Ar-H), 7.3- 7.53 (m, 5H, Ar-H), 7.78 (d, 1H, .7= 8.3 Hz, Ar-H), 11.66 (bs, 1H, NH). $^{13}$C NMR (300 MHz, DMSO-$d_6$, TMS) δ 55.48, 55.69, 55.91, 98.44, 104.98, 105.74, 109.22, 113.72, 114.58, 127.87, 128.01, 128.45, 131.54, 136.30, 145.06, 148.40, 150.32, 153.42, 158.53, 160.43, 162.59 ESI-MS: m/z 419 $(M+H)^+$.

**6-(benzyloxy)-2-(4-hydroxylphenyl)-7-methoxyquinazolin-4(3H)-one** (**8f):** Yield 70%, mp:271-273°C. IR (KBr) v 3081, 2936, 1664, 1608, 1498, 1442, 1388, 1277, 1221, 1179, 1099, 998, 950, 842, 782, 737, 696, 593, 523, 495, cm$^{-1}$. $^1$H NMR (300 MHz, DMSO-$d_6$, TMS) δ 3.93 (s, 3H, $OCH_3$), 5.24 (s, 2H, $OCH_2$), 6.83 (d, 2H, $J$ = 8.68 Hz, Ar-H), 7.16 (s, 1H, Ar-H), 7.48 (s, 1H, Ar-H), 7.29 (m, 5H, Ar-H), 8.03 (d, 2H, $J$ = 8.49 Hz, Ar-H), 9.75 (bs, 1H, OH). $^{13}$C NMR (300 MHz, DMSO-$d_6$, TMS) δ 55.68, 69.93, 105.13, 109.18, 113.60, 115.26, 123.35, 127.83, 128, 128.47, 129.13, 136.32, 144.93, 148.28, 150.69, 153.57, 161.57. ESI-MS: m/z 376 $(M+H)^+$.

**6-(benzyloxy)-7-methoxy-2-styrylquinazolin-4(3H)-one (8g):** Yield 75%, m.p: 239-241°C. IR (KBr) v 3027, 2923, 1660, 1609, 1485, 1442, 1380, 1268, 1217, 1173, 1096, 985, 914, 869, 850, 785, 754, 699, 585, 493 cm'1 $^1$H NMR (300 MHz, DMSO-$d_6$, TMS) δ 3.75 (s, 3H, $OCH_3$), 5.04 (s, 2H, $OCH_2$), 6.12 (d, 1H, $J$= 16 Hz, Ar-H), 6.46 (d, 1H, $J$= 16 Hz), 7.21 (s, 1H, Ar-H), 7.27-7.66 (m, 10H, Ar-H), 7.84 (s, 1H, Ar-H). ESI-MS: m/z 375 $(M+H)^+$.

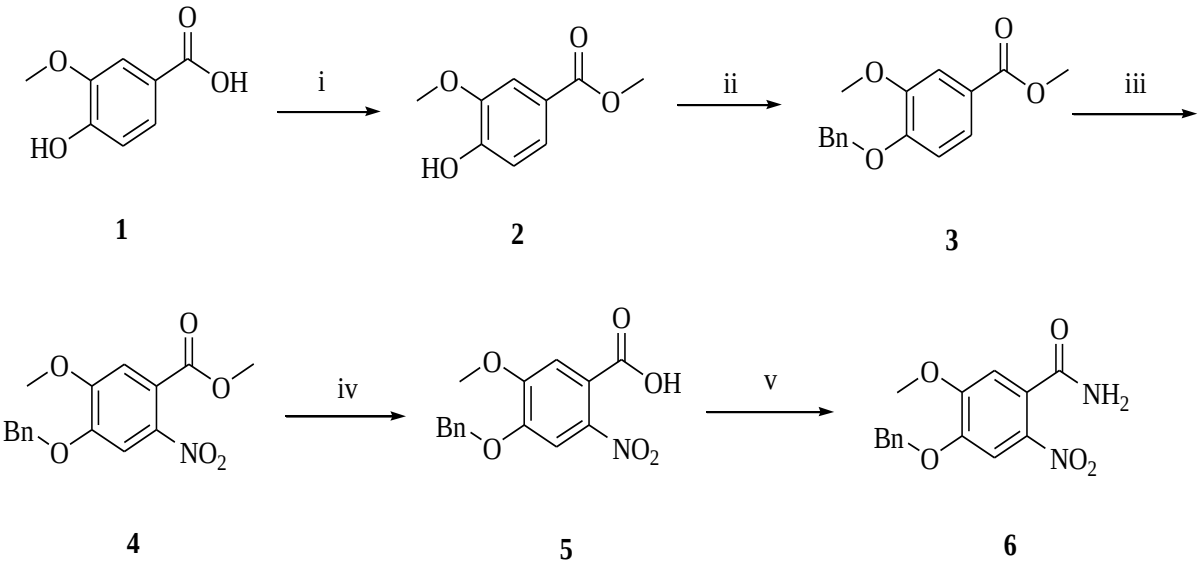
**6-(benzyloxy)-7-methoxy-2-phenethylquinazolin-4(3H)-one (8h):** Yield 72%, m.p: 232-234°C. $^1$H NMR (300 MHz, DMSO-$d_6$, TMS) δ 2.71-2.9 (t, 2H, $J$= 6.61 Hz, $CH_2$), 2.95-3.17 (t, 2H, $J$= 6.61 Hz, $CH_2$), 3.84 (s, 3H $OCH_3$), 5.2 (s, 2H, $OCH_2$), 7.02 (s, 1H, Ar-H), 7.2 (s, 1H, Ar-H), 7.01-7.42 (m, 5H, Ar-H), 7.35-7.02 (m, 5H, Ar-H). $^{13}$C NMR (300 MHz, DMSO-c/6, TMS) δ 32.55, 36.14, 55.62, 69.90, 105.03, 108.90, 113.77, 126.02, 127.79, 127.96, 128.26, 128.43, 136.32, 140.74, 144.76, 148.19, 153.37, 154.94, 161.08. ESI-MS: m/z 387 $(M+H)^+$.

