## 5. EXPERIMENTAL

The experimental has been subcategorized into two parts:

5.1 Chemical work

5.2 Biological work

5.3 Computational Study

### 5.1 Chemical work

All the chemicals and solvents used in the work were characterized and purified using standard laboratory techniques prior to use. Progress and completion of the reactions were monitored using thin layer chromatography (TLC) on aluminium supported silica gel 60 G plates; with the use of ultra violet light (254 nm), Iodine vapours, ninhydrin reagent and KMnO4 solution as visualizing agent. Melting points of the compounds were recorded using Veego-melting point apparatus using open glass capillary method and were uncorrected. Purification of the synthesized compound was done using column chromatography taking silica gel (100-200 mesh diameter) as stationary phase. IR spectra for all the compounds were recorded using Bruker FT-IR ALPHA-T spectrophotometer using KBr disc method to obtain spectra of % transmission v/s wavelength ($cm^{-1}$). $^{1}$H-NMR of the synthesized compound were recorded on Bruker Advance-II 500/400 MHz spectrometer in DMSO-$d_6$ OR $CDCl_3$ with TMS as internal standard. Multiplicities of the proton in $^{1}$H-NMR are given as singlet (s), doublet (d), doublet of doublet (dd), triplet (t), multiplet (m), and chemical shift values are expressed as δ ppm, and coupling constant (*J*) in Hz. Mass spectra were recorded on Water make and Acquity model mass spectrometer with UPLC connected with single quadrapole (SQ) detector.

The experimental work carried out has been discussed under the following two main heads:

5.1.1. Synthesis of pyrazolone based multifunctional anti-AD agents **(66-121)** and

5.1.2. Synthesis of pyrimidinone based multifunctional anti-AD agents **(122-150)**

#### 5.1.1. Pyrazolone based multifunctional anti-AD agents (66-121)

##### 5.1.1.1. 5-(Chloromethyl)quinolin-8-ol hydrochloride (65)

In a 25ml RBF, 8-hydroxyquinoline (1gm, 6.89 mol), formaldehyde (1.35ml, 45 mol) and conc. HCl (2.95 ml, 80.82 mol) was stirred at 0 ºC. The reaction mixture was treated with dry HCl gas was for 6 hrs. Progress of the reaction was monitored by the TLC after completion of reaction yellow solid was collected and washed with ethanol.

Anal:

Melting Point : 295-296ºC decomposed [Reported 294-296 ºC][1]

Yield : 90%

**5.1.1.2. Ethyl 2-((8-hydroxyquinolin-5-yl)methyl)-3-oxobutanoate (66)**

In a 25ml two neck RBF containing 3ml of *n*-Hexane in sodium hydride was carefully added and resulting solution was kept aside for 5 min. Solvent carefully decanted in a beaker containing methanol and sodium hydride mass slowly flushed with stream of nitrogen. Anh. DMF added to the RBF followed by addition of ethyl 3-oxobutanoate and stirred for 10min. 5-(chloromethyl)quinolin-8-ol hydrochloride was added in the reaction mixture at R.T. The progress of the reaction mixture was monitored by the TLC. After completion of the reaction, crushed ice added into the solution and extracted with chloroform and dried over $Na_2SO_4$ and solvent evaporated with rotary evaporator which offered brown solid

Anal:

Melting Point : 74-78$^{o}$C

Yield : 70%

$R_f$ value : 0.4

IR (KBr, $cm^{-1}$) : 3332, 2970, 1709, 1225 and 840

Mass ( m/z ) : 288.46 $[M+H]^+$

$^1$H-NMR (DMSO, δ) :δ 9.69 (s, 1H), 8.84-8.85 (d, 1H), at δ 8.47-8.49 (d, 1H), 7.56-7.59 (q, 1H), δ 7.23-7.25 (d, 1H), δ 6.94-6.96 (d, 1H), 3.95-4.04(m, 3H), 3.31-3.48 (m, 2H), 2.17 (s, 3H), 0.99-1.02 (s, 3H).

**5.1.1.3. 4-((8-Hydroxyquinolin-5-yl)methyl)-5-methyl-1*H*-pyrazol-3(2*H*)-one (67)**

In a 25ml RBF, Ethyl 2-((8-hydroxyquinolin-5-yl)methyl)-3-oxobutanoate (1 gm, 2.86 mM)and hydrazine hydrate (0.286 ml, 5.72 mM)was dissolved in ethanol at R.T. The reaction mixture was shifted on oil bath and refluxed for overnight. The progress of the reaction mixture was monitored by the TLC. After completion of the reaction excess amount of ethanol was evaporated with the aid of rotary evaporator. Crushed ice was added into the solution which offered colourless solid.

Anal:

Melting Point : 212-215ºC

Yield : 60%

| | |
|---|---|
| $R_f$ value | : 0.4, Chloroform: Methanol (09:01) |
| IR (KBr, $cm^{-1}$) | : 3333, 3048, 1713, 1174 and 840 |
| Mass (m/z ) | : 256.39 $[M+H]^+$ |
| $^1$H-NMR (DMSO, δ) | : 10.43 (s, 1H), 9.58 (s, 1H), 8.82-8.83 (d, 1H), 8.62-8.60 (d, 1H), 7.53-7.56 (dd, 1H), 7.16-7.18 (d, 1H), 6.98-6.96 (d, 1H), 3.89 (s, 2H), 1.90 (s, 3H). |

### 5.1.1.4. 2-Benzyl-1,2-dihydro-4-((8-hydroxyquinolin-5-yl)methyl)-3-methylpyrazol-5 one (68)

In 25ml of single-neck RBF, 1,2-dihydro-4-((8-hydroxyquinolin-5-yl) methyl)-3-methylpyrazol-5-one (0.6 gm, 2.35 mM) and potassium carbonate (0.38 gm, 2.29 mM) was added in DMF and stirred for 15 min at R.T. 1-(Bromomethyl)benzene (0.33 ml, 2.31 mM ) was added in reaction mixture and allowed to stir for 1hrs. Reaction mixture was monitored by TLC. After completion of reaction, crushed ice was added extracted with chloroform, dried over $Na_2SO_4$ and the solvent was evaporated which offered brown solid. Further purification was done by column chromatography to offered brown colour compound

Anal:

| | |
|---|---|
| Melting Point | : >250℃ |
| Yield | : 63% |
| $R_f$ value | : 0.4, Chloroform: Methanol (09:01) |
| IR (KBr, $cm^{-1}$) | : 3309, 3029, 2924, 1633 and 1150 |
| Mass (m/z) | : 346.3 $[M+H]^+$ |
| $^1$HNMR | : 9.51 (s, 1H), 8.85 (dd, *J* = 4.2, 1.6 Hz, 1H), 8.62 (dd, *J* = 8.6, 1.7 Hz, 1H), 7.57 (dd, *J* = 8.5, 4.2 Hz, 1H), 7.36 – 7.24 (m, 5H), 6.98 (dd, *J* = 7.8, 2.5 Hz, 2H), 5.04 (s, 2H), 3.93 (s, 2H), 1.97 (s, 3H). |

### 5.1.1.5. 2-(2,6-Difluorobenzyl)-1,2-dihydro-4-((8-hydroxyquinolin-5-yl)methyl)-3methyl pyrazol-5-one (69)

In 25ml of single-neck RBF, 1,2-dihydro-4-((8-hydroxyquinolin-5-yl)methyl)-3-methylpyrazol-5-one (0.6 gm, 2.35 mM) and potassium carbonate (0.38 gm, 2.29 mM) was added in DMF and stirred for 15 min at R.T. 2-(Bromomethyl)-1,3-difluorobenzene (0.58 gm, 2.33 mM) was added in reaction mixture and allowed to stir for 1hrs. Reaction mixture was

monitored by TLC. After completion of reaction, crushed ice was added extracted with chloroform, dried over $Na_2SO_4$ and the solvent was evaporated which offered brown solid. Further purification was done by column chromatography to offered brown colour compound. Anal:

| | |
|---|---|
| Melting Point | : 162-165℃ |
| Yield | : 68% |
| $R_f$ value | : 0.55, Chloroform: Methanol (09:01) |
| IR (KBr, $cm^{-1}$) | : 3314, 2957, 2924, 1698 and 1152 |
| Mass (m/z) | : 382.2 $[M+H]^+$ |
| $^1$HNMR | : 9.53 (s, 1H), 8.84 (d, *J* = 5.7 Hz, 1H), 8.61 (d, *J* = 10.2 Hz, 1H), 7.56 (dd, *J* = 8.6, 4.2 Hz, 1H), 7.43 – 7.39 (m, 1H), 7.18 – 7.12 (m, 2H), 7.08 (d, *J* = 8.1 Hz, 1H), 6.97 (d, *J* = 7.9 Hz, 1H), 5.03 (s, 2H), 3.88 (s, 2H), 2.14 (s, 3H). |

**5.1.1.6. 2-(4-(Trifluoromethyl)benzyl)-1,2-dihydro-4-((8-hydroxyquinolin-5-yl)methyl)-3-methylpyrazol-5-one (70)**

In 25ml of single-neck RBF, 1,2-dihydro-4-((8-hydroxyquinolin-5-yl) methyl)-3-methylpyrazol-5-one (0.6 gm, 2.35 mM) and potassium carbonate (0.38 gm, 2.29 mM) was added in DMF and stirred for 15 min at R.T. 1-(Bromomethyl)-2-(trifluoromethyl) benzene (0.42 ml, 2.33 mM) was added in reaction mixture and allowed to stir for 1hrs. Reaction mixture was monitored by TLC. After completion of reaction, crushed ice was added extracted with chloroform, dried over $Na_2SO_4$ and the solvent was evaporated which offered brown solid. Further purification was done by column chromatography to offered white colour compound. Anal:

| | |
|---|---|
| Melting Point | : 169-171℃ |
| Yield | : 60% |
| $R_f$ value | : 0.58, Chloroform: Methanol (09:01) |
| IR (KBr, $cm^{-1}$) | : 3391, 2958, 1696 and 1153 |
| Mass (m/z) | : 414.2 $[M+H]^+$ |
| $^1$HNMR (DMSO, δ) | : 11.53 (s, 1H), 9.53 (s, 1H), 8.82 (dd, *J* = 4.1, 1.6 Hz, 1H), 8.52 (dd, *J* = 8.6, 1.6 Hz, 1H), 7.74 (d, *J* = 7.6 Hz, 1H), 7.60 (t, *J* = 6.9 Hz, 1H), 7.53 (d, *J* = 7.5 Hz, 2H), 7.46 (dd, *J* = 8.6, 4.1 Hz, |

1H), 7.19 (d, *J* = 7.9 Hz, 1H), 6.98 (d, *J* = 7.8 Hz, 1H), 5.33 (s, 2H), 3.96 (s, 2H), 2.00 (s, 3H).

### 5.1.1.7. 2-(3,5-Difluorobenzyl)-1,2-dihydro-4-((8-hydroxyquinolin-5-yl)methyl)-3-methyl pyrazol-5-one (71)

In 25ml of single-neck RBF, 1,2-dihydro-4-((8-hydroxyquinolin-5-yl) methyl)-3-methylpyrazol-5-one (0.6 gm, 2.35 mM) and potassium carbonate (0.38 gm, 2.29 mM) was added in DMF and stirred for 15 min at R.T. 1-(Bromomethyl)-3,5-difluorobenzene (0.58 gm, 2.33 mM) was added in reaction mixture and allowed to stir for 1hrs. Reaction mixture was monitored by TLC. After completion of reaction, crushed ice was added extracted with chloroform, dried over $Na_2SO_4$ and the solvent was evaporated which offered brown solid. Further purification was done by column chromatography to offered white colour compound.

Anal:

| | |
|---|---|
| Melting Point | : 183-185℃ |
| Yield | : 62% |
| $R_f$ value | : 0.55, Chloroform: Methanol (09:01) |
| IR (KBr, $cm^{-1}$) | : 3306, 2920, 1627 and 1113 |
| Mass (m/z) | : 382.1 $[M+H]^+$ |
| $^1$HNMR | : 12.35 (s, 1H), 9.49 (s, 1H), 8.78 (dd, *J* = 4.1, 1.6 Hz, 1H), 8.35 (dd, *J* = 8.6, 1.6 Hz, 1H), 7.69 – 7.64 (m, 1H), 7.58 – 7.46 (m, 3H), 7.12 (d, *J* = 7.9 Hz, 1H), 6.79 (d, *J* = 7.8 Hz, 1H), 3.97 (s, 2H), 2.14 (s, 3H). |

### 5.1.1.8. 2-(4-Chlorobenzyl)-1,2-dihydro-4-((8-hydroxyquinolin-5-yl)methyl)-3-methyl pyrazol-5-one (72)

In 25ml of single-neck RBF, 1,2-dihydro-4-((8-hydroxyquinolin-5-yl) methyl)-3-methylpyrazol-5-one (0.6 gm, 2.35 mM) and potassium carbonate (0.38 gm, 2.29 mM) was added in DMF and stirred for 15 min at R.T. 1-(Bromomethyl)-4-chlorobenzene (0.58 gm, 2.35 mM) was added in reaction mixture and allowed to stir for 1hrs. Reaction mixture was monitored by TLC. After completion of reaction, crushed ice was added extracted with chloroform, dried over $Na_2SO_4$ and the solvent was evaporated which offered brown solid. Further purification was done by column chromatography to offered white colour compound.

Anal:

Melting Point : 193-196℃

Yield : 64%

$R_f$ value : 0.56, Chloroform: Methanol (09:01)

IR (KBr, $cm^{-1}$) : 3356, 3076, 2924, 1695 and 1161

Mass (m/z) : 380.13 $[M+H]^+$**,** 382.08 $[M+2]^+$

$^1$HNMR : 11.51 (s, 1H), 9.56 (s, 1H), 8.83 (dd, *J* = 4.2, 1.5 Hz, 1H), 8.53 (dd, *J* = 8.6, 1.6 Hz, 1H), 7.48 (dd, *J* = 8.6, 4.1 Hz, 1H), 7.41 – 7.31 (m, 4H), 7.17 (d, *J* = 7.9 Hz, 1H), 6.97 (d, *J* = 7.8 Hz, 1H), 5.15 (s, 2H), 3.93 (s, 2H), 1.99 (s, 3H).

**5.1.1.9. 2-(2,6-Dichlorobenzyl)-1,2-dihydro-4-((8-hydroxyquinolin-5-yl)methyl)-3-methyl pyrazol-5-one (73)**

In 25ml of single-neck RBF, 1,2-dihydro-4-((8-hydroxyquinolin-5-yl) methyl)-3-methylpyrazol-5-one (0.6 gm, 2.35 mM) and potassium carbonate (0.38 gm, 2.29 mM) was added in DMF and stirred for 15 min at R.T. 2-(Bromomethyl)-1,3-dichlorobenzene (0.67 gm, 2.35 mM) was added in reaction mixture and allowed to stir for 1hrs. Reaction mixture was monitored by TLC. After completion of reaction, crushed ice was added extracted with chloroform, dried over $Na_2SO_4$ and the solvent was evaporated which offered brown solid. Further purification was done by column chromatography to offered white colour compound.

Anal:

Melting Point : 176-179℃

Yield : 62%

$R_f$ value : 0.58, Chloroform: Methanol (09:01)

IR (KBr, $cm^{-1}$) : 3357, 3090, 2919, 1626, and 1152

Mass (m/z) : 414.04 $[M+H]^+$, 416.04 $[M+2]^+$

$^1$HNMR (DMSO, δ) : 11.55 (s, 1H), 9.56 (s, 1H), 8.83 (dd, *J* = 4.2, 1.5 Hz, 1H), 8.52 (dd, *J* = 8.6, 1.6 Hz, 1H), 7.64 (d, *J* = 1.5 Hz, 1H), 7.49 (dd, *J* = 8.6, 4.2 Hz, 1H), 7.36 (d, *J* = 1.6 Hz, 2H), 7.19 (d, *J* = 7.9 Hz, 1H), 6.98 (d, *J* = 7.9 Hz, 1H), 5.20 (s, 2H), 3.95 (s, 2H), 2.00 (s, 3H).

**5.1.1.10. 2-(2-(Trifluoromethyl)benzyl)-1,2-dihydro-4-((8-hydroxyquinolin-5-yl)methyl)-3-methylpyrazol-5-one (74)**

In 25ml of single-neck RBF, 1,2-dihydro-4-((8-hydroxyquinolin-5-yl) methyl)-3-methylpyrazol-5-one (0.6 gm, 2.35 mM) and potassium carbonate (0.38 gm, 2.29 mM) was added in DMF and stirred for 15 min at R.T. 2-(Bromomethyl)-1,3-dichlorobenzene (0.67 gm, 2.35 mM) was added in reaction mixture and allowed to stir for 1hrs. Reaction mixture was monitored by TLC. After completion of reaction, crushed ice was added extracted with chloroform, dried over $Na_2SO_4$ and the solvent was evaporated which offered brown solid. Further purification was done by column chromatography to offered white colour compound.
Anal:

| | |
|---|---|
| Melting Point | : 175-178℃ |
| Yield | : 66% |
| $R_f$ value | : 0.53, Chloroform: Methanol (09:01) |
| IR (KBr, $cm^{-1}$) | **:** 3347, 3028, 2922, 1588 and 1161 |
| Mass (m/z) | : 414.2 $[M+H]^+$ |
| $^1$HNMR (DMSO, δ) | :11.53 (s, 1H), 9.56 (s, 1H), 8.83 (dd, *J* = 4.1, 1.6 Hz, 1H), 8.54 (dd, *J* = 8.6, 1.6 Hz, 1H), 7.68 (d, *J* = 8.1 Hz, 3H), 7.52 (d, *J* = 8.0 Hz, 3H), 7.19 (d, *J* = 7.8 Hz, 1H), 6.98 (d, *J* = 7.8 Hz, 1H), 5.26 (s, 2H), 3.96 (s, 3H), 2.00 (s, 3H). |

### 5.1.1.11. 2-(2,5-Dimethylbenzyl)-1,2-dihydro-4-((8-hydroxyquinolin-5-yl)methyl)-3 methyl pyrazol-5-one (75)

In 25ml of single-neck RBF, 1,2-dihydro-4-((8-hydroxyquinolin-5-yl) methyl)-3-methylpyrazol-5-one (0.6 gm, 2.35 mM) and potassium carbonate (0.38 gm, 2.29 mM) was added in DMF and stirred for 15 min at R.T. 2-(Bromomethyl)-1,4-dimethylbenzene (0.56 gm, 2.35 mM) was added in reaction mixture and allowed to stir for 1hrs. Reaction mixture was monitored by TLC. After completion of reaction, crushed ice was added extracted with chloroform, dried over $Na_2SO_4$ and the solvent was evaporated which offered brown solid. Further purification was done by column chromatography to offered brown colour compound.
Anal:

| | |
|---|---|
| Melting Point | : 166-168℃ |
| Yield | : 66% |
| $R_f$ value | : 0.59, Chloroform: Methanol (09:01) |
| IR (KBr, $cm^{-1}$) | : 3311, 2956, 2921, 1684 and 1151 |
| Mass (m/z) | :374.2 $[M+H]^+$ |

$^{1}$HNMR (DMSO, δ) **:** 9.51 (s, 1H), 8.78 (d, *J* = 10.4 Hz, 1H), 8.61 (d, *J* = 10.3 Hz, 1H), 7.59 (dd, *J* = 9.0, 4.1 Hz, 1H), 6.96 (d, *J* = 7.8 Hz, 1H), 6.91 – 6.84 (m, 3H), 6.73 (s, 1H), 4.94 (s, 2H), 3.92 (s, 2H), 2.18 (s, 6H), 2.06 (s, 3H).

