DOI:10.7598/cst2016.1140
ISSN:2278-3458

Chemical Science Transactions
2016, **5(1),** 61-74

RESEARCH ARTICLE

Synthesis of New Pyrazole Derivatives Containing Quinoline Moiety *via* Chalcones: A Novel Class of Potential Antibacterial and Antifungal Agents

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Received 29 September 2015 / Accepted 28 October 2015

Abstract: In the present investigation a new class of quinoline derivatives containing pyrazole moiety have been designed and synthesized by condensation of 2-(quinolin-8-yloxy)acetohydrazide with various chalcones. These newly synthesized quinoline derivatives containing pyrazole moiety were screened for their minimum inhibitory concentration by antibacterial activity against two kinds of strains *i.e. Staphylococcus aureus, Escherichia coli* and antifungal activity against *Aspergillus niger*. The results showed that some of the compounds exhibited moderate to good antibacterial activity against both the strains and a few compounds were active in antifungal activity. The structure–activity relationships were briefly discussed. The studies indicated that variation of substituent in the aromatic rings changes the antibacterial activity and compounds containing electron withdrawing groups exhibited potential antifungal activity.

Keywords: Quinolin-8-ol, Ethyl chloroacetate, Hydrazine hydrate, Chalcone, Pyrazole, Antibacterial activity and Antifungal activity

Introduction

A wide range of antimicrobial agents have been discovered to prolong the lifespan of people but unfortunately microbial resistance resulted in a dwindling pool of effective antibiotics. At this instance, resistance to existing antifungal agents is also a major threat and hence there is a pressing need for the development of new antimicrobial agents which may be effective against the resistant microbes.

Quinoline[1-5] has its own prominence in drug discovery programs. Quinoline along with its derivatives is reported to exhibit a wide spectrum of biological properties such as antimicrobial[6], antimalarial[7] and antitubercular[8] activities. Quinoline and its derivatives are widely used as fungicides, biocides, antibiotics, alkaloids, dyes, rubber chemicals and flavoring agents. They are also used in manufacturing oil soluble dyes, food colorants, pharmaceuticals, pH indicators and other organic compounds.

Pyrazoles[9-13] are potential bioactive agents due to their wide spectrum of pharmacological activities like anti-inflammatory, antimicrobial, antihypertensive, antitumor, anticonvulsant, antitubercular, hypoglycemic and analgesic. Chalcones[14-18] represents important building blocks for both natural and synthetic bioactive compounds. Chalcones are fine synthons for different heterocyclic rings. So it was planned to synthesize some new pyrazoles from chalcones with the hope that they may possess better antimicrobial activities.

Looking at the importance of quinoline and pyrazole nucleus, it was thought that it would be worthwhile to design and synthesize some new quinoline derivatives bearing pyrazole moiety and screen them for potential biological activities.

Experimental

All chemicals and reagents were procured from Merck India limited. Melting points were determined in open capillary on a Mel-Temp apparatus and are uncorrected. The progress of the reaction was monitored by TLC (silica gel H, BDH, ethyl acetate-hexane, 3:5). The IR spectra were recorded on IR 200 FT-IR spectrometer as KBr pellets. The wave numbers were given in cm^{-1}. The ^1H NMR spectra were recorded in $CDCl_3$/DMSO-d_6 on a Jeol JNM λ-400 MHz machine. The ^{13}C NMR spectra were recorded in $CDCl_3$/DMSO-d_6 on a Jeol JNM spectrometer operating at 125 MHz. All chemical shifts were measured in δ (ppm) using TMS as an internal standard. The mass spectra were recorded on VG 7070H mass spectrometer. The microanalyses were performed on Perkin-Elmer 240 C elemental analyzer. The microwave syntheses were carried out in a domestic microwave oven (LG MH2548QPS) wherever it was specified.

Biological activity

The minimum inhibitory concentration[19,20] of the compounds **7a-o** was determined by broth dilution method. The respective clinical strain was spread separately on the Mueller-Hinton broth[21] medium for antibacterial activity and Sabouraud dextrose agar (SDA) broth for antifungal activity. The synthesized compounds were dissolved in DMSO at different concentrations such as 100, 87.5, 75, 62.5, 50, 37.5, 25, 12.5, 6.25, 3.13, 1.56, 0.78, 0.39 and 0.19 µg/mL and 2 mL of these solutions were taken in test tubes. Then 2 µL of test organism suspension was added and incubated at 37 ºC for 24 h for bacteria and 48 h for fungi studies. The drugs ofloxacin and fluconazole were used as standards for comparison of antibacterial and antifungal activities respectively. The minimum inhibitory concentration was the lowest concentration of test compound that inhibit the visible growth of the organism and was determined in triplicates. The results are tabulated in the Table 2.

*Synthesis of ethyl 2-(quinolin-8-yloxy)acetate **2***

A mixture of quinolin-8-ol **1** (0.01 mol), ethyl chloroacetate (0.01 mol), anhydrous K_2CO_3 (1.38 g, 0.01 mol) and DMF was stirred at room temperature for 8 h. The reaction mixture was diluted with ice-cold water. The separated solid was filtered, washed with water and recrystallized from ethanol to afford ethyl 2-(quinolin-8-yloxy)acetate **2**.

*Characterization data of **2***

Yield 80%. m.p. 56-58 ºC. IR (KBr)ν_{max} : 3065 (C-H stretch in aromatics), 2920 (C-H stretch in CH_3/CH_2), 1730 (C=O stretch), 1215, 1015 (sp^2/sp^3 C-O stretch) cm^{-1}. ^1H NMR (DMSO-d_6) : δ 1.28 (t, J = 6.8 Hz, 3H, ester CH_3), 4.29 (q, J = 7.2 Hz, 2H, ester CH_2), 4.95 (s, 2H, OCH_2), 6.98 (d, J = 2.4 Hz , 1H, quinoline-H_7), 7.44-7.47 (m, 3H, quinoline-H_3, -H_5, -H_6), 8.15 (dd, J = 2.0, 6.8, 1.6 Hz, 1H, quinoline-H_4), 8.96 (dd, J = 1.6, 2.4, 2.0 Hz, 1H, quinoline-H_2) ppm.

^{13}C NMR (DMSO-d_6): δ 13.8 (ester CH_3), 63.2 (ester CH_2), 67.1 (OCH_2), 112.3, 121.4, 122.5, 124.0, 129.1, 136.2, 139.2, 155.2, 153.5, 165.6 (aromatic carbons) ppm. MS *m/z*: found 231 [M^+]; calcd. 231. Anal. $C_{13}H_{13}NO_3$. Found C 66.48 (67.52), H 5.53 (5.67), N 5.98 (6.06).

*Synthesis of 2-(quinolin-8-yloxy)acetohydrazide **3***

A solution of ethyl 2-(quinolin-8-yloxy)acetate **2** (0.01 mole) and hydrazine hydrate (0.015 mole) in ethanol (25 mL) was refluxed for 5 h. The excess of solvent was distilled off and the reaction mixture was cooled. The separated solid was filtered, washed with petroleum ether and recrystallized from water to afford **3**.

