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## SYNTHESIS OF BENZO[G]QUINOXALINE-5,10-DIONE BASED PYRAZOLINE DERIVATIVES AND THEIR ANTIMYCOBACTERIAL ACTIVITY

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**ABSTRACT:** Eleven new compounds belonging to series 7-[5-(substituted) phenyl - 4, 5-dihydro-1*H*-pyrazol-3-yl]-2,3-diphenyl-5*H*, 10*H* - benzo[g] quinoxaline - 5, 10 - dione (Compound 7a-k) were synthesized by multistep synthetic scheme. The newly synthesized compounds were screened for their *in-vitro* antimycobacterial activity against *Mycobacterium tuberculosis* H<sub>37</sub>Rv by L.J. Slope (Conventional) Method. Compound 7j having 4-CH<sub>3</sub> at phenyl ring attached to 5-position of pyrazoline ring and compound 7i having 3,4-(OCH<sub>3</sub>)<sub>2</sub> group on the above mentioned position have been observed as most and least active antimycobacterial compounds respectively.

**INTRODUCTION:** Nitrogen containing benzene fused heterocyclic ring, quinoxaline is the important components of antibiotics *viz.* hinomycin, levomycin and actinoleutin, that are inhibitors of gram positive bacteria and various transplantable tumours <sup>1-7</sup>. Quinoxaline derivatives have also been observed to exhibit wide range of pharmacological activities like antifungal <sup>8-10</sup>, antibacterial <sup>11-12</sup>, antitubercular <sup>8-9, 11, 13-15</sup> *etc.* In literature, various methods have been explained for synthesis of quinoxaline ring systems by reaction of *ortho*-phenylenediamine with various  $\alpha$ ,  $\beta$ -dicarbonyl moieties <sup>16</sup>, oximes <sup>17-18</sup>, phenacyl bromides *via* oxidative cyclization <sup>19</sup>, ethyl pyruvate and  $\alpha$ -bromo ketones in presence of FeCl<sub>3</sub> <sup>20</sup>,  $\alpha$ -hydroxyimino ketone derivatives <sup>21</sup> *etc.*

Synthesis of various fused quinoxalines by intramolecular cyclization of NH and N-alkyl quaternary salts of 2-quinoxaline-2-carboxyl aldehyde hydrazones have also been reported <sup>22</sup>. Various methods for synthesis of benzo[g] quinoxaline scaffold include Bis-S<sub>RN1</sub> Methodology <sup>23</sup>, regiospecific displacement <sup>24</sup>, reaction of diethylester of naphthalenebis(oxamate) with *tert*-BuNH<sub>2</sub> <sup>25</sup>, Diels-Alder Condensation <sup>6</sup> *etc.*

Tuberculosis (TB) is one of the major cause for death now-a-days worldwide. Quinoxaline ring containing antileprotic and antitubercular drug clofazimine (CZM) is widely used for treatment of multidrug resistant tuberculosis. In *Mycobacterium tuberculosis*, CZM is reduced by NADH-dehydrogenase (NDH-2) in order to release reactive oxygen species and reoxidized by O<sub>2</sub> <sup>26</sup>. CZM also competes with mycobacterial menaquinone (MK-4) for its reduction by NDH-2 <sup>27</sup>.

**MATERIALS AND METHODS: Chemistry:** Melting points were determined in open capillary

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tubes and are uncorrected. All the Fourier-Transform Infra-Red (FT-IR) spectra were recorded using KBr pellets on Shimadzu FT-8400 Spectrophotometer. The  $^1\text{H-NMR}$  and  $^{13}\text{C-NMR}$  spectra were recorded on Bruker-Spectrospin DCX NMR spectrometer using tetramethylsilane (TMS)

as an internal standard. Chemical shifts ( $\delta$ ) are expressed in ppm. The purity of the compounds was checked by thin layer chromatography (TLC) on Merck Silica Gel 60<sub>F254</sub> precoated sheets using Toluene: Ethylacetate: Formic acid (5:4:1) solution as mobile phase (solvent).

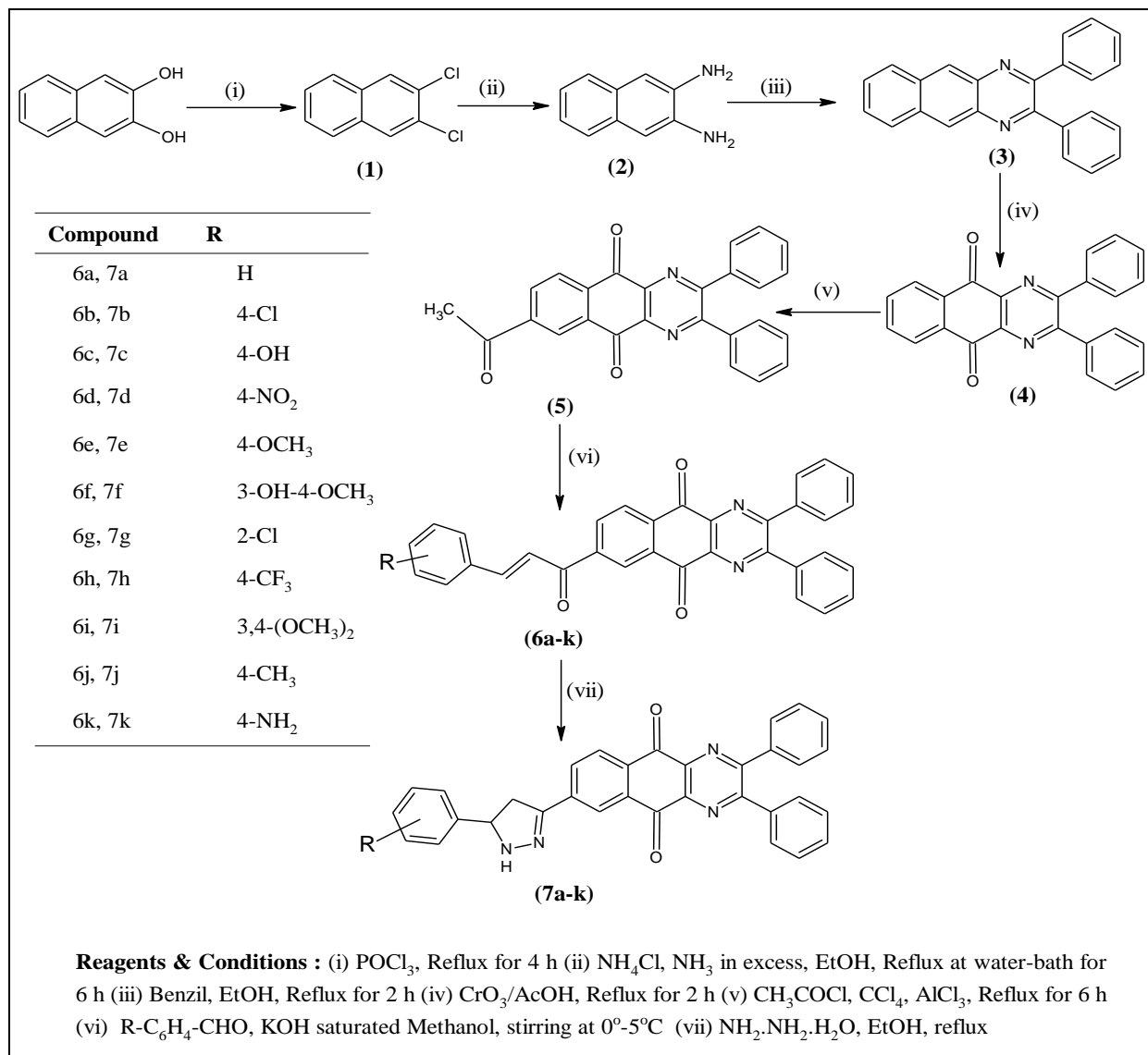


FIG. 1: REACTION SCHEME

### General Procedure for the Synthesis of Titled Compounds:

**2, 3-Dichloronaphthalene (1):** 2, 3-dihydroxynaphthalene (5 gm) was dissolved in phosphorus oxychloride (90 ml) in parts at 0° - 5°C with occasionally stirring and refluxed for about 4 hours till the appearance of clear dark pinkish solution. The solution was cooled and poured into ice-cold water. A dark pinkish solid appeared and was filtered. The solid was dried and recrystallized with dimethylformamide (DMF). Pinkish crystalline solid;

yield 85%;  $R_f$  0.72; mp 185°C; FT-IR ( $\nu_{\max}$ , cm<sup>-1</sup>): 756 (*ortho*-disubstituted aromatic ring), 856 (*meta*-disubstituted aromatic ring), 1160 (C-Cl, aryl), 1384 (C=C, sp<sup>2</sup>, aromatic);  $^1\text{H-NMR}$  (CDCl<sub>3</sub>, 300 MHz,  $\delta$ ): 8.16-8.20 (q, 2H, A<sub>2</sub>B<sub>2</sub> pattern, Ar-H, J=5-6 Hz), 7.74-7.79 (m, 2H, Ar-H, J=4.5-6 Hz), 7.50-7.53 (m, 2H, Ar-H, J=1-4 Hz).