### 5.1.1.12. 2-(4- Fluorobenzyl)-1,2-dihydro-4-((8-hydroxyquinolin-5-yl)methyl)-3-methyl pyrazol-5-one (76)

In 25ml of single-neck RBF, 1,2-dihydro-4-((8-hydroxyquinolin-5-yl) methyl)-3-methylpyrazol-5-one (0.6 gm, 2.35 mM) and potassium carbonate (0.38 gm, 2.29 mM) was added in DMF and stirred for 15 min at R.T. 1-(Bromomethyl)-4-fluorobenzene (0.29 ml, 2.34 mM) was added in reaction mixture and allowed to stir for 1hrs. Reaction mixture was monitored by TLC. After completion of reaction, crushed ice was added extracted with chloroform, dried over $Na_2SO_4$ and the solvent was evaporated which offered brown solid. Further purification was done by column chromatography to offered white colour compound.
Anal:

Melting Point : 194-197°C

Yield : 64%

$R_f$ value : 0.55, Chloroform: Methanol (09:01)

IR (KBr, $cm^{-1}$) : 3287, 2921, 1673, 1503 and 1411

$^{1}$HNMR (DMSO, δ) **:** 9.53 (s, 1H), 8.84 (dd, *J* = 4.2, 1.6 Hz, 1H), 8.61 (dd, *J* = 8.6, 1.7 Hz, 1H), 7.57 (dd, *J* = 8.6, 4.1 Hz, 1H), 7.16 – 7.08 (m, 5H), 6.97 (d, *J* = 7.8 Hz, 1H), 5.01 (s, 2H), 3.91 (s, 2H), 1.97 (s, 3H).

### 5.1.1.13. 2-(3-Chlorobenzyl)-1,2-dihydro-4-((8-hydroxyquinolin-5-yl)methyl)-3-methyl pyrazol-5-one (77)

In 25ml of single-neck RBF, 1,2-dihydro-4-((8-hydroxyquinolin-5-yl) methyl)-3-methylpyrazol-5-one (0.6 gm, 2.35 mM) and potassium carbonate (0.38 gm, 2.29 mM) was added in DMF and stirred for 15 min at R.T. 1-(Bromomethyl)-3-chlorobenzene (0.37 ml, 2.35 mM) was added in reaction mixture and allowed to stir for 1hrs. Reaction mixture was monitored by TLC. After completion of reaction, crushed ice was added extracted with chloroform, dried over $Na_2SO_4$ and the solvent was evaporated which offered brown solid. Further purification was done by column chromatography to offered white colour compound.
Anal:

Melting Point : 181-184℃

Yield : 59%

$R_f$ value : 0.57, Chloroform: Methanol (09:01)

IR (KBr, $cm^{-1}$) : 3322, 3156, 2922, 1692 and 1173

Mass (m/z) : 380.13 $[M+H]^+$, 382.8 $[M+H]^+$

$^1$HNMR (DMSO, δ) : 11.52 (s, 1H), 9.55 (s, 1H), 8.83 (dd, *J* = 4.1, 1.5 Hz, 1H), 8.55 (dd, *J* = 8.7, 1.6 Hz, 1H), 7.49 (dd, *J* = 8.6, 4.2 Hz, 1H), 7.41 – 7.31 (m, 4H), 7.19 (d, *J* = 7.9 Hz, 1H), 6.97 (dd, *J* = 7.8, 2.9 Hz, 1H), 5.18 (s, 2H), 3.94 (s, 2H), 2.00 (s, 3H).

**5.1.1.14. 2-(3,5-Dimethylbenzyl)-1,2-dihydro-4-((8-hydroxyquinolin-5-yl)methyl)-3 methyl pyrazol-5-one (78)**

In 25ml of single-neck RBF, 1,2-dihydro-4-((8-hydroxyquinolin-5-yl) methyl)-3-methylpyrazol-5-one (0.6 gm, 2.35 mM) and potassium carbonate (0.38 gm, 2.29 mM) was added in DMF and stirred for 15 min at R.T. 1-(Bromomethyl)-3-chlorobenzene (0.37 ml, 2.35 mM) was added in reaction mixture and allowed to stir for 1hrs. Reaction mixture was monitored by TLC. After completion of reaction, crushed ice was added extracted with chloroform, dried over $Na_2SO_4$ and the solvent was evaporated which offered brown solid. Further purification was done by column chromatography to offered white colour compound.
Anal:

Melting Point : 201-204℃

Yield : 64%

$R_f$ value : 0.53, Chloroform: Methanol (09:01)

IR (KBr, $cm^{-1}$) : 3314, 2971, 2915, 1604 and 1153

Mass (m/z) : 374.2 $[M+H]^+$

$^1$HNMR : 11.47 (s, 1H), 9.54 (s, 2H), 8.83 (dd, *J* = 4.3, 1.6 Hz, 1H), 8.56 (dd, *J* = 8.7, 1.6 Hz, 1H), 7.47 (dd, *J* = 8.6, 4.1 Hz, 1H), 7.19 (d, *J* = 7.8 Hz, 1H), 6.98 (d, *J* = 2.9 Hz, 1H), 6.90 (s, 2H), 6.85 (s, 1H), 5.07 (s, 2H), 3.92 (s, 2H), 2.22 (s, 6H), 2.13 (s, 3H).

**5.1.1.15. 2-(4-Methylbenzyl)-1,2-dihydro-4-((8-hydroxyquinolin-5-yl) methyl)-3-methylpyrazol-5-one (79)**

In 25ml of single-neck RBF, 1,2-dihydro-4-((8-hydroxyquinolin-5-yl) methyl)-3-methylpyrazol-5-one (0.6 gm, 2.35 mM) and potassium carbonate (0.38 gm, 2.29 mM) was

added in DMF and stirred for 15 min at R.T. 1-(Bromomethyl)-4-methylbenzene (0.39 ml, 2.35 mM) was added in reaction mixture and allowed to stir for 1hrs. Reaction mixture was monitored by TLC. After completion of reaction, crushed ice was added extracted with chloroform, dried over $Na_2SO_4$ and the solvent was evaporated which offered brown solid. Further purification was done by column chromatography to offered white colour compound.

Anal:

| | |
|---|---|
| Melting Point | : 177-180℃ |
| Yield | : 66% |
| $R_f$ value | : 0.56, Chloroform: Methanol (09:01) |
| IR (KBr, $cm^{-1}$) | : 3139, 2912, 1592 and 1148 |
| Mass (m/z) | : 360.16 $[M+H]^+$ |
| $^1$HNMR (DMSO, δ) | : 11.48 (s, 1H), 9.54 (s, 1H), 8.82 (dd, *J* = 4.1, 1.6 Hz, 1H), 8.54 (dd, *J* = 8.6, 1.6 Hz, 1H), 7.46 (dd, *J* = 8.6, 4.1 Hz, 1H), 7.24 (d, *J* = 8.1 Hz, 2H), 7.19 – 7.12 (m, 3H), 6.96 (d, *J* = 7.8 Hz, 1H), 5.11 (s, 2H), 3.91 (s, 2H), 2.29 (s, 3H), 1.98 (s, 3H). |

**5.1.1.16. Phenyl4-((8-hydroxyquinolin-5-yl) methyl)-3-methyl-5-oxo-1*H*-pyrazole-2(5*H*)-carboxylate (80)**

In 25ml of single-neck RBF, 1,2-dihydro-4-((8-hydroxyquinolin-5-yl)methyl)-3-methylpyrazol-5-one (1 gm) and potassium carbonate (1.54 gm) was added in DMF and stirred for 15 min at R.T. Phenyl chloroformate was added in reaction mixture and stirred for 1 hr. Reaction mixture was monitored by TLC. After completion of reaction, crushed ice was added to get the desired product. Further purification was done by column chromatography to offered white colour compound.

Anal:

| | |
|---|---|
| Melting Point | : 237-239℃ |
| Yield | : 60% |
| $R_f$ value | : 0.8, Chloroform: Methanol (09:01) |
| IR (KBr, $cm^{-1}$) | : 3333, 3023, 2919, 1746 and 1222 |
| Mass (m/z) | : 376.3 $[M+H]^+$ |
| $^1$HNMR (DMSO, δ) | : 11.32 (s, 1H), 9.62 (s, 1H), 8.87 (dd, *J* = 4.1, 1.5 Hz, 1H), 8.62 (dd, *J* = 8.7, 1.6 Hz, 1H), 7.62 (dd, *J* = 8.6, 4.2 Hz, 1H), 7.50 – |

7.43 (m, 2H), 7.35 – 7.28 (m, 3H), 7.15 (d, *J* = 8.0 Hz, 1H), 7.00 (d, *J* = 7.9 Hz, 1H), 4.02 (s, 2H), 2.39 (s, 3H).

### 5.1.1.17. Methyl 4-((8-hydroxyquinolin-5-yl)methyl)-3-methyl-5-oxo-1*H*-pyrazole-2(5*H*)-carboxylate (81)

In 25ml of single-neck RBF, 1,2-dihydro-4-((8-hydroxyquinolin-5-yl)methyl)-3-methylpyrazol-5-one (1 gm) and potassium carbonate (1.54 gm) was added in DMF and stirred for 15 min at R.T. Methyl chloroformate was added in reaction mixture and stirred for 1 hr. Reaction mixture was monitored by TLC. After completion of reaction, crushed ice was added to get the desired product. Further purification was done by column chromatography to offered white colour compound.

Anal:

| | |
|---|---|
| Melting Point | : 191-194℃ |
| Yield | : 70% |
| $R_f$ value | : 0.7, Chloroform: Methanol (09:01) |
| IR (KBr, $cm^{-1}$) | : 3399, 3094, 2910, 1750, 1707 and 1210 |
| Mass (m/z) | : 314.12 $[M+H]^+$ |
| $^1$HNMR (DMSO, δ) | : 12.27 (s, 1H), 9.61 (s, 1H), 8.59 (dd, *J* = 8.6, 1.6 Hz, 1H), 8.36 (dd, *J* = 8.6, 1.6 Hz, 1H), 7.55 (dd, *J* = 8.6, 4.1 Hz, 1H), 7.15 (d, *J* = 7.8 Hz, 1H), 6.98 (d, *J* = 7.9 Hz, 1H), 3.95 (s, 3H), 3.84 (s, 2H), 2.07 (s, 3H). |

### 5.1.1.18. Benzyl 4-((8-hydroxyquinolin-5-yl)methyl)-3-methyl-5-oxo-1*H*-pyrazole-2(5*H*)-carboxylate (82)

In 25ml of single-neck RBF, 1,2-dihydro-4-((8-hydroxyquinolin-5-yl)methyl)-3-methylpyrazol-5-one (1 gm) and potassium carbonate (1.54 gm) was added in DMF and stirred for 15 min at R.T. Benzyl chloroformate (0.58 gm, 0.38 ml) was added in reaction mixture and stirred for 1 hr. Reaction mixture was monitored by TLC. After completion of reaction, crushed ice was added to get the desired product. Further purification was done by column chromatography to offered white colour compound.

Anal:

| | |
|---|---|
| Melting Point | : 217-220℃ |
| Yield | : 85% |
| $R_f$ value | : 0.74, Chloroform: Methanol (09:01) |

IR (KBr, $cm^{-1}$) : 3334, 3028, 2940, 1729, 1630 and 1224

Mass (m/z) : 390.14 $[M+H]^+$

$^1$HNMR (DMSO, δ) :11.13 (s, 1H), 9.61 (s, 1H), 8.86 (dd, *J* = 4.2, 1.5 Hz, 1H), 8.58 (dd, *J* = 8.6, 1.6 Hz, 1H), 7.59 (dd, *J* = 8.6, 4.2 Hz, 1H), 7.48 – 7.36 (m, 5H), 7.09 (d, *J* = 7.9 Hz, 1H), 6.97 (d, *J* = 7.9 Hz, 1H), 5.31 (s, 2H), 3.96 (s, 2H), 2.35 (s, 3H).

**5.1.1.19. Pentyl 4-((8-hydroxyquinolin-5-yl)methyl)-3-methyl-5-oxo-1*H*-pyrazole-2(5*H*)-carboxylate (83)**

In 25ml of single-neck RBF, 1,2-dihydro-4-((8-hydroxyquinolin-5-yl)methyl)-3-methylpyrazol-5-one (1 gm) and potassium carbonate (1.54 gm) was added in DMF and stirred for 15 min at R.T. n-Pentyl chloroformate (0.456 gm, 0.43 ml) was added in reaction mixture and stirred for 1 hr. Reaction mixture was monitored by TLC. After completion of reaction, crushed ice was added to get the desired product. Further purification was done by column chromatography to offered white colour compound.

Anal:

Melting Point : 217-220℃

Yield : 68%

$R_f$ value : 0.90, Chloroform: Methanol (09:01)

IR (KBr, $cm^{-1}$) : 3355, 3023, 2919, 1731, 1624 and 1218

Mass (m/z) : 370.18 $[M+H]^+$

$^1$HNMR (DMSO, δ) : 11.10 (s, 1H), 9.60 (s, 1H), 8.86 (dd, *J* = 4.2, 1.5 Hz, 1H), 8.59 (dd, *J* = 8.6, 1.6 Hz, 1H), 7.60 (dd, *J* = 8.6, 4.1 Hz, 1H), 7.10 (d, *J* = 7.9 Hz, 1H), 6.98 (d, *J* = 7.9 Hz, 1H), 4.24 (t, *J* = 6.6 Hz, 2H), 3.96 (s, 2H), 2.34 (s, 3H), 1.67 (p, *J* = 6.9 Hz, 2H), 1.35 – 1.30 (m, 4H), 0.90 – 0.85 (m, 3H).

**5.1.1.20. 2,2,2-Trichloroethyl 4-((8-hydroxyquinolin-5-yl)methyl)-3-methyl-5-oxo-1*H*-pyrazole-2(5*H*)-carboxylate (84)**

In 25ml of single-neck RBF, 1,2-dihydro-4-((8-hydroxyquinolin-5-yl)methyl)-3-methylpyrazol-5-one (1 gm) and potassium carbonate (1.54 gm) was added in DMF and stirred for 15 min at R.T. 2,2,2-Trichloroethyl chloroformate (0.908 gm, 0.53 ml) was added in reaction mixture and stirred for 1 hr. Reaction mixture was monitored by TLC. After

completion of reaction, crushed ice was added to get the desired product. Further purification was done by column chromatography to offered white colour compound

Anal:

Melting Point : 210-212℃

Yield : 70%

$R_f$ value : 0.80, Chloroform: Methanol (09:01)

IR (KBr, $cm^{-1}$) : 3355, 3021, 2943, 1740, 1684 and 1216

$^1$HNMR (DMSO, δ) : 11.40 (s, 1H), 9.62 (s, 1H), 8.86 (dd, *J* = 4.1, 1.6 Hz, 1H), 8.59 (dd, *J* = 8.6, 1.6 Hz, 1H), 7.61 (dd, *J* = 8.6, 4.2 Hz, 1H), 7.12 (d, *J* = 7.9 Hz, 1H), 6.98 (d, *J* = 7.9 Hz, 1H), 5.11 (s, 2H), 3.99 (s, 2H), 2.39 (s, 3H).

**5.1.1.21. (9*H*-Fluoren-9-yl) methyl 4-((8-hydroxyquinolin-5-yl) methyl)-3-methyl-5-oxo-1*H*-pyrazole-2(5*H*)-carboxylate (85)**

In 25ml of single-neck RBF, 1,2-dihydro-4-((8-hydroxyquinolin-5-yl)methyl)-3-methylpyrazol-5-one (1 gm) and potassium carbonate (1.54 gm) was added in DMF and stirred for 15 min at R.T. (9*H*-Fluoren-9-yl)methyl chloroformate (2.02 gm, 1.06 ml) was added in reaction mixture and stirred for 1 hr. Reaction mixture was monitored by TLC. After completion of reaction, crushed ice was added to get the desired product. Further purification was done by column chromatography to offered white colour compound.

Anal:

Melting Point : 200-203℃

Yield : 78%

$R_f$ value : 0.85, Chloroform: Methanol (09:01)

IR (KBr, $cm^{-1}$) : 3338, 2992, 2893, 1742, 1627 and 1218

Mass (m/z) : 478.10 $[M+H]^+$

$^1$HNMR (DMSO, δ) : 11.10 (s, 1H), 9.61 (s, 1H), 8.86 (dd, *J* = 4.2, 1.5 Hz, 1H), 8.57 (dd, *J* = 8.6, 1.6 Hz, 1H), 7.89 (d, *J* = 4.9 Hz, 2H), 7.76 (d, *J* = 7.3 Hz, 2H), 7.60 (dd, *J* = 8.6, 4.1 Hz, 1H), 7.42 (t, *J* = 7.2 Hz, 2H), 7.35 (d, *J* = 7.5 Hz, 2H), 7.05 (d, *J* = 7.9 Hz, 1H), 6.97 (d, *J* = 7.9 Hz, 1H), 4.71 (d, *J* = 6.2 Hz, 2H), 4.40 (t, *J* = 6.3 Hz, 1H), 3.93 (s, 2H), 2.04 (s, 3H).