*Characterization data of **3***

Yield 76%. m.p. 124-126 ºC. IR (KBr)ν_{max} : 3325 (N-H stretch), 3060 (C-H stretch in aromatics), 2895 (C-H stretch in CH_3/CH_2), 1660 (C=O stretch), 1285, 1035 (sp^2/sp^3 C-O stretch) cm^{-1}. ^{1}H NMR (DMSO-d_6) : δ 3.98 (s, 2H, NH_2), 4.87 (s, 2H, CH_2O), 7.17 (dd, J = 1.2, 5.6, 1.6 Hz, 1H, quinoline-H_7), 7.47-7.54 (m, 3H, quinoline-H_3, -H_5, -H_6), 8.20 (dd, J = 2.0, 6.8, 1.2 Hz, 1H, quinoline-H_4), 8.93 (dd, J = 1.2, 3.2, 1.2 Hz, 1H, quinoline-H_2), 9.75 (s, 1H, NH) ppm.

^{13}C NMR (DMSO-d_6): δ 67.5 (OCH_2), 112.4, 121.6, 122.5, 123.6, 130.0, 135.9, 139.4, 153.5, 154.6, 162.7 (aromatic carbons) ppm. MS *m/z*: found 217 [M^+]; calcd. 217. Anal. $C_{11}H_{11}N_3O_2$. Found C 60.14 (60.82), H 4.98 (5.10), N 19.17 (19.34).

*General procedure for the synthesis of 1,3-bis(substituted phenyl)prop-2-en-1-ones **6a-o***

A number of known and novel chalcone derivatives were prepared by Claisen- Schmidt condensation of appropriate aldehyde and acetophenone derivatives.

To a solution of substituted acetophenone **5** (0.01 mol) in ethanol (20 mL), substituted aromatic benzaldehyde **4** (0.01 mol) was added and cooled to 5-10 ºC in an ice bath. To this cold solution, sodium hydroxide (30%) was added and stirred magnetically for 1 h and then left overnight or longer, monitored by TLC. The resultant solution was diluted with ice water and acidified with dilute HCl. The chalcone separated as solid was collected by filtration after washing with water and recrystallized from ethanol.

The physical and analytical characterization data of 1,3-bis(substituted phenyl)prop-2-en-1-ones **6a-o** are presented in Table 1.

*Characterization data of **6a***

Recrystallised from ethanol as yellow solid in 91% yield. m.p. 56-58 ºC. IR (KBr)ν_{max} : 3064 (C-H stretch in aromatics), 2938 (C-H stretch in CH_3/CH_2), 1675 (C=O stretch), 1618 (C=C stretch in olefins), 1596 (C=C stretch) cm^{-1}.

^{1}H NMR (DMSO-d_6) : δ 7.38 - 7.40 (m, 3H, Ar-H), 7.54 (d, J = 15.6 Hz, 1H, =CH-C=O), 7.63 - 7.65 (m, 2H, Ar-H), 7.66 - 7.68 (m, 2H, Ar'-H), 7.76 -7.78 (m, 1H, Ar'-H), 7.84 - 7.86 (m, 2H, Ar'-H), 8.04 (d, J = 15.6 Hz, 1H, =CH) ppm.

^{13}C NMR (DMSO-d_6): δ 121.5 (=C-H adjacent to carbonyl), 145.6 (=C-H), 126.8, 128.1, 128.6, 128.8, 129.3, 134.4, 135.3, 138.2 (aromatic carbons), 190.8 (C=O) ppm. MS *m/z*: found 208 [M^+]; calcd. 208. Anal. $C_{15}H_{12}O$. Found C 86.39 (86.51), H 5.79 (5.81).

Table 1. Physical and analytical characterization data of 1,3-bis(substituted phenyl)prop-2-en-1-ones **6a-o**

S. No.	Compound	R_1	R_2	Colour	Melting point, ºC
1	**6a**	-H	-H	Yellow	56-58
2	**6b**	-H	*p*-OH	Lemon yellow	172-174
3	**6c**	-H	*o*-OH	Golden yellow	68-70
4	**6d**	-H	*p*-Cl	Light yellow	124-126
5	**6e**	-H	*p*-NO_2	Dark yellow	92-94
6	**6f**	*p*-OCH_3	-H	Lemon yellow	126-128
7	**6g**	*p*-OCH_3	*p*-OH	Golden yellow	224-226
8	**6h**	*p*-OCH_3	*o*-OH	Golden yellow	134-136
9	**6i**	*p*-OCH_3	*p*-Cl	Light yellow	170-172
10	**6j**	*p*-OCH_3	*p*-NO_2	Dark yellow	128-130
11	**6k**	*o*-OH	-H	Brownish yellow	100-102
12	**6l**	*o*-OH	*p*-OH	Yellow	182-184
13	**6m**	*o*-OH	*o*-OH	Yellow	150-152
14	**6n**	*o*-OH	*p*-Cl	Lemon yellow	236-238
15	**6o**	*o*-OH	*p*-NO_2	Chocolate brown	196-198

Synthesis of 1-(substituted 3,5-diphenyl-4,5-dihydro-1*H*-pyrazol-1-yl)-2-(quinolin-8-yloxy)ethanones 7a-o

*Synthesis of 1-(3,5-diphenyl-4,5-dihydro-1H-pyrazol-1-yl)-2-(quinolin-8-yloxy) ethanone **7a***

Conventional method

To a solution of **6a** (0.01 mol) in glacial acetic acid (25 mL, 0.01 mol), 2-(quinolin-8-yloxy) acetohydrazide **3** (0.01 mol) was added. The mixture was refluxed for 6-7 h and left overnight. The reaction mixture was poured onto crushed ice and the solid mass was filtered, washed with ethanol, dried and purified by recrystallization from ethanol to afford **7a.**

Microwave method

To the solution of **6a** (0.01 mol) in glacial acetic acid (25 mL, 0.01 mol), 2-(quinolin-8-yloxy) acetohydrazide **3** (0.01 mol) was added. The mixture was irradiated under MW at 80% power for 10-12 min and the reaction mixture was allowed to attain room temperature and poured on crushed ice. The precipitated solid mass was filtered, washed with ethanol, dried and purified by recrystallization from ethanol to afford **7a** (Figure 1). Compounds **7b-7o** are prepared on the same lines.

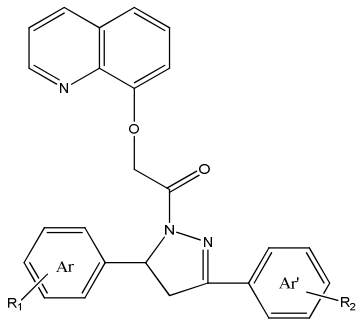


Figure 1. Structure of the compounds **7a-o** (*Refer* Table 1)

Characterization data of 7a-o

*1-(3,5-Diphenyl-4,5-dihydro-1H-pyrazol-1-yl)-2-(quinolin-8-yloxy)ethanone **7a***

Recrystallised from ethanol as yellow solid in 92% yield. m.p. 86-88 ºC. IR (KBr)ν_{max} : 3074 (C-H stretch in aromatics), 2935 (C-H stretch in CH_3/CH_2), 1672 (C=O stretch), 1632 (C=N stretch), 1349 (C-N stretch), 1164, 1061 (sp^2/sp^3 C-O stretch) cm^{-1}.