**2,3-Diaminonaphthalene (2):** Compound 1 (2 gm) was dissolved in absolute ethanol and ammonium chloride (1.5 gm), dil. HCl (in catalytic amount) and excess of strong ammonia solution were added

and then refluxed for 6 hours on water bath till dark greenish colour permanently persists. Reaction solution was cooled and kept in deep freezer for overnight. Greenish crystalline solid was filtered, dried and recrystallized with methanol. Dark greenish crystals; yield 75%;  $R_f$  0.89; mp 150°C; FT-IR ( $\nu_{\max}$ ,  $\text{cm}^{-1}$ ): 758, 854, 1473 (aromatic =C-N), 1500 (aromatic C=C), 1681 (N-H), 3049 (N-H);  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ , 500 MHz,  $\delta$ ): 7.45-7.46 (dd, 2H, Ar-H,  $J=3.5-4$  Hz), 7.12-7.14 (dd, 2H, Ar-H,  $J=3-3.5$  Hz), 7.09 (s, 2H, Ar-H), 7.05 (s, 4H, Ar-NH<sub>2</sub>).

**2,3-Diphenylbenzo[g]quinoxaline (3):** Equimolar quantities of compound 2 (0.001 mol) and benzil (0.001 mol) were dissolved in ethanol (30 ml) and refluxed for 2 hours. Reaction solution was cooled and kept for overnight. Yellow crystalline solid was filtered, dried and recrystallized with ethanol: methanol solution (1:1). Yellow crystalline solid; yield 72%;  $R_f$  0.83; mp 170°C; FT-IR ( $\nu_{\max}$ ,  $\text{cm}^{-1}$ ): 725 (*mono*-substituted aromatic ring), 785, 820, 875, 1475, 1510, 1660 (quinoxaline C=N);  $^1\text{H-NMR}$  ( $\text{DMSO-}d_6$ , 500 MHz,  $\delta$ ): 8.73-8.77 (m, 10H, Ar-H,  $J=2.5-4$  Hz), 8.28 (s, 2H, Ar-H), 8.03-8.07 (m, 4H, Ar-H,  $J=2.5-4$  Hz).

**2,3-Diphenylbenzo[g]quinoxaline-5,10-dione (4):** Compound 3 (1.2 gm) was dissolved in glacial acetic acid (30 ml) and added to a solution of chromium trioxide (1.1 gm) in 12 ml of glacial acetic acid : water solution (1:1). This solution was heated at 80 °C for 2 hours and then poured into ice-chilled water (1500 ml). Resulting solid was filtered, dried and recrystallized with methanol. White solid; yield 65%;  $R_f$  0.78; mp 162°C; FT-IR ( $\nu_{\max}$ ,  $\text{cm}^{-1}$ ): 718, 795, 875, 1450, 1594 (aromatic C=C), 1676 (quinoxaline C=N);  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ , 500 MHz,  $\delta$ ): 8.13-8.15 (d, 2H, Ar-H,  $J=8.5$  Hz), 7.85-7.88 (t, 4H, Ar-H,  $J=2.5-10.5$  Hz), 7.81-7.82 (d, 2H, Ar-H,  $J=8$  Hz), 7.50-7.53 (t, 6H, Ar-H,  $J=7.5$  Hz).

**7-Acetyl-2,3-diphenylbenzo[g]quinoxaline-5, 10-dione (5):** Anhydrous aluminium trichloride (1 gm) was dissolved in carbon tetrachloride (30 ml). Acetyl chloride (2 ml) was added to it under cold conditions (0° - 5°C). Compound 4 (120 mg) was dissolved in this solution and stirred at room temperature for 6 hours. Yellow crystalline solid was filtered, dried and recrystallized with chloroform. Yellow crystalline solid; yield 48%;  $R_f$

0.74; mp 225°C; FT-IR ( $\nu_{\max}$ ,  $\text{cm}^{-1}$ ): 725, 775, 810, 875, 1450 (aromatic =C-N), 1500 (aromatic C=C), 1593 (cyclic >C=O), 1672 (quinoxaline C=N), 1974 (aromatic >C=O), 3063 (C-H, CH<sub>3</sub>);  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ , 500 MHz,  $\delta$ ): 7.97-7.98 (d, 4H, Ar-H,  $J=8$  Hz), 7.65-7.68 (t, 3H, Ar-H,  $J=7.5$  Hz), 7.50-7.53 (t, 6H, Ar-H,  $J=7.5-8$  Hz), 7.26 (s, 3H, CH<sub>3</sub>CO)

**Synthesis of 7 -[3-(substituted) phenylprop – 2 -enoyl]-2,3-diphenyl-5H,10H-benzo[g] quinoxaline -5,10-dione (Compound 6a-k):** Compound 5 (0.01 mol) and appropriate benzaldehyde derivative (0.15 mol) were dissolved in methanol saturated with KOH and stirred at 0° - 5 °C till the solid appeared. Reaction time may vary from 15 minutes to 4 hours. Solid was filtered, dried and recrystallized with methanol: ethanol (1:1) solution.

**7-[3-phenylprop-2-enoyl]-2,3-diphenyl-5H, 10H-benzo[g]quinoxaline - 5, 10-dione (6a):** Yellow solid; yield 65%;  $R_f$  0.78; mp 156°C; FT-IR ( $\nu_{\max}$ ,  $\text{cm}^{-1}$ ): 750 (*mono*-substituted aromatic ring), 783 (*ortho*-disubstituted aromatic ring), 972 (*meta*-disubstituted aromatic ring), 980 (>C-C=C), 1290 (C=N), 1384 (C-N), 1483 (Ar-C=O), 1581 (enoyl >C=O), 1620 (cyclic >C=O), 1680 (>C=O, conjugated with phenyl);  $^1\text{H-NMR}$  ( $\text{DMSO-}d_6$ , 500 MHz,  $\delta$ ): 8.14 (bs, 3H, Ar-H), 7.88 (bs, 5H, Ar-H), 7.74-7.76 (d, 2H, CH=CH,  $J=12$  Hz), 7.35-7.65 (m, 10H, Ar-H); MS-ESI: 492.1 (m/z, M<sup>+</sup>); Analysis calculated for C<sub>33</sub>H<sub>20</sub>N<sub>2</sub>O<sub>3</sub>: C, 80.47; H, 4.09; N, 5.69; O, 9.75. Found: C, 80.45; H, 4.07; N, 5.70; O, 9.77.

**7-[3-(4-chlorophenyl)prop-2-enoyl]-2,3-diphenyl -5H, 10H-benzo[g]quinoxaline-5,10-dione (6b):** Yellow solid; yield 65%;  $R_f$  0.75; mp 185°C; FT-IR ( $\nu_{\max}$ ,  $\text{cm}^{-1}$ ): 723, 780, 972, 980, 1172 (aryl C-Cl), 1290, 1382, 1485, 1590, 1620, 1680;  $^1\text{H-NMR}$  ( $\text{DMSO-}d_6$ , 500 MHz,  $\delta$ ): 8.11-8.15 (m, 1H, CH=CH\*-CO-,  $J=2.5-7.5$  Hz), 8.05-8.07 (d, 1H, \*CH=CH-CO-,  $J=8$  Hz), 7.91-7.97 (m, 3H, Ar-H,  $J=7.5-16$  Hz), 7.77-7.88 (m, 4H, Ar-H,  $J=3-11$  Hz), 7.45-7.56 (m, 5H, Ar-H,  $J=2.5-15.5$  Hz), 7.32-7.38 (m, 5H, Ar-H,  $J=5-7$  Hz);  $^{13}\text{C-NMR}$  ( $\text{DMSO-}d_6$ , 125 MHz,  $\delta$ ): 189.50, 188.96, 167.55, 161.86, 153.55, 142.00, 138.29, 135.48, 135.39, 134.18, 134.13, 133.41, 131.31, 131.17, 131.04, 130.91, 130.71, 130.17, 129.86, 129.68, 129.53, 129.41, 129.29, 129.25, 129.20, 128.88, 128.53, 126.70, 127.24, 114.89; MS-ESI: 526.1 (m/z, M<sup>+</sup>);

Analysis calculated for  $C_{33}H_{19}ClN_2O_3$ : C, 75.21; H, 3.63; Cl, 6.73; N, 5.32; O, 9.11. Found: C, 75.20; H, 3.64; Cl, 6.72; N, 5.31; O, 9.11.