**5.1.1.22. Ethyl 4-((8-hydroxyquinolin-5-yl) methyl)-3-methyl-5-oxo-1*H*-pyrazole-2(5*H*)-carboxylate (86)**

In 25ml of single-neck RBF, 1,2-dihydro-4-((8-hydroxyquinolin-5-yl)methyl)-3-methylpyrazol-5-one (1 gm) and potassium carbonate (1.54 gm) was added in DMF and stirred for 15 min at R.T. Ethyl chloroformate (0.85 gm, 0.74 ml) was added in reaction mixture and stirred for 1 hr. Reaction mixture was monitored by TLC. After completion of reaction, crushed ice was added to get the desired product. Further purification was done by column chromatography to offered white colour compound.

Anal:

| | |
|---|---|
| Melting Point | : 246-249°C |
| Yield | : 60 |
| $R_f$ value | : 0.8, Chloroform: Methanol (09:01) |
| IR (KBr, $cm^{-1}$) | : 3359, 2985, 2921, 1739, 1620 and 1209 |
| Mass (m/z) | : 328.11 $[M+H]^+$ |
| $^1$HNMR (DMSO, δ) | : 11.11 (s, 1H), 9.60 (s, 1H), 8.86 (dd, *J* = 4.2, 1.5 Hz, 1H), 8.59 (dd, *J* = 8.7, 1.6 Hz, 1H), 7.60 (dd, *J* = 8.7, 4.2 Hz, 1H), 7.10 (d, *J* = 7.9 Hz, 1H), 6.98 (d, *J* = 7.9 Hz, 1H), 4.29 (q, *J* = 7.1 Hz, 2H), 3.96 (s, 2H), 2.34 (s, 3H), 1.29 (t, *J* = 7.1 Hz, 3H). |

**5.1.1.23. Isobutyl 4-((8-hydroxyquinolin-5-yl)methyl)-3-methyl-5-oxo-1*H*-pyrazole2(5*H*)-carboxylate (87)**

In 25ml of single-neck RBF, 1,2-dihydro-4-((8-hydroxyquinolin-5-yl)methyl)-3-methylpyrazol-5-one (1 gm) and potassium carbonate (1.54 gm) was added in DMF and stirred for 15 min at R.T. Isobutyl chloroformate (1.07 gm, 1.02 ml) was added in reaction mixture and stirred for 1 hr. Reaction mixture was monitored by TLC. After completion of reaction, crushed ice was added to get the desired product. Further purification was done by column chromatography to offered white colour compound.

Anal:

| | |
|---|---|
| Melting Point | : 212-215°C |
| Yield | : 63% |
| $R_f$ value | : 0.8, Chloroform: Methanol (09:01) |
| IR (KBr, $cm^{-1}$) | : 3315, 2989, 2918, 1728, 1636 and 1226 |
| Mass (m/z) | : 356.16 $[M+H]^+$ |

$^1$HNMR (DMSO, δ) : 11.11 (s, 1H), 9.60 (s, 1H), 8.86 (dd, *J* = 4.2, 1.5 Hz, 1H), 8.59 (dd, *J* = 8.6, 1.6 Hz, 1H), 7.60 (dd, *J* = 8.6, 4.2 Hz, 1H), 7.10 (d, *J* = 7.9 Hz, 1H), 6.98 (d, *J* = 7.8 Hz, 1H), 4.04 (d, *J* = 6.7 Hz, 2H), 3.96 (s, 2H), 2.34 (s, 3H), 1.98 (dt, *J* = 13.4, 6.7 Hz, 1H), 0.94 (d, *J* = 6.7 Hz, 6H).

**5.1.1.24. 2-Methyl-*N*-(4-methylbenzyl)acetamide (88)**

In 25ml of single-neck RBF, *p*-tolylmethanamine (1.047ml, 8.26mM) and potassium carbonate (1.48 ml, 10.724mM) was added in DCM and stirred the reaction mixture for a while. Chloroacetylchloride (1.30ml, 16.46mM) was added drop wise in the reaction mixture at 0ºC and stirred it at room temp. Excess amount of DCM was evaporated after completion of reaction followed by addition of crushed ice. The obtained solid was filtered by using vacuum filtration and taken for further reaction without any purification.

Anal:

Melting Point : 160-162ºC (Lit.: 164-166 ºC)[2]

Yield : 75%

$R_f$ value : 0.4, *n*-Hexane:Ethylacetate (16:04)

IR (KBr, $cm^{-1}$) : 3278, 2951, 2359, 1649, 1237, 806

**5.1.1.25. 2-Methoxy-*N*-(4-methoxybenzyl)acetamide (89)**

In 25ml of single-neck RBF,4-methoxy-benzylamine (0.95 ml, 7.29mM) and potassium carbonate ( 1.30gm, 9.42mM) was added in DCM and stirred the reaction mixture for a while. Chloroacetylchloride (1.15 ml, 14.51mM) was added drop wise in the reaction mixture at 0ºC and stirred it at room temp. Excess amount of DCM was evaporated after completion of reaction followed by addition of crushed ice. The obtained solid was filtered by using vacuum filtration and taken for further reaction without any purification.

Anal:

Melting Point : 118-120ºC (Lit.: 121-122 ºC)[2]

Yield : 75%

$R_f$ value : 0.4, *n*-Hexane:Ethylacetate (16:04)

IR (KBr, $cm^{-1}$) : 3278, 2915, 1649, 1513, 1108, 806

**5.1.1.26. 2-Chloro-*N*-(4-chlorobenzyl)acetamide (90)**

In 25ml of single-neck RBF, (4-chlorophenyl)methanamine (0.006 ml, 7.06mM)and potassium carbonate (1.26gm, 9.42mM) was added in DCM and stirred the reaction mixture

for a while. Chloroacetylchloride (1.11ml, 14.51mM) was added drop wise in the reaction mixture at 0ºC and stirred it at room temp. Excess amount of DCM was evaporated after completion of reaction followed by addition of crushed ice. The obtained solid was filtered by using vacuum filtration and taken for further reaction without any purification.

Anal:

| | |
|---|---|
| Melting Point | : 275-276ºC [Lit.: 275-278ºC][3] |
| Yield | : 78% |
| $R_f$ value | : 0.4, *n*-Hexane:Ethylacetate (16:04) |
| IR (KBr, $cm^{-1}$) | : 3264, 2386, 1646, 1432, 1226, 432 |

**5.1.1.27. 2-Fluoro-*N*-(4-fluorobenzyl)acetamide (91)**

In 25ml of single-neck RBF,4-fluoro-benzylamine (0.91ml, 8 mM) and potassium carbonate (1.43 ml, 10.362 mM) was added in DCM and stirred the reaction mixture for a while. Chloroacetylchloride (1.26 ml, 15.929 mM) was added drop wise in the reaction mixture at 0ºC and stirred it at room temp. Excess amount of DCM was evaporated after completion of reaction followed by addition of crushed ice. The obtained solid was filtered by using vacuum filtration and taken for further reaction without any purification.

Anal:

| | |
|---|---|
| Melting Point | : 107-109ºC [Lit. : 111-112 ºC][4] |
| Yield | : 73% |
| $R_f$ value | : 0.4, *n*-Hexane:Ethylacetate (16:04) |
| IR (KBr, $cm^{-1}$) | : 3280, 2952, 2342, 1650, 1064, 854 |

**5.1.1.28. 2-(4-((8-Hydroxyquinolin-5-yl)methyl)-5-methyl-3-oxo-2,3-dihydro-1*H*-pyrazol-1-yl)-*N*-(4-methylbenzyl)acetamide (92)**

In 25ml of single-neck RBF, 4-((8-hydroxyquinolin-5-yl)methyl)-5-methyl-1*H*-pyrazol-3(2*H*)-one (0.5 gm, 1.958 mM) and potassium carbonate (0.324 gm, 2.347 mM ) was added in DMF and stirred for 15 min at R.T. 2-Chloro-*N*-(4-methylbenzyl)acetamide (0.387 gm, 1.959 mM) was added in reaction mixture and heated at 80ºC for 12hrs. Reaction mixture was monitored by TLC. After completion of reaction, crushed ice was added extracted with chloroform, dried over $Na_2SO_4$ and the solvent was evaporated with which offered brown solid. Further purification was done by column chromatography to offered colourless compound.

Anal:

Melting Point : 184-187ºC

Yield : 90%

$R_f$ value : 0.7, Chloroform: Methanol (09:01)

IR (KBr, $cm^{-1}$) : 3377, 2959, 1654, 1412, 1210, 896

Mass (m/z) : 417.25 $[M+H]^+$

$^1$HNMR (DMSO, δ) : 11.58 (s, 1H), 9.56 (s, 1H), 8.86-8.87 (d, 1H), 8.64-8.66 (d, 1H), 8.24-8.26 (s, 1H), 7.54-7.56 (q, 1H), 7.24-7.26 (d, 1H), 7.13-7.19 (m, 3H), 6.90-7.02 (d, 1H), 4.65 (s, 2H), 4.28-4.33 (d, 2H), 4.05 (s, 2H), 2.31-2.32 (s, 3H), 1.19-2.03 (s, 3H)

**5.1.1.29. 2-(4-((8-hydroxyquinolin-5-yl)methyl)-5-methyl-3-oxo-2,3-dihydro-1*H*-pyrazol-1-yl)-*N*-(4-methoxybenzyl)acetamide (93)**

In 25ml of single-neck RBF, 4-((8-hydroxyquinolin-5-yl)methyl)-5-methyl-1*H*-pyrazol-3(2*H*)-one (0.5 gm, 1.958 mM) and potassium carbonate (0.324 gm, 2.347 mM) was added in DMF and stirred for 15 min at R.T. 2-Chloro-*N*-(4-methoxybenzyl)acetamide (0.418 gm, 1.957 mM) was added in reaction mixture and heated at 80ºC for 12hrs. Reaction mixture was monitored by TLC. After completion of reaction, crushed ice was added extracted with chloroform, dried over $Na_2SO_4$ and the solvent was evaporated with which offered brown solid. Further purification was done by column chromatography to offered colourless compound.

Anal:

Melting Point : 188-192ºC

Yield : 80%

$R_f$ value : 0.8, Chloroform: Methanol (09:01)

IR (KBr, $cm^{-1}$) : 3279, 2959, 1658, 1462, 1274, 783

Mass (m/z) : 433.23 $[M+H]^+$

$^1$HNMR (DMSO, δ) : 11.54 (s, 1H), 9.54 (s, 1H), 8.82-8.83 (d, 1H), 8.18-8.21 (t, 1H), 7.60-7.70 (m, 1H), 7.49-7.52 (q, 1H), 6.84-7.22 (m, 5H), 4.25-4.26 (d, 2H), 4.59 (s, 2H), 4.10-4.15 (q, 2H), 4.00 (s, 2H), 3.73 (s, 3H), 1.95 (s, 3H).

**5.1.1.30. *N*-(4-Chlorobenzyl)-2-(4-((8-hydroxyquinolin-5-yl)methyl)-5-methyl-3-oxo-2,3-dihydro-1*H*-pyrazol-1-yl)acetamide (94)**

In 25ml of single-neck RBF, 4-((8-hydroxyquinolin-5-yl)methyl)-5-methyl-1*H*-pyrazol-3(2*H*)-one (0.5 gm, 1.958 mM) and potassium carbonate (0.324 gm, 2.347 mM) was added in DMF and stirred for 15 min at R.T. 2-Chloro-*N*-(4-chlorobenzyl)acetamide (0.495 gm, 1.859 mM) was added in reaction mixture and heated at 80ºC for 12hrs. Reaction mixture was monitored by TLC. After completion of reaction, crushed ice was added extracted with chloroform, dried over $Na_2SO_4$ and the solvent was evaporated which offered brown solid. Further purification was done by column chromatography to offered colourless compound.

Anal:

| | |
|---|---|
| Melting Point | : 196-198ºC |
| Yield | : 74% |
| $R_f$ value | : 0.62, Chloroform: Methanol (09:01) |
| IR (KBr, $cm^{-1}$) | : 3274, 2959, 1662, 1492 and 854 |

**5.1.1.31. *N*-(4-Fluorobenzyl)-2-(4-((8-hydroxyquinolin-5-yl)methyl)-5-methyl-3-oxo-2,3-dihydro-1*H*-pyrazol-1-yl)acetamide (95)**

In 25ml of single-neck RBF, 4-((8-hydroxyquinolin-5-yl)methyl)-5-methyl-1*H*-pyrazol-3(2*H*)-one (0.5 gm, 1.958 mM) and potassium carbonate (0.324 gm, 2.347 mM) was added in DMF and stirred for 15 min at R.T. 2-Chloro-*N*-(4-fluorobenzyl)acetamide (0.395 gm, 1.959 mM) was added in reaction mixture and heated at 80ºC for 12hrs. Reaction mixture was monitored by TLC. After completion of reaction, crushed ice was added extracted with chloroform, dried over $Na_2SO_4$ and the solvent was evaporated which offered brown solid. Further purification was done by column chromatography to offered colourless compound.

Anal:

| | |
|---|---|
| Melting Point | : 192-194ºC |
| Yield | : 80% |
| $R_f$ value | : 0.65, Chloroform: Methanol (09:01) |
| IR (KBr, $cm^{-1}$) | : 3358, 3305, 2924, 1638, 1487, 1281, 1113, 886 |
| Mass (m/z) | : 421.22 $[M+H]^+$ |
| $^1$HNMR (DMSO, δ) | : 11.59 (s, 1H), 9.57 (s, 1H), 8.86-8.89 (d, 1H), 8.64-8.67 (d, 1H), 8.32-8.34 (t, 1H), 7.75-7.77 (m, 1H), 7.70-7.72 (q, 1H), 7.54-7.56 (t, 1H), 7.19-7.24 (d, 1H), 7.13-7.18 (t, 1H), 7.02-7.12 (d, |

1H), 4.66 (d, 2H), 4.30-4.36 (d, 2H), 4.17-4.19 (t, 1H), 3.90-4.05 (s, 2H), 1.19-2.02 (s, 3H).

**5.1.1.32. Ethyl 2-(8-hydroxyquinolin-5-yl)methyl)-3-oxo-3-phenylpropanoate (96)**

In a 25ml two neck RBF containing 3ml of *n*-Hexane in sodium hydride was carefully added and resulting solution was kept aside for 5 min. Solvent carefully decanted in a beaker containing methanol and sodium hydride mass slowly flushed with stream of nitrogen. Anh. DMF added to the RBF followed by addition of benzyl acetoacetate and stirred for 10min. 5-(Chloromethyl)quinolin-8-ol hydrochloride was added in the reaction mixture at R.T. The progress of the reaction mixture was monitored by the TLC. After completion of the reaction, crushed ice added into the solution and extracted with chloroform and dried over $Na_2SO_4$ and solvent evaporated with rotary evaporator which offered brown solid.

Anal:

| | |
|---|---|
| Melting Point | : 76-80ºC |
| Yield | : 80% |
| $R_f$ value | : 0.55, *n*-Hexane:Ethylacetate (12:08) |
| IR (KBr, $cm^{-1}$) | : 3334, 2970, 1734, 1687, 1276 and 840 |
| Mass (m/z) | : 350.59 $[M+H]^+$ |
| $^1$HNMR (DMSO, δ) | : 9.63 (s, 1H), 8.84-8.85 (d, 1H), 8.55-8.58 (d, 1H), 7.86-7.88 (d, 2H), 7.57-7.63 (m, 2H), 7.45-7.49 (t, 2H), 7.27-7.29 (s, 1H), 6.94-6.96 (d, 1H), 4.96-4.99 (t,- 1H), 3.88-3.96 (m, 2H), 3.51-3.60 (t, 2H), 0.89-0.92 (t, 3H). |

**5.1.1.33. Ethyl 2-(8-hydroxyquinolin-5-yl)methyl)-3-oxo-3-phenylpropanoate (97)**

In a 25ml RBF, Ethyl 2-((8-hydroxyquinolin-5-yl)methyl)-3-oxo-3-phenylpropanoate and hydrazine hydrate was dissolved in ethanol at R.T. The reaction mixture was shifted on oil bath and refluxed for overnight. The progress of the reaction mixture was monitored by the TLC. After completion of the reaction excess amount of ethanol was evaporated with the aid of rotary evaporator. Crushed ice was added into the solution which offered colourless solid.

Anal:

| | |
|---|---|
| Melting Point | : 212-215ºC |
| Yield | : 60% |
| $R_f$ value | : 0.4, *n*-Hexane:Ethylacetate (12:08) |

IR (KBr, $cm^{-1}$) : 3324, 2959, 2359, 1198, 1679 and 833

Mass (m/z) : 318.50 $[M+H]^+$

$^1$HNMR (DMSO, δ) : 11.57 (s, 1H), 9.52 (s, 1H), 8.85-8.87(s, 1H), 8.56-8.58 (d, 1H),7.54-7.57 (q, 1H), 7.39-7.41 (t, 2H), 7.31-7.34 (t, 2H), 7.27-7.29 (t, 1H), 6.99-7.00 (d, 1H), 6.93-6.94 (d, 1H), 3.18 (s, 2H)

**5.1.1.34. 2-(2,6-Difluorobenzyl)-1,2-dihydro-4-((8-hydroxyquinolin-5-yl) methyl)-3-phenylpyrazol-5-one (98)**

In 25ml of single-neck RBF, 1,2-dihydro-4-((8-hydroxyquinolin-5-yl) methyl)-3-phenylpyrazol-5-one (0.6 gm, 1.89 mM) and potassium carbonate (0.31 gm, 2.27 mM) was added in DMF and stirred for 15 min at R.T. 2-(Bromomethyl)-1,3-difluorobenzene (0.47 gm, 2.22 mM) was added in reaction mixture and allowed to stir for 1hrs. Reaction mixture was monitored by TLC. After completion of reaction, crushed ice was added extracted with chloroform, dried over $Na_2SO_4$ and the solvent was evaporated which offered brown solid. Further purification was done by column chromatography to offered white colour compound.
Anal:

Melting Point : 165-167°C

Yield : 65%

$R_f$ value : 0.56, *n*-Hexane: Ethyl acetate, (10:10)

IR (KBr, $cm^{-1}$) : 3291, 2998, 2919, 1628 and 1212

Mass (m/z) : 444.2 $[M+H]^+$

$^1$HNMR (DMSO, δ) : 12.35 (s, 1H), 9.54 (s, 1H), 8.83 (dd, *J* = 4.2, 1.5 Hz, 1H), 8.47 (dd, *J* = 8.6, 1.6 Hz, 1H), 7.49 – 7.45 (m, 2H), 7.40 – 7.31 (m, 5H), 7.11 (t, *J* = 8.1 Hz, 2H), 6.91 (d, *J* = 8.0 Hz, 1H), 6.85 (d, *J* = 7.9 Hz, 1H), 5.28 (s, 2H), 4.06 (s, 2H).