^{1}H NMR (DMSO-d_6): δ 4.92 (s, 2H, OCH_2), 3.16-3.21 (dd, J = 5.2, 12.4, 4.8 Hz, 1H, pyrazole-H_4), 3.74-3.81 (dd, J = 12, 5.6. 12.4, 1H, pyrazole-H_4), 5.65-5.69 (dd, J =12, 7.2, 12.4 Hz, 1H, pyrazole-H_5), 7.30-7.46 (m, 5H, Ar-H), 7.40-7.62 (m, 5H, Ar'-H), 7.38 (d, 1H, quinoline-H_7), 7.60 (t, 1H, quinoline-H_3), 7.66(d, 1H, quinoline-H_5), 7.76 (t, 1H, quinoline-H_6), 8.32 (d, 1H, quinoline-H_4), 8.89 (d, 1H, quinoline-H_2) ppm.

^{13}C NMR (DMSO-d_6): δ 39.2 (pyrazole CH_2), 66.8 (pyrazole CH), 67.5 (OCH_2), 112.5, 121.7, 122.6, 123.6, 126.5, 126.6, 128.2, 128.6, 128.8, 130.1, 131.1, 136.1, 136.3, 139.5, 141.3, 152.9, 154.6 (aromatic carbons), 151.2 (pyrazole C), 168.7 (C=O) ppm. MS *m/z* : found 407 [M^+]; calcd. 407. Anal. $C_{26}H_{21}N_3O_2$. Found C 75.98 (76.64), H 5.09 (5.19), N 10.18 (10.31).

*1-(3-(4-Hydroxyphenyl)-5-phenyl-4,5-dihydro-1H-pyrazol-1-yl)-2-(quinolin-8-yloxy)ethanone **7b***

Recrystallised from ethanol as yellow solid in 88% yield. m.p. 172-174 ºC. IR (KBr)ν_{max} : 3368 (O-H stretch), 3012 (C-H stretch in aromatics), 2968 (C-H stretch in CH_3/CH_2), 1663 (C=O stretch), 1628 (C=N stretch), 1339 (C-N stretch), 1172, 1017 (sp^2/sp^3 C-O stretch) cm^{-1}.

^{1}H NMR (DMSO-d_6) : δ 4.95 (s, 2H, OCH_2), 3.19-3.24 (dd, J = 4.4, 12.8, 4.8 Hz, ,1H, pyrazole-H_4), 3.78-3.85 (dd, J = 12.8, 6.4, 8.2 Hz, 1H, pyrazole-H_4), 5.36 (s, 1H, OH), 5.65-5.69 (dd, J = 4.0, 6.8, 4.4 Hz, 1H, pyrazole-H_5), 7.24-7.48 (m, 5H, Ar-H), 6.85, 6.88 (d, J =10 Hz, 2H, Ar'-H), 7.94 & 7.96 (d, J = 8 Hz, 2H, Ar'-H), 7.41 (d, 1H, quinoline-H_7), 7.62 (t, 1H, quinoline-H_3), 7.68 (d, 1H, quinoline-H_5), 7.79 (t, 1H, quinoline-H_6), 8.31 (d, 1H, quinoline-H_4), 8.86 (d, 1H, quinoline-H_2) ppm.

^{13}C NMR (DMSO-d_6): δ 39.4 (pyrazole CH_2), 66.6 (pyrazole CH), 67.8 (OCH_2), 111.8, 115.4, 121.6, 122.5, 123.8, 126.5, 126.6, 128.5, 128.6, 128.8, 130.0, 135.9, 140.2, 141.3, 151.9, 155.1, 157.8 (aromatic carbons), 151.4 (pyrazole C), 168.4 (C=O) ppm. MS *m/z* : found 423 [M^+]; calcd. 423. Anal. $C_{26}H_{21}N_3O_3$. Found C 73.13 (73.74), H 4.92 (5.00), N 9.74 (9.92).

*1-(3-(2-Hydroxyphenyl)-5-phenyl-4,5-dihydro-1H-pyrazol-1-yl)-2-(quinolin-8-yloxy)ethanone **7c***

Recrystallised from ethanol as lemon yellow solid in 90% yield. m.p. 70-72 ºC. IR (KBr)ν_{max}: 3392 (O-H stretch), 3021 (C-H stretch in aromatics), 2953 (C-H stretch in CH_3/CH_2), 1672 (C=O stretch), 1634 (C=N stretch), 1343 (C-N stretch), 1163, 1033 (sp^2/sp^3 C-O stretch) cm^{-1}.

^{1}H NMR (DMSO-d_6): δ 4.91 (s, 2H, OCH_2), 3.11-3.16 (dd, J = 5.2, 12.4, 5.6 Hz, 1H, pyrazole-H_4), 3.69-3.76 (dd, J = 12, 5.6, 12.4 Hz, 1H, pyrazole-H_4), 5.38 (s, 1H, OH), 5.58-5.62 (dd, J = 4.4, 7.2, 4.8 Hz, 1H, pyrazole-H_5), 7.31-7.41 (m, 5H, Ar-H), 6.98-7.56 (m, 4H, Ar'-H), 7.46 (d, 1H, quinoline-H_7), 7.61 (t, 1H, quinoline-H_3), 7.65 (d, 1H, quinoline-H_5), 7.74 (t, 1H, quinoline-H_6), 8.35 (d, 1H, quinoline-H_4), 8.87 (d, 1H, quinoline-H_2) ppm.

^{13}C NMR (DMSO-d_6): δ 40.4 (pyrazole CH_2), 66.3 (pyrazole CH), 67.3 (OCH_2), 111.4, 117.6, 118.6, 121.5, 121.6, 122.5, 123.5, 126.5, 126.8, 129.0, 130.2, 132.2, 132.3, 135.8, 140.1,

141.6, 152.8, 155.2, 161.41 (aromatic carbons), 151.4 (pyrazole C), 168.5 (C=O) ppm. MS *m/z* : found 423 [M^+]; calcd. 423. Anal. $C_{26}H_{21}N_3O_3$. Found C 73.18 (73.74), H 4.91 (5.00), N 9.76 (9.92).

1-(3-(4-Chlorophenyl)-5-phenyl-4,5-dihydro-1H-pyrazol-1-yl)-2-(quinolin-8-yloxy) ethanone ***7d***

Recrystallised from ethanol as cream solid in 94% yield. m.p. 124-126 ºC. IR (KBr)ν_{max} : 3068 (C-H stretch in aromatics), 2865 (C-H stretch in CH_3/CH_2), 1665 (C=O stretch), 1628 (C=N stretch), 1352 (C-N stretch), 1193, 1017 (sp^2/sp^3 C-O stretch), 1082 (C-Cl stretch in aromatics) cm^{-1}.

^{1}H NMR (DMSO-d_6) : δ 4.95 (s, 2H, OCH_2), 3.08-3.13 (dd, J = 4.0, 12.4, 4.4 Hz, 1H, pyrazole-H_4), 3.67-3.74 (dd, J = 12.0, 4.4, 12.4 Hz, 1H, pyrazole-H_4), 5.60-5.64 (dd, J = 4.8, 7.2, 5.2 Hz, 1H, pyrazole-H_5), 7.33-7.44 (m, 5H, Ar-H), 7.50, 7.53 (d, J = 8.8 Hz, 2H, Ar'-H), 7.92, 7.94 (d, J = 8.8 Hz, 2H, Ar'-H), 7.48 (d, 1H, quinoline-H_7), 7.64 (t, 1H, quinoline-H_3), 7.69 (d, 1H, quinoline-H_5), 7.76 (t, 1H, quinoline-H_6), 8.32 (d, 1H, quinoline-H_4), 8.92 (d, 1H, quinoline-H_2) ppm.