**7-[3-(4-hydroxyphenyl)prop-2-enoyl]-2,3-diphenyl-5H,10H-benzo[g]quinoxaline-5,10-dione (6c):** Red Solid; yield 62%;  $R_f$  0.78; mp 180°C; FT-IR ( $\nu_{max}$ ,  $cm^{-1}$ ): 690, 780, 880, 960, 980, 1199 (phenolic C-O), 1290, 1384, 1483, 1581, 1680, 1749, 3078 (phenolic C-O-H);  $^1H$ -NMR (DMSO- $d_6$ , 500 MHz,  $\delta$ ): 8.11-8.16 (m, 1H, CH=CH\*-CO-, J=2.5-8 Hz), 8.01 (s, 1H, Ar-H), 7.82-7.88 (m, 5H, Ar-H, J=2-11 Hz), 7.53-7.56 (t, 1H, \*CH=CH-CO-, J=7.5 Hz), 7.41-7.47 (m, 5H, Ar-H, J=3-12 Hz), 7.33-7.38 (m, 2H, Ar-H, J=5-7.5 Hz), 7.00-7.04 (dd, 4H, Ar-H, J=8.5 Hz), 5.83-5.86 (dd, 1H, Ar-OH, J=8 Hz); MS-ESI: 508.1 (m/z,  $M^+$ ); Analysis calculated for  $C_{33}H_{20}N_2O_4$ : C, 77.94; H, 3.96; N, 5.51; O, 12.58. Found: C, 77.93; H, 3.97; N, 5.50; O, 12.57.

**7-[3-(4-nitrophenyl)prop-2-enoyl]-2,3-diphenyl-5H,10H-benzo[g]quinoxaline-5,10-dione (6d):** Brown solid; yield 55%;  $R_f$  0.78; mp 160°C; FT-IR ( $\nu_{max}$ ,  $cm^{-1}$ ): 680, 783, 837, 972, 1080, 1290, 1380, 1404 (-NO<sub>2</sub>, *sym.*), 1483, 1560 (-NO<sub>2</sub>, *asym.*), 1581, 1645, 1701;  $^1H$ -NMR (DMSO- $d_6$ , 500 MHz,  $\delta$ ): 8.11-8.15 (dd, 4H, Ar-H,  $J_1=7.5$  Hz,  $J_2=3.5$  Hz), 7.81-7.88 (m, 5H, Ar-H, J=3-10.5 Hz), 7.78 (s, 1H, Ar-H), 7.69-7.72 (d, 2H, CH=CH-CO-, J=15.5 Hz), 7.62-7.65 (t, 2H, Ar-H, J=7-7.5 Hz), 7.45-7.56 (m, 5H, Ar-H); MS-ESI: 537.2 (m/z,  $M^+$ ); Analysis calculated for  $C_{33}H_{19}N_3O_5$ : C, 73.74; H, 3.56; N, 7.82; O, 14.88. Found: C, 73.72; H, 3.57; N, 7.83; O, 14.87.

**7-[3-(4-methoxyphenyl)prop-2-enoyl]-2,3-diphenyl-5H,10H-benzo[g]quinoxaline-5,10-dione (6e):** White solid; yield 43%;  $R_f$  0.70; mp 160°C; FT-IR ( $\nu_{max}$ ,  $cm^{-1}$ ): 680, 783, 840, 965, 980, 1130 (C-O-C, *sym.*), 1263 (C-O-C, *asym.*), 1290, 1380, 1483, 1580, 1616, 1640;  $^1H$ -NMR (DMSO- $d_6$ , 500 MHz,  $\delta$ ): 8.11-8.15 (m, 1H, CH=CH-CO-, J=3.5-7.5 Hz), 7.98 (s, 1H, Ar-H), 7.77-7.88 (m, 5H, Ar-H, J=1.5-15.5 Hz), 7.64-7.72 (m, 1H, Ar-H, J=8-15.5 Hz), 7.41-7.46 (m, 5H, Ar-H, J=2.5-12 Hz), 7.33-7.38 (m, 1H, Ar-H, J=5-7.5 Hz), 7.02-7.04 (d, 2H, Ar-H, J=8.5 Hz), 6.83-6.85 (d, 2H, Ar-H, J=8.5 Hz), 5.82-5.85 (dd, 1H, CH=CH,  $J_1=J_2=7$  Hz), 3.68 (s, 3H, CH<sub>3</sub>O); MS-ESI: 522.2 (m/z,  $M^+$ ); Analysis calculated for  $C_{34}H_{22}N_2O_4$ : C, 78.15; H,

4.24; N, 5.36; O, 12.25. Found: C, 78.14; H, 4.26; N, 5.34; O, 12.24.

**7-[3-(3-hydroxy-4-methoxyphenyl)prop-2-enoyl]-2,3-diphenyl-5H,10H-benzo[g]quinoxaline-5,10-dione (6f):** Yellow solid; yield 50%;  $R_f$  0.80; mp 155°C; FT-IR ( $\nu_{max}$ ,  $cm^{-1}$ ): 680, 742, 891, 964, 972, 1114 (C-O-C, *sym.*), 1163 (C-O, phenolic), 1226 (C-O-C, *asym.*), 1288, 1377, 1498, 1595, 1608, 1629, 3064 (O-H, phenolic);  $^1H$ -NMR (DMSO- $d_6$ , 500 MHz,  $\delta$ ): 9.60 (s, 1H, Ar-H), 8.52 (s, 1H, Ar-OH), 8.11-8.15 (q, 2H, Ar-H, J=3-7.5 Hz), 7.78-7.87 (m, 3H, Ar-H, J=3-15.5 Hz), 7.69-7.72 (d, 1H, Ar-H, J=16 Hz), 7.62-7.65 (t, 1H, Ar-H, J=7-7.5 Hz), 7.53-7.56 (t, 1H, CH=CH\*-CO-, J=7-7.5 Hz), 7.45-7.46 (d, 2H, Ar-H, J=7 Hz), 7.32-7.37 (m, 3H, Ar-H, J=5-7.5 Hz), 7.28-7.29 (d, 1H, \*CH=CH-CO-, J=7.5 Hz), 7.23 (s, 1H, Ar-H), 6.99-7.01 (d, 1H, Ar-H, J=8.5 Hz), 6.80-6.82 (d, 1H, Ar-H, J=8 Hz), 3.74-3.80 (d, 3H, CH<sub>3</sub>O, J=2.5 Hz);  $^{13}C$ -NMR (DMSO- $d_6$ , 125 MHz,  $\delta$ ): 189.98, 189.51, 166.15, 161.86, 153.54, 149.80, 144.53, 140.92, 139.23, 138.28, 133.41, 130.91, 130.30, 130.17, 129.28, 129.25, 129.22, 128.88, 128.53, 127.75, 125.55, 119.96, 116.39, 114.89, 110.30, 55.85; MS-ESI: 538.2 (m/z,  $M^+$ ); Analysis calculated for  $C_{34}H_{22}N_2O_5$ : C, 75.83; H, 4.12; N, 5.20; O, 14.85. Found: C, 75.82; H, 4.11; N, 5.21; O, 14.85.

**7-[3-(2-chlorophenyl)prop-2-enoyl]-2,3-diphenyl-5H,10H-benzo[g]quinoxaline-5,10-dione (6g):** Red solid; yield 60%;  $R_f$  0.82; mp 140°C; FT-IR ( $\nu_{max}$ ,  $cm^{-1}$ ): 690, 780, 838, 970, 990, 1089 (C-Cl, aryl), 1247, 1375, 1473, 1577, 1614, 1640;  $^1H$ -NMR (DMSO- $d_6$ , 500 MHz,  $\delta$ ): 8.12-8.16 (m, 1H, Ar-H, J=3.5-7.5 Hz), 8.05-8.06 (d, 1H, Ar-H, J=7.5 Hz), 7.82-7.88 (m, 2H, Ar-H, J=2.5-8.5 Hz), 7.78-7.80 (d, 1H, Ar-H, J=7 Hz), 7.62-7.75 (m, 2H, Ar-H, J=7.5-16.5 Hz), 7.46-7.56 (m, 3H, Ar-H, J=6.5-20.5 Hz), 7.31-7.38 (m, 3H, Ar-H, J=1.5-8 Hz), 7.20-7.29 (m, 2H, Ar-H, J=6-9.5 Hz), 6.99-7.01 (d, 2H, CH=CH-CO-, J=8 Hz), 6.86-6.91 (q, 1H, Ar-H, J=7-12.5 Hz), 6.57-6.64 (m, 1H, Ar-H, J=4.5-8.5 Hz); MS-ESI: 526.2 (m/z,  $M^+$ ); Analysis calculated for  $C_{33}H_{19}ClN_2O_3$ : C, 75.21; H, 3.63; Cl, 6.73; N, 5.32; O, 9.11. Found: C, 75.20; H, 3.62; Cl, 6.74; N, 5.32; O, 9.12.

