5. EXPERIMENTAL

The experimental has been subcategorized into three parts:

5.1 Computational studies

5.2 Chemical work

5.3 Biological screening

5.1 Computational studies

5.1.1 Hardware and software used in the computational work

5.1.1.1 Hardware

Pharmacophore modelling, 3D-QSAR modelling, virtual screening, were performed on PC with Microsoft windows operating system with the following specifications:

- Model : Dell
- Processor : Intel(R)core
- Memory : 8GB
- Data cache : 4×32
- Operating system : Microsoft Windows

5.1.1.2 Softwares

- Pharmacophore modelling, 3D-QSAR, virtual screening were performed using PHASE from Schrodinger, LLC New York, NY.[1,2]
- Docking studies were carried out using GLIDE (5.5) Schrodinger, LLC New York, NY,2009[3] and autodock[4,5] softwares.
- Physicochemical and pharmacokinetic properties were computed by utilizing Qikprop[6], SwissADME[7] and Derek[8] softwares.

5.1.2 Selection of dataset

Many scaffolds have been reported in recent years showing DprE1 inhibition. After conducting a thorough literature survey, it was found that 566 compounds from various classes such as benzothiazinones[9-10], azaindoles[11,12], aminoquinolones[13], quinoxalines[14], triazoles[15,16] etc. were reported as DprE1 inhibitors. The first criterion for dataset was a reported IC_{50} value for DprE1 enzyme. Further, compounds with unclear stereochemistry or biological activity were not included in the study. So, out of these 566 compounds, 300 compounds were selected for which, activity was defined in terms of IC_{50} value. The dataset was generated in such a way that it contains most active, moderately active and least active

compounds covering all structural variations. To get robust dataset, compounds having similar structures with similar biological activity were omitted from the final selection.

Finally, a set of 150 compounds with IC_{50} value ranging from 100 to 0.003 μM were selected in such a way that the data set provide both structural and biological variations. IC_{50} value of these compounds were converted to pIC_{50} values by taking negative logarithm of IC_{50} values (pIC_{50} = -logIC_{50}). This dataset consisting 140 structures was scrutinized into a model generating set comprising of 140 compounds and an external test set consisting of 10 compounds.

5.1.3 Development of pharmacophore model using PHASE

The development of pharmacophore model was done using PHASE, version 2.5 (SchrÖdinger)[1,2,17]. Grid points corresponding to the atoms in the molecule aligned to a reference compound were determined. These grid points were utilized to generate 3D descriptors for corelating with biological activity by using PLS analysis. Structure of the compounds were drawn and cleaned using 'building tools' of Maestro software.

Following steps were carried out to obtain suitable pharmacophore:

- Structures were imported to the "develop pharmacophore model" and minimized by using two-step process i.e. cleaning (geometric refining) using Ligprep module[18]. Conformations were generated by using ConfGen search method with OPLS-2005 force field. A maximum of 1000 conformers per structure with 100 conformers per rotatable bond were generated by a pre-process of 50 steps and a distance-dependent dielectric solvation was applied. Activity threshold was kept as. Active above 6.9 and inactive below 5.0.
- A set of pharmacophore features for selected compounds (1-140) was generated by selecting create sites option. Site points were created for each conformer of the compounds. For creating pharmacophore sites, a default setting having Aromatic ring (R), negative (N), positive (P), hydrophobic (H), H-bond donor (D), and acceptor (A) features were used.
- Common pharmacophore hypothesis for the set of active ligands were generated using these features. A set of variants formed by a set of features was used to identify the common pharmacophore using a tree based partitioning algorithm with a criterion that the selected must match maximum number of active compounds.
- The generated common pharmacophore of all variants was scored active and inactive compounds to identify a set of hypotheses having best alignment for most of the

compounds. The common hypothesis so formed were scored by setting the root mean square deviation (RMSD) value below 1.2 and vector score value to 0.5.

- All the hypothesis were scored so as to make rank making it easier to choose among all the generated hypothesis.
- The most appropriate hypothesis was selected for further exploration. All the generated pharmacophore hypothesis were ranked on the basis of various parameters such as survival score and survival minus 'inactive'. Higher survival score indicates better mapping of the pharmacophore with the active ligands and the fitness score confirms the quality of the pharmacophore that can be defined as how well the compounds could be mapped to a pharmacophore model.