^{13}C NMR (DMSO-d_6) : δ 39.8 (pyrazole CH_2), 66.5 (pyrazole CH), 66.8 (OCH_2), 112.6, 121.6, 122.5, 123.8, 125.9, 127.0, 128.1, 128.5, 128.8, 129.9, 134.6, 135.9, 136.8, 139.8, 141.6, 150.2, 155.1 (aromatic carbons), 151.4 (pyrazole C), 169.3 (C=O) ppm. MS *m/z* : found 441 [M^+]; calcd. 441. Anal. $C_{26}H_{20}ClN_3O_2$. Found C 70.28 (70.67), H 4.45 (4.56), N 9.38 (9.51).

1-(3-(4-Nitrophenyl)-5-phenyl-4,5-dihydro-1H-pyrazol-1-yl)-2-(quinolin-8-yloxy) ethanone ***7e***

Recrystallised from ethanol as orange solid in 93% yield. m.p. 94-96 ºC. IR (KBr)ν_{max} : 3060 (C-H stretch in aromatics), 2924 (C-H stretch in CH_3/CH_2), 1665 (C=O stretch), 1522 (N-O stretch), 1342 (C-N stretch), 1177, 1032 (sp^2/sp^3 C-O stretch) cm^{-1}.

^{1}H NMR (DMSO-d_6) : δ 4.94 (s, 2H, OCH_2), 3.17-3.23 (dd, J = 5.2, 12.4, 5.6 Hz, 1H, pyrazole-H_4), 3.76-3.83 (dd, J = 12.4, 5.6, 12.8 Hz, 1H, pyrazole-H_4), 5.64-5.68 (dd, J = 4.0, 6.8, 4.4 Hz, 1H, pyrazole-H_5), 7.29-7.47 (m, 5H, Ar-H), 8.14, 8.16 (d, J = 8.8 Hz, 2H, Ar'-H), 8.29, 8.32 (d, J = 9.2 Hz, 2H, Ar'-H), 7.51 (d, 1H, quinoline-H_7), 7.55 (t, 1H, quinoline-H_3), 7.65 (d, 1H, quinoline-H_5), 7.79 (t, 1H, quinoline-H_6), 8.35 (d, 1H, quinoline-H_4), 8.87 (d, 1H, quinoline-H_2) ppm.

^{13}C NMR (DMSO-d_6) : δ 40.1 (pyrazole CH_2), 66.6 (pyrazole CH), 67.2 (OCH_2), 111.9, 118.9, 121.8, 123.5, 126.7, 126.8, 126.9, 127.6, 128.6, 130.2, 136.0, 140.2, 141.8, 142.7, 149.9, 150.3, 154.8 (aromatic carbons), 151.1 (pyrazole C), 168.9 (C=O) ppm. MS *m/z* : found 452 [M^+]; calcd. 452. Anal. $C_{26}H_{20}N_4O_4$. Found C 68.54 (69.02), H 4.39 (4.46), N 12.27 (12.38).

1-(5-(4-Methoxyphenyl)-3-phenyl-4,5-dihydro-1H-pyrazol-1-yl)-2-(quinolin-8-yloxy)ethanone ***7f***

Recrystallised from ethanol as light brown solid in 91% yield. m.p. 126-128 ºC. IR (KBr)ν_{max} : 3082 (C-H stretch in aromatics), 2996 (C-H stretch in CH_3/CH_2), 1668 (C=O stretch), 1630 (C=N stretch), 1361 (C-N stretch), 1225, 1062 (sp^2/sp^3 C-O stretch) cm^{-1}.

^{1}H NMR (DMSO-d_6) : δ 3.86 (s, 3H, OCH_3), 4.92 (s, 2H, OCH_2), 3.12-3.17 (dd, J = 4.8, 13.2, 4.4 Hz, 1H, pyrazole-H_4), 3.78-3.85 (dd, J = 13.2, 4.4. 13.6, 1H, pyrazole-H_4), 5.66-5.70 (dd, J = 4.4, 7.2, 4.8 Hz, 1H, pyrazole-H_5), 6.89, 6.91 (d, J = 8 Hz, 2H, Ar-H), 7.12, 7.14

(d, J = 8 Hz, 2H, Ar-H), 7.54-7.69 (m, 5H, Ar'-H), 7.51 (d, 1H, quinoline-H_7), 7.58 (t, 1H, quinoline-H_3), 7.63 (d, 1H, quinoline-H_5), 7.78 (t, 1H, quinoline-H_6), 8.31 (d, 1H, quinoline-H_4), 8.82 (d, 1H, quinoline-H_2) ppm.

^{13}C NMR (DMSO-d_6) : δ 39.7 (pyrazole CH_2), 55.9 (OCH_3), 66.4 (pyrazole CH), 66.9 (OCH_2), 112.8, 114.2, 121.6, 122.4, 123.5, 126.7, 128.3, 128.6, 129.8 (2), 135.8, 136.8, 139.7, 139.8, 151.8, 154.3, 158.6 (aromatic carbons), 151.9 (pyrazole C), 168.5 (C=O) ppm. MS *m/z*: found 437 [M^+]; calcd. 437. Anal. $C_{27}H_{23}N_3O_3$. Found C 73.74 (74.12), H 5.24 (5.30), N 9.44 (9.60).

1-(3-(4-Hydroxyphenyl)-5-(4-methoxyphenyl)-4,5-dihydro-1H-pyrazol-1-yl)-2-(quinolin-8-yloxy)ethanone ***7g***

Recrystallised from ethanol as orange solid in 86% yield. m.p. 226-228 ºC. IR (KBr)ν_{max} : 3373 (O-H stretch), 2988 (C-H stretch in aromatics), 2913 (C-H stretch in CH_3/CH_2), 1672 (C=O stretch), 1631 (C=N stretch), 1598 (C=C stretch), 1185, 1042 (sp^2/sp^3 C-O stretch) cm^{-1}.

^{1}H NMR (DMSO-d_6) : δ 3.87 (s, 3H, OCH_3), 4.90 (s, 2H, OCH_2), 3.15-3.20 (dd, J = 4.8, 12.4, 4.4 Hz, ,1H, pyrazole-H_4), 3.70-3.77 (dd, J = 12.0, 4.8, 12.4 Hz, 1H, pyrazole-H_4), 5.39 (s, 1H, OH), 5.61-5.65 (dd, J = 4.0, 6.8, 4.4 Hz, 1H, pyrazole-H_5), 6.85, 6.87 (d, J = 8 Hz, 2H, Ar-H), 7.08, 7.10 (d, J = 8 Hz, 2H, Ar-H), 6.81, 6.84 (d, J =12 Hz, 2H, Ar'-H), 7.92, 7.94 (d, J = 8 Hz, 2H, Ar'-H), 7.54 (d, 1H, quinoline-H_7), 7.61 (t, 1H, quinoline-H_3), 7.65 (d, 1H, quinoline-H_5), 7.76 (t, 1H, quinoline-H_6), 8.36 (d, 1H, quinoline-H_4), 8.80 (d, 1H, quinoline-H_2) ppm.

^{13}C NMR (DMSO-d_6) : δ 40.1 (pyrazole CH_2), 55.6 (OCH_3), 66.5 (pyrazole CH), 67.4 (OCH_2), 111.8, 114.3, 116.8, 121.5, 122.7, 123.8, 126.7, 128.9, 129.3, 129.9, 134.8, 135.9, 140.5, 152.5, 154.4, 158.9, 160.2 (aromatic carbons), 151.9 (pyrazole C), 168.9 (C=O) ppm. MS *m/z*: found 453 [M^+]; calcd. 453. Anal. $C_{27}H_{23}N_3O_4$. Found C 70.98 (71.51), H 5.06 (5.11), N 9.11 (9.27).