**7-[3-(4-trifluoromethyl)phenylprop-2-enoyl]-2,3-diphenyl-5H,10H-benzo[g]quinoxaline-5,10-dione (6h):** Brown solid; yield 42%;  $R_f$  0.78; mp



152°C; FT-IR ( $\nu_{\max}$ ,  $\text{cm}^{-1}$ ): 680, 783, 837, 972, 1018, 1263, 1290 (aryl C-F), 1380, 1483, 1581, 1680;  $^1\text{H-NMR}$  (DMSO- $d_6$ , 500 MHz,  $\delta$ ): 7.95-7.97 (d, 4H, Ar-H,  $J=7.5$  Hz), 7.61 (s, 1H, Ar-H), 7.53-7.58 (q, 2H, Ar-H,  $J=7.5-9.5$  Hz), 7.45-7.50 (q, 5H, Ar-H,  $J=7-8$  Hz), 7.27-7.33 (m, 5H, Ar-H,  $J=1.5-12$  Hz), 7.38-7.41 (d, 2H, CH=CH-CO,  $J=16.5$  Hz);  $^{13}\text{C-NMR}$  (DMSO- $d_6$ , 125 MHz,  $\delta$ ): 189.51, 188.15, 170.12, 161.87, 153.56, 146.27, 140.93, 138.29, 136.73, 133.42, 132.11, 131.32, 130.92, 130.18, 129.68, 129.58, 129.29, 129.26, 129.22, 128.88, 128.75, 128.61, 127.76, 120.36, 114.89-119.98 (t,  $\text{CF}_3$ ), 113.71; MS-ESI: 560.1 ( $m/z$ ,  $M^+$ ); Analysis calculated for  $\text{C}_{34}\text{H}_{19}\text{F}_3\text{N}_2\text{O}_3$ : C, 72.85; H, 3.42; F, 10.17; N, 5.00; O, 8.56. Found: C, 72.84; H, 3.41; F, 10.18; N, 4.99; O, 8.57.

**7-[3-(3,4-dimethoxyphenyl)prop-2-enoyl] - 2, 3-diphenyl-5H,10H-benzo[g] quinoxaline - 5, 10-dione (6i):** Brick red solid; yield 68%;  $R_f$  0.75; mp. 170°C; FT-IR ( $\nu_{\max}$ ,  $\text{cm}^{-1}$ ): 680, 740, 840, 972, 980, 1112 (C-O-C, *sym.*), 1253 (C-O-C, *asym.*), 1290, 1382, 1480, 1581, 1640, 1680;  $^1\text{H-NMR}$  (DMSO- $d_6$ , 500 MHz,  $\delta$ ): 8.05-8.07 (d, 3H, Ar-H,  $J=7.5$  Hz), 7.77-7.78 (d, 4H, Ar-H,  $J=8$  Hz), 7.60-7.73 (m, 6H, Ar-H,  $J=7-15.5$  Hz), 7.30-7.35 (m, 2H, CH=CH-CO,  $J=6.5-9.5$  Hz), 6.96-6.98 (d, 3H, Ar-H,  $J=8.5$  Hz), 3.87 (s, 6H,  $\text{OCH}_3$ ); MS-ESI: 552.2 ( $m/z$ ,  $M^+$ ); Analysis calculated for  $\text{C}_{35}\text{H}_{24}\text{N}_2\text{O}_5$ : C, 76.08; H, 4.38; N, 5.07; O, 14.48. Found: C, 76.07; H, 4.39; N, 5.06; O, 14.48.

**7-[3-(4-methylphenyl)prop-2-enoyl] - 2, 3 - di phenyl-5H,10H-benzo[g]quinoxaline-5, 10-dione (6j):** White solid; yield 40%;  $R_f$  0.70; mp 144°C; FT-IR ( $\nu_{\max}$ ,  $\text{cm}^{-1}$ ): 710, 783, 877, 972, 980, 1290, 1382, 1483, 1581, 1640, 1680, 2356 (C-H,  $\text{CH}_3$ );  $^1\text{H-NMR}$  (DMSO- $d_6$ , 500 MHz,  $\delta$ ): 7.80-7.88 (m, 5H, Ar-H,  $J=4-11.5$  Hz), 7.77 (s, 1H, Ar-H), 7.70-7.73 (m, 2H, Ar-H,  $J=4-8$  Hz), 7.62-7.67 (q, 1H, CH=CH\*-CO), 7.45-7.47 (d, 1H, \*CH=CH-CO,  $J=7$  Hz), 7.34-7.39 (m, 5H, Ar-H,  $J=6.5-7.5$  Hz), 6.99-7.00 (d, 4H, Ar-H,  $J=9$  Hz), 3.80 (s, 3H,  $\text{CH}_3$ ); MS-ESI: 506.1 ( $m/z$ ,  $M^+$ ); Analysis calculated for  $\text{C}_{34}\text{H}_{22}\text{N}_2\text{O}_3$ : C, 80.62; H, 4.38; N, 5.53; O, 9.48. Found: C, 80.61; H, 4.39; N, 5.51; O, 9.49.

**7-[3-(4-aminophenyl)prop-2-enoyl]-2,3-diphenyl-5H, 10H-benzo[g] quinoxaline- 5, 10 - dione (6k):** Light yellowish solid; yield 66%;  $R_f$  0.79; mp 134°C; FT-IR ( $\nu_{\max}$ ,  $\text{cm}^{-1}$ ): 692, 765, 813, 831,

1012, 1290, 1382, 1463, 1585, 1614 (N-H,  $1^\circ$ amine, bend), 3139 (N-H,  $1^\circ$ amine, str.);  $^1\text{H-NMR}$  (DMSO- $d_6$ , 500 MHz,  $\delta$ ): 7.96 (s, 1H, Ar-H), 7.82-7.90 (m, 5H, Ar-H,  $J=2-10.5$  Hz), 7.41-7.47 (m, 5H, Ar-H,  $J=3.5-8.5$  Hz), 7.34-7.38 (m, 1H, CH=CH\*-CO,  $J=4.5-8$  Hz), 7.02-7.04 (d, 1H, Ar-H,  $J=8.5$  Hz), 6.92-6.94 (d, 2H, Ar-H,  $J=9$  Hz), 6.83-6.85 (d, 1H, Ar-H,  $J=8.5$  Hz), 6.61-6.63 (d, 2H, Ar-H,  $J=8.5$  Hz), 5.77-5.80 (dd, 1H, \*CH=CH-CO,  $J_1=J_2=3$  Hz), 3.78-3.87 (m, 2H,  $\text{NH}_2$ ,  $J=5.5-11.5$  Hz); MS-ESI: 507.1 ( $m/z$ ,  $M^+$ ); Analysis calculated for  $\text{C}_{33}\text{H}_{21}\text{N}_3\text{O}_3$ : C, 78.09; H, 4.17; N, 8.28; O, 9.46. Found: C, 78.08; H, 4.17; N, 8.26; O, 9.47.

**Synthesis of 7-[5-(substituted) phenyl - 4, 5-dihydro-1H-pyrazol-3-yl]-2,3-diphenyl-5H, 10H-benzo[g]quinoxaline-5,10-dione (7a-k):**Compound 6(a-k) (0.005 mol) and hydrazine hydrate (1 ml) were refluxed in absolute ethanol under anhydrous conditions till the solid appeared with brisk bumping. Solid was filtered, dried and recrystallized.