Based on 41 active ligands in the data-set, several 3-point and 4-point pharmacophore hypothesis were generated. These alignments were further used to develop 3D-QSAR model.

5.1.4 Development of 3D-QSAR model

An attempt was made to develop an atom-based 3D-QSAR model because it is based on the considerations of the entire molecular space. The molecular and structural alignment acquired through pharmacophore model generation was used to build 3D-QSAR model by applying partial least square (PLS) factors. To generate QSAR model, PLS utilized to linearly corelate independent variables as descriptors and dependant variable as biological activity. The compounds in training set were covered with regular grid of cubes. Each cube generally represents six bits expressing six different class of atoms i.e. hydrophobic group (H), H-bond donor (D), positive ionic (P), negative ionic (N), electron withdrawing (W) and others. Various 3-D QSAR models were generated and each model was validated by the internal test set. The generated model were evaluated by different parameters such as cross-validated coefficient, F-value, predictive r^2, modified r^2, Pearson-R etc.

The 140 compounds were divided into two sets i.e. training (112) and test set (28) by following the rule (a) both training and test set compounds contain representative from each class to ensure structural diversity; (b) both, training and test sets covered the bioactivities (IC_{50}) as wide as possible. If there was only one compound with maximum order of biological activity in a class, such a compound was assigned to the training set.

5.1.5 Virtual screening

A virtual screening was carried out for Asinex database containing 2,12,526 compounds having diverse chemical scaffolds with an aim to identify potential hit for DprE1

inhibitor. The Asinex database having 3D structures were downloaded from the official site and optimized using OPLS 2005 force field in ligprep option in Maestro 9.0[19,20]. The generated pharmacophore model was used as a primary screen to search the database to retrieve structures fitting the pharmacophore hypothesis. The compounds retrieved from this stage were further screened by utilizing molecular docking studies using Glide 5.5[3,21]. Firstly, high throughput virtual screening (HTVS) method with flexible docking with a limit of five retained poses per molecule was employed. The compounds so obtained were re-docked using standard precision (SP) method to get higher precision. The docking was repeated again by using extra precision (XP) method. The resultant compounds were screened using another filter i.e., Lipinski rule of five by using the Qikprop feature of Meastro[6].

5.1.6 Docking of the designed compounds using Autodock

5.1.6.1 Ligand preparation

The compounds were drawn using Chem-draw software and minimized using discovery studio[22]. After minimization, the structures were prepared using an autodock tool and converted into pdbqt format which was required for performing the docking studies using autodock vina[4,5].

5.1.6.2 Protein preparation

There are approximately 35 crystal structures available for the enzyme DprE1. The crystal structure used to perform binding interaction studies in the active site of the DprE1 enzyme is 4p8n and is downloaded from the RCSB site of the protein data bank[23]. The PDB ID is chosen on the basis of its origin and resolution[24]. The crystal structure was minimized using Discovery studio where bound ligand and all water molecules were removed and the protein was further prepared using Auto dock MGL tools provided by the Scripps research institute. In auto dock tools the PDB is converted into pdbqt format that was required for binding studies predication in auto dock vina.

5.1.6.3 Grid generation

The grid generation was done using auto dock tools where the protein and ligand molecule were selected and the grid box was generated with dimensions x-axis 17.734, y-axis -13.785, and z-axis 2.687.

5.1.6.4 Protein-ligand interaction

The receptor and all the ligand molecules were converted into pdbqt format in autodock and docked in autodock vina. The interactions were visualized using the discovery studio. Different types of interactions formed between a protein and ligand complex were observed.

5.1.7 ADMET predictions of the designed compounds

ADME calculations of the all compounds was performed by the SwissADME web server[7]. The server is reported to have a strong database to predict various physiochemical properties like water solubility, lipophilicity, drug likeness, medicinal and pharmacokinetics properties with high accuracy.