1-(3-(2-Hydroxyphenyl)-5-(4-methoxyphenyl)-4,5-dihydro-1H-pyrazol-1-yl)-2-(quinolin-8-yloxy)ethanone ***7h***

Recrystallised from ethanol as lemon yellow solid in 92% yield. m.p. 136-138 ºC. IR (KBr)ν_{max} : 3347 (O-H stretch), 2987 (C-H stretch in CH_3/CH_2), 1682 (C=O stretch), 1638 (C=N stretch), 1604 (C=C stretch in aromatics), 1176, 1029 (sp^2/sp^3 C-O stretch) cm^{-1}.

^{1}H NMR (DMSO-d_6) : δ 3.87 (s, 3H, OCH_3), 4.88 (s, 2H, OCH_2), 3.10-3.15 (dd, J = 5.2, 12.4, 5.6 Hz, 1H, pyrazole-H_4), 3.71-3.78 (dd, J = 12.0, 5.6, 12.4 Hz, 1H, pyrazole-H_4), 5.37 (s, 1H, OH), 5.57-5.61 (dd, J = 4.4, 6.8, 4.0 Hz, 1H, pyrazole-H_5), 6.86, 6.88 (d, 2H, Ar-H), 7.21, 7.23 (d, 2H, Ar-H), 6.95-7.48 (m, 4H, Ar'-H), 7.52 (d, 1H, quinoline-H_7), 7.62 (t, 1H, quinoline-H_3), 7.66 (d, 1H, quinoline-H_5), 7.78 (t, 1H, quinoline-H_6), 8.32 (d, 1H, quinoline-H_4), 8.81 (d, 1H, quinoline-H_2) ppm.

^{13}C NMR (DMSO-d_6) : δ 40.5 (pyrazole CH_2), 55.7 (OCH_3), 66.4 (pyrazole CH), 66.9 (OCH_2), 112.8, 114.4, 117.9, 118.8, 121.3, 121.6, 122.8, 123.7, 126.4, 129.9, 131.9, 132.5, 133.8, 135.8, 138.9, 150.2, 154.9, 158.2, 162.6 (aromatic carbons), 151.6 (pyrazole C), 168.8 (C=O) ppm. MS *m/z*: found 453 [M^+]; calcd. 453. Anal. $C_{27}H_{23}N_3O_4$. Found C 71.12 (71.51), H 5.02 (5.11), N 9.14 (9.27).

1-(3-(4-Chlorophenyl)-5-(4-methoxyphenyl)-4,5-dihydro-1H-pyrazol-1-yl)-2-(quinolin-8-yloxy)ethanone ***7i***

Recrystallised from ethanol as cream solid in 94% yield. m.p. 170-172 ºC. IR (KBr)ν_{max} : 3074 (C-H stretch in aromatics), 2932 (C-H stretch in CH_3/CH_2), 1658 (C=O stretch), 1632

(C=N stretch), 1606 (C=C stretch in aromatics), 1184, 1028 (sp^2/sp^3 C-O stretch), 1076 (C-Cl stretch in aromatics) cm^{-1}.

^1H NMR (DMSO-d_6) : δ 3.86 (s, 3H, OCH_3), 4.92 (s, 2H, OCH_2), 3.21-3.26 (dd, J= 4.8, 12.4, 4.4 Hz, 1H, pyrazole-H_4), 3.84-3.91 (dd, J= 12.0, 4.8, 12.4 Hz, 1H, pyrazole-H_4), 5.80-5.84 (dd, J= 4.4, 7.2, 4.8 Hz, 1H pyrazole-H_5), 6.80 & 6.82 (d, 2H, Ar-H), 7.11 & 7.13 (d, 2H, Ar-H), 7.45, 7.47 (d, J = 8.0 Hz, 2H, Ar'-H), 7.95, 7.97 (d, J = 8.0 Hz, 2H, Ar'-H), 7.49 (d, 1H, quinoline-H_7), 7.56 (t, 1H, quinoline-H_3), 7.65 (d, 1H, quinoline-H_5), 7.76 (t, 1H, quinoline-H_6), 8.35 (d, 1H, quinoline-H_4), 8.84 (d, 1H, quinoline-H_2) ppm.

^{13}C NMR (DMSO-d_6) : δ 39.8 (pyrazole CH_2), 55.6 (OCH_3), 66.4 (pyrazole CH), 66.8 (OCH_2), 113.2, 114.3, 121.4, 122.6, 123.8, 126.4, 128.4, 128.9, 130.1, 134.4, 134.7, 135.4, 136.5, 138.6, 151.5, 154.9, 158.4 (aromatic carbons), 151.2 (pyrazole C), 168.5 (C=O) ppm. MS *m/z*: found 471 [M^+]; calcd. 471. Anal. $C_{27}H_{22}ClN_3O_3$. Found C 68.33 (68.71), H 4.61 (4.70), N 8.75 (8.90).

1-(5-(4-methoxyphenyl)-3-(4-nitrophenyl)-4,5-dihydro-1H-pyrazol-1-yl)-2-(quinolin-8-yloxy)ethanone ***7j***

Recrystallised from ethanol as light brown solid in 93% yield. m.p. 128-130 ºC. IR (KBr)ν_{max} : 3065 (C-H stretch in aromatics), 2824 (C-H stretch in CH_3/CH_2), 1668 (C=O stretch), 1636 (C=N stretch), 1561 (N-O stretch), 1498 (C=C stretch in aromatics), 1196, 1046 (sp^2/sp^3 C-O stretch) cm^{-1}.

^1H NMR (DMSO-d_6) : δ 3.86 (s, 3H, OCH_3), 4.95 (s, 2H, OCH_2), 3.16-3.21 (dd, J = 4.8, 13.2, 4.4 Hz, 1H, pyrazole-H_4), 3.77-3.86 (dd, J = 12.8, 4.8, 13.2 Hz, 1H, pyrazole-H_4), 5.58-5.62 (dd, J = 4.4, 7.2, 4.8 Hz, 1H pyrazole-H_5), 6.84 & 6.86 (d, J = 8.4 Hz, 2H, Ar-H), 7.14 & 7.16 (d, J = 8.4 Hz, 2H, Ar-H), 8.12 & 8.14 (d, J = 8.4 Hz, 2H, Ar'-H), 8.27& 8.29 (d, J = 8.4 Hz, 2H, Ar'-H), 7.38 (d, 1H, quinoline-H_7), 7.61 (t, 1H, quinoline-H_3), 7.62 (d, J =8.4 Hz, 1H, quinoline-H_5), 7.63 (t, 1H, quinoline-H_6), 8.33 (d, 1H, quinoline-H_4), 8.86 (d, 1H, quinoline-H_2) ppm.

^{13}C NMR (DMSO-d_6) : δ 40.1 (pyrazole CH_2), 55.9 (OCH_3), 66.4 (pyrazole CH), 67.2 (OCH_2), 106.8, 114.5, 118.6, 121.6, 124.3, 126.8, 127.1, 127.6, 130.5, 134.2, 136.8, 140.3, 142.3, 149.4, 150.2, 156.1, 158.9 (aromatic carbons), 151.6 (pyrazole C), 170.2 (C=O) ppm. MS *m/z*: found 482 [M^+]; calcd. 482. Anal. $C_{27}H_{22}N_4O_5$. Found C 66.88 (67.21), H 4.53 (4.60), N 11.49 (11.61).