**7-[5-phenyl-4,5-dihydro-1H-pyrazol-3-yl] - 2, 3-diphenyl-5H,10H-benzo[g] quinoxaline - 5, 10 - dione (7a):** White solid, yield 55%, mp 136°C,  $R_f$  0.70; FT-IR ( $\nu_{\max}$ ,  $\text{cm}^{-1}$ ): 696, 757, 829, 985, 1147 (=N-N, pyrazoline), 1353 (C-N, pyrazoline), 1379, 1583 (C=N, pyrazoline), 1656, 1749, 2358 (C-C, cyclic, pyrazoline), 3058 (N-H, pyrazoline);  $^1\text{H-NMR}$  (DMSO- $d_6$ , 500 MHz,  $\delta$ ): 8.59 (s, 1H, Ar-H), 7.86-7.95 (m, 5H, Ar-H), 7.72-7.75 (d, 1H, Ar-H,  $J=11$  Hz), 7.64-7.67 (t, 1H, Ar-H,  $J=7-7.5$  Hz), 7.54-7.57 (t, 2H, pyrazoline-H,  $J=7.5-8$  Hz), 7.32-7.46 (m, 10H, Ar-H), 7.23-7.24 (d, 1H, pyrazoline-H,  $J=7.5$  Hz), 6.83-6.88 (q, 1H, pyrazoline-N-H,  $J=5.5-8.5$  Hz);  $^{13}\text{C-NMR}$  (DMSO- $d_6$ , 125 MHz,  $\delta$ ): 189.68, 176.58, 155.40, 153.56, 144.53, 143.47, 140.93, 139.24, 138.01, 135.12, 133.66, 131.36, 131.14, 131.03, 130.92, 130.18, 129.41, 129.40, 129.29, 129.26, 129.16, 129.01, 128.98, 128.54, 127.59, 127.39, 125.75, 122.52, 63.31, 42.86; MS-ESI: 506.5 ( $m/z$ ,  $M^+$ ); Analysis calculated for  $\text{C}_{33}\text{H}_{22}\text{N}_4\text{O}_2$ : C, 78.25; H, 4.38; N, 11.06; O, 6.32. Found: C, 78.15; H, 4.41; N, 10.98; O, 6.46.

**7-[5-(4-chlorophenyl)-4,5-dihydro-1H-pyrazol-3-yl]-2,3-diphenyl-5H, 10 H-benzo[g]quinoxaline - 5,10-dione (7b):** Yellow solid, yield 68%, mp 184°C,  $R_f$  0.86; FT-IR ( $\nu_{\max}$ ,  $\text{cm}^{-1}$ ): 684, 759, 840,

1018, 1176 (=N-N, pyrazoline, C-Cl, aryl), 1342, 1384, 1593, 1610, 1749, 2360, 3168; <sup>1</sup>H-NMR (DMSO-*d*<sub>6</sub>, 500 MHz, δ): 8.14-8.15 (d, 1H, pyrazoline-H, J=6.5 Hz), 8.05 (s, 1H, Ar-H), 7.88 (bs, 2H, Ar-H), 7.74-7.75 (d, 4H, Ar-H, J=7.5 Hz), 7.44-7.47 (t, 1H, pyrazoline-H, J=6-7.5 Hz), 7.34-7.36 (d, 4H, Ar-H, J=8 Hz), 7.23-7.25 (d, 3H, Ar-H, J=8 Hz), 7.11-7.13 (d, 3H, Ar-H, J=8.5 Hz), 5.86-5.89 (dd, 2H, pyrazoline-H, J<sub>1</sub>=J<sub>2</sub>=3 Hz); <sup>13</sup>C-NMR (DMSO-*d*<sub>6</sub>, 125 MHz, δ): 191.49, 189.68, 161.14, 153.55, 150.48, 144.53, 140.93, 139.24, 138.00, 135.11, 133.66, 131.14, 130.91, 130.17, 129.40, 129.29, 129.26, 129.01, 128.53, 125.80, 124.12, 122.51, 115.85, 115.95, 110.46, 56.03, 55.97; MS-ESI: 540.2 (m/z, M<sup>+</sup>); Analysis calculated for C<sub>33</sub>H<sub>21</sub>ClN<sub>4</sub>O<sub>2</sub>: C, 73.26; H, 3.91; Cl, 6.55; N, 10.36; O, 5.91. Found: C, 73.20; H, 3.96; Cl, 6.42; N, 10.38; O, 6.04.

**7-[5-(4-hydroxyphenyl)-4,5-dihydro-1H-pyrazol-3-yl]-2,3-diphenyl-5H,10H-benzo[g]quinoxaline-5,10-dione (7c):** White solid, yield 65%, mp 174°C, R<sub>f</sub> 0.79; FT-IR (ν<sub>max</sub>, cm<sup>-1</sup>): 684, 759, 840, 1018, 1145, 1249 (C-O, phenolic), 1342, 1384, 1593, 1610, 1747, 2360, 3170, 3375 (O-H, phenolic); <sup>1</sup>H-NMR (DMSO-*d*<sub>6</sub>, 500 MHz, δ): 8.14-8.15 (q, 1H, Ar-OH, J=1.5-3.5 Hz), 8.02 (s, 1H, Ar-H), 7.85-7.86 (t, 5H, Ar-H, J=2-6 Hz), 7.73-7.76 (d, 1H, Ar-H, J=15 Hz), 7.64-7.67 (t, 1H, pyrazoline-H, J=2-8.5 Hz), 7.54-7.57 (t, 1H, Ar-H, J<sub>1</sub>=J<sub>2</sub>=7.5 Hz), 7.41-7.47 (m, 5H, Ar-H, J=5-10 Hz), 7.32-7.38 (m, 2H, pyrazoline-H, J=2-8.5 Hz), 7.03-7.04 (d, 2H, Ar-H, J=8.5 Hz), 6.83-6.85 (d, 2H, Ar-H, J=8.5 Hz), 5.83-5.86 (q, 1H, pyrazoline-H, J=3-8 Hz); MS-ESI: 522.3 (m/z, M<sup>+</sup>); Analysis calculated for C<sub>33</sub>H<sub>22</sub>N<sub>4</sub>O<sub>3</sub>: C, 75.85; H, 4.24; N, 10.72; O, 9.19. Found: C, 75.88; H, 4.21; N, 10.65; O, 9.26.

**7-[5-(4-nitrophenyl)-4,5-dihydro-1H-pyrazol-3-yl]-2,3-diphenyl-5H,10H-benzo[g]quinoxaline-5,10-dione (7d):** Dark brown solid, yield 48%, mp 148°C, R<sub>f</sub> 0.76; FT-IR (ν<sub>max</sub>, cm<sup>-1</sup>): 684, 759, 840, 995, 1176, 1342, 1382, 1461 (-NO<sub>2</sub>, *sym.*), 1512 (-NO<sub>2</sub>, *asym.*), 1593, 1610, 1725, 2536, 3170; <sup>1</sup>H-NMR (DMSO-*d*<sub>6</sub>, 500 MHz, δ): 8.13-8.15 (d, 3H, Ar-H, J=6.5 Hz), 7.88-7.95 (q, 4H, Ar-H, J=3-19 Hz), 7.72-7.75 (d, 1H, pyrazoline-N-H, J=9.5 Hz), 7.64-7.67 (t, 1H, Pyrazoline-H, J<sub>1</sub>=J<sub>2</sub>=7 Hz), 7.55-7.58 (t, 2H, pyrazoline-H, J<sub>1</sub>=J<sub>2</sub>=7.5 Hz), 7.33-7.47 (m, 10H, Ar-H); MS-ESI: 551.4 (m/z, M<sup>+</sup>);

Analysis calculated for C<sub>33</sub>H<sub>21</sub>N<sub>5</sub>O<sub>4</sub>: C, 71.86; H, 3.84; N, 12.70; O, 11.60. Found: C, 71.84; H, 3.89; N, 12.66; O, 11.61.

**7-[5-(4-methoxyphenyl)-4,5-dihydro-1H-pyrazol-3-yl]-2,3-diphenyl-5H,10H-benzo[g]quinoxaline-5,10-dione (7e):** Light silver solid, yield 72%, mp 164°C, R<sub>f</sub> 0.71; FT-IR (ν<sub>max</sub>, cm<sup>-1</sup>): 688, 759, 833, 1006, 1126 (C-O-C, *sym.*), 1166, 1288 (C-O-C, *asym.*), 1359, 1388, 1585, 1614, 1740, 2360, 3136; <sup>1</sup>H-NMR (DMSO-*d*<sub>6</sub>, 500 MHz, δ): 8.14-8.157 (d, 1H, Ar-H, J=8 Hz), 7.91-7.96 (q, 1H, Ar-H, J=2.5-16.5 Hz), 7.85-7.88 (q, 4H, Ar-H, J=2-8.5 Hz), 7.82 (s, 1H, Ar-H), 7.61-7.70 (m, 1H, pyrazoline-H, J=2.5-9 Hz), 7.32-7.57 (m, 10H, Ar-H, J=4.5-17 Hz), 6.92-6.94 (d, 2H, pyrazoline-H, J=8.5 Hz), 6.61-6.73 (m, 3H, Ar-OCH<sub>3</sub>, J=8.5-18 Hz), 5.77-5.80 (dd, 1H, pyrazoline-N-H, J<sub>1</sub>=J<sub>2</sub>=2.5 Hz); MS-ESI: 536.2 (m/z, M<sup>+</sup>); Analysis calculated for C<sub>34</sub>H<sub>24</sub>N<sub>4</sub>O<sub>3</sub>: C, 76.11; H, 4.51; N, 10.44; O, 8.95. Found: C, 76.07; H, 4.55; N, 10.40; O, 8.98.