**5.1.1.35. 2-Benzyl-1,2-dihydro-4-((8-hydroxyquinolin-5-yl) methyl)-3-phenylpyrazol-5-one (99)**

In 25ml of single-neck RBF, 1,2-dihydro-4-((8-hydroxyquinolin-5-yl) methyl)-3-phenylpyrazol-5-one (0.6 gm, 1.89 mM) and potassium carbonate (0.31 gm, 2.24 mM) was added in DMF and stirred for 15 min at R.T. 1-(Bromomethyl) benzene (0.38 gm, 2.22 mM) was added in reaction mixture and allowed to stir for 1hrs. Reaction mixture was monitored by TLC. After completion of reaction, crushed ice was added extracted with chloroform, dried

over $Na_2SO_4$ and the solvent was evaporated which offered brown solid. Further purification was done by column chromatography to offered white colour compound.

Anal:

| | |
|---|---|
| Melting Point | : 178-181°C |
| Yield | : 63% |
| $R_f$ value | : 0.55, *n*-Hexane: Ethyl acetate, (10:10) |
| IR (KBr, $cm^{-1}$) | : 3330, 3146, 2912, 1703 and 1222 |
| Mass (m/z) | : 408.3 $[M+H]^+$ |
| $^1$HNMR (DMSO, δ) | : 12.26 (s, 1H), 9.57 (s, 1H), 8.85 (d, *J* = 5.7 Hz, 1H), 8.51 (d, *J* = 10.3 Hz, 1H), 7.51 (dd, *J* = 8.6, 4.1 Hz, 1H), 7.43 – 7.26 (m, 10H), 6.99 (d, *J* = 8.0 Hz, 1H), 6.92 (s, 1H), 5.23 (s, 2H), 4.15 (s, 2H). |

### 5.1.1.36. 2-(3-Fluorobenzyl)-1,2-dihydro-4-((8-hydroxyquinolin-5-yl) methyl)-3-phenyl pyrazol-5-one (100)

In 25ml of single-neck RBF, 1,2-dihydro-4-((8-hydroxyquinolin-5-yl) methyl)-3-phenylpyrazol-5-one (0.6 gm, 1.89 mM) and potassium carbonate (0.31 gm, 2.27 mM) was added in DMF and stirred for 15 min at R.T. 1-(Bromomethyl)-3-fluorobenzene (0.43 gm, 2.26 mM) was added in reaction mixture and allowed to stir for 1hrs. Reaction mixture was monitored by TLC. After completion of reaction, crushed ice was added extracted with chloroform, dried over $Na_2SO_4$ and the solvent was evaporated which offered brown solid. Further purification was done by column chromatography to offered white colour compound.

Anal:

| | |
|---|---|
| Melting Point | : 182-185°C |
| Yield | : 65% |
| $R_f$ value | : 0.55, *n*-Hexane: Ethyl acetate, (10:10) |
| IR (KBr, $cm^{-1}$) | : 3330, 2951, 2916, 1704 and 1223 |
| Mass (m/z) | : 426.72 $[M+H]^+$ |

### 5.1.1.37. 2-(2-(Trifluoromethyl) benzyl)-1,2-dihydro-4-((8-hydroxyquinolin-5-yl)methyl) -3-phenylpyrazol-5-one (101)

In 25ml of single-neck RBF, 1,2-dihydro-4-((8-hydroxyquinolin-5-yl) methyl)-3-phenyl pyrazol-5-one (0.6 gm, 1.89 mM) and potassium carbonate (0.31 gm, 2.27 mM) was added in DMF and stirred for 15 min at R.T. 1-(Bromomethyl)-2-(trifluoromethyl) benzene (0.54 gm, 2.25 mM) was added in reaction mixture and allowed to stir for 1hrs. Reaction mixture was monitored by TLC. After completion of reaction, crushed ice was added extracted with chloroform, dried over $Na_2SO_4$ and the solvent was evaporated which offered brown solid. Further purification was done by column chromatography to offered white colour compound.
Anal:

| | |
|---|---|
| Melting Point | : 149-152°C |
| Yield | : 62% |
| $R_f$ value | : 0.56, *n*-Hexane: Ethyl acetate, (10:10) |
| IR (KBr, $cm^{-1}$) | : 3329, 3015, 2912, 1725 and 1221 |
| Mass (m/z) | : 476.2 $[M+H]^+$ |
| $^1$HNMR (DMSO, δ) | : 12.31 (s, 1H), 9.58 (s, 1H), 8.85 (dd, *J* = 4.2, 1.5 Hz, 1H), 8.50 (dd, *J* = 8.6, 1.6 Hz, 1H), 7.72 (d, *J* = 7.9 Hz, 1H), 7.59 – 7.33 (m, 9H), 7.02 (d, *J* = 7.9 Hz, 1H), 6.94 (d, *J* = 7.9 Hz, 1H), 5.40 (s, 2H), 4.18 (s, 2H). |

**5.1.1.38. 2-(4-Nitrobenzyl)-1,2-dihydro-4-((8-hydroxyquinolin-5-yl) methyl)-3-phenyl pyrazol-5-one (102)**

In 25ml of single-neck RBF, 1,2-dihydro-4-((8-hydroxyquinolin-5-yl) methyl)-3-phenylpyrazol-5-one (0.6 gm, 1.89 mM) and potassium carbonate (0.31 gm, 2.24 mM) was added in DMF and stirred for 15 min at R.T. 1-(Bromomethyl)-4-nitrobenzene (0.49 gm, 2.26 mM) was added in reaction mixture and allowed to stir for 1hrs. Reaction mixture was monitored by TLC. After completion of reaction, crushed ice was added extracted with chloroform, dried over $Na_2SO_4$ and the solvent was evaporated which offered brown solid. Further purification was done by column chromatography to offered white colour compound.
Anal:

| | |
|---|---|
| Melting Point | : 149-152°C |
| Yield | : 62% |
| $R_f$ value | : 0.56, *n*-Hexane: Ethyl acetate, (10:10) |
| IR (KBr, $cm^{-1}$) | : 3305, 2944, 2904, 1708, and 1225 |

Mass (m/z) : 453.2 $[M+H]^+$

$^1$HNMR (DMSO, δ) : 12.30 (s, 1H), 9.60 (s, 1H), 8.86 (dd, *J* = 4.1, 1.5 Hz, 1H), 8.50 (dd, *J* = 8.7, 1.6 Hz, 1H), 7.57 – 7.47 (m, 5H), 7.41 (ddd, *J* = 8.2, 7.1, 5.5 Hz, 4H), 7.02 (d, *J* = 7.9 Hz, 1H), 6.96 (d, *J* = 7.9 Hz, 1H), 5.37 (s, 2H), 4.19 (s, 2H).

**5.1.1.39. 2-(3-Methoxybenzyl)-1,2-dihydro-4-((8-hydroxyquinolin-5-yl) methyl)-3-phenyl pyrazol-5-one (103)**

In 25ml of single-neck RBF, 1,2-dihydro-4-((8-hydroxyquinolin-5-yl) methyl)-3-phenylpyrazol-5-one (0.6 gm, 1.89 mM) and potassium carbonate (0.31 gm, 1.89 mM) was added in DMF and stirred for 15 min at R.T. 1-(Bromomethyl)-3-methoxybenzene (0.45 gm, 1.89 mM) was added in reaction mixture and allowed to stir for 1hrs. Reaction mixture was monitored by TLC. After completion of reaction, crushed ice was added extracted with chloroform, dried over $Na_2SO_4$ and the solvent was evaporated which offered brown solid. Further purification was done by column chromatography to offered white colour compound.

Anal:

Melting Point : 166-169°C

Yield : 62%

$R_f$ value : 0.55, *n*-Hexane: Ethyl acetate, (10:10)

IR (KBr, $cm^{-1}$) : 3351, 3002, 2962, 1704 and 1222

Mass (m/z) : 438.3 $[M+H]^+$

$^1$HNMR (DMSO, δ) : 12.26 (s, 1H), 9.56 (s, 1H), 8.85 (dd, *J* = 4.2, 1.5 Hz, 1H), 8.53 (dd, *J* = 8.6, 1.6 Hz, 1H), 7.51 (dd, *J* = 8.6, 4.1 Hz, 1H), 7.43 – 7.32 (m, 6H), 7.24 – 7.16 (m, 2H), 7.00 – 6.97 (m, 1H), 6.91 (d, *J* = 7.9 Hz, 1H), 6.83 (dd, *J* = 8.2, 2.6 Hz, 1H), 5.20 (s, 2H), 4.15 (s, 2H), 3.66 (s, 3H).

**5.1.1.40. 2-(4-Fluorobenzyl)-1,2-dihydro-4-((8-hydroxyquinolin-5-yl) methyl)-3-phenyl pyrazol-5-one (104)**

In 25ml of single-neck RBF, 1,2-dihydro-4-((8-hydroxyquinolin-5-yl) methyl)-3-phenylpyrazol-5-one (0.6 gm, 1.89 mM) and potassium carbonate (0.31 gm, 2.27 mM) was added in DMF and stirred for 15 min at R.T. 1-(Bromomethyl)-4-fluorobenzene (0.43 gm, 2.26 mM) was added in reaction mixture and allowed to stir for 1hrs. Reaction mixture was

monitored by TLC. After completion of reaction, crushed ice was added extracted with chloroform, dried over $Na_2SO_4$ and the solvent was evaporated which offered brown solid. Further purification was done by column chromatography to offered white colour compound.
Anal:

| | |
|---|---|
| Melting Point | : 197-200°C |
| Yield | : 64% |
| $R_f$ value | : 0.55, *n*-Hexane: Ethyl acetate, (10:10) |
| IR (KBr, $cm^{-1}$) | : 3186, 2890, 2832, 1598 and 1224 |
| Mass (m/z) | : 426.17 $[M+H]^+$ |
| $^1$HNMR (DMSO, δ) | : 9.50 (s, 1H), 8.81 (dd, *J* = 4.2, 1.5 Hz, 1H), 8.35 (dd, *J* = 8.6, 1.6 Hz, 1H), 7.47 (dd, *J* = 8.6, 4.1 Hz, 1H), 7.39 – 7.33 (m, 5H), 7.22 – 7.18 (m, 2H), 7.03 – 6.98 (m, 2H), 6.92 – 6.86 (m, 2H), 4.97 (s, 2H), 3.91 (s, 2H). |

**5.1.1.41. 2-(4-Methylbenzyl)-1,2-dihydro-4-((8-hydroxyquinolin-5-yl) methyl)-3-phenyl pyrazol-5-one (105)**

In 25ml of single-neck RBF, 1,2-dihydro-4-((8-hydroxyquinolin-5-yl) methyl)-3-phenylpyrazol-5-one (0.6 gm, 1.89 mM) and potassium carbonate (0.31 gm, 2.27 mM) was added in DMF and stirred for 15 min at R.T. 1-(Bromomethyl)-4-methylbenzene (0.42 gm, 2.26 mM) was added in reaction mixture and allowed to stir for 1hrs. Reaction mixture was monitored by TLC. After completion of reaction, crushed ice was added extracted with chloroform, dried over $Na_2SO_4$ and the solvent was evaporated which offered brown solid. Further purification was done by column chromatography to offered white colour compound.
Anal:

| | |
|---|---|
| Melting Point | : 190-192°C |
| Yield | : 65% |
| $R_f$ value | : 0.53, *n*-Hexane: Ethyl acetate, (10:10) |
| IR (KBr, $cm^{-1}$) | : 3325, 2945, 2914, 1642 and 1223 |
| Mass (m/z) | : 422.99 $[M+H]^+$ |
| $^1$HNMR (DMSO, δ) | : 12.24 (s, 1H), 9.56 (s, 1H), 8.85 (dd, *J* = 4.1, 1.6 Hz, 1H), 8.51 (dd, *J* = 8.6, 1.6 Hz, 1H), 7.51 (dd, *J* = 8.6, 4.2 Hz, 1H), 7.43 – 7.29 (m, 5H), 7.20 (d, *J* = 8.1 Hz, 2H), 7.11 (d, *J* = 7.9 Hz, 2H), |

6.97 (d, *J* = 7.9 Hz, 1H), 6.91 (d, *J* = 7.9 Hz, 1H), 5.17 (s, 2H), 4.13 (s, 2H), 2.27 (s, 3H).

**5.1.1.42. 2-(3-Chlorobenzyl)-1,2-dihydro-4-((8-hydroxyquinolin-5-yl) methyl)-3-phenyl pyrazol-5-one (106)**

In 25ml of single-neck RBF, 1,2-dihydro-4-((8-hydroxyquinolin-5-yl) methyl)-3-phenylpyrazol-5-one (0.6 gm, 1.89 mM) and potassium carbonate (0.31 gm, 2.27 mM) was added in DMF and stirred for 15 min at R.T. 1-(Bromomethyl)-3-chlorobenzene (0.46 gm, 2.23 mM) was added in reaction mixture and allowed to stir for 1hrs. Reaction mixture was monitored by TLC. After completion of reaction, crushed ice was added extracted with chloroform, dried over $Na_2SO_4$ and the solvent was evaporated which offered brown solid. Further purification was done by column chromatography to offered white colour compound.
Anal:

| | |
|---|---|
| Melting Point | : 185-189℃ |
| Yield | : 68% |
| $R_f$ value | : 0.52, *n*-Hexane: Ethyl acetate, (10:10) |
| IR (KBr, $cm^{-1}$) | : 3233, 2890, 2840, 1577 and 1221 |
| Mass (m/z) | : 442.2 $[M+H]^+$, 444.2 $[M+2]^+$ |
| $^1$HNMR (DMSO, δ) | : 12.28 (s, 1H), 9.56 (s, 1H), 8.85 (dd, *J* = 4.2, 1.5 Hz, 1H), 8.51 (dd, *J* = 8.6, 1.6 Hz, 1H), 7.51 (dd, *J* = 8.6, 4.2 Hz, 1H), 7.44 – 7.32 (m, 8H), 7.28 – 7.23 (m, 1H), 6.99 (d, *J* = 7.9 Hz, 1H), 6.92 (d, *J* = 7.9 Hz, 1H), 5.23 (s, 2H), 4.16 (s, 2H). |

**5.1.1.43. 2-(4-Chlorobenzyl)-1,2-dihydro-4-((8-hydroxyquinolin-5-yl) methyl)-3-phenyl pyrazol-5-one (107)**

In 25ml of single-neck RBF, 1,2-dihydro-4-((8-hydroxyquinolin-5-yl) methyl)-3-phenylpyrazol-5-one (0.6 gm, 1.89 mM) and potassium carbonate (0.31 gm, 2.27 mM) was added in DMF and stirred for 15 min at R.T. 1-(Bromomethyl)-4-chlorobenzene (0.46 gm, 2.23 mM) was added in reaction mixture and allowed to stir for 1hrs. Reaction mixture was monitored by TLC. After completion of reaction, crushed ice was added extracted with chloroform, dried over $Na_2SO_4$ and the solvent was evaporated which offered brown solid. Further purification was done by column chromatography to offered white colour compound.
Anal:

Melting Point : 175-178℃

Yield : 69%

$R_f$ value : 0.58, *n*-Hexane: Ethyl acetate, (10:10)

IR (KBr, $cm^{-1}$) : 3307, 2944, 2911, 1675 and 1222

Mass (m/z) : 442.2 $[M+H]^+$, 444.2 $[M+2]^+$

$^1$HNMR (DMSO, δ) : 12.27 (s, 1H), 9.58 (s, 1H), 8.85 (dd, *J* = 4.1, 1.6 Hz, 1H), 8.50 (dd, *J* = 8.6, 1.6 Hz, 1H), 7.51 (dd, *J* = 8.6, 4.2 Hz, 1H), 7.45 – 7.27 (m, 9H), 6.98 (d, *J* = 8.0 Hz, 1H), 6.93 (d, *J* = 7.9 Hz, 1H), 5.21 (s, 2H), 4.15 (s, 2H).

### 5.1.1.44. 2-(3,5-Dimethylbenzyl)-1,2-dihydro-4-((8-hydroxyquinolin-5-yl)methyl)-3-phenylpyrazol-5-one (108)

In 25ml of single-neck RBF, 1,2-dihydro-4-((8-hydroxyquinolin-5-yl) methyl)-3-phenylpyrazol-5-one (0.6 gm, 1.89 mM) and potassium carbonate (0.31 gm, 2.27 mM) was added in DMF and stirred for 15 min at R.T. 1-(Bromomethyl)-3,5-dimethylbenzene (0.45 gm, 2.26 mM) was added in reaction mixture and allowed to stir for 1hrs. Reaction mixture was monitored by TLC. After completion of reaction, crushed ice was added extracted with chloroform, dried over $Na_2SO_4$ and the solvent was evaporated which offered brown solid. Further purification was done by column chromatography to offered white colour compound.
Anal:

Melting Point : 209-211℃

Yield : 63%

$R_f$ value : 0.55, *n*-Hexane: Ethyl acetate, (10:10)

IR (KBr, $cm^{-1}$) : 3291, 2998, 2919, 1628 and 1212

Mass (m/z) : 436.28 $[M+H]^+$

$^1$HNMR (DMSO, δ) : 12.24 (s, 1H), 9.57 (s, 1H), 8.85 (dd, *J* = 4.2, 1.5 Hz, 1H), 8.51 (dd, *J* = 8.6, 1.6 Hz, 1H), 7.51 (dd, *J* = 8.6, 4.2 Hz, 1H), 7.44 – 7.31 (m, 6H), 6.99 (d, *J* = 8.0 Hz, 1H), 6.92 (d, *J* = 7.9 Hz, 1H), 6.87 (s, 2H), 5.13 (s, 2H), 4.14 (s, 2H), 2.19 (s, 6H).