5.1.8 Molecular simulations

The protein stability after binding to the ligand can be successfully understood by applying molecular dynamics simulations. Molecular dynamics stimulation for DNA-ligand complex was performed using GROMACS version 2020.2 software package for 10ns[25,26], in PARAM Shavak supercomputer. The force field used for generating receptor and ligand topology is CHARMM36[27] all atom force field and the water model used was TIP3P[28]. Before processing for dynamics, the complex is immersed in a dodecahedral box filled with water molecules. The system was neutralized by adding ions and energy minimization was carried out for 500 steps by using steepest descent minimization. The complex was equilibrated using an NVT group (constant number of particles, volume and temperature) by gradually increasing temperature from 0 to 300K and NPT group (the number of particles, pressure and temperature). After equilibrating, the complex MD simulation was performed for 10ns. The analysis was performed using VMD[29].

5.2 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 and ^{13}C-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.

SECTION I

5.2.1 3-Amino-4-phenyl-*1H*-pyrazol-5(*4H*)-one (**106**)

In a single neck 25 ml RBF, ethyl 2-cyano-2-phenylacetate (**105**, 0.4 gm, 0.0021 M) was added to ethanol. To this solution, hydrazine hydrate 90% (0.21 gm, 0.0042 M) was added drop-wise and the reaction mixture was stirred vigorously for 5 mins. Aqueous NaOH solution was added to the reaction and further stirred for 15 mins. The completion of reaction mixture was monitored by TLC. Upon completion, the reaction mixture was neutralized by dilute HCl to yield white solid product which was filtered under vacuum. The product was used for further reaction without purification. (0.39 gm, 98 %); m.p. 250-252 °C.

Anal:

TLC : R_f 0.4 (Chloroform: Methanol; 20:1)

IR (KBr, cm^{-1}) : 3485, 3304, 3255, 3152, 1647, 1620, 1433, 1314, 929, and 775.

Mass (m/z) : 176 [M+1], 177 [M+2]

5.2.2 5-Methyl-3-phenylpyrazolo[1,5-*a*] pyrimidine-2,7(1*H*,4*H*)-dione (**107**)

In a single neck 25-ml RBF, 3-amino-4-phenyl-1*H*-pyrazol-5(4*H*)-one (**106**, 0.4 gm, 0.0022 M) was dissolved in acetic acid. To this, ethyl acetoacetate (0.858 gm, 0.0066 M) was added drop wise and stirred at room temperature for 10 minutes. The reaction mixture was then transferred to 90 °C for overnight. The reaction was monitored by TLC. Upon completion the reaction mixture was diluted with ice cold water to obtain white solid product. The product was used for further reactions without purification. (0.36 gm, 91 %); m.p. >250 °C.

Anal:

TLC : R_f 0.45 (Chloroform: Methanol; 20:1)

IR (KBr, cm^{-1}) : 3066, 3022, 2948, 1688, 1645, 1606, 1500, 1442, 879, and 759.

Mass (m/z) : 242 $[M+1]^+$.

^{1}H NMR [500 MHz, DMSO-d_6, δ] : 12.04 (s, 1H), 11.52 (s, 1H), 7.45-7.43 (d, 2H), 7.36-7.33 (t, *J* =7.7 Hz, 2H), 7.21-7.18 (t, *J* =7.3 Hz, 1H), 2.37 (s, 3H), 2.19 (s, 1H).

5.2.3 1-Bromo-5-methyl-3-phenylpyrazolo[1,5-*a*]pyrimidine-2,7(1*H*,4*H*)-dione (**108**)

In a 10 ml 2-neck RBF, kept on ice-bath 5-methyl-3-phenylpyrazolo[1,5-*a*]pyrimidine-2,7(1*H*,4*H*)-dione (**107**, 0.4gm, 0.0016 M) was dissolved in chloroform. To this *N*-bromosuccinimide (NBS) (0.284 gm, 0.0016 M) was added in portions. Once NBS was added, benzoyl peroxide was added and the reaction mixture was stirred at rt for 10 mins. Reaction mixture was further refluxed for 6 hours and the progress was monitored by TLC. Once the reaction was completed, excess chloroform was evaporated using rotary evaporator to obtain brownish residue. To the residue, crushed ice was added to obtain buff coloured solid, which was filtered with aid of vacuum. The crude was purified by using recrystallization using methanol as solvent to obtain white needle crystals. (0.35 gm, 89 %); m.p. >250 °C.