**7-[5-(3-hydroxy-4-methoxyphenyl)-4,5-dihydro-1H-pyrazol-3-yl]-2,3-diphenyl-5H,10H-benzo[g]quinoxaline-5,10-dione (7f):** Red solid, yield 72%, mp 156°C, R<sub>f</sub> 0.75; FT-IR (ν<sub>max</sub>, cm<sup>-1</sup>): 702, 790, 819, 979, 1116 (C-O-C, *sym.*), 1172, 1253 (C-O-C, *asym.*), 1292 (C-O, phenolic), 1342, 1373, 1591, 1654, 1899, 2347, 3072, 3386 (O-H, phenolic); <sup>1</sup>H-NMR (DMSO-*d*<sub>6</sub>, 500 MHz, δ): 8.14-8.15 (d, 1H, Ar-H, J=6.5 Hz), 8.03 (s, 1H, Ar-H), 7.85-7.95 (m, 5H, Ar-H, J=7-19 Hz), 7.55-7.58 (t, 1H, pyrazoline-H, J<sub>1</sub>=J<sub>2</sub>=7.5 Hz), 7.43-7.47 (q, 5H, Ar-H, J=6.5-8 Hz), 7.33-7.38 (m, 1H, Ar-H, J=6.5-7 Hz), 6.83-6.85 (d, 1H, Ar-H, J=8 Hz), 6.76 (s, 1H, Ar-H), 6.56-6.57 (d, 1H, Ar-H, J=7.5 Hz), 5.83-5.86 (dd, 1H, pyrazoline-N-H, J<sub>1</sub>=J<sub>2</sub>=3 Hz), 3.81-3.87 (q, 2H, pyrazoline-H, J=6.5-11 Hz), 3.33 (s, 3H, OCH<sub>3</sub>), 3.12-3.16 (dd, 1H, Ar-OH, J<sub>1</sub>=J<sub>2</sub>=3 Hz); MS-ESI: 552.1 (m/z, M<sup>+</sup>); Analysis calculated for C<sub>34</sub>H<sub>24</sub>N<sub>4</sub>O<sub>4</sub>: C, 73.90; H, 4.38; N, 10.14; O, 11.58. Found: C, 73.88; H, 4.39; N, 10.08; O, 11.35.

**7-[5-(2-chlorophenyl)-4,5-dihydro-1H-pyrazol-3-yl]-2,3-diphenyl-5H,10H-benzo[g]quinoxaline-5,10-dione (7g):** Brown solid, yield 72%, mp 158°C, R<sub>f</sub> 0.79; FT-IR (ν<sub>max</sub>, cm<sup>-1</sup>): 703, 775, 831, 983, 1174, 1209 (C-Cl, aryl), 1334, 1384, 1600, 1654, 1917, 2374, 3058; <sup>1</sup>H-NMR (DMSO-*d*<sub>6</sub>, 500 MHz, δ): 8.02 (s, 1H, Ar-H), 7.92-7.97 (d, 1H, Ar-H, J=22 Hz), 7.83-7.86 (t, 5H, Ar-H, J=6-9 Hz), 7.42-

7.47 (t, 5H, Ar-H, J=8.5-15.5 Hz), 7.32-7.37 (m, 1H, Ar-H, J=4.5-8.5 Hz), 7.03-7.04 (d, 1H, Ar-H, J=9 Hz), 6.93-6.94 (d, 2H, Ar-H, J=9 Hz), 6.83-6.85 (d, 1H, Ar-H, J=8.5 Hz), 6.61-6.63 (d, 2H, pyrazoline-H, J=9 Hz), 5.83-5.86 (dd, 1H, pyrazoline-N-H,  $J_1=J_2=3$  Hz), 5.78-5.80 (dd, 1H, pyrazoline-H,  $J_1=7.5$  Hz,  $J_2=8$  Hz); MS-ESI: 540.2 (m/z,  $M^+$ ); Analysis calculated for  $C_{33}H_{21}ClN_4O_2$ : C, 73.26; H, 3.91; Cl, 6.55; N, 10.36; O, 5.91. Found: C, 73.20; H, 3.99; Cl, 6.60; N, 10.40; O, 5.81.

**7-[5-(4-trifluoromethylphenyl)-4,5-dihydro-1H-pyrazol-3-yl]-2,3-diphenyl-5H,10H-benzo[g]quinoxaline-5,10-dione (7h):** Dark brown solid, yield 67%, mp 180°C,  $R_f$  0.81; FT-IR ( $\nu_{max}$ ,  $cm^{-1}$ ): 696, 757, 831, 1072, 1093, 1263 (C-F, aryl), 1353, 1384, 1583, 1670, 1876, 2393, 3143;  $^1H$ -NMR (DMSO- $d_6$ , 500 MHz): 8.14-8.15 (t, 1H, pyrazoline-H, J=4-8 Hz), 8.11 (s, 1H, Ar-H), 7.81-7.95 (m, 4H, Ar-H, J=3.5-9.5 Hz), 7.54-7.67 (m, 2H, Ar-H, J=2-9 Hz), 7.31-7.49 (m, 10H, Ar-H, J=5.5-10 Hz), 7.10-7.14 (t, 2H, pyrazoline-H, J=8-10.5 Hz), 5.88-5.91 (dd, 1H, pyrazoline-N-H,  $J_1=J_2=3.5$  Hz); MS-ESI: 574.1 (m/z,  $M^+$ ); Analysis calculated for  $C_{34}H_{21}F_3N_4O_2$ : C, 71.08; H, 3.68; F, 9.92; N, 9.75; O, 5.57. Found: C, 71.11; H, 3.65; F, 9.90; N, 9.75; O, 5.59.

**7-[5-(3,4-dimethoxyphenyl)-4,5-dihydro-1H-pyrazol-3-yl]-2,3-diphenyl-5H,10H-benzo[g]quinoxaline-5,10-dione (7i):** Light silver solid, yield 72%, mp 164°C,  $R_f$  0.71; FT-IR ( $\nu_{max}$ ,  $cm^{-1}$ ): 688, 763, 840, 1026, 1139 (C-O-C, *sym.*), 1166, 1307 (C-O-C, *asym.*), 1350, 1382, 1587, 1680, 1753, 2302, 3149;  $^1H$ -NMR (DMSO- $d_6$ , 500 MHz,  $\delta$ ): 8.59 (s, 1H, Ar-H), 8.13-8.14 (d, 2H, Ar-H, J=3 Hz), 7.86-7.95 (m, 3H, Ar-H, J=3-20.5 Hz), 7.64-7.75 (m, 2H, pyrazoline-H), 7.32-7.47 (m, 10H, Ar-H), 7.23-7.24 (d, 1H, pyrazoline-H, J=8 Hz), 6.86-6.88 (d, 1H, pyrazoline-H, J=8 Hz), 4.34 (s, 3H, OCH<sub>3</sub>), 3.81 (s, 3H, OCH<sub>3</sub>); MS-ESI: 566.4 (m/z,  $M^+$ ); Analysis calculated for  $C_{35}H_{26}N_4O_4$ : C, 74.19; H, 4.63; N, 9.89; O, 11.29. Found: C, 74.20; H, 4.65; N, 9.85; O, 11.30.