### 5.1.1.45. 2-(2-Fluorobenzoyl)-1,2-dihydro-4-((8-hydroxyquinolin-5-yl)methyl)-3-phenylpyrazol-5-one (109)

In 25ml of single-neck RBF, 1,2-dihydro-4-((8-hydroxyquinolin-5-yl) methyl)-3-phenylpyrazol-5-one (0.6 gm, 1.89 mM) and potassium carbonate (0.31 gm, 2.27 mM) was added in DMF and stirred for 15 min at R.T. 2-Fluorobenzoyl bromide (0.46 gm, 2.26 mM) was added in reaction mixture and allowed to stir for 1hrs. Reaction mixture was monitored by TLC. After completion of reaction, crushed ice was added extracted with chloroform, dried over $Na_2SO_4$ and the solvent was evaporated which offered brown solid. Further purification was done by column chromatography to offered white colour compound.

Anal:

| | |
|---|---|
| Melting Point | : 192-194°C |
| Yield | : 65% |
| $R_f$ value | : 0.55, *n*-Hexane: Ethyl acetate, (10:10) |
| IR (KBr, $cm^{-1}$) | : 3291, 2958, 2924, 1728 and 1072 |
| Mass (m/z) | : 440.2 $[M+H]^+$ |
| $^1$HNMR (DMSO, δ) | : 9.54 (s, 1H), 8.87 (dd, *J* = 4.2, 1.5 Hz, 1H), 8.58 (dd, *J* = 8.6, 1.6 Hz, 1H), 7.57 (dd, *J* = 8.6, 4.1 Hz, 1H), 7.48 – 7.25 (m, 9H), 6.98 (d, *J* = 8.0 Hz, 1H), 6.92 (d, *J* = 7.9 Hz, 1H), 4.12 (s, 2H). |

### 5.1.1.46 Phenyl 4-((8-hydroxyquinolin-5-yl)methyl)-5-oxo-3-phenyl-1*H*-pyrazole-2(5*H*)-carboxylate (110)

In 25ml of single-neck RBF, 1,2-dihydro-4-((8-hydroxyquinolin-5-yl)methyl)-3-phenylpyrazol-5-one (1 gm, 3.1 mM) and potassium carbonate (0.65 gm, 4.7 mM) was added in DMF and stirred for 15 min at R.T. Phenyl chloroformate (0.79 ml, 6.3 mM) was added in reaction mixture and stirred for 1 hr. Reaction mixture was monitored by TLC. After completion of reaction, crushed ice was added to get the desired product. Further purification was done by column chromatography to offered white colour compound.

Anal:

| | |
|---|---|
| Melting Point | : 213-215°C |
| Yield | : 64% |
| $R_f$ value | : 0.82, Chloroform: Methanol (09:01) |
| IR (KBr, $cm^{-1}$) | : 3287, 3020, 2873, 1760, 1661 and 1213 |

$^1$HNMR (DMSO, δ) : 9.53 (s, 1H), 8.86 (dd, *J* = 4.2, 1.6 Hz, 1H), 8.57 (dd, *J* = 8.6, 1.7 Hz, 1H), 7.57 (dd, *J* = 8.6, 4.1 Hz, 1H), 7.40 – 7.28 (m, 10H), 6.97 (d, *J* = 7.9 Hz, 1H), 6.92 (d, *J* = 7.9 Hz, 1H), 4.12 (s, 2H).

### 5.1.1.47. Methyl 4-((8-hydroxyquinolin-5-yl)methyl)-5-oxo-3-phenyl-1*H*-pyrazole-2(5*H*)-carboxylate (111)

In 25ml of single-neck RBF, 1,2-dihydro-4-((8-hydroxyquinolin-5-yl) methyl)-3-phenylpyrazol-5-one (1 gm, 3.1 mM) and potassium carbonate (0.65 gm, 4.7 mM) was added in DMF and stirred for 15 min at R.T. Methyl chloroformate (0.79 ml, 6.3 mM) was added in reaction mixture and stirred for 1 hr. Reaction mixture was monitored by TLC. After completion of reaction, crushed ice was added to get the desired product. Further purification was done by column chromatography to offered white colour compound.

Anal:

Melting Point : 206-209°C

Yield : 70%

$R_f$ value : 0.86, Chloroform: Methanol (09:01)

IR (KBr, $cm^{-1}$) : 3210, 2923, 1730, 1654, 890

$^1$HNMR (DMSO, δ) : 9.57 (s, 1H), 8.81 (dd, *J* = 4.1, 1.8 Hz, 1H), 8.31 (dd, *J* = 39.0, 1.7 Hz, 1H), 7.49 – 7.31 (m, 6H), 6.90 (dd, *J* = 10.5, 2.5 Hz, 2H), 3.89 (s, 2H), 3.70 (s, 3H).

### 5.1.1.48. Benzyl 4-((8-hydroxyquinolin-5-yl)methyl)-5-oxo-3-phenyl-1*H*-pyrazole-2(5*H*)-carboxylate (112)

In 25ml of single-neck RBF, 1,2-dihydro-4-((8-hydroxyquinolin-5-yl)methyl)-3-phenylpyrazol-5-one (1 gm, 3.1 mM) and potassium carbonate (0.65 gm, 4.7 mM) was added in DMF and stirred for 15 min at R.T. Benzyl chloroformate (0.86 ml, 6.3 mM) was added in reaction mixture and stirred for 1 hr. Reaction mixture was monitored by TLC. After completion of reaction, crushed ice was added to get the desired product. Further purification was done by column chromatography to offered white colour compound.

Anal:

Melting Point : 226-229°C

Yield : 65%

$R_f$ value : 0.85, Chloroform: Methanol (09:01)

IR (KBr, $cm^{-1}$) : 3327, 2965, 2917, 1753, 1623 and 1220

$^1$HNMR (DMSO, δ) : δ 11.30 (s, 1H), 9.56 (s, 1H), 8.84 (dd, *J* = 4.1, 1.7 Hz, 1H), 8.36 (dd, *J* = 8.6, 1.7 Hz, 1H), 7.52 (dd, *J* = 8.6, 4.2 Hz, 1H), 7.39 – 7.29 (m, 10H), 6.94 (d, *J* = 7.8 Hz, 1H), 6.88 (d, *J* = 3.4 Hz, 1H), 5.17 (s, 2H), 3.82 (s, 2H).

### 5.1.1.49. Pentyl 4-((8-hydroxyquinolin-5-yl)methyl)-5-oxo-3-phenyl-1H-pyrazole-2(5H)-carboxylate (113)

In 25ml of single-neck RBF, 1,2-dihydro-4-((8-hydroxyquinolin-5-yl)methyl)-3-phenylpyrazol-5-one (1 gm, 3.1 mM) and potassium carbonate (0.65 gm, 4.7 mM) was added in DMF and stirred for 15 min at R.T. *N*-Pentyl chloroformate was added in reaction mixture and stirred for 1 hr. Reaction mixture was monitored by TLC. After completion of reaction, crushed ice was added to get the desired product. Further purification was done by column chromatography to offered white colour compound.

Anal:

Melting Point : 217-220℃

Yield : 68%

$R_f$ value : 0.95, Chloroform: Methanol (09:01)

IR (KBr, $cm^{-1}$) : 3321, 2934, 1780, 1210, 890

### 5.1.1.50. 2,2,2-Trichloroethyl4-((8-hydroxyquinolin-5-yl)methyl)-5-oxo-3-phenyl-1H-pyrazole-2(5*H*)-carboxylate (114)

In 25ml of single-neck RBF, 1,2-dihydro-4-((8-hydroxyquinolin-5-yl)methyl)-3-phenylpyrazol-5-one and potassium carbonate was added in DMF and stirred for 15 min at R.T. 2,2,2-Trichloroethyl chloroformate was added in reaction mixture and stirred for 1 hr. Reaction mixture was monitored by TLC. After completion of reaction, crushed ice was added to get the desired product. Further purification was done by column chromatography to offered white colour compound.

Anal:

Melting Point : 210-212℃

Yield : 70%

$R_f$ value : 0.80, Chloroform: Methanol (09:01)

IR (KBr, $cm^{-1}$) : 3290, 2943, 1768, 1654 and 1129

### 5.1.1.51. (9*H*-Fluoren-9-yl) methyl 4-((8-hydroxyquinolin-5-yl) methyl)-3-methyl-5-oxo-1*H*-pyrazole-2(5*H*)-carboxylate (115)

In 25ml of single-neck RBF, 1,2-dihydro-4-((8-hydroxyquinolin-5-yl)methyl)-3-phenylpyrazol-5-one and potassium carbonate was added in DMF and stirred for 15 min at R.T. (9*H*-Fluoren-9-yl)methyl chloroformate was added in reaction mixture and stirred for 1 hr. Reaction mixture was monitored by TLC. After completion of reaction, crushed ice was added to get the desired product. Further purification was done by column chromatography to offered white colour compound.

Anal:

Melting Point : >250 ℃

Yield : 65%

$R_f$ value : 0.80, Chloroform: Methanol (09:01)

IR (KBr, $cm^{-1}$) : 3317, 2976, 1732, 1636 and 1224

### 5.1.1.52. Ethyl4-((8-hydroxyquinolin-5-yl)methyl)-5-oxo-3-phenyl-1*H*-pyrazole-2(5*H*)-carboxylate (116)

In 25ml of single-neck RBF, 1,2-dihydro-4-((8-hydroxyquinolin-5-yl)methyl)-3-phenylpyrazol-5-one (1 gm, 3.1 mM) and potassium carbonate (0.65 gm, 4.7 mM) was added in DMF and stirred for 15 min at R.T. Ethyl chloroformate (0.60 ml, 6.3 mM) was added in reaction mixture and stirred for 1 hr. Reaction mixture was monitored by TLC. After completion of reaction, crushed ice was added to get the desired product. Further purification was done by column chromatography to offered white colour compound.

Anal:

Melting Point : >250 ℃

Yield : 62%

$R_f$ value : 0.85, Chloroform: Methanol (09:01)

IR (KBr, $cm^{-1}$) : 3321, 3029, 2888, 1745, 1663, 1223

Mass (m/z) **:** 390.98 $[M+H]^+$

### 5.1.1.53. Isobutyl 4-((8-hydroxyquinolin-5-yl)methyl)-5-oxo-3-phenyl-1*H*-pyrazole-2(5*H*)-carboxylate (117)

In 25ml of single-neck RBF, 1,2-dihydro-4-((8-hydroxyquinolin-5-yl)methyl)-3-phenylpyrazol-5-one (1 gm, 3.1 mM) and potassium carbonate (0.65 gm, 4.7 mM) was added

in DMF and stirred for 15 min at R.T. Ethyl chloroformate (0.60 ml, 6.3 mM) was added in reaction mixture and stirred for 1 hr. Reaction mixture was monitored by TLC. After completion of reaction, crushed ice was added to get the desired product. Further purification was done by column chromatography to offered white colour compound.

Anal:

| | |
|---|---|
| Melting Point | : >250 ℃ |
| Yield | : 65% |
| $R_f$ value | : 0.85, Chloroform: Methanol (09:01) |
| IR (KBr, $cm^{-1}$) | : 3331, 2987, 1756, 1635 and 1176 |

**5.1.1.54. *N*-(4-Fluorobenzyl)-2-(4-((8-hydroxyquinolin-5-yl)methyl)-3-oxo-5-phenyl-2,3-dihydro-1*H*-pyrazol-1-yl)acetamide (118)**

In 25ml of single-neck RBF, 4-((8-hydroxyquinolin-5-yl)methyl)-5-phenyl-1*H*-pyrazol-3(2*H*)-one (0.5 gm, 1.577 mM ) and potassium carbonate (0.324 gm, 2.34 mM) was added in DMF and stirred for 15 min at R.T. 2-Chloro-*N*-(4-fluorobenzyl)acetamide (0.395 gm, 1.960 mM ) was added in reaction mixture and heated at 80ºC for 12hrs. Reaction mixture was monitored by TLC. After completion of reaction, crushed ice was added extracted with chloroform, dried over $Na_2SO_4$ and the solvent was evaporated which offered brown solid. Further purification was done by column chromatography to offered colourless compound.

Anal:

| | |
|---|---|
| Melting Point | : 180-183ºC |
| Yield | : 80 % |
| $R_f$ value | : 0.60, Chloroform: Methanol (09:01) |
| IR (KBr, $cm^{-1}$) | : 3281, 2949, 1679, 1475, 1377 and 827 |
| Mass ( m/z ) | : 483.22 $[M+H]^+$ |
| $^1$HNMR (DMSO, δ) | : 12.30 (s, 1H), 9.54 (s, 1H), 8.85-8.86 (d, 1H), 8.54-8.56 (d, 1H), 8.26-8.29 (t, 1H), 7.52-7.55 (m, 1H), 7.33-7.42 (m, 5H), 7.24-7.28 (t, 1H), 7.07-7.12 (t, 1H), 7.01-7.03 (d, 1H), 6.88-6.90 (d, 2H), 4.672 (s, 2H), 4.29-4.30 (d, 2H), 4.26 (s, 2H). |

**5.1.1.55. 2-(4-((8-Hydroxyquinolin-5-yl)methyl)-3-oxo-5-phenyl-2,3-dihydro-1*H*-pyrazol-1-yl)-*N*-(4-methoxybenzyl)acetamide (119)**

In 25ml of single-neck RBF, 4-((8-hydroxyquinolin-5-yl)methyl)-5-phenyl-1H-pyrazol-3(2*H*)-one (0.5 gm, 1.577 mM )and potassium carbonate (0.261gm, 1.891 mM ) was added in DMF and stirred for 15 min at R.T. 2-Chloro-*N*-(4-methoxybenzyl)acetamide was added in reaction mixture and heated at 80ºC for 12hrs. Reaction mixture was monitored by TLC. After completion of reaction, crushed ice was added extracted with chloroform, dried over $Na_2SO_4$ and the solvent was evaporated which offered brown solid. Further purification was done by column chromatography to offered colourless compound.

Anal:

| | |
|---|---|
| Melting Point | : 176-180ºC |
| Yield | : 80 % |
| $R_f$ value | : 0.60, Chloroform: Methanol (09:01) |
| IR (KBr, $cm^{-1}$) | : 3306, 3067, 2924, 1664, 1547, 1247, 1074 and 818 |
| Mass ( m/z ) | **:** 495.26 $[M+H]^+$ |
| $^1$HNMR (DMSO, δ) | : 12.34 (s, 1H), 9.57 (s, 1H), 8.88-8.89 (d, 1H), 8.56-8.58 (d, 1H), 8.16-8.18 (t, 1H), 7.70-7.75 (t, 1H), 7.34-7.45 (q, 1H), 7.34-7.45 (m, 5H), 7.15-7.16 (d, 1H), 7.04-7.06 (d, 1H), 6.91-6.93 (d, 1H), 6.85-6.86 (d, 1H), 4.69 (s, 2H), 4.25-4.28 (t, 2H), 4.16-4.18 (t, 1H), 3.74-3.59 (s, 3H). |

### 5.1.1.56. *N*-(4-Chlorobenzyl)-2-(4-((8-hydroxyquinolin-5-yl)methyl)-5-oxo-3-phenyl-1*H*-pyrazol-2(5*H*)-yl)acetamide (120)

In 25ml of single-neck RBF, 4-((8-hydroxyquinolin-5-yl)methyl)-5-phenyl-1H-pyrazol-3(2*H*)-one (0.5 gm, 1.577 mM )and potassium carbonate (0.261gm, 1.891 mM ) was added in DMF and stirred for 15 min at R.T. 2-Chloro-*N*-(4-chlorobenzyl)acetamide was added in reaction mixture and heated at 80ºC for 12hrs. Reaction mixture was monitored by TLC. After completion of reaction, crushed ice was added extracted with chloroform, dried over $Na_2SO_4$ and the solvent was evaporated which offered brown solid. Further purification was done by column chromatography to offered colourless compound.

| | |
|---|---|
| Melting Point | : 184-187ºC |
| Yield | : 78 % |
| $R_f$ value | : 0.72, Chloroform: Methanol (09:01) |
| IR (KBr, $cm^{-1}$) | : 3288, 2926, 1679, 1495 and 822. |

Mass (m/z) **:** 499.19 $[M+H]^+$ and 501.12 $[M+2]^+$.

**5.1.1.57. *N*-(4-Methylbenzyl)-2-(4-((8-hydroxyquinolin-5-yl)methyl)-5-oxo-3-phenyl-1*H*-pyrazol-2(5*H*)-yl)acetamide (121)**

In 25ml of single-neck RBF, 4-((8-hydroxyquinolin-5-yl)methyl)-5-phenyl-1H-pyrazol-3(2*H*)-one (0.5 gm, 1.577 mM )and potassium carbonate (0.261gm, 1.891 mM ) was added in DMF and stirred for 15 min at R.T. 2-Chloro-*N*-(4-methylbenzyl)acetamide was added in reaction mixture and heated at 80ºC for 12hrs. Reaction mixture was monitored by TLC. After completion of reaction, crushed ice was added extracted with chloroform, dried over $Na_2SO_4$ and the solvent was evaporated which offered brown solid. Further purification was done by column chromatography to offered colourless compound.

Melting Point : 176-178ºC

Yield : 84 %

$R_f$ value : 0.76, Chloroform: Methanol (09:01)

IR (KBr, $cm^{-1}$) : 3305, 2926, 1663, 1474, 1246 and 818.

**5.1.2. Pyrimidinone based multifunctional anti-AD agents (122-150)**

**5.1.2.1. 2,3-Dihydro-5-((8-hydroxyquinolin-5-yl)methyl)-6-methyl-2-thioxopyrimidin-4(1*H*)-one (122)**

In 50ml of single-neck RBF, ethyl 2-((8-hydroxyquinolin-5-yl)methyl)-3-oxobutanoate (5 gm, 1.7 mM), thiourea (1.59 gm, 1.2 mM), 1,8-Diazabicyclo(5.4.0)undec-7-ene (5.3 gm, 3.4 mM) was added. Reaction mixture will allow to reflux at 80℃ for 24 Hr. Reaction mixture was monitored by TLC. After completion of reaction, crushed ice was added and neutralize with 5% HCl to get precipitate. Further purification was done by column chromatography to offered colourless compound.