Anal:

TLC : R_f 0.4 (Chloroform: Methanol; 18:2)

IR (KBr, cm^{-1}) : 3056, 2962, 1634, 1578, 1527, 1260 and 694.

Mass (m/z) : 320 $[M]^+$, 322 $[M+2]^+$

^{1}H NMR [400 MHz, DMSO-d_6, δ] : 11.58 (s, 1H), 11.28 (s, 1H), 7.52-7.50 (dd, *J* =8.1 & 1.2 Hz, 2H), 7.43-7.40 (t, 2H), 7.28-7.24 (t, 1H), 5.55 (s, 1H), 2.27 (s, 3H).

5.2.4 6-Chloro-5-methyl-3-phenylpyrazolo[1,5-*a*]pyrimidine-2,7(1*H*,4*H*)-dione (**109**)

In a 25 ml single neck RBF containing glacial acetic acid, 3-amino-4-phenyl-1*H*-pyrazol-5 (4*H*)-one (**106**, 0.4 gm, 0.0022 M) was added and stirred for 5 mins under cooling conditions. To this, ethyl 2-chloroacetoacetate (0.918 gm, 0.0056 M) was added and stirred further for 5 mins. The reaction mixture was refluxed for 3 hours. The progress of the reaction was monitored by TLC. Upon completion, crushed ice was added to the reaction

mixture to obtain precipitates. The compound was filtered under vacuum to yield white solid compound. (0.36 gm, 90 %); m.p. >250 °C. (**Sii**)

Anal:

TLC : R_f 0.45 (Chloroform: Methanol; 20:1)

IR (KBr, cm^{-1}) : 3057, 2598, 1715, 1697, 1648, 1525, 1257 and 758.

Mass (m/z) : 297 $[M+ Na]^+$ adduct.

^{1}H NMR [400 MHz, DMSO-d_6, δ] : 12.05 (s, 1H), 11.58 (s, 1H), 7.52-7.50 (d, *J*=7.6, 2H), 7.45-7.41(t, *J*=7.6, 2H), 7.3-7.2 (t, *J*=7.2, 1H), 2.43 (s, 3H), 1.90 (s, 1H).

5.2.5 5-(Chloromethyl)-3-phenylpyrazolo[1,5-*a*]pyrimidine-2,7(1*H*,4*H*)-dione (**110**)

In a 25 ml single neck RBF containing glacial acetic acid, 3-amino-4-phenyl-1*H*-pyrazol-5 (4*H*)-one (**106**, 0.4 gm, 0.0022 M) was added and stirred for 5 mins under cooling conditions. To this, ethyl 4-chloroacetoacetate (0.918 gm, 0.0056 M) was added and stirred further for 5 mins. The reaction mixture was refluxed for 3 hours. The progress of the reaction was monitored by TLC. Upon completion, crushed ice was added to the reaction mixture to obtain precipitates. The compound was filtered under vacuum to yield white solid compound. (0.36 gm, 90 %); m.p. 246-248 ℃. (**Siii**)

Anal:

TLC : R_f 0.51 (Chloroform: Methanol; 20:1)

IR (KBr, cm^{-1}) : 3176, 3064, 2998, 2951, 1692, 1646, 1606, 1502, 1297, 913, 753.

Mass (m/z) : 276 [M+1]

^{1}H-NMR [500 MHz, DMSO-d_6, δ] : 12.01 (s, 1H), 11.39 (s, 1H), 7.56 (s, 2H), 7.46-7.43 (d, *J* = 7.6 Hz, 2H), 7.30-7.27 (t, *J* = 7.4 Hz, 1H), 5.90 (s, 1H), 4.65 (s, 2H).

5.2.6 5-((Benzylamino)methyl)-3-phenylpyrazolo[1,5-*a*]pyrimidine-2,7(1*H*,4*H*)-dione (111)

In a single neck 25 ml RBF, benzyl amine (0.186 gm, 0.00174 M) was dissolved in a mixture of anhydrous K_2CO_3 in dry DMF. This mixture was allowed to stir at room temperature. To this mixture, 5-(chloromethyl)3-phenylpyrazolo[1,5-*a*]pyrimidine-

2,7(1*H*,4*H*)-dione (**110**, 0.4 gm, 0.00145 M) was added. The resulting reaction mixture was heated at 80 °C for 5 hours. The reaction was monitored by TLC. Upon, completion, crushed ice was added to the reaction mixture to obtain the desired compound, filtered under vacuum to obtain crude solid. The crude was further purified by column chromatography using silica gel (6% methanol) afforded brown semi-solid compound. (0.27 gm, 69 %).