**7-[5-(4-methylphenyl)-4,5-dihydro-1H-pyrazol-3-yl]-2,3-diphenyl-5H,10H-benzo[g]quinoxaline-5,10-dione (7j):** Red solid, yield 69%, mp 164°C,  $R_f$  0.73; FT-IR ( $\nu_{max}$ ,  $cm^{-1}$ ): 688, 763, 838, 1004,

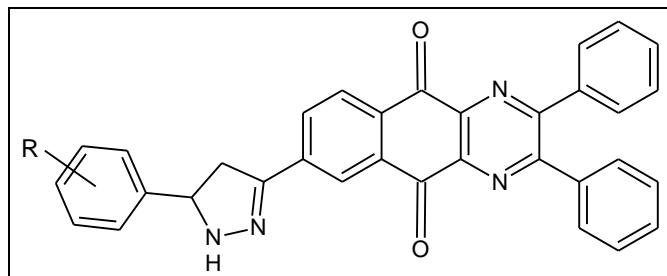
1157, 1352, 1377, 1583, 1612, 1810, 2374, 2835 (C-H, *sp*<sup>3</sup>, CH<sub>3</sub>), 3155;  $^1H$ -NMR (DMSO- $d_6$ , 500 MHz,  $\delta$ ): 8.11-8.15 (q, 4H, Ar-H, J=3.5-8.5 Hz), 7.78-7.85 (q, 6H, Ar-H, J=3.5-15.5 Hz), 7.69-7.72 (d, 2H, Ar-H, J=15.5 Hz), 7.62-7.65 (t, 2H, pyrazoline-H, J=7-7.5 Hz), 7.53-7.56 (t, 4H, Ar-H, J=7.5 Hz), 7.45-7.47 (d, 1H, Ar-H, J=7 Hz), 7.34-7.35 (d, 1H, pyrazoline-H, J=7.5 Hz), 6.99-7.01 (d, 1H, pyrazoline-H, J=9 Hz), 3.80 (s, 3H, CH<sub>3</sub>);  $^{13}C$ -NMR (DMSO- $d_6$ , 125 MHz,  $\delta$ ): 207.01, 176.37, 155.45, 153.56, 144.53, 139.24, 133.66, 131.85, 130.92, 130.17, 129.74, 129.40, 129.29, 129.26, 129.01, 128.94, 128.53, 128.51, 127.81, 127.61, 122.51, 62.68, 42.68, 21.54; MS-ESI: 520.2 (m/z,  $M^+$ ); Analysis calculated for  $C_{34}H_{24}N_4O_2$ : C, 78.44; H, 4.65; N, 10.76; O, 6.15. Found: C, 78.40; H, 4.66; N, 10.78; O, 6.16.

**Compound 7(k): 7-[5-(4-aminophenyl)-4,5-dihydro-1H-pyrazol-3-yl]-2,3-diphenyl-5H,10H-benzo[g]quinoxaline-5,10-dione (7k):** Orange solid, yield 70%, mp 158°C,  $R_f$  0.80; FT-IR ( $\nu_{max}$ ,  $cm^{-1}$ ): 740, 779, 835, 999, 1170, 1377, 1390, 1585, 1602 (>C=O, cyclic, conjugated, 1° amine, N-H, bend), 1757, 2374, 3058 (N-H, pyrazoline), 3236 (1° amine, N-H, str.);  $^1H$ -NMR (DMSO- $d_6$ , 500 MHz,  $\delta$ ): 7.95-7.97 (bd, 2H, Ar-NH<sub>2</sub>, J=7.5 Hz), 7.82-7.88 (m, 3H, Ar-H, J=2.5-21.5 Hz), 7.44-7.47 (t, 1H, pyrazoline-H, J=6-7 Hz), 7.32-7.38 (m, 1H, pyrazoline-N-H, J=3-7.5 Hz), 7.23-7.25 (d, 5H, Ar-H, J=8 Hz), 7.02-7.03 (d, 5H, Ar-H, J=8.5 Hz), 6.83-6.84 (d, 4H, Ar-H, J=8.5 Hz), 5.81-5.84 (dd, 2H, pyrazoline-H,  $J_1=J_2=2.5$  Hz); MS-ESI: 521.5 (m/z,  $M^+$ ); Analysis calculated for  $C_{33}H_{23}N_5O_2$ : C, 75.99; H, 4.44; N, 13.43; O, 6.14. Found: C, 76.01; H, 4.42; N, 13.39; O, 6.18.

**In-vitro Antimycobacterial Screening:** The newly synthesized compounds were submitted for their antimycobacterial activity against *Mycobacterium tuberculosis* H<sub>37</sub>Rv by L.J. Slope (Conventional) Method<sup>28-29</sup>. Each compound was diluted to obtain 2000  $\mu$ g/ml concentration (as a stock solution).

Inoculum Size for *M. tuberculosis* was adjusted to 1 mg/ml. L. J. Medium was used as nutrient medium. Isoniazid (0.20 $\mu$ g/ml) and rifampicin (0.25 $\mu$ g/ml) were used as standard drug.



**TABLE 1: ANTIMYCOBACTERIAL SCREENING OF COMPOUNDS (7a-k) AGAINST MYCOBACTERIUM TUBERCULOSIS H<sub>37</sub>Rv, MIC (µg/ml) (L. J. SLOPE METHOD)**

Compound	R	MIC (µg/mL)
7a	H	---
7b	4-Cl	125
7c	4-OH	100
7d	4-NO <sub>2</sub>	62.5
7e	4-OCH <sub>3</sub>	250
7f	3-OH-4-OCH <sub>3</sub>	100
7g	2-Cl	125
7h	4-CF <sub>3</sub>	250
7i	3,4-(OCH <sub>3</sub> ) <sub>2</sub>	1000
7j	4-CH <sub>3</sub>	12.5
7k	4-NH <sub>2</sub>	250
Rifampicin	---	0.25
Isoniazid	---	0.20

**Primary screen:** 500 µg/ml, 250 µg/ml, and 125 µg/ml concentrations of the compounds were considered for primary screening. The compounds found active in primary screening were further tested in second set of dilution against *M. tuberculosis*.

**Secondary screen:** The compounds found active in primary screening were similarly diluted to obtain 100 µg/ml, 50 µg/ml, 25 µg/ml, 12.5 µg/ml, 6.250 µg/ml, 3.125 µg/ml and 1.5625 µg/ml concentrations and were tested.

**Reading Result:** The result was expressed in term of Minimum Inhibitory concentration (MIC). The highest dilution inhibiting 99% of *M. tuberculosis* population was considered as MIC.

## RESULT AND DISCUSSION:

**Chemistry:** 2, 3 - Dihydroxynaphthalene on refluxing with phosphorus oxychloride yields 2, 3-dichloronaphthalene (1). Compound 1 on refluxing with ammonium chloride in excess of ammonia, catalytic amount of dil. HCl and ethanol undergoes amination (nucleophilic substitution) and furnishes 2,3-diaminonaphthalene (2).

Compound 2 on refluxing with equimolar quantity of benzil in ethanol undergoes nucleophilic addition followed by dehydration to yield 2,3-diphenylbenzo[g] quinoxaline (3). Compound 3 undergoes aromatic oxidation on refluxing with equimolar mixture of chromium trioxide and glacial acetic acid in water, furnishes 2,3-diphenylbenzo[g]quinoxaline-5,10-dione (4).

Compound 4 on acetylation reaction with acetylchloride and anhydrous aluminium chloride in carbon tetrachloride yields 7-acetyl - 2, 3-diphenylbenzo[g]quinoxaline-5, 10-dione (5).

Compound 5 on stirring with appropriate substituted benzaldehydes in potassium hydroxide saturated with methanol furnishes 7-[3-(substituted) phenylprop-2-enoyl]-2,3-diphenyl - 5H, 10H-benzo [g] quinoxaline - 5, 10-dione (6a-k) (*Cannizzaro Reaction*). Compound 6(a-k) were further refluxed with hydrazine hydrochloride in ethanol under anhydrous conditions to furnish 7-[5-(substituted) phenyl-4,5-dihydro-1H-pyrazol-3-yl]-2,3-diphenyl-5H, 10H - benzo [g] quinoxaline - 5, 10 - dione (Compound 7a-k). The structures of all the newly synthesized compounds (7a-k) belonging to series 7-[5-(substituted)phenyl-4,5-dihydro - 1H-pyrazol-3-yl]-2,3-diphenyl-5H,10H-benzo[g]quinoxaline-5, 10 - dione (Compound 7a-k) were confirmed by FT-IR, <sup>1</sup>H-NMR, MS-ESI spectral data interpretation and their elemental analysis.