Anal:

Melting Point : 182-185ºC

Yield : 63 %

$R_f$ value : 0.21, Chloroform: Methanol (09:01)

IR (KBr, $cm^{-1}$) : 3283, 3046, 2837, 1641 and 1226

Mass (m/z) **:** 299.4 $[M+H]^+$

$^1$HNMR (DMSO, δ) : 12.48 (s, 1H), 12.28 (s, 1H), 9.59 (s, 1H), 8.87 (dd, *J* = 4.2, 1.6 Hz, 1H), 8.60 (dd, *J* = 8.6, 1.7 Hz, 1H), 7.61 (dd, *J* = 8.6, 4.1 Hz, 1H), 7.03 (d, *J* = 8.1 Hz, 1H), 6.96 (d, *J* = 7.9 Hz, 1H), 3.98 (s, 2H), 2.06 (s, 3H).

### 5.1.2.2. 2-(Benzylthio)-5-((8-hydroxyquinolin-5-yl) methyl)-6-methylpyrimidin-4(3*H*)-one (123)

In 25ml of single-neck RBF, 2,3-dihydro-5-((8-hydroxyquinolin-5-yl) methyl)-6-methyl-2-thioxopyrimidin-4(1*H*)-one (0.6 gm, 2 mM), potassium carbonate (0.55 gm, 3.98 mM) was added in DMF and stirred for 15 min at R.T. 1-(Bromomethyl) benzene (0.34 ml, 2.39 mM) was added in reaction mixture and allowed to stir for 1hr. Reaction mixture was monitored by TLC. After completion of reaction, crushed ice was added and neutralize with 5% HCl to get precipitate. Further purification was done by column chromatography to offered white colour compound.

Anal:

Melting Point : 212-214℃

Yield : 65%

$R_f$ value : 0.44, Chloroform: Methanol (09:01)

IR (KBr, $cm^{-1}$) : 3313, 3026, 2937, 1633, and 1224

Mass (m/z) : 390.1 $[M+H]^+$

$^1$HNMR (DMSO, δ) : 9.57 (s, 1H), 8.87 (dd, *J* = 4.1, 1.6 Hz, 1H), 8.65 (dd, *J* = 8.6, 1.6 Hz, 1H), 7.61 (dd, *J* = 8.6, 4.1 Hz, 1H), 7.43 (d, *J* = 6.9 Hz, 2H), 7.35 –7.24 (m, 3H), 6.96 (s, 2H), 4.40 (s, 2H), 4.09 (s, 2H), 2.17 (s, 3H).

### 5.1.2.3. 2-(4-Fluorobenzylthio)-5-((8-hydroxyquinolin-5-yl) methyl)-6-methylpyrimidin-4(3*H*)-one (124)

In 25ml of single-neck RBF, 2,3-dihydro-5-((8-hydroxyquinolin-5-yl) methyl)-6-methyl-2-thioxopyrimidin-4(1*H*)-one (0.6 gm, 2 mM), potassium carbonate (0.55 gm, 2 mM) was added in DMF and stirred for 15 min at R.T. 1-(Bromomethyl)-4-fluorobenzene (0.49 ml, 3.9 mM) was added in reaction mixture and allowed to stir for 1hrs. Reaction mixture was monitored by TLC. After completion of reaction, crushed ice was added and neutralize with

5% HCl to get precipitate. Further purification was done by column chromatography to offered white colour compound.

Anal:

| | |
|---|---|
| Melting Point | : 255-257℃ |
| Yield | : 63% |
| $R_f$ value | : 0.44, Chloroform: Methanol (09:01) |
| IR (KBr, $cm^{-1}$) | : 3325, 3044, 2937, 1644, and 1228 |
| Mass (m/z) | : 408.12 $[M+H]^+$ |
| $^1$HNMR (DMSO, δ) | : 12.70 (s, 1H), 9.58 (s, 1H), 8.87 (dd, *J* = 4.2, 1.6 Hz, 1H), 8.65 (dd, *J* = 8.6, 1.7 Hz, 1H), 7.61 (dd, *J* = 8.6, 4.1 Hz, 1H), 7.48 (dd, *J* = 8.7, 5.5 Hz, 2H), 7.16 (d, *J* = 8.9 Hz, 2H), 6.96 (s, 2H), 4.39 (s, 2H), 4.09 (s, 2H), 2.16 (s, 3H). |

### 5.1.2.4. 2-(3-Methoxybenzylthio)-5-((8-hydroxyquinolin-5-yl) methyl)-6-methyl pyrimidin-4(3*H*)-one (125)

In 25ml of single-neck RBF, 2,3-dihydro-5-((8-hydroxyquinolin-5-yl) methyl)-6-methyl-2-thioxopyrimidin-4(1*H*)-one (0.6 gm, 2 mM), potassium carbonate (0.55 gm, 2 mM) was added in DMF and stirred for 15 min at R.T. 1-(Bromomethyl)-3-methoxybenzene (0.33 ml, 2 mM) was added in reaction mixture and allowed to stir for 1hrs. Reaction mixture was monitored by TLC. After completion of reaction, crushed ice was added and neutralize with 5% HCl to get precipitate. Further purification was done by column chromatography to offered white colour compound.

Anal:

| | |
|---|---|
| Melting Point | : 242-244℃ |
| Yield | : 61% |
| $R_f$ value | : 0.45, Chloroform: Methanol (09:01) |
| IR (KBr, $cm^{-1}$) | : 3307, 3046, 2833, 1649 and 226 |
| Mass (m/z) | **:** 420.09 $[M+H]^+$ |
| $^1$HNMR (DMSO, δ) | : 12.73 (s, 1H), 9.59 (s, 1H), 8.88 (dd, *J* = 4.2, 1.6 Hz, 1H), 8.65 (dd, *J* = 8.6, 1.7 Hz, 1H), 7.61 (dd, *J* = 8.6, 4.2 Hz, 1H), 7.24 (t, *J* = 7.9 Hz, 1H), 7.04 – 6.94 (m, 4H), 6.83 (dd, *J* = 8.1, 3.0 Hz, 1H), 4.37 (s, 2H), 4.09 (s, 2H), 3.73 (s, 3H), 2.17 (s, 3H). |

### 5.1.2.5. 2-(3,4-Dichlorobenzylthio)-5-((8-hydroxyquinolin-5-yl) methyl)-6-methyl pyrimidin-4(3*H*)-one (126)

In 25ml of single-neck RBF, 2,3-dihydro-5-((8-hydroxyquinolin-5-yl) methyl)-6-methyl-2-thioxopyrimidin-4(1*H*)-one (0.6 gm, 2 mM), potassium carbonate (0.55 gm, 2 mM) was added in DMF and stirred for 15 min at R.T. 1,2-*di*Chloro-4-(chloromethyl) benzene (0.33 ml, 2 mM) was added in reaction mixture and allowed to stir for 1hrs. Reaction mixture was monitored by TLC. After completion of reaction, crushed ice was added and neutralize with 5% HCl to get precipitate. Further purification was done by column chromatography to offered white colour compound.

Anal:

| | |
|---|---|
| Melting Point | : 253-256℃ |
| Yield | : 60% |
| $R_f$ value | : 0.45, Chloroform: Methanol (09:01) |
| IR (KBr, $cm^{-1}$) | : 3313, 2977, 2942, 1652 and 1227 |
| Mass (m/z) | **:** 458.04 $[M]^+$**,** 460 $[M+2]^+$ |
| $^1$HNMR (DMSO, δ) | : 12.73 (s, 1H), 9.59 (s, 1H), 8.88 (d, *J* = 5.4 Hz, 1H), 8.69 – 8.61 (m, 1H), 7.75 (s, 1H), 7.65 – 7.54 (m, 2H), 7.46 (d, *J* = 10.4 Hz, 1H), 7.00 – 6.90 (m, 2H), 4.38 (s, 2H), 4.09 (s, 2H), 2.17 (s, 3H). |

### 5.1.2.6. 2-(3-Chlorobenzylthio)-5-((8-hydroxyquinolin-5-yl) methyl)-6-methyl pyrimidin-4(3*H*)-one (127)

In 25ml of single-neck RBF, 2,3-dihydro-5-((8-hydroxyquinolin-5-yl) methyl)-6-methyl-2-thioxopyrimidin-4(1*H*)-one (0.6 gm, 2 mM), potassium carbonate (0.55 gm, 2 mM) was added in DMF and stirred for 15 min at R.T. 1-Chloro-3-(chloromethyl)benzene (0.30 ml, 2 mM) was added in reaction mixture and allowed to stir for 1hrs. Reaction mixture was monitored by TLC. After completion of reaction, crushed ice was added and neutralize with 5% HCl to get precipitate. Further purification was done by column chromatography to offered colourless compound.

Anal:

| | |
|---|---|
| Melting Point | : 246-249℃ |
| Yield | : 62% |
| $R_f$ value | : 0.56, Chloroform: Methanol (09:01) |

IR (KBr, $cm^{-1}$) : 3305, 3043, 2873, 1658 and 1226

Mass (m/z) **:** 424.09 $[M+H]^+$, 426.07 $[M+2]^+$

$^1$HNMR (DMSO, δ) : 12.77 (s, 1H), 9.58 (s, 1H), 8.87 (dd, *J* = 4.0, 1.6 Hz, 1H), 8.65 (dd, *J* = 8.6, 1.7 Hz, 1H), 7.61 (dd, *J* = 8.6, 4.1 Hz, 1H), 7.54 (s, 1H), 7.44 – 7.30 (m, 3H), 6.96 (d, *J* = 7.5 Hz, 2H), 4.39 (s, 2H), 4.08 (s, 2H), 2.16 (s, 3H).

### 5.1.2.7. 2-(3,5-Dimethoxybenzylthio)-5-((8-hydroxyquinolin-5-yl)methyl)-6-methyl pyrimidin-4(3*H*)-one (128)

In 25ml of single-neck RBF, 2,3-dihydro-5-((8-hydroxyquinolin-5-yl) methyl)-6-methyl-2-thioxopyrimidin-4(1*H*)-one (0.6 gm, 2 mM), potassium carbonate (0.55 gm, 2 mM) was added in DMF and stirred for 15 min at R.T. 1-(Bromomethyl)-3,5-dimethoxybenzene (0.55 ml, 2 mM) was added in reaction mixture and allowed to stir for 1hrs. Reaction mixture was monitored by TLC. After completion of reaction, crushed ice was added and neutralize with 5% HCl to get precipitate. Further purification was done by column chromatography to offered white colour compound.

Anal:

Melting Point : 213-216℃

Yield : 59%

$R_f$ value : 0.44, Chloroform: Methanol (09:01)

IR (KBr, $cm^{-1}$) : 3322, 3026, 2835, 1650, and 1227

Mass (m/z) **:** 450.14 $[M+H]^+$

### 5.1.2.8. 2-(2-Methylbenzylthio)-5-((8-hydroxyquinolin-5-yl) methyl)-6-methylpyrimidin-4(3*H*)-one (129)

In 25ml of single-neck RBF, 2,3-dihydro-5-((8-hydroxyquinolin-5-yl)methyl)-6-methyl-2-thioxopyrimidin-4(1*H*)-one (0.6 gm, 2 mM) , potassium carbonate (0.55 gm, 2 mM) was added in DMF and stirred for 15 min at R.T. 1-(Chloromethyl)-2-methylbenzene (0.31 ml, 2 mM) was added in reaction mixture and allowed to stir for 1hrs. Reaction mixture was monitored by TLC. After completion of reaction, crushed ice was added and neutralize with 5% HCl to get precipitate. Further purification was done by column chromatography to offered white colour compound.

Anal:

Melting Point : >250℃

Yield : 58%

$R_f$ value : 0.44, Chloroform: Methanol (09:01)

IR (KBr, $cm^{-1}$) : 3320, 3018, 2940, 1631, and 1134

Mass (m/z) : 404.03 $[M+H]^+$

$^1$HNMR (DMSO, δ) : 9.58 (s, 1H), 8.87 (dd, *J* = 4.2, 1.6 Hz, 1H), 8.66 (dd, *J* = 8.6, 1.7 Hz, 1H), 7.61 (dd, *J* = 8.6, 4.2 Hz, 1H), 7.41 (d, *J* = 6.7 Hz, 1H), 7.21 – 7.12 (m, 3H), 6.96 (s, 2H), 4.41 (s, 2H), 4.09 (s, 2H), 2.36 (s, 3H), 2.17 (s, 3H).

### 5.1.2.9. 2-(4-Bromobenzylthio)-5-((8-hydroxyquinolin-5-yl) methyl)-6-methylpyrimidin-4(3*H*)-one (130)

In 25ml of single-neck RBF, 2,3-dihydro-5-((8-hydroxyquinolin-5-yl)methyl)-6-methyl-2-thioxopyrimidin-4(1*H*)-one (0.6 gm, 2 mM) , potassium carbonate (0.55 gm, 2 mM) was added in DMF and stirred for 15 min at R.T. 1-Bromo-4-(bromomethyl)benzene (0.6 gm, 2 mM) was added in reaction mixture and allowed to stir for 1hrs. Reaction mixture was monitored by TLC. After completion of reaction, crushed ice was added and neutralize with 5% HCl to get precipitate. Further purification was done by column chromatography to offered white colour compound.

Anal:

Melting Point : 247-249℃

Yield : 65%

$R_f$ value : 0.53, Chloroform: Methanol (09:01)

IR (KBr, $cm^{-1}$) : 3331, 2973, 2939, 1652, and 1260

Mass (m/z) **:** 470.01 $[M+H]^+$, 471.93 $[M+2]^+$

$^1$HNMR (DMSO, δ) : 9.60 (s, 1H), 8.87 (dd, *J* = 4.1, 1.5 Hz, 1H), 8.65 (dd, *J* = 8.7, 1.6 Hz, 1H), 7.61 (dd, *J* = 8.6, 4.2 Hz, 1H), 7.52 (d, *J* = 6.4 Hz, 2H), 7.41 (d, *J* = 8.4 Hz, 2H), 6.95 (s, 2H), 4.37 (s, 2H), 4.08 (s, 2H), 2.16 (s, 3H).

### 5.1.2.10. 2-(4-Chlorobenzylthio)-5-((8-hydroxyquinolin-5-yl) methyl)-6-methylpyrimidin-4(3*H*)-one (131)

In 25ml of single-neck RBF, 2,3-dihydro-5-((8-hydroxyquinolin-5-yl)methyl)-6-methyl-2-thioxopyrimidin-4(1*H*)-one (0.6 gm, 2 mM) , potassium carbonate (0.55 gm, 2 mM) was added in DMF and stirred for 15 min at R.T. 1-Chloro-4-(chloromethyl)benzene (0.31 ml, 2 mM) was added in reaction mixture and allowed to stir for 1hrs. Reaction mixture was monitored by TLC. After completion of reaction, crushed ice was added and neutralize with 5% HCl to get precipitate. Further purification was done by column chromatography to offer off white colour compound.

Anal:

| | |
|---|---|
| Melting Point | : 232-235℃ |
| Yield | : 61% |
| $R_f$ value | : 0.56, Chloroform: Methanol (09:01) |
| IR (KBr, $cm^{-1}$) | : 3319, 3011, 2923, 1653, and 1133 |
| Mass (m/z) | **:** 424.09 $[M+H]^+$, 426.07 $[M+2]^+$ |
| $^1$HNMR (DMSO, δ) | : 12.71 (s, 1H), 9.59 (s, 1H), 8.88 (dd, *J* = 4.0, 1.6 Hz, 1H), 8.65 (dd, *J* = 8.7, 1.6 Hz, 1H), 7.61 (dd, *J* = 8.6, 4.1 Hz, 1H), 7.44 (d, *J* = 6.8 Hz, 2H), 7.33 (t, *J* = 7.3 Hz, 2H), 6.96 (s, 2H), 4.41 (s, 2H), 4.09 (s, 2H), 2.17 (s, 3H). |

### 5.1.2.11. 2-(2,4-dichlorobenzylthio)-5-((8-hydroxyquinolin-5-yl)methyl)-6-methyl pyrimidin-4(3*H*)-one (132)

In 25ml of single-neck RBF, 2,3-dihydro-5-((8-hydroxyquinolin-5-yl)methyl)-6-methyl-2-thioxopyrimidin-4(1*H*)-one (0.6 gm, 2 mM) , potassium carbonate (0.55 gm, 2 mM) was added in DMF and stirred for 15 min at R.T. 2,4-Dichloro-1-(chloromethyl)benzene (0.33 ml, 2 mM) was added in reaction mixture and allowed to stir for 1hrs. Reaction mixture was monitored by TLC. After completion of reaction, crushed ice was added and neutralize with 5% HCl to get precipitate. Further purification was done by column chromatography to offered white colour compound.

Anal:

| | |
|---|---|
| Melting Point | : 172-175℃ |
| Yield | : 56% |
| $R_f$ value | : 0.45, Chloroform: Methanol (09:01) |
| IR (KBr, $cm^{-1}$) | : 3321, 3027, 2974, 1646, and 1260 |

Mass (m/z) **:** 458.04 $[M]^+$, 461.98 $[M+2]^+$

**5.1.2.12. 2-(4-Methylbenzylthio)-5-((8-hydroxyquinolin-5-yl)methyl)-6-methylpyrimidin-4(3*H*)-one (133)**

In 25ml of single-neck RBF, 2,3-dihydro-5-((8-hydroxyquinolin-5-yl)methyl)-6-methyl-2-thioxopyrimidin-4(1*H*)-one (0.6 gm, 2 mM) , potassium carbonate (0.55 gm, 2 mM) was added in DMF and stirred for 15 min at R.T. 1-(Chloromethyl)-4-methylbenzene (0.31 ml, 2 mM) was added in reaction mixture and allowed to stir for 1hrs. Reaction mixture was monitored by TLC. After completion of reaction, crushed ice was added and neutralize with 5% HCl to get precipitate. Further purification was done by column chromatography to offered white colour compound.

Anal:

Melting Point : 242-245℃

Yield : 53%

$R_f$ value : 0.48, Chloroform: Methanol (09:01)

IR (KBr, $cm^{-1}$) : 3324, 3022, 2976, 1650, and 1223

Mass (m/z) **:** 404.03 $[M+H]^+$

$^1$HNMR (DMSO, δ) : 9.59 (s, 1H), 8.87 (dd, *J* = 4.2, 1.5 Hz, 1H), 8.65 (dd, *J* = 8.6, 1.6 Hz, 1H), 7.61 (dd, *J* = 8.6, 4.2 Hz, 1H), 7.34 – 7.28 (m, 2H), 7.13 (d, *J* = 7.8 Hz, 2H), 6.96 (s, 2H), 4.35 (s, 2H), 4.08 (s, 2H), 2.27 (s, 3H), 2.16 (s, 3H).