**6-(benzyloxy)-7-methoxy-2-(4-(trifluoromethyl) phenylquinazolin-4(3H)-one (8i)**: Yield 73%, m.p: 256-258 °C. $^{1}$H NMR (300 MHz, DMSO-$d_6$, TMS) δ 3.94 (s, 3H, $OCH_3$), 5.28 (s, 2H, $OCH_2$), 7.31 (s, 1H, Ar-H), 7.41 (s, 1H, Ar-H), 7.34-7.54 (m, 5H, Ar-H), 7.84 (d, 2H, *J* = 7.74 Hz, Ar-H), 8.37 (d, 2H, *J* = 8.30 Hz, Ar-H), 12.57 (broad singlet, 1H, NH). $^{13}$C NMR (300 MHz, DMSO-$d_6$,, TMS) δ 55.65, 56.03, 60.07, 104.70, 104.87, 108.12, 113.74, 127.80, 139.81, 144.70, 148.45, 150.17, 152.82, 154.68, 161.66. ESI-MS: m/z 427 $(M+H)^+$

**2-(4-aminophenyl)-6-(benzyloxy)-7-methoxyquinazolin-4(3H)-one (8j):** Yield 72%, m.p:261-262°C. $^{1}$H NMR (300 MHz, DMSO-$d_6$, TMS) δ 3.95 (s, 3H, $OCH_3$), 5.25 (s, 2H, $CH_2$), 6.7 (d, 2H, *J* = 8.498 Hz, Ar-H), 7.16 (s, 1H, Ar-H), 7.2 (s, 1H, Ar-H), 7.01-7.42 (m, 5H, Ar-H), 7.95 (d, 2H, *J* = 8.68 Hz, Ar-H). $^{I3}$C NMR (300 MHz, DMSO-J6, TMS) δ 55.65, 69.87, 105.16, 108.95, 113.01, 113.25, 113.75, 119.01, 127.51, 127.74, 127.83, 127.97, 128.47, 128.66, 136.38, 145.28, 147.87, 151.10, 151.68, 153.51, 161.63. ESI-MS: m/z 374 $(M+H)^+$