1-(5-(2-Hydroxyphenyl)-3-phenyl-4,5-dihydro-1H-pyrazol-1-yl)-2-(quinolin-8-yloxy)ethanone ***7k***

Recrystallised from ethanol as yellow solid in 72% yield. m.p. 100-102 ºC. IR (KBr)ν_{max} : 3410 (O-H stretch), 3071 (C-H stretch in aromatics), 2865 (C-H stretch in CH_3/CH_2), 1675 (C=O stretch), 1632 (C=N stretch), 1486 (C=C stretch in aromatics), 1186, 1042 (sp^2/sp^3 C-O stretch) cm^{-1}.

^1H NMR (DMSO-d_6) : δ 4.94 (s, 2H, OCH_2), 3.18-3.23 (dd, J = 5.2, 13.2, 5.6 Hz, 1H, pyrazole-H_4), 3.78-3.85 (dd, J = 12.8, 5.6. 13.2, 1H, pyrazole-H_4), 5.38 (s, 1H, OH), 5.70-5.74 (dd, J = 4.0, 6.8, 4.4 Hz, 1H, pyrazole-H_5), 6.94-7.10 (m, 4H, Ar-H), 7.48-7.68 (m, 5H, Ar'-H), 7.54 (d, 1H, quinoline-H_7), 7.58 (t, 1H, quinoline-H_3), 7.60 (d, 1H, quinoline-H_5), 7.65 (t, 1H, quinoline-H_6), 8.32 (d, 1H, quinoline-H_4), 8.86 (d, 1H, quinoline-H_2) ppm.

^{13}C NMR (DMSO-d_6): δ 40.6 (pyrazole CH_2), 58.3 (pyrazole CH), 66.8 (OCH_2), 108.9, 115.6, 117.8, 121.2, 121.9, 126.4, 126.7, 128.4, 128.6, 128.9, 130.1 (2), 131.2, 136.2, 136.5,

140.3, 150.1, 154.8, 155.8 (aromatic carbons), 151.8 (pyrazole C), 169.8 (C=O) ppm. MS *m/z*: found 423 [M^+]; calcd. 423. Anal. $C_{26}H_{21}N_3O_3$. Found C 73.32 (73.74), H 4.95 (5.00), N 9.77 (9.92).

1-(5-(2-Hydroxyphenyl)-3-(4-hydroxyphenyl)-4,5-dihydro-1H-pyrazol-1-yl)-2-(quinolin-8-yloxy)ethanone ***7l***

Recrystallised from ethanol as yellow solid in 70% yield. m.p. 182-184 ºC. IR (KBr)ν_{max} : 3315 (O-H stretch), 3024 (C-H stretch in aromatics), 2843 (C-H stretch in CH_3/CH_2), 1681 (C=O stretch), 1628 (C=N stretch), 1480 (C=C stretch in aromatics), 1171, 1034 (sp^2/sp^3 C-O stretch) cm^{-1}.

^{1}H NMR (DMSO-d_6) : δ 4.95 (s, 2H, OCH_2), 3.15-3.20 (dd, J = 4.4, 12.4, 4.0 Hz, 1H, pyrazole-H_4), 3.76-3.83 (dd, J = 12.0, 4.0, 12.4 Hz, 1H, pyrazole-H_4), 5.39 (s, 2H, OH), 5.67-5.71 (dd, J = 4.4, 7.2, 4.8 Hz, 1H, pyrazole-H_5), 6.87-7.08 (m, 4H, Ar-H), 6.80-6.83 (d, J = 12 Hz, 2H, Ar'-H), 7.91, 7.93 (d, J = 8 Hz, 2H, Ar'-H), 7.51 (d, 1H, quinoline-H_7), 7.58 (t, 1H, quinoline-H_3), 7.65 (d, 1H, quinoline-H_5), 7.76 (t, 1H, quinoline-H_6), 8.34 (d, 1H, quinoline-H_4), 8.81 (d, 1H, quinoline-H_2) ppm.

^{13}C NMR (DMSO-d_6) : δ 40.3 (pyrazole CH_2), 59.8 (pyrazole CH), 67.2 (OCH_2), 108.9, 115.9, 116.2, 118.2, 120.8, 121.7, 126.1, 126.8, 128.4, 128.8, 128.9, 129.6, 130.6, 135.9, 140.1, 148.2, 154.7, 155.8, 159.6 (aromatic carbons), 151.6 (pyrazole C), 169.4 (C=O) ppm. MS *m/z*: found 439 [M^+]; calcd. 439. Anal. $C_{26}H_{21}N_3O_4$. Found C 70.67 (71.06), H 4.76 (4.82), N 9.41 (9.56).

1-(3,5-Bis(2-hydroxyphenyl)-4,5-dihydro-1H-pyrazol-1-yl)-2-(quinolin-8-yloxy)ethanone ***7m***

Recrystallised from ethanol as yellow solid in 65% yield. m.p. 150-152 ºC. IR (KBr)ν_{max} : 3318 (O-H stretch), 3041 (C-H stretch in aromatics), 2827 (C-H stretch in CH_3/CH_2), 1678 (C=O stretch), 1641 (C=N stretch), 1493 (C=C stretch in aromatics), 1164, 1039 (sp^2/sp^3 C-O stretch) cm^{-1}.

^{1}H NMR (DMSO-d_6) : δ 4.86 (s, 2H, OCH_2), 3.14-3.19 (dd, J = 4.8, 12.4, 4.4 Hz, 1H, pyrazole-H_4), 3.80-3.87 (dd, J = 12.0, 4.8, 12.4 Hz, 1H, pyrazole-H_4), 5.37 (s, 2H, OH), 5.73-5.77 (dd, J = 4.4, 7.2, 4.8 Hz, 1H, pyrazole-H_5), 6.88-7.10 (m, 4H, Ar-H), 6.94-7.51 (m, 4H, Ar'-H), 7.48 (d, 1H, quinoline-H_7), 7.59 (t, 1H, quinoline-H_3), 7.63 (d, 1H, quinoline-H_5), 7.75 (t, 1H, quinoline-H_6), 8.36 (d, 1H, quinoline-H_4), 8.84 (d, 1H, quinoline-H_2) ppm.

^{13}C NMR (DMSO-d_6) : δ 40.5 (pyrazole CH_2), 59.2 (pyrazole CH), 67.2 (OCH_2), 108.1, 115.9, 117.5, 118.2, 118.6, 121.3, 121.5, 121.7, 126.4, 126.7, 128.2, 130.1, 130.5, 131.9, 132.3, 135.9, 140.2, 148.9, 154.6, 154.9, 162.8 (aromatic carbons), 151.6 (pyrazole C), 169.1 (C=O) ppm. MS *m/z*: found 439 [M^+]; calcd. 439. Anal. $C_{26}H_{21}N_3O_4$. Found C 70.74 (71.06), H 4.77 (4.82), N 9.42 (9.56).