**5.1.2.13. 5-((8-Hydroxyquinolin-5-yl) methyl)-6-methyl-2-(phenethylthio) pyrimidin-4(3*H*)-one (134)**

In 25ml of single-neck RBF, 2,3-dihydro-5-((8-hydroxyquinolin-5-yl)methyl)-6-methyl-2-thioxopyrimidin-4(1*H*)-one (0.6 gm, 2 mM) , potassium carbonate (0.55 gm, 2 mM) and potassium iodide (0.33 gm, 2 mM) was added in DMF and stirred for 15 min at R.T. 1-(2-Bromoethyl)benzene (0.32 ml, 2 mM) was added in reaction mixture and allowed to stir for 1hrs. Reaction mixture was monitored by TLC. After completion of reaction, crushed ice was added and neutralize with 5% HCl to get precipitate. Further purification was done by column chromatography to offered white colour compound.

Anal:

Melting Point : 212-214℃

Yield : 65%

$R_f$ value : 0.48, Chloroform: Methanol (09:01)

IR (KBr, $cm^{-1}$) : 3307, 3026, 2916, 1648, and 1225

Mass (m/z) **:** 404.12 $[M+H]^+$

$^1$HNMR (DMSO, δ) : 12.65 (s, 1H), 9.58 (s, 1H), 8.88 (dd, *J* = 4.2, 1.6 Hz, 1H), 8.66 (dd, *J* = 8.6, 1.7 Hz, 1H), 7.61 (dd, *J* = 8.6, 4.1 Hz, 1H), 7.35 – 7.19 (m, 5H), 6.96 (s, 2H), 4.08 (s, 2H), 3.40 – 3.34 (m, 2H), 2.97 (t, *J* = 7.6 Hz, 2H), 2.15 (s, 3H).

### 5.1.2.14. 5-((8-Hydroxyquinolin-5-yl) methyl)-6-methyl-2-(methylthio) pyrimidin-4(3*H*)-one (135)

In 25ml of single-neck RBF, 2,3-dihydro-5-((8-hydroxyquinolin-5-yl)methyl)-6-methyl-2-thioxopyrimidin-4(1*H*)-one (0.6 gm, 2 mM) , potassium carbonate (0.55 gm, 2 mM) was added in DMF and stirred for 15 min at R.T. Methyl iodide (0.15 ml, 2 mM) was added in reaction mixture and allowed to stir for 1hrs. Reaction mixture was monitored by TLC. After completion of reaction, crushed ice was added and neutralize with 5% HCl to get precipitate. Further purification was done by column chromatography to offered white colour compound.
Anal:

Melting Point : >250℃

Yield : 63%

$R_f$ value : 0.48, Chloroform: Methanol (09:01)

IR (KBr, $cm^{-1}$) : 3331, 2912, 1655, and 1224

Mass (m/z) : 314 $[M+H]^+$

$^1$HNMR (DMSO, δ) : 9.56 (s, 1H), 8.87 (dd, *J* = 4.2, 1.5 Hz, 1H), 8.65 (dd, *J* = 8.6, 1.6 Hz, 1H), 7.61 (dd, *J* = 8.6, 4.1 Hz, 1H), 6.95 (s, 2H), 4.09 (s, 2H), 2.49 (s, 3H), 2.13 (s, 3H).

### 5.1.2.15. 2,3-Dihydro-5-((8-hydroxyquinolin-5-yl)methyl)-6-phenyl-2-thioxopyrimidin-4(1*H*)-one (136)

In 50ml of single-neck RBF, ethyl 2-((8-hydroxyquinolin-5-yl)methyl)-3-oxo-3-phenylpropanoate (5 gm, 1.4 mM), thiourea (1.3 gm, 1.7 mM), 1,8-Diazabicyclo [5.4.0]undec-7-ene (4.41 gm, 2.8 mM) was added. Reaction mixture will allow to reflux at 80℃ for 24 Hr.

Reaction mixture was monitored by TLC. After completion of reaction, crushed ice was added and neutralize with 5% HCl to get precipitate. Further purification was done by column chromatography to offered white colour compound.

Anal:

| | |
|---|---|
| Melting Point | : 189-192℃ |
| Yield | : 63% |
| $R_f$ value | : 0.48, Chloroform: Methanol (09:01) |
| IR (KBr, $cm^{-1}$) | : 3389, 3030, 2853, 1654, and 1129 |
| $^1$HNMR (DMSO, δ) | : 12.62 (s, 1H), 12.50 (s, 1H), 9.57 (s, 1H), 8.82 (dd, *J* = 4.2, 1.6 Hz, 1H), 8.30 (dd, *J* = 8.6, 1.7 Hz, 1H), 7.51 – 7.47 (m, 1H), 7.42 – 7.34 (m, 5H), 7.03 (d, *J* = 7.9 Hz, 1H), 6.92 (d, *J* = 7.9 Hz, 1H), 3.79 (s,2H). |

### 5.1.2.16. 2,3-Dihydro-5-((8-hydroxyquinolin-5-yl)methyl)-6-phenyl-2-thioxopyrimidin4 (1*H*)-one (137)

In 25ml of single-neck RBF, 2,3-dihydro-5-((8-hydroxyquinolin-5-yl)methyl)-6-phenyl-2-thioxopyrimidin-4(1*H*)-one (0.6 gm, 1.6 mM), potassium carbonate (0.45 gm, 1.6 mM) was added in DMF and stirred for 15 min at R.T. 1-(Bromomethyl)benzene (0.23 ml, 1.6 mM) was added in reaction mixture and allowed to stir for 1hrs. Reaction mixture was monitored by TLC. After completion of reaction, crushed ice was added and neutralize with 5% HCl to get precipitate. Further purification was done by column chromatography to offered white colour compound.

Anal:

| | |
|---|---|
| Melting Point | : 196-198℃ |
| Yield | : 63% |
| $R_f$ value | : 0.48, Chloroform: Methanol (09:01) |
| IR (KBr, $cm^{-1}$) | : 3341, 3025, 2840, 1634, and 1227 |
| $^1$HNMR (DMSO, δ) | : 9.59 (s, 1H), 8.86 (dd, *J* = 4.1, 1.6 Hz, 1H), 8.42 (dd, *J* = 8.7, 1.6 Hz, 1H), 7.55 – 7.51 (m, 1H), 7.39 – 7.25 (m, 11H), 6.97 (q, *J* = 7.9 Hz, 2H), 4.47 (s, 2H), 4.15 (s, 2H). |

### 5.1.2.17. 2-(4-Fluorobenzylthio)-5-((8-hydroxyquinolin-5-yl)methyl)-6-phenylpyrimidin-4(3*H*)-one (138)

In 25ml of single-neck RBF, 2,3-dihydro-5-((8-hydroxyquinolin-5-yl)methyl)-6-phenyl-2-thioxopyrimidin-4(1*H*)-one (0.6 gm, 1.6 mM) , potassium carbonate (0.45 gm, 1.6 mM) was added in DMF and stirred for 15 min at R.T. 1-(Bromomethyl)-4-fluorobenzene (0.24 ml, 1.6 mM) was added in reaction mixture and allowed to stir for 1hrs. Reaction mixture was monitored by TLC. After completion of reaction, crushed ice was added and neutralize with 5% HCl to get precipitate. Further purification was done by column chromatography to offered white colour compound.

Anal:

| | |
|---|---|
| Melting Point | : > 250°C |
| Yield | : 59 % |
| $R_f$ value | : 0.44, Chloroform: Methanol (09:01) |
| IR (KBr, $cm^{-1}$) | : 3328, 3039, 2829, 1640, and 1225 |
| Mass (m/z) | **:** 470.08 $[M+H]^+$ |
| $^1$HNMR (DMSO, δ) | : 12.95 (s, 1H), 9.60 (s, 1H), 8.86 (dd, *J* = 4.2, 1.6 Hz, 1H), 8.40 (dd, *J* = 8.6, 1.7 Hz, 1H), 7.53 (dd, *J* = 8.6, 4.1 Hz, 1H), 7.48 – 7.32 (m, 7H), 7.19 – 7.12 (m, 2H), 6.95 (s, 2H), 4.43 (s, 2H), 4.05 (s, 2H). |

### 5.1.2.18. 2-(3-Methoxybenzylthio)-5-((8-hydroxyquinolin-5-yl)methyl)-6-phenyl pyrimidin-4(3*H*)-one. (139)

In 25ml of single-neck RBF, 2,3-dihydro-5-((8-hydroxyquinolin-5-yl)methyl)-6-phenyl-2-thioxopyrimidin-4(1*H*)-one (0.6 gm, 1.6 mM) , potassium carbonate (0.45 gm, 1.6 mM) was added in DMF and stirred for 15 min at R.T. 1-(bromomethyl)-3-methoxybenzene (0.28 ml, 1.6 mM) was added in reaction mixture and allowed to stir for 1hrs. Reaction mixture was monitored by TLC. After completion of reaction, crushed ice was added and neutralize with 5% HCl to get precipitate. Further purification was done by column chromatography to offered white colour compound.

Anal:

| | |
|---|---|
| Melting Point | : 183-185°C |
| Yield | : 62 % |
| $R_f$ value | : 0.65, Chloroform: Methanol (09:01) |
| IR (KBr, $cm^{-1}$) | : 3339, 3039, 2833, 1643 and 1223 |

Mass (m/z) **:** 482 $[M+H]^+$

$^1$HNMR (DMSO, δ) : 12.93 (s, 1H), 9.58 (s, 1H), 8.86 (dd, *J* = 4.2, 1.5 Hz, 1H), 8.40 (dd, *J* = 8.7, 1.6 Hz, 1H), 7.53 (dd, *J* = 8.6, 4.1 Hz, 1H), 7.47 (d, *J* = 9.6 Hz, 2H), 7.36 (t, *J* = 8.1 Hz, 3H), 7.23 (t, *J* = 8.1 Hz, 1H), 6.97 (d, *J* = 17.8 Hz, 4H), 6.82 (d, *J* = 9.6 Hz, 1H), 4.41 (s, 2H), 4.06 (s, 2H), 3.61 (s, 3H).

### 5.1.2.19. 2-(3,4-Dichlorobenzylthio)-5-((8-hydroxyquinolin-5-yl)methyl)-6-phenyl pyrimidin-4(3*H*)-one. (140)

In 25ml of single-neck RBF, 2,3-dihydro-5-((8-hydroxyquinolin-5-yl)methyl)-6-phenyl-2-thioxopyrimidin-4(1*H*)-one (0.6 gm, 1.6 mM) , potassium carbonate (0.45 gm, 1.6 Mm) was added in DMF and stirred for 15 min at R.T. 1,2-Dichloro-4-(chloromethyl)benzene (0.27 ml, 1.6 mM) was added in reaction mixture and allowed to stir for 1hrs. Reaction mixture was monitored by TLC. After completion of reaction, crushed ice was added and neutralize with 5% HCl to get precipitate. Further purification was done by column chromatography to offered white colour compound.

Anal:

Melting Point : 158-160℃

Yield : 60 %

$R_f$ value : 0.55, Chloroform: Methanol (09:01)

IR (KBr, $cm^{-1}$) : 3323, 3049, 2928, 1646, and 1222

$^1$HNMR (DMSO, δ) : 9.57 (s, 1H), 8.86 (d, *J* = 4.3 Hz, 1H), 8.52 (d, *J* = 8.8 Hz, 1H), 7.98 (d, *J* = 7.7 Hz, 1H), 7.65 – 7.33 (m, 8H), 6.98 (dd, *J* = 15.8, 8.1 Hz, 2H), 4.47 (s, 2H), 4.13 (s, 2H).

### 5.1.2.20. 2-(2-Methylbenzylthio)-5-((8-hydroxyquinolin-5-yl)methyl)-6-phenylpyrimidin-4(3*H*)-one (141)

In 25ml of single-neck RBF, 2,3-dihydro-5-((8-hydroxyquinolin-5-yl)methyl)-6-phenyl-2-thioxopyrimidin-4(1*H*)-one (0.6 gm, 1.6 mM) , potassium carbonate (0.45 gm, 1.6 mM) was added in DMF and stirred for 15 min at R.T. 1-(Chloromethyl)-2-methylbenzene (0.26 ml, 1.6 mM) was added in reaction mixture and allowed to stir for 1hrs. Reaction mixture was monitored by TLC. After completion of reaction, crushed ice was added and neutralize

with 5% HCl to get precipitate. Further purification was done by column chromatography to offered white colour compound.

Anal:

| | |
|---|---|
| Melting Point | : 195-198℃ |
| Yield | : 62 % |
| $R_f$ value | : 0.53, Chloroform: Methanol (09:01) |
| IR (KBr, $cm^{-1}$) | : 3357, 3061, 2974, 1651, and 1156 |
| $^1$HNMR (DMSO, δ) | : 12.92 (s, 1H), 9.59 (s, 1H), 8.86 (dd, *J* = 4.2, 1.6 Hz, 1H), 8.41 (dd, *J* = 8.6, 1.7 Hz, 1H), 7.56 – 7.41 (m, 6H), 7.22 – 7.11 (m, 4H), 6.95 (s, 2H), 4.44 (s, 2H), 4.05 (s, 2H), 2.34 (s, 3H). |

### 5.1.2.21. 2,3-Dihydro-5-((8-hydroxyquinolin-5-yl)methyl)-2-imino-6-methylpyrimidin-4 (1*H*)-one (142)

In 50ml of single-neck RBF, ethyl 2-((8-hydroxyquinolin-5-yl)methyl)-3-oxobutanoate (1 gm, 3.4 mM), guanidine nitrate (0.51 gm, 4.1 mM), 1,8-Diazabicyclo [5.4.0]undec-7-ene (1 gm, 6.9 mM) was added. Reaction mixture will allow to reflux at 80℃ for 24 Hr. Reaction mixture was monitored by TLC. After completion of reaction, crushed ice was added and neutralize with 5% HCl to get precipitate. Further purification was done by column chromatography to offered white colour compound.

Anal:

| | |
|---|---|
| Melting Point | : 204-207℃ |
| Yield | : 54 % |
| $R_f$ value | : 0.63, Chloroform: Methanol (09:01) |
| IR (KBr, $cm^{-1}$) | : 3323, 3049, 2892, 1655, and 1147 |
| $^1$HNMR (DMSO, δ) | : 11.08 (s, 1H), 9.55 (s, 1H), 8.86 (dd, *J* = 4.2, 1.6 Hz, 1H), 8.68 (dd, *J* = 8.6, 1.7 Hz, 1H), 7.59 (dd, *J* = 8.6, 4.1 Hz, 1H), 7.03 – 6.94 (m, 1H), 6.57 (s, 1H), 3.99 (s, 2H), 1.96 (s, 3H). |

### 5.1.2.22. 2-(Dibenzylamino)-5-((8-hydroxyquinolin-5-yl)methyl)-6-methylpyrimidin-4 (3*H*)-one (143)

In 25ml of single-neck RBF, 2,3-dihydro-5-((8-hydroxyquinolin-5-yl)methyl)-2-imino-6-methylpyrimidin-4(1*H*)-one (0.6 gm, 2.1 mM) , potassium carbonate (0.58 gm, 4.2

mM) was added in DMF and stirred for 15 min at R.T. 1-(Bromomethyl)benzene (0.30 ml, 2.5 mM) was added in reaction mixture and allowed to stir for 1hrs. Reaction mixture was monitored by TLC. After completion of reaction, crushed ice was added and neutralize with 5% HCl to get precipitate. Further purification was done by column chromatography to offered white colour compound.

Anal:

| | |
|---|---|
| Melting Point | : 195-198℃ |
| Yield | : 65 % |
| $R_f$ value | : 0.49, Chloroform: Methanol (09:01) |
| IR (KBr, $cm^{-1}$) | : 3347, 3033, 1666, and 1452 |
| Mass (m/z) | **:** 463.69 $[M+H]^+$ |
| $^1$HNMR (DMSO, δ) | : 8.88 (dd, *J* = 4.1, 1.6 Hz, 1H), 8.61 (dd, *J* = 8.6, 1.7 Hz, 1H), 7.58 – 7.51 (m, 3H), 7.44 – 7.33 (m, 3H), 7.20 (q, *J* = 4.7 Hz, 5H), 7.13 (d, *J* = 8.1 Hz, 1H), 6.83 (d, *J* = 8.0 Hz, 1H), 6.41 (s, 1H), 5.30 (s, 2H), 5.24 (s, 2H), 4.15 (s, 2H), 2.09 (s, 3H). |

### 5.1.2.23. 2-(Bis(3-chlorobenzyl)amino)-5-((8-hydroxyquinolin-5-yl)methyl)-6-methyl pyrimidin-4(3*H*)-one (144)

In 25ml of single-neck RBF, 2,3-dihydro-5-((8-hydroxyquinolin-5-yl)methyl)-2-imino-6-methylpyrimidin-4(1*H*)-one (0.6 gm, 2.1 mM) , potassium carbonate (0.58 gm, 4.2 mM) was added in DMF and stirred for 15 min at R.T. 1-(Bromomethyl)-3-chlorobenzene (0.52 gm, 2.5 mM) was added in reaction mixture and allowed to stir for 1hrs. Reaction mixture was monitored by TLC. After completion of reaction, crushed ice was added and neutralize with 5% HCl to get precipitate. Further purification was done by column chromatography to offered white colour compound.

Anal:

| | |
|---|---|
| Melting Point | : 215-218℃ |
| Yield | : 62 % |
| $R_f$ value | : 0.52, Chloroform: Methanol (09:01) |
| IR (KBr, $cm^{-1}$) | : 3344, 3061, 1672, and 1169 |
| Mass (m/z) | **:** 533.80 $[M+H]^+$, 535.97 $[M+2]^+$ |

$^1$HNMR (DMSO, δ) : 8.90 (dd, *J* = 4.1, 1.6 Hz, 1H), 8.66 (dd, *J* = 8.6, 1.7 Hz, 1H), 7.62 – 7.34 (m, 7H), 7.26 (d, *J* = 2.0 Hz, 1H), 7.20 – 7.12 (m, 2H), 7.05 (d, *J* = 8.1 Hz, 2H), 5.29 (s, 2H), 5.18 (s, 2H), 4.09 (s, 2H), 2.00 (s, 3H).