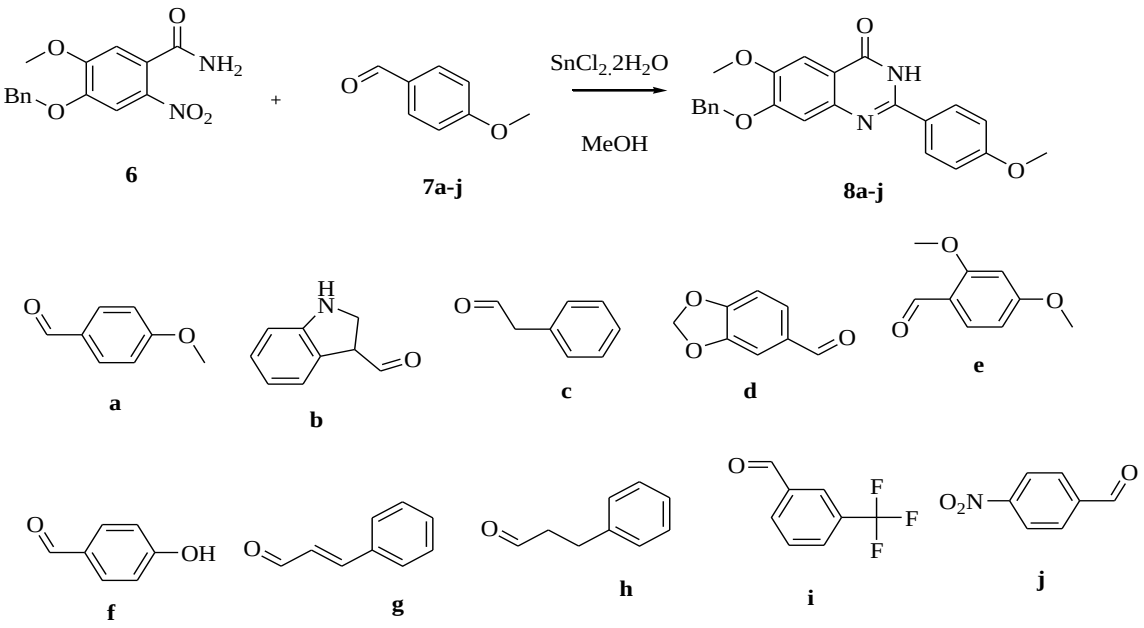
## RESULTS AND DISCUSSION

We are successful in synthesizing **6-benzyloxy- 7-methoxyquinazolin-4(3H)-ones (8a-j** ) in good yields via 4-(benzyloxy)-5-methoxy-2-nitrobenzamide (**6**) as shown in scheme 1 and 2.




**Reagents and conditions** : **(i)** $H_2SO_4$, MeOH, reflux, 4 hours,
**(ii)** benzyl chloride, $K_2CO_3$, acetone, reflux, 12 hours,
**(iii**) $SnCl_4$, $HNO_3$ (fuming), $CH_2C1_2$, 5 minutes,
**(iv)** NaOH (5 %), heat 4 h, **(v)** $SOC1_2$, cat. DMF, ammonia (aq.).

**Scheme-1.** Synthesis of 4-benzyloxy-5-methoxy-2-nitrobenzamide




**Scheme-2.**Synthesis of compounds 8a-j

Etherification of compound **1** was brought out in presence of conc.sulphuric acid in methanol to obtain compound **2** in 90 % yields [14]. $^1$H NMR spectrum of compound **2** showed the presence of singlet for methoxy group at δ 3.91 additions to the spectra of compound **1**. Benzylation of free phenolic -OH group in compound **2** was carried out in presence of Benzyl chloride and $K_2CO_3$ in acetone to obtain benzylated compound **3** in 85 %. It was characterized by its $^1$H NMR spectra which showed the characteristic peak of $CH_2$ group of OBn group at δ 5.16. This was followed by nitration employing the literature method [15] to provide the 4-benzyloxy-5-methoxy-2-nitrobenzoate **4**. Nitration of compound **3** was carried out in presence of nitrating mixture of Stannic chloride and Nitric acid (fuming) to get nitrated product **4** in 80 % yield. Formation of compound **4** was characterized from the $^1$H NMR which showed two singlets for two aromatic protons at δ 7.04 and δ 7.47. Compound **4** was hydrolyzed using Sodium hydroxide (5 %) to afford benzoic acid **5** in 90 % yields. Formation of compound **5** was characterized from the $^1$H NMR which showed the disappearance of methoxy group of ester group. Thus, the substituted o-nitro benzanilide (**6**) was obtained by converting nitro acid compound **5** to its acid chloride in presence of thionyl chloride, followed by treating with Ammonia (aq.) in 90 % yield as shown in **Scheme 1**. $^1$H NMR spectrum of compound **6** showed the presence of two broad singlets for two NH protons of amide bond at δ 7.60 and δ 7.99 along with two singlets for $CH_3$ and $CH_2$ groups at δ 3.91 and δ 5.24 respectively. Further it was confirmed with ESI-MS peak at 303$(M+H)^+$.