1-(3-(4-Chlorophenyl)-5-(2-hydroxyphenyl)-4,5-dihydro-1H-pyrazol-1-yl)-2-(quinolin-8-yloxy)ethanone ***7n***

Recrystallised from ethanol as brown solid in 93% yield. m.p. 236-238 ºC. IR (KBr)ν_{max} : 3287 (O-H stretch), 2986 (C-H stretch in aromatics), 1737 (C=O stretch), 1637 (C=N stretch), 1591 (C=C stretch in aromatics), 1178, 1012 (sp^2/sp^3 C-O stretch), 1091 (C-Cl stretch in aromatics) cm^{-1}.

^{1}H NMR (DMSO-d_6) : δ 4.75 (s, 2H, OCH_2), 3.52-3.57 (dd, J = 4.8, 13.2, 4.4 Hz, 1H, pyrazole-H_4), 3.67-3.74 (dd, J = 12.8, 4.8, 13.2 Hz, 1H, pyrazole-H_4), 5.36 (s, 1H, OH),

5.82-5.86 (dd, J = 4.4, 6.8, 4.8 Hz, 1H, pyrazole-H_5), 6.90-7.12 (m, 4H, Ar-H), 7.52, 7.55 (d, J = 8.8 Hz, 2H, Ar'-H), 7.96, 7.98 (d, J = 8.8 Hz, 2H, Ar'-H), 7.50 (d, 1H, quinoline-H_7), 7.59 (t, 1H, quinoline-H_3), 7.75 (d, 1H, quinoline-H_5), 7.77 (t, 1H, quinoline-H_6), 8.25 (d, 1H, quinoline-H_4), 8.91 (d, 1H, quinoline-H_2) ppm.

^{13}C NMR (DMSO-d_6) : δ 40.3 (pyrazole CH_2), 59.8 (pyrazole CH), 66.9 (OCH_2), 111.4, 115.6, 117.9, 121.3, 121.7, 126.4, 126.7, 128.2, 128.3, 129.1, 129.6, 130.8, 134.6, 135.4, 136.5, 140.1, 148.6, 154.8, 155.6 (aromatic carbons), 151.8 (pyrazole C), 169.5 (C=O) ppm. MS *m/z*: found 457 [M^+]; calcd. 457. Anal. $C_{26}H_{20}ClN_3O_3$. Found C 67.76 (68.20), H 4.33 (4.40), N 9.11 (9.18).

1-(5-(2-Hydroxyphenyl)-3-(4-nitrophenyl)-4,5-dihydro-1H-pyrazol-1-yl)-2-(quinolin-8-yloxy)ethanone ***7o***

Recrystallised from ethanol as brown solid in 88% yield. m.p. 196-198 ºC. IR (KBr)ν_{max} : 3439 (O-H stretch), 3058 (C-H stretch in aromatics), 1662 (C=O stretch), 1603 (C=N stretch), 1528 (N-O stretch), 1418 (C-N stretch, 1090, 1009 (sp^2/sp^3 C-O stretch) cm^{-1}.

^{1}H NMR (DMSO-d_6) : δ 4.98 (s, 2H, OCH_2), 3.51-3.56 (dd, J = 12.0, 5.6, 12.4 Hz, 1H, pyrazole-H_4), 3.74-3.79 (dd, J = 4.8, 12.4, 5.2 Hz, 1H, pyrazole-H_4), 5.37 (s, 1H, OH), 5.85-5.88 (dd, J = 4.8, 6.8, 4.4 Hz, 1H pyrazole-H_5), 6.93-7.03 (m, 4H, Ar-H), 8.15, 8.18 (d, J = 9.2 Hz, 2H, Ar'-H), 8.33, 8.36 (d, J = 9.2 Hz, 2H, Ar'-H), 7.35 (d, 1H, quinoline-H_7), 7.38 (t, 1H, quinoline-H_3), 7.90 (d, 1H, quinoline-H_5), 7.92 (t, 1H, quinoline-H_6), 8.38 (d, 1H, quinoline-H_4), 8.72 (d, 1H, quinoline-H_2) ppm.

^{13}C NMR (DMSO-d_6) : δ 40.1 (pyrazole CH_2), 59.8 (pyrazole CH), 67.2 (OCH_2), 111.4, 115.6, 118.3, 121.4, 121.6, 126.7, 126.8, 126.9, 127.8, 128.2, 129.8, 130.4, 135.6, 140.3, 143.4, 149.2, 149.9, 154.6, 155.8 (aromatic carbons), 151.8 (pyrazole C), 169.3 (C=O) ppm. MS *m/z*: found 468 [M^+]; calcd. 468. Anal. $C_{26}H_{20}N_4O_5$. Found C 66.23 (66.66), H 4.26 (4.30), N 11.85 (11.96).

Results and Discussion

A novel series of ring systems derived from quinolin-8-ol **1** have been synthesized in good yields using the synthetic route outlined in Scheme 1. IR, ^{1}H NMR, ^{13}C NMR, Mass and chemical analysis data were in agreement with the proposed structures of all newly synthesized compounds.

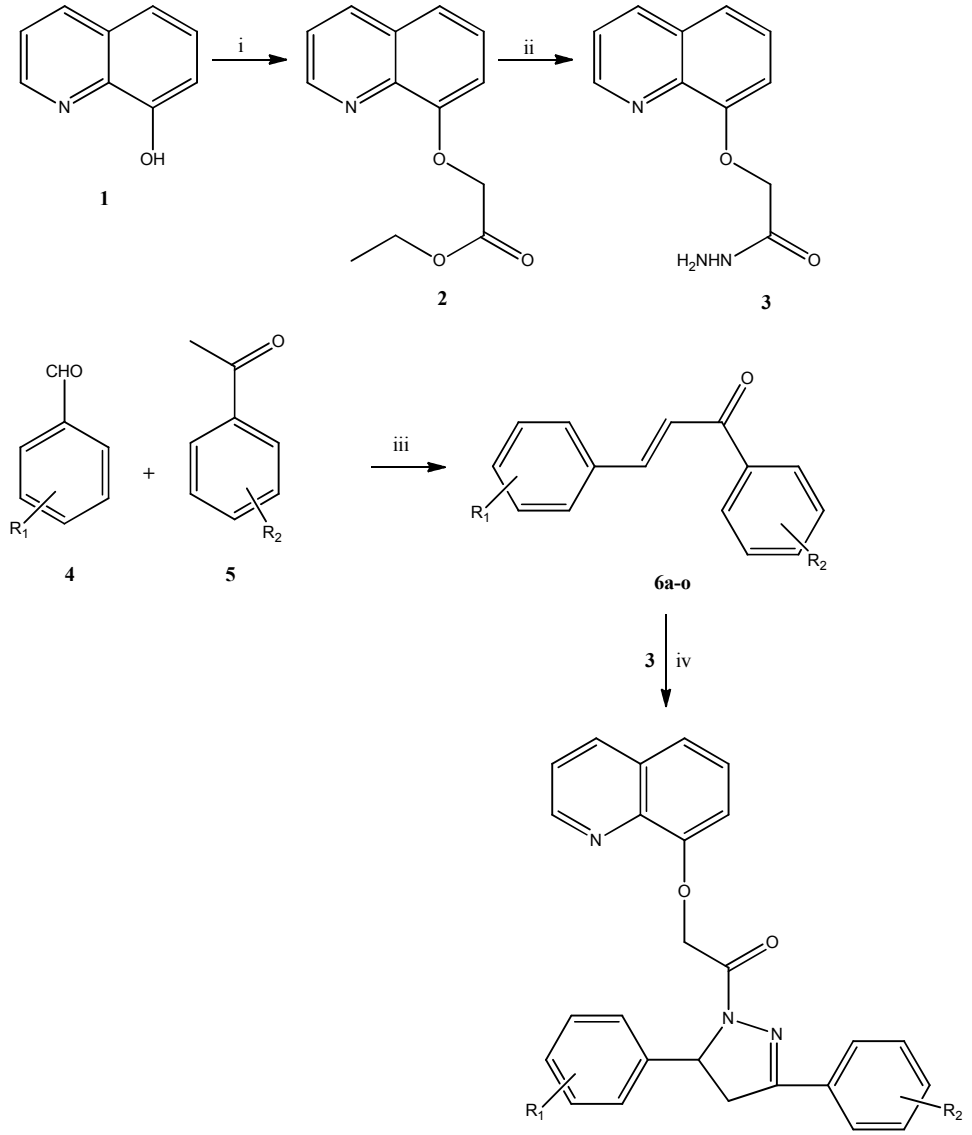
In the IR spectrum of **2,** a strong absorption band for carbonyl group at 1730 cm^{-1} confirms the formation of acetate. ^{1}H NMR spectrum showed a 3H triplet at δ 1.38 and 2H quartet at 4.29 corresponding to CH_3-CH_2 group and the singlet at 4.95 correspond to OCH_2.