### 5.1.2.24. 2-(Bis(4-bromobenzyl)amino)-5-((8-hydroxyquinolin-5-yl)methyl)-6-methyl pyrimidin-4(3*H*)-one (145)

In 25ml of single-neck RBF, 2,3-dihydro-5-((8-hydroxyquinolin-5-yl)methyl)-2-imino-6-methylpyrimidin-4(1*H*)-one (0.6 gm, 2.1 mM) , potassium carbonate (0.58 gm, 4.2 mM) was added in DMF and stirred for 15 min at R.T. 1-Bromo-4-(bromomethyl)benzene (0.63 gm, 2.4 mM) was added in reaction mixture and allowed to stir for 1hrs. Reaction mixture was monitored by TLC. After completion of reaction, crushed ice was added and neutralize with 5% HCl to get precipitate. Further purification was done by column chromatography to offered white colour compound.

Anal:

Melting Point : 224-227°C

Yield : 61 %

$R_f$ value : 0.47, Chloroform: Methanol (09:01)

IR (KBr, $cm^{-1}$) : 3274, 3162, 2875, 1619, and 1093

$^1$HNMR (DMSO, δ) : 8.89 (dd, *J* = 4.1, 1.6 Hz, 1H), 8.61 (dd, *J* = 8.6, 1.7 Hz, 1H), 7.63 – 7.55 (m, 3H), 7.50 (d, *J* = 8.3 Hz, 2H), 7.42 – 7.38 (m, 2H), 7.12 (dd, *J* = 11.6, 8.2 Hz, 2H), 6.81 (d, *J* = 8.0 Hz, 1H), 6.40 (s, 2H), 5.25 (d, *J* = 7.3 Hz, 4H), 4.14 (s, 2H), 2.10 (s, 3H).

### 5.1.2.25. 2-(Bis(4-fluorobenzyl)amino)-5-((8-hydroxyquinolin-5-yl)methyl)-6-methyl pyrimidin-4(3*H*)-one (146)

In 25ml of single-neck RBF, 2,3-dihydro-5-((8-hydroxyquinolin-5-yl)methyl)-2-imino-6-methylpyrimidin-4(1*H*)-one (0.6 gm, 2.1 mM) , potassium carbonate (0.58 gm, 4.2 mM) was added in DMF and stirred for 15 min at R.T. 1-Bromo-4-(fluoromethyl)benzene (0.53 gm, 2.4 mM) was added in reaction mixture and allowed to stir for 1hrs. Reaction mixture was monitored by TLC. After completion of reaction, crushed ice was added and neutralize with

5% HCl to get precipitate. Further purification was done by column chromatography to offered white colour compound.

Anal:

| | |
|---|---|
| Melting Point | : >250°C |
| Yield | : 66 % |
| $R_f$ value | : 0.51, Chloroform: Methanol (09:01) |
| IR (KBr, $cm^{-1}$) | : 3334, 2825, 1636, and 993 |
| Mass (m/z) | **:** 499.74 $[M+H]^+$. |

### 5.1.2.26. 2-(Bis(2,5-difluorobenzyl)amino)-5-((8-hydroxyquinolin-5-yl)methyl)-6-methyl pyrimidin-4(3*H*)-one (147)

In 25ml of single-neck RBF, 2,3-dihydro-5-((8-hydroxyquinolin-5-yl)methyl)-2-imino-6-methylpyrimidin-4(1*H*)-one (0.6 gm, 2.1 mM) , potassium carbonate (0.58 gm, 4.2 mM) was added in DMF and stirred for 15 min at R.T. 1-Bromo-2,5-(difluoromethyl)benzene (0.33 gm, 2.4 mM) was added in reaction mixture and allowed to stir for 1hrs. Reaction mixture was monitored by TLC. After completion of reaction, crushed ice was added and neutralize with 5% HCl to get precipitate. Further purification was done by column chromatography to offered white colour compound.

Anal:

| | |
|---|---|
| Melting Point | : >250°C |
| Yield | : 63 % |
| $R_f$ value | : 0.58, Chloroform: Methanol (09:01) |
| IR (KBr, $cm^{-1}$) | : 3406, 2910, 1656, and 933 |
| Mass (m/z) | **:** 535.80 $[M+H]^+$. |

### 5.1.2.27. 2,3-Dihydro-5-((8-hydroxyquinolin-5-yl)methyl)-2-imino-6-phenylpyrimidin-4 (1*H*)-one (148)

In 50ml of single-neck RBF, ethyl 2-((8-hydroxyquinolin-5-yl)methyl)-3-oxo-3-phenylpropanoate (1 gm, 2.8 mM), guanidine nitrate (0.41 gm, 3.4 mM), 1,8-Diazabicyclo [5.4.0]undec-7-ene (0.88 gm, 5.7 mM) was added. Reaction mixture will allow to reflux at 80°C for 24 Hr. Reaction mixture was monitored by TLC. After completion of reaction, crushed ice was added and neutralize with 5% HCl to get precipitate. Further purification was done by column chromatography to offered white colour compound.

Anal:

| | |
|---|---|
| Melting Point | : 212-215℃ |
| Yield | : 56 % |
| $R_f$ value | : 0.34, Chloroform: Methanol (09:01) |
| IR (KBr, $cm^{-1}$) | : 3323, 3049, 1655, 1230, 890 |
| $^1$HNMR (DMSO, δ) | : 11.04 (s, 1H), 9.49 (s, 1H), 8.83 (dd, *J* = 4.1, 1.5 Hz, 1H), 8.38 (dd, *J* = 8.6, 1.6 Hz, 1H), 7.52 – 7.22 (m, 6H), 6.95 (s, 1H), 6.51 (s, 1H), 3.91(s, 2H). |

### 5.1.2.28. 2-(Bis(4-fluorobenzyl)amino)-5-((8-hydroxyquinolin-5-yl)methyl)-6-phenyl pyrimidin-4(3*H*)-one (149)

In 25ml of single-neck RBF, 2,3-dihydro-5-((8-hydroxyquinolin-5-yl)methyl)-2-imino-6-phenylpyrimidin-4(1*H*)-one (0.6 gm, 1.7 mM) , potassium carbonate (0.47 gm, 3.4 mM) was added in DMF and stirred for 15 min at R.T. 1-(Bromomethyl)benzene (0.24 ml, 2 mM) was added in reaction mixture and allowed to stir for 1hrs. Reaction mixture was monitored by TLC. After completion of reaction, crushed ice was added and neutralize with 5% HCl to get precipitate. Further purification was done by column chromatography to offered white colour compound.

Anal:

| | |
|---|---|
| Melting Point | : 234-237℃ |
| Yield | : 55 % |
| $R_f$ value | : 0.34, Chloroform: Methanol (09:01) |
| IR (KBr, $cm^{-1}$) | : 3347, 3061, 3033, 1666, and 1174 |
| Mass (m/z) | **:** 525.75 $[M+H]^+$. |
| $^1$HNMR (DMSO, δ) | : 8.85 (dd, *J* = 4.1, 1.6 Hz, 1H), 8.40 (dd, *J* = 8.6, 1.7 Hz, 1H), 7.57 – 7.26 (m, 16H), 7.17 – 7.13 (m, 2H), 7.01 (d, *J* = 8.0 Hz, 1H), 5.24 (d, *J* = 12.8 Hz, 4H), 4.00 (s, 2H). |

### 5.1.2.29. 2-(Bis(4-fluorobenzyl)amino)-5-((8-hydroxyquinolin-5-yl)methyl)-6-phenyl pyrimidin-4(3*H*)-one (150)

In 25ml of single-neck RBF, 2,3-dihydro-5-((8-hydroxyquinolin-5-yl)methyl)-2-imino-6-phenylpyrimidin-4(1*H*)-one (0.6 gm, 1.7 mM) , potassium carbonate (0.47 gm, 3.4

mM) was added in DMF and stirred for 15 min at R.T. 1-(Bromomethyl)-4-fluorobenzene (0.26 ml, 2 mM) was added in reaction mixture and allowed to stir for 1hrs. Reaction mixture was monitored by TLC. After completion of reaction, crushed ice was added and neutralize with 5% HCl to get precipitate. Further purification was done by column chromatography to offered white colour compound.

Anal:

| | |
|---|---|
| Melting Point | : 223-225℃ |
| Yield | : 62 % |
| $R_f$ value | : 0.34, Chloroform: Methanol (09:01) |
| IR (KBr, $cm^{-1}$) | : 3321, 3041, 1666, and 1155 |
| Mass (m/z) | **:** 561.73 $[M+H]^+$. |
| $^1$HNMR (DMSO, δ) | : 8.85 (dd, *J* = 4.0, 1.6 Hz, 1H), 8.40 (dd, *J* = 8.7, 1.7 Hz, 1H), 7.60 (dd, *J* = 8.4, 5.6 Hz, 2H), 7.49 (dd, *J* = 8.6, 4.1 Hz, 1H), 7.37 – 7.15 (m, 13H), 7.01 (d, *J* = 8.1 Hz, 1H), 5.22 (d, *J* = 17.0 Hz, 4H), 4.00 (s, 2H) |

## 5.2 Biological screening

### 5.2.1 AChE and BuChE Inhibition assay

A modified version of Ellman's colorimetric assay was adapted into a high-throughput format for measuring the enzymatic activity of BuChE and AChE[5]. Reagents were obtained from Sigma-Aldrich (St. Louis, MO, USA) and included butyrylthiocholine iodide (BTC), acetylthiocholine iodide (ATC), and 5,5′-dithiobis(2-nitrobenzoic acid) (DTNB). Details of the assay modifications have been described previously. To enable high-throughput testing in 384-well plates, the protocol was further optimized. Briefly, AChE activity was measured using 25 µL per well of a 1:400 diluted solution of lysed pooled human red blood cells (RBCs) and a 1:768 diluted pure recombinant human AChE protein (final concentration: 3.5 ng/mL; Sigma, Cat. No. C1682). The RBC source was prepared by centrifuging frozen RBCs to remove plasma, followed by lysis in an equivalent volume of phosphate buffer to produce a lysed RBC solution. This solution was diluted fourfold and subsequently mixed with an equal volume of glycerol. The resulting stock solution was aliquoted into small volumes and stored at -20 °C for future use.

For BuChE activity measurement, 25 µL/well of a 1:400 diluted pooled human plasma solution was used. During the initial stage of in vitro screening, wells were preincubated at

room temperature for 10–30 minutes with 25 µL/well of synthesized compounds at a concentration of 30 µM. The final concentration of compounds in each well was adjusted to 10 µM. Each well then received 25 µL of a cocktail mix prepared in Na/K phosphate buffer. This mix contained DTNB (final concentration: 0.4 mM), BTC (final concentration: 1 mM), or ATC (final concentration: 0.5 mM). Absorbance changes were measured at 412 nm over 15–20 minutes, with one-minute intervals, using a microplate spectrophotometer reader (Infinite M1000, Tecan). Percentage inhibition of enzyme activity was calculated relative to control wells containing the enzyme incubated with the compound vehicle (DMSO), using SOFTmax PRO 3.1.2 software.

**5.2.2. MAO-B Inhibition Assay**

MAO-B activity in STHdhQ7/Q7 cells was assessed using the Amplex® Red Monoamine Oxidase Assay Kit (Invitrogen, USA)[6,7]. Cells were lysed using M-PER™ Mammalian Protein Extraction Reagent (Thermo Fisher Scientific) supplemented with a 1× protease inhibitor cocktail (Sigma-Aldrich). The lysates were incubated on ice for 30 minutes and centrifuged at 14,000 rpm for 15 minutes at 4°C. The resulting supernatant was collected for analysis. Protein concentration was determined using the Bradford assay (Bio-Rad Protein Assay Dye Reagent Concentrate, Bio-Rad), and 4 µg of protein per well was utilized for the MAO-B activity assay. Benzylamine hydrochloride served as the substrate for the MAO-B enzyme, with sodium phosphate buffer (0.05 M, pH 7.4) used for all reactions and dilutions. Each reaction had a final volume of 200 µL, containing the substrate, 10 µM of the test compound, and DMSO as the co-solvent. The effect of test compounds on MAO-B activity was determined by quantifying H2O2 production from benzylamine using the Amplex® Red assay kit. In the assay, 100 µL of sodium phosphate buffer (0.05 M, pH 7.4) containing 10 µM of the test compound and 4 µg of cell lysate protein was incubated in a 96-well plate at 37°C for 1 hour to ensure binding and reaction equilibrium. The reaction was then initiated by adding Amplex® Red reagent (200 µM final concentration), horseradish peroxidase (1 U/mL), and benzylamine hydrochloride (1 mM final concentration). The mixture was incubated at room temperature for 1 hour. Fluorescence intensity, proportional to H2O2 and resorufin production, was measured at an excitation wavelength of 560 nm and an emission wavelength of 590 nm using a Synergy HTX Multi-Mode Microplate Reader (BioTek Instruments). Control experiments were performed simultaneously by substituting the test compounds (new compounds and reference inhibitors) with vehicle controls. Background fluorescence was subtracted, and data were normalized to wells without inhibitors (0 µM) to calculate percentage

inhibition. $IC_{50}$ values were determined using dose-response curves fitted with a variable slope model in GraphPad Prism (version 6). Initial concentrations of the test compounds ranged from 0 to 10 µM for $IC_{50}$ calculations.

**5.2.3. Cytotoxicity assay (MTT assay)**

The MTT assay was employed to assess the cytotoxic effects of compounds 106, 107, 118 and 138 at varying concentrations, specifically 10 nM, 100 nM, 1 µM, 2 µM, and 10 µM. These evaluations were conducted utilizing STHdhQ7/Q7 (mouse striatal cells) cells as the experimental model[8].

**Material and Method**

The 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) assay was conducted following the method described by Mosmann (1983)[9]. The study utilized *STHdh*$^{Q7/Q7}$ cells, a transgenic mouse striatal cell line expressing human huntingtin protein with a polyglutamine repeat of 7.Cells were cultured in Dulbecco's Modified Eagle's Medium (DMEM, Gibco, Invitrogen, USA) supplemented with 10% fetal bovine serum (FBS, Gibco, Invitrogen, USA) and 1% penicillin-streptomycin (Pen-Strep, Gibco, Invitrogen, USA). Cultures were maintained at 37°C in a humidified atmosphere containing 5% $CO_2$.

Initially, $5 \times 10^3$ cells were seeded into each well of a 96-well plate. After an initial incubation, the culture media was replaced, and the test compounds were added in triplicate at specified concentrations. Cells treated with an equal volume of dimethyl sulfoxide (DMSO) in complete media served as the untreated control. Following a 24-hour incubation with the test compounds, the media was replaced, and 10 µL of MTT solution (5 mg/mL in 1× phosphate-buffered saline) was added to each well. Plates were incubated in the dark at 37°C for 4 hours to allow the formation of formazan crystals. The media was then carefully removed, and 100 µL of DMSO was added to each well to dissolve the crystals. After a 30-minute incubation in the dark, absorbance was measured at 570 nm using a Synergy HTX Multi-Mode Microplate Reader (BioTek Instruments). A decrease in the intensity of the purple color indicated reduced cell viability following treatment with the test compounds. The percentage of cell viability was calculated by comparing the absorbance of treated samples to that of the untreated controls.

**5.2.4. Metal chelating activity**

To evaluate the metal-chelating ability of the selected compounds, a metal-chelating assay was performed using ferrozine and ferrous chloride, following the method described by Dinis et al., 1994. Ferrozine forms a purple-colored complex upon chelation with $Fe^{2+}$ ions[10]. However, the presence of competing chelating agents reduces the formation of this complex,

resulting in a decrease in the intensity of the purple color. This reduction in color intensity reflects the chelating activity of the compounds, indicating their ability to compete with ferrozine for binding to ferrous ions[11,12].

**Material and Method**

In this modified assay, ferrous chloride (2 mM) and ferrozine (5 mM) solutions were prepared in distilled water. Test compounds, dissolved in DMSO to achieve a final concentration of 10 µM, were mixed with 5 µL of 2 mM ferrous chloride and incubated for 20 minutes. A solution of 10 µM EDTA was used as a standard. After the incubation, 0.2 mL of the ferrozine solution (5 mM) was added to each mixture. The samples were allowed to equilibrate at room temperature for 10 minutes, after which their absorbance was measured at 562 nm using a spectrophotometer.The $Fe^{2+}$ chelating activity (%) of each compound was determined by quantifying the inhibition of the ferrous iron–ferrozine complex formation using a predefined calculation formula.

$$\% \text{ MCA} = ((\text{Abs control} - \text{Abs sample})/ \text{Abs control}) \times 100$$

Where, MCA is the Metal chelation Activity; Abs control is the absorbance of ferrous chloride + ferrozine + DMSO; Abs sample is the absorbance of ferrous chloride + ferrozine + compounds.

**5.3 Computational Study**

In order to evaluate the binding affinity and orientation of synthesized ligands within the active sites of target receptors, an in-silico molecular docking approach was employed. The synthesized compounds were docked into the active sites of human acetylcholinesterase (*h*AChE), human butyrylcholinesterase (*h*BuChE), and human monoamine oxidase B (*h*MAO-B) using Maestro 13.5 (Schrödinger LLC). Co-crystallized protein structures of *h*AChE (PDB: 4EY7), *h*BuChE (PDB: 5K5E), and *h*MAO-B (PDB: 2V5Z) were retrieved from the Protein Data Bank (RCSB.org), and the proteins were prepared using the "Protein Preparation Wizard" in Schrödinger suite 2023. The chemical structures of the ligands were drawn using ChemDraw 16.0 and imported into the Schrödinger suite, where ligand preparation was carried out using LigPrep with the OPLS force field for energy minimization.

Before performing molecular docking, the binding site was validated by redocking the co-crystallized ligands into the active site of the respective proteins, with a grid generated around the binding site of the co-crystallized ligand. Docking of the prepared ligands was then performed using the Standard Precision (SP) method, followed by Extra Precision (XP)

docking for the top ligands obtained from the SP results. The docking scores (kcal/mol) and binding modes were analyzed for all docked ligands. Validation of the docking protocol was achieved by comparing the binding interactions of donepezil (for AChE) and safinamide (for MAO-B) with their respective target enzymes. This approach ensured a comprehensive evaluation of the binding affinity and molecular interactions of the synthesized compounds, providing valuable insights into their potential as enzyme inhibitors.

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