FT-IR spectrum of 7-[5-phenyl-4,5-dihydro-1H-pyrazol-3-yl]-2, 3-diphenyl-5H, 10H - benzo [g] quinoxaline-5,10-dione (7a) showed bands at 696 cm<sup>-1</sup>, 757 cm<sup>-1</sup>, 829 cm<sup>-1</sup>, 985 cm<sup>-1</sup>, 1147 cm<sup>-1</sup>, 1353 cm<sup>-1</sup>, 1379 cm<sup>-1</sup>, 1583 cm<sup>-1</sup>, 1656 cm<sup>-1</sup>, 1749 cm<sup>-1</sup>, 2358 cm<sup>-1</sup> and 3058 cm<sup>-1</sup> belonging to mono-substituted aromatic ring, ortho-disubstituted aromatic ring, para-disubstituted aromatic ring, meta- disubstituted aromatic ring, = N - N (pyrazoline), C-N (pyrazoline), C-N (quinoxaline), C=N (pyrazoline), >C=O (cyclic, conjugated, C=N (quinoxaline), C-C (cyclic, pyrazoline) and N-H (pyrazoline) respectively. In <sup>1</sup>H-NMR spectrum of compound (7a), a singlet at 8.59 ppm belonging to one aromatic proton present at C-6 of quinoxaline-5,10-dione ring. A multiplet at 7.86-7.95 ppm confirms five aromatic protons of phenyl ring attached to C-5 of pyrazoline ring.



A doublet at 7.72-7.75 ppm with J value of 11 Hz confirmed one aromatic proton at C-9 of quinoxaline-5,10-dione ring. A triplet at 7.64-7.67 ppm with J value 7-7.5 Hz confirmed one aromatic proton at C-8 of quinoxaline-5,10-dione ring. A triplet at 7.54-7.57 ppm with J value 7.5-8 Hz belonged to two protons at C-4 of pyrazoline ring. A multiplet at 7.32-7.46 ppm confirmed ten aromatic protons of two phenyl rings present at C-2 and C-3 of quinoxaline-5,10-dione ring. A doublet at 7.23-7.24 ppm having J value 7.5 Hz belonged to one proton attached to C-5 of pyrazoline ring. A quartet at 6.83-6.88 ppm with J value 5.5-8.5 Hz belonged to one proton attached at N-1 of pyrazoline ring.

<sup>13</sup>C-NMR spectrum of compound (7a) showed the prominent peaks at 189.68 ppm (C<sub>5</sub>, C<sub>10</sub> of quinoxaline-5,10-dione ring), 176.58 ppm (C<sub>4a</sub>, C<sub>10a</sub> of quinoxaline-5,10-dione ring), 155.40 ppm (C<sub>3</sub> of quinoxaline-5,10-dione ring), 153.56 ppm (C<sub>2</sub> of quinoxaline-5,10-dione ring), 144.53 ppm (C<sub>3</sub> of pyrazoline), 143.47 ppm (C<sub>1</sub> of phenyl ring attached to C-3 of quinoxaline-5,10-dione ring), 140.93 ppm (C<sub>1</sub> of phenyl ring attached to C-2 of quinoxaline-5,10-dione ring), 139.24 ppm (C<sub>1</sub> of phenyl ring attached to C-5 of pyrazoline ring), 138.01 ppm (C<sub>5</sub> of phenyl ring attached to C-2 of quinoxaline-5,10-dione ring), 135.12 ppm (C<sub>7</sub> of quinoxaline-5,10-dione ring), 133.66 ppm (C<sub>5a</sub>, C<sub>9a</sub> of quinoxaline-5,10-dione ring), 131.36 ppm (C<sub>2</sub> of phenyl ring attached to C-5 of pyrazoline ring), 131.14 ppm (C<sub>4</sub> of phenyl ring attached to C-2 of quinoxaline-5,10-dione ring), 131.03 ppm (C<sub>4</sub> of phenyl ring attached to C-3 of quinoxaline-5,10-dione ring), 130.92 ppm (C<sub>5</sub> of phenyl ring attached to C-3 of quinoxaline-5,10-dione ring), 130.18 ppm (C<sub>6</sub> of phenyl ring attached to C-5 of pyrazoline ring), 129.41 ppm (C<sub>2</sub> of phenyl ring attached to C-3 of quinoxaline-5,10-dione ring), 129.40 ppm (C<sub>2</sub> of phenyl ring attached to C-2 of quinoxaline-5,10-dione ring), 129.29 ppm (C<sub>6</sub> of phenyl ring attached to C-3 of quinoxaline-5,10-dione ring), 129.26 ppm (C<sub>6</sub> of phenyl ring attached to C-2 of quinoxaline-5,10-dione ring), 129.16 ppm (C<sub>3</sub> of phenyl ring attached to C-2 of quinoxaline-5,10-dione ring), 129.01 ppm (C<sub>9</sub> of quinoxaline-5,10-dione ring), 128.98 ppm (C<sub>3</sub> of phenyl ring attached to C-3 of quinoxaline-5,10-dione ring), 128.54 ppm (C<sub>6</sub> of quinoxaline-5,10-dione ring), 127.59 ppm (C<sub>3</sub> of phenyl ring attached to C-5 of pyrazoline ring),

127.39 ppm (C<sub>5</sub> of phenyl ring attached to C-5 of pyrazoline ring), 125.75 ppm (C<sub>8</sub> of quinoxaline-5,10-dione ring), 122.52 ppm (C<sub>4</sub> of phenyl ring attached to C-5 of pyrazoline ring), 63.31 ppm (C<sub>5</sub> of pyrazoline ring) and 42.86 ppm (C<sub>4</sub> of pyrazoline ring). ESI-MS spectrum of compound (7a) showed M<sup>+</sup> peak at 506.5, close to its molecular weight. Similarly, structures of other compounds of the newly synthesized series viz. 7-[5-(substituted) phenyl-4, 5-dihydro-1H-pyrazol-3-yl]-2,3-diphenyl-5H,10H-benzo[g] quinoxaline - 5, 10-dione (7a-k) were confirmed.

**Biological Activity (In-vitro Antimycobacterial Screening):** The newly synthesized compounds 7b, 7c, 7d, 7e, 7f, 7g, 7h, 7i, 7j and 7k of the series 7-[5-(substituted)phenyl-4,5-dihydro-1H-pyrazol-3-yl]-2,3-diphenyl-5H,10H-benzo[g]quinoxaline - 5, 10-dione (Compound 7a-k) were screened for their antimycobacterial activity against *Mycobacterium tuberculosis H<sub>37</sub>Rv* by L.J. Slope (Conventional) Method to observe the effect of substitution at phenyl ring attached to 5-position of pyrazoline ring attached to C-7 of the series 7-[5-(substituted) phenyl-4,5-dihydro-1H-pyrazol-3-yl]-2,3-diphenyl-5H,10H-benzo[g] quinoxaline - 5, 10 - dione (Compound 7a-k). Isoniazid and Rifampicin were used as standard drugs.

Compound 7j having electron donating 4-CH<sub>3</sub> group on phenyl ring attached to the above mentioned position has been observed as the most active antimycobacterial compound. Compounds 7d, 7b, 7g having electron withdrawing 4-NO<sub>2</sub>, 4-Cl, 2-Cl groups and compounds 7c and 7f having electron donating 4-OH and 3-OH-4-OCH<sub>3</sub> groups respectively on phenyl ring attached to above mentioned position have exhibited significant antimycobacterial activity.

While compounds 7e and 7k having electron donating 4-OCH<sub>3</sub> and 4-NH<sub>2</sub> groups respectively and compound 7h having electron withdrawing 4-CF<sub>3</sub> group on phenyl ring attached to above mentioned position, have exhibited moderate antimycobacterial activity. Compound 7i having electron donating 3, 4-(OCH<sub>3</sub>)<sub>2</sub> group on phenyl ring attached to above mentioned position has been observed as the least active antimycobacterial compound of the newly synthesized series 7-[5-(substituted)phenyl-4,5-dihydro-1H-pyrazol-3-yl]-

2,3-diphenyl - 5*H*, 10*H*-benzo[*g*]quinoxaline-5,10-dione (Compound 7a-k).

**CONCLUSION:** After the interpretation of the results obtained after antimycobacterial screening, Structure Activity Relationship (SAR) may be established, for the series 7-[5-(*Substituted*)phenyl]-4,5-dihydro-1*H*-pyrazol-3-yl]-2,3-diphenyl-5*H*, 10*H*-benzo[*g*]quinoxaline-5,10-dione (Compound 7a-k), as “substitution with smaller functional group at the *ortho* and *para*-position of phenyl ring attached to 5-position of pyrazoline ring attached to C-7 of 2,3-diphenylbenzo[*g*] quinoxaline - 5, 10 - dione nucleus increases antimycobacterial activity, while substitution with larger functional groups at the *para*-position of phenyl ring present at the above mentioned position produces moderate active antimycobacterial compounds. Compounds with more powerful electron donating groups like 3,4-(OCH<sub>3</sub>)<sub>2</sub> group at phenyl ring attached to above mentioned position produces least active antimycobacterial compound.”

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