Anal:

TLC : R_f 0.41 (Chloroform: Methanol; 18:2)

IR (KBr, cm^{-1}) : 3399, 2922, 1679, 1645, 1525, 1251, 1139 and 762.

Mass (m/z) : 347 $[M+1]^+$.

^{1}H-NMR [500 MHz, DMSO-d_6, δ] : 8.30 (s, 1H), 7.57-7.55 (d, 2H), 7.47-7.39 (m, 6H), 7.31-7.10 (t, 2H), 5.94 (s, 1H), 4.24 (s, 2H), 4.17 (s, 2H).

5.2.7 5-((4-Fuorobenzylamino)methyl)-3-phenylpyrazolo[1,5-*a*]pyrimidine-2,7(1*H*,4*H*)-dione (112)

In a single neck 25 ml RBF, 4-flourobenzyl amine (0.362 gm, 0.0029 M) was dissolved in a mixture of anhydrous K_2CO_3 in dry DMF. This mixture was allowed to stir at room temperature. To this mixture, 5-(chloromethyl)3-phenylpyrazolo[1,5-*a*]pyrimidine-2,7(1*H*,4*H*)-dione (**110**, 0.4 gm, 0.00145 M) was added. The resulting reaction mixture was heated at 80 °C for 5 hours. The reaction was monitored by TLC. Upon, completion, crushed ice was added to the reaction mixture to obtain the desired compound, filtered under vacuum to obtain crude solid. The crude was further purified by column chromatography using silica gel (8% methanol) afforded greenish colored compound. (0.27 gm, 69 %); m.p. 198-200 ℃.

Anal:

TLC : R_f 0.4 (Chloroform: Methanol; 19:1)

IR (KBr, cm^{-1}) : 2922, 2853, 1726, 1640, 1578, 1438, 1228, 875 and 699.

Mass (m/z) : 365 $[M+1]^+$.

^{1}H-NMR [500 MHz, DMSO-d_6, δ] : 9.49 (s, 2H), 8.07 (d, *J* = 7.7 Hz, 2H), 7.60 – 7.48 (m, 4H), 7.37-7.34 (t, *J* = 7.6 Hz, 2H), 7.15-7.12 (t, *J* = 7.3 Hz, 1H), 5.65 (s, 1H), 4.09 (s, 2H), 3.87 (s, 2H).

5.2.8 5-((4-Chlorobenzylamino)methyl)-3-phenylpyrazolo[1,5-*a*]pyrimidine-2,7(1*H*,4*H*)-dione (113)

In a single neck 25 ml RBF, 4-chlorobenzyl amine (0.408 gm, 0.0029 M) was dissolved in a mixture of anhydrous K_2CO_3 in dry DMF. This mixture was allowed to stir at room temperature. To this mixture, 5-(chloromethyl)3-phenylpyrazolo[1,5-*a*]pyrimidine-2,7(1*H*,4*H*)-dione (**110**, 0.4 gm, 0.00145 M) was added. The resulting reaction mixture was heated at 80 °C for 5 hours. The reaction was monitored by TLC. Upon, completion, crushed ice was added to the reaction mixture to obtain the desired compound, filtered under vacuum to obtain crude solid. The crude was further purified by column chromatography using silica gel (8% methanol) afforded off-white colored compound. (0.31 gm, 79 %); m.p. 229-231 ℃.

Anal:

TLC : R_f 0.35 (Chloroform: Methanol; 19:1)

IR (KBr, cm^{-1}) : 3056, 2925, 2856, 1723, 1641, 1577, 1315, 1092, 914 and 701.

Mass (m/z) : 381 $[M+1]^+$.