In the IR spectrum of **3**, a broad absorption band at around 3325 cm^{-1} was due to hydrazide NH while strong absorption at 1660 was attributed to amide carbonyl. ^{1}H NMR spectrum showed a singlet at δ 3.98 and 9.75 which were accounted for NH_2 and NH and the singlet at 4.87 correspond to OCH_2.

In the IR spectrum of **6a**, an absorption band at around 1618 cm^{-1} is attributed to C=C stretching and a strong absorption band at 1675 cm^{-1} corresponds to carbonyl C=O stretching. ^{1}H NMR spectrum showed two doublets at 7.54 and 8.06 which were accounted for CH=CH and these results confirmed the formation of chalcone.

Reaction of compound **3** with **6a-o** in glacial acetic acid resulted in the formation of 1-(substituted 3,5-diphenyl-4,5-dihydro-1*H*-pyrazol-1-yl)-2-(quinolin-8-yloxy)ethanones **7a-o** in good yields. IR spectrum of **7a** revealed a band at 1632 cm^{-1} due to C=N stretching in

pyrazole ring. The ^{1}H NMR spectrum of **7a** showed two double doublets at δ 3.16 - 3.21 and 3.74 - 3.81 which indicate the presence of a pair of hydrogens at 4th position and a double doublet at 5.65 -5.69 indicate the presence of one hydrogen at 5th position in the pyrazole ring. A singlet was observed at δ 4.92 due to OCH_2 protons. The mass spectrum of **7a** showed molecular ion peak M^+ at *m/z* 407 corresponding to molecular formula $C_{26}H_{21}N_3O_2$.



(i) $ClCH_2COOC_2H_5$, K_2CO_3, DMF (ii) N_2H_4,,H_2O, ErOH (iii) NaOH, ErOH (iv) Giacial acetic acid R_1=(a) to (e)-H, (f) to (i) p-OCH_3, (k) to (o) o-OH R_2=(a), (f), (k) –H, (b), (g), (l) p-OH, (c), (h), (m) o-OH, (d), (i), (n) p-Cl, (e), (i), (o) p-NO_2

Scheme 1. Synthesis of 1-(substituted 3,5-diphenyl-4-5-dihydro-1H-pyrazol-1-yl)-2-(quinoline-8-yloxy)ethanones **7a-o**

These newly synthesized quinoline derivatives containing pyrazole **7a-o** were screened for their minimum inhibitory concentration by antibacterial activity against two kinds of strains *i.e.* gram-positive organism *Staphylococcus aureus* and gram-negative organism *Escherichia coli* and antifungal activity against *Aspergillus niger.* The newly synthesized quinoline derivatives containing pyrazole moiety were found potent in the concentration range 100-62.5 µg/mL compared to the standard drugs, 0.19 µg/mL for ofloxacin and 1.56 µg/mL for Fluconazole. The minimum inhibitory concentrations (MICs) of 1-(substituted 3,5-diphenyl-4,5-dihydro-1*H*-pyrazol-1-yl)-2-(quinolin-8-yloxy)ethanones **7a-o** are presented in Table 2.

Table 2. Minimum inhibitory concentration (MICs) of 1-(substituted 3,5-diphenyl-4,5-dihydro-1*H*-pyrazol-1-yl)-2-(quinolin-8-yloxy)ethanones **7a-o**

Minimum Inhibitory concentration, Concentration in µg/mL				
S. No.	Compound	Gram-positive organisms[a]	Gram-negative organisms[a]	Fungi[b]
1	**7a**	62.5	100	NA
2	**7b**	75	87.5	NA
3	**7c**	75	87.5	NA
4	**7d**	87.5	75	75
5	**7e**	87.5	62.5	87.5
6	**7f**	87.5	100	NA
7	**7g**	75	87.5	NA
8	**7h**	75	87.5	NA
9	**7i**	87.5	75	87.5
10	**7j**	87.5	75	100
11	**7k**	62.5	100	NA
12	**7l**	75	87.5	NA
13	**7m**	75	87.5	NA
14	**7n**	100	75	75
15	**7o**	87.5	75	75
16	Ofloxacin	0.19	0.19	
17	Fluconazole			1.56

The compounds **7a, 7b, 7c, 7g, 7h, 7k, 7l** and **7m** were more potent against *Staphylococcus aureus* and **7d, 7e, 7f, 7i, 7j** and **7o** have moderate potencies. Compound **7n** was weakly potent towards *S. aureus.*

Compound 7e was more potent towards *Escherichia coli* and **7d, 7i, 7j, 7n** and **7o** have moderate potencies. Compounds **7a, 7b, 7c, 7f, 7g, 7h, 7k, 7l** and **7m** were weakly potent towards *E. coli.*

Surprisingly only few compounds showed significant antifungal inhibition with **7d, 7n** and **7o** being more potent whereas **7e, 7i** and **7j** were weakly potent towards *Aspergillus niger.* The results showed that some of the compounds exhibited moderate to good activity against both the strains in antibacterial activity and few compounds were active in antifungal activity.

The studies indicated that variation of substituent in the aromatic rings changes the antibacterial activity significantly. Further compounds containing electron withdrawing groups in Ar' were only potent compared to the other compounds under investigation in antifungal activity.

Conclusion

The compounds 1-(substituted 3,5-diphenyl-4,5-dihydro-1*H*-pyrazol-1-yl)-2-(quinolin-8-yloxy)ethanones **7a-o** have been successfully synthesized and the structures are established by spectral analysis. The spectral data are consistent with the structure of the newly synthesized compounds. The minimum inhibitory concentration (MIC) of the synthesized compounds was studied using broth dilution method. The results revealed that majority of the tested compounds exhibited moderate to good activity against the control ofloxacin in antibacterial activity and only few compounds exhibit significant antifungal inhibition.

Acknowledgement

The authors wish to thank the University Grants Commission, New Delhi for award of Junior Research Fellowships to Mr. G. Manjunath, Mr. M. Mahesh and Mr. G. Bheemaraju under SAP and DST, New Delhi for its support under FIST. The authors also thank the Department of Biochemistry, Sri Krishnadevaraya University for helping in anti-microbial screening.

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