The reaction sequence employed for the synthesis of title compounds is shown in (**Scheme 2**). The one pot reaction of ortho-nitero key intermediate compound **(6)**, react with (aromatic/aliphatic aldehydes) of anisaldehyde **(7a)** in presence of $SnCl_2.2H_2O$ in MeOH was heated at reflux temperature for 3-4 hours to yield 6-(benzyloxy)-7-methoxy-2-(4-methoxyphenyl)quinazolin-4(3H)-one (**8a**)**.** In the $^1$H NMR (300MHz,DMSO-$d_6$) spectrum of 6-(benzyloxy)-7-methoxy-2-(4-methoxyphenyl)quinazolin-4(3H)-one **(8a)** appeared at δ 3.86 (s, 3H, $OCH_3$), 3.96 (s, 3H, $OCH_3$), 5.25 (s, 2H, $OCH_2$), 6.96 (d, 2H, *J*= 9.44 Hz, Ar-H), 7.17 (s, 1H, Ar-H), 7.37 (s, 1H, Ar-H), 7.27-7.42 (m, 5H, Ar-H), 8.16 (d, 2H, *J* = 8.39 Hz, Ar-H). $^{13}$C NMR (300 MHz, DMSO-$d_6$, TMS) δ 55.39, 55.71, 69.99, 105.05, 105.13, 109.23, 113.72, 113.92, 124.91, 127.19, 127.88, 128.06, 128.49, 129.05, 136.32, 148.42, 150.46, 153.60, 161.51. IR (KBr) v 3423, 2923, 1636, 1609, 1500, 1441, 1388, 1267, 1220, 1182, 1102, 1031,948,858, 732, 694, 524 $cm^{-1}$. ESI-MS: m/z 389 $(M+H)^+$.

## APPLICATIONS

**Antimicrobial Activity:** In view of developing new class of antimicrobial agents, synthesized novel compounds were screened for their In vitro antimicrobial activities to determine zone of inhibition at 100 μg $mL^{-1}$ against two Gram-positive bacteria (Staphylococcus aureus, Bacillus subtillis and two Gram-negative bacteria Escherichia coli, Pseudomonas aeuroginosa, as well as two fungi Aspergillus niger, Aspergillus fumigates strains using Cup plate method [11,12] where inoculated Muller-Hilton agar for bacteria and Sabouraud dextrose agar for fungi was poured onto the sterilized Petri dishes (25–30 mL each Petri dish). The poured material was allowed to set (30 min.) and thereafter the 'CUPS' (06mm diameter) was made by punching into the agar surface with a sterile cork borer and scooping out the punched part of the agar. Into these cups the test compound solution (0.1mL) was added with the help of a micro pipette. The plates were incubated at 37° C for 14h for bacteria and 30 h for fungi and the results were noted. The test solution was prepared by DMSO as solvent.

The obtained results, depicted in table 1, revealed that all the synthesized compounds **8a-j** could effectively, to some extent, inhibit the growth of all tested strains In vitro. In antibacterial studies, all the compounds tested were found less active towards Bacillus subtillis, as compared to other one strain of bacteria. Most of the compounds showed moderate to good activity against Staphylococcus aureus, Pseudomonas aeuroginosa. Compounds **8a**, **8h** and **8i** have shown good antibacterial activity against Staphylococcus aureus. **8a, 8b** and **8i** have shown moderate activity against Escherichia coli. Out of two strains of fungi, these compounds were found to be less active against Aspergillus niger whereas showed moderate to good activity against Aspergillus fumigatus.

**Table1.** Antimicrobial activity of title compounds 8a-j

| Compound | **Gram positive bacteria** | | **Gram negative bacteria** | | **Fungi** | |
|---|---|---|---|---|---|---|
| | Aureus | subtillis | coli | aeuroginosa | niger | fumigatus |
| **8a** | 15 | 12 | 11 | 13 | 11 | 18 |
| **8b** | 13 | 12 | 15 | 12 | 10 | 18 |
| **8c** | 14 | 10 | 15 | 12 | 11 | 15 |
| **8d** | 13 | 11 | 12 | 11 | 12 | 18 |
| **8e** | 13 | 10 | 10 | 11 | 11 | 18 |
| **8f** | 14 | 11 | 10 | 13 | 13 | 16 |
| **8g** | 13 | 10 | 12 | 12 | 13 | 18 |
| **8h** | 16 | 10 | 14 | 14 | 14 | 18 |
| **8i** | 15 | 13 | 16 | 14 | 14 | 18 |
| **8j** | 13 | 11 | 13 | 13 | 13 | 18 |

## CONCLUSIONS

We developed methodology for the synthesis of novel 6-(Benzyloxy)-7-Methoxyquinazolin-4(3H)-ones **8a-j** [13-15] using aliphatic/aromatic aldehydes in good yields. The structures of all the compounds were confirmed by their spectral and analytical data. All the newly synthesized compounds were screened for their MIC and zone of inhibition against four strains of bacteria and two strains of fungi. Most of the compounds have shown moderate to good antibacterial and antifungal properties whereas some compounds have shown promising antifungal properties, which were further used to determine MBC and MFC against some selected strains of bacteria and fungi. It is evident from the results that 6-(Benzyloxy)-7-Methoxyquinazolin-4(3H)-ones are potential antimicrobial agents.

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