^{1}H-NMR [500 MHz, DMSO-d_6, δ] : 9.45 (s, 2H), 8.02 (d, *J* = 7.8 Hz, 2H), 7.54 – 7.44 (m, 4H), 7.33-7.30 (t, *J* = 7.6 Hz, 2H), 7.11-7.09 (t, *J* = 7.4 Hz, 1H), 5.61 (s, 1H), 4.04 (s, 2H), 3.83 (s, 2H).

5.2.9 5-((4-Methylbenzylamino)methyl)-3-phenylpyrazolo[1,5-*a*]pyrimidine-2,7(1*H*,4*H*)-dione (114)

In a single neck 25 ml RBF, 4-methylbenzyl amine (0.350 gm, 0.0029 M) was dissolved in a mixture of anhydrous K_2CO_3 in dry DMF. This mixture was allowed to stir at room temperature. To this mixture, 5-(chloromethyl)3-phenylpyrazolo[1,5-*a*]pyrimidine-2,7(1*H*,4*H*)-dione (**110**, 0.4 gm, 0.00145 M) was added. The resulting reaction mixture was heated at 80 °C for 5 hours. The reaction was monitored by TLC. Upon, completion, crushed ice was added to the reaction mixture to obtain the desired compound, filtered under vacuum to obtain crude solid. The crude was further purified by column chromatography using silica gel (8% methanol) afforded white colored compound. (0.27 gm, 69 %); m.p. 210-212 ℃.

Anal:

TLC : R_f 0.39 (Chloroform: Methanol; 19:1)

IR (KBr, cm^{-1}) : 3055, 2924, 2859, 1728, 1643, 1578, 1538, 1440, 1121, 1039 and 911.

Mass (m/z) : 361$[M+1]^+$, 359 $[M+2]^+$.

^{1}H-NMR [500 MHz, DMSO-d_6, δ] : 8.24 (d, 2H), 7.40-7.38 (d, 2H), 7.35-7.34 (d, 1H), 7.28-7.22 (m, 4H), 7.03-7.00 (t, 1H), 5.54 (s, 1H), 4.14 (s, 2H), 4.0 (s, 1H), 3.85 (s, 2H), 2.33 (s, 3H).

5.2.10 5-((3,4-Dichlorobenzylamino)methyl)-3-phenylpyrazolo[1,5-*a*]pyrimidine-2,7(1*H*,4*H*)-dione (115)

In a single neck 25 ml RBF, 3,4-dichlorobenzyl amine (0.306 gm, 0.00174 M) was dissolved in a mixture of anhydrous K_2CO_3 in dry DMF. This mixture was allowed to stir at room temperature. To this mixture, 5-(chloromethyl)3-phenylpyrazolo[1,5-*a*]pyrimidine-2,7(1*H*,4*H*)-dione (**110**, 0.4 gm, 0.00145 M) was added. The resulting reaction mixture was heated at 80 °C for 5 hours. The reaction was monitored by TLC. Upon, completion, crushed ice was added to the reaction mixture to obtain the desired compound, filtered under vacuum to obtain crude solid. The crude was further purified by column chromatography using silica gel (8% methanol) afforded white colored compound. (0.34 gm, 87 %); m.p. 190-192 °C. (**Sv**)

Anal:

TLC : R_f 0.49 (Chloroform: Methanol; 18:2)

IR (KBr, cm^{-1}) : 3444, 2926, 2627, 1613, 1560, 1473, 1218, 1131, 815.

Mass (m/z) : 415 $[M]^+$.

^{1}H-NMR [400 MHz, DMSO-d_6, δ] : 9.3 (s, 2H), 7.83-7.81 (d, *J*=7.2, 2H), 7.71 (s, 1H), 7.64-7.626 (d, J=8.0, 1H), 7.43-7.42 (d, 1H), 7.36-7.32 (t, J=7.8, 2H), 7.16-7.13 (t, J=7.4,1H), 5.7 (s, 1H), 3.95 (s, 2H), 3.77 (s, 2H)

5.2.11 5-((4-Methoxybenzylamino)methyl)-3-phenylpyrazolo[1,5-*a*]pyrimidine-2,7(1*H*,4*H*)-dione (116)

In a single neck 25 ml RBF, 4-methoxybenzyl amine (0.397 gm, 0.0029 M) was dissolved in a mixture of anhydrous K_2CO_3 in dry DMF. This mixture was allowed to stir at room temperature. To this mixture, 5-(chloromethyl)3-phenylpyrazolo[1,5-*a*]pyrimidine-2,7(1*H*,4*H*)-dione (**110**, 0.4 gm, 0.00145 M) was added. The resulting reaction mixture was heated at 80 °C for 5 hours. The reaction was monitored by TLC. Upon, completion, crushed ice was added to the reaction mixture to obtain the desired compound, filtered under vacuum

to obtain crude solid. The crude was further purified by column chromatography using silica gel (8% methanol) afforded white colored compound. (0.34 gm, 86 %); m.p. 252-253 ℃. (**Svi**)

Anal:

TLC : R_f 0.35 (Chloroform: Methanol; 18:2)

IR (KBr, cm^{-1}) : 3433, 2928, 2843, 1727, 1540, 1443, 1252, 1031 and 700.

Mass (m/z) : 377 $[M+1]^+$.

^{1}H-NMR [500 MHz, DMSO-d_6, δ] : 9.69 (s, 2H), 8.32-8.30 (d, J = 8.0 Hz, 2H), 7.51 – 7.49 (m, 2H), 7.33-7.30 (t, J = 7.7 Hz, 2H), 7.08 –7.02 (m, 3H), 5.59 (s, 1H), 4.21 (s, 2H), 3.97 (s, 2H), 3.82 (s, 3H).

^{13}C-NMR [126 MHz, DMSO-d_6, δ] : 162.56, 159.37, 155.41, 134.42, 131.06, 127.49, 125.20, 125.07, 122.76, 113.86, 93.18, 87.44, 55.07, 49.84, 48.99.

5.2.12 5-((Phenylamino)methyl)-3-phenylpyrazolo[1,5-*a*]pyrimidine-2,7(1*H*,4*H*)-dione (117)

In a single neck 25 ml RBF, aniline (0.161 gm, 0.00174 M) was dissolved in a mixture of anhydrous K_2CO_3 in dry DMF. This mixture was allowed to stir at room temperature. To this mixture, 5-(chloromethyl)3-phenylpyrazolo[1,5-*a*]pyrimidine-2,7(1*H*,4*H*)-dione (**110**, 0.4 gm, 0.00145 M) was added. The resulting reaction mixture was heated at 80 °C for 5 hours. The reaction was monitored by TLC. Upon, completion, crushed ice was added to the reaction mixture to obtain the desired compound, filtered under vacuum to obtain crude solid. The crude was further purified by column chromatography using silica gel (8% methanol) afforded white colored compound. (0.34 gm, 85 %); m.p. >250 ℃. (**Sviii**)

Anal:

TLC : R_f 0.4 (Chloroform: Methanol; 20:1)

IR (KBr, cm^{-1}) : 3370, 3056, 1612, 1516, 1434, 1258 and 763.

Mass (m/z) : 333 $[M+1]^+$.

^{1}H-NMR [400 MHz, DMSO-d_6, δ] : 11.56 (s, 1H), 11.32(s, 1H),7.54-7.52(s, 2H), 7.46-7.42 (t, 2H), 7.30-7.26(t, 1H), 7.11-7.07(t, 2H), 6.62-6.57(m, 3H), 6.24(s, 1H), 5.62 (s, 1H), 4.25(s, 2H).

5.2.13 5-((4-Fluorophenylamino)methyl)-3-phenylpyrazolo[1,5-*a*]pyrimidine-2,7(1*H*,4*H*)-dione (118)

In a single neck 25 ml RBF, 4-fluroaniline (0.193 gm, 0.00174 M) was dissolved in a mixture of anhydrous K_2CO_3 in dry DMF. This mixture was allowed to stir at room temperature. To this mixture, 5-(chloromethyl)3-phenylpyrazolo[1,5-*a*]pyrimidine-2,7(1*H*,4*H*)-dione (**110**, 0.4 gm, 0.00145 M) was added. The resulting reaction mixture was heated at 80 °C for 5 hours. The reaction was monitored by TLC. Upon, completion, crushed ice was added to the reaction mixture to obtain the desired compound, filtered under vacuum to obtain crude solid. The crude was further purified by column chromatography using silica gel (8% methanol) afforded buff colored compound. (0.35 gm, 89 %); m.p. >250 ℃.

Anal:

TLC : R_f 0.44 (Chloroform: Methanol; 20:1)

IR (KBr, cm^{-1}) : 3443, 2926, 2627, 1613, 1560, 1401, 1218, 1131 and 770.

Mass (m/z) : 351 $[M+1]^+$.

^{1}H-NMR [400 MHz, DMSO-d_6, δ] : 11.57 (s, 1H), 11.32 (s, 1H), 7.54 (d, *J* = 6.8 Hz, 2H), 7.45 (t, *J* = 7.8 Hz, 3H), 7.29 (t, *J* = 7.3 Hz, 1H), 6.94 (t, *J* = 8.9 Hz, 2H), 6.65 – 6.57 (m, 2H), 5.63 (s, 1H), 4.25 – 4.20 (m, 2H).

5.2.14 5-((2-Chlorophenylamino)methyl)-3-phenylpyrazolo[1,5-*a*]pyrimidine-2,7(1*H*,4*H*)-dione (119)

In a single neck 25 ml RBF, 2-chloroaniline (0.22 gm, 0.00174 M) was dissolved in a mixture of anhydrous K_2CO_3 in dry DMF. This mixture was allowed to stir at room temperature. To this mixture, 5-(chloromethyl)3-phenylpyrazolo[1,5-*a*]pyrimidine-2,7(1*H*,4*H*)-dione (**110**, 0.4 gm, 0.00145 M) was added. The resulting reaction mixture was heated at 80 °C for 5 hours. The reaction was monitored by TLC. Upon, completion, crushed ice was added to the reaction mixture to obtain the desired compound, filtered under vacuum to obtain crude solid. The crude was further purified by column chromatography using silica gel (8% methanol) afforded white colored compound. (0.36 gm, 91 %); m.p. 248-250 ℃.

Anal:

TLC : R_f 0.4 (Chloroform: Methanol; 20:1)

IR (KBr, cm^{-1}) : 3376, 3058, 1616, 1517, 1153, 1084 and 697.

Mass (m/z) : 367 $[M+1]^+$.

^{1}H-NMR [400 MHz, DMSO-d_6, δ] : 11.46 (d, *J* = 97.6 Hz, 2H), 7.55 (d, *J* = 6.8 Hz, 2H), 7.46 (t, *J* = 7.7 Hz, 2H), 7.30 (t, *J* = 7.3 Hz, 1H), 6.95 (t, *J* = 8.9 Hz, 2H), 6.62 (dd, *J* = 9.0, 4.5 Hz, 2H), 5.64 (s, 1H), 4.24 (s, 2H).

5.2.15 5-((4-Methoxyphenylamino)methyl)-3-phenylpyrazolo[1,5-*a*]pyrimidine-2,7(1*H*,4*H*)-dione (120)

In a single neck 25 ml RBF, 4-methoxyaniline (0.214 gm, 0.00174 M) was dissolved in a mixture of anhydrous K_2CO_3 in dry DMF. This mixture was allowed to stir at room temperature. To this mixture, 5-(chloromethyl)3-phenylpyrazolo[1,5-*a*]pyrimidine-2,7(1*H*,4*H*)-dione (**110**, 0.4 gm, 0.00145 M) was added. The resulting reaction mixture was heated at 80 °C for 5 hours. The reaction was monitored by TLC. Upon, completion, crushed ice was added to the reaction mixture to obtain the desired compound, filtered under vacuum to obtain crude solid. The crude was further purified by column chromatography using silica gel (8% methanol) afforded white colored compound. (0.36 gm, 90 %); m.p. >250 ℃.

Anal:

TLC : R_f 0.51 (Chloroform: Methanol; 20:1)

IR (KBr, cm^{-1}) : 3407, 3064, 1619, 1514, 1150, 1019, 752 and 700.

Mass (m/z) : 363 $[M+1]^+$.

^{1}H-NMR [400 MHz, DMSO-d_6, δ] : 11.39 (d, *J* = 67.1 Hz, 2H), 7.52 (d, *J* = 7.6 Hz, 3H), 7.45 (t, *J* = 7.7 Hz, 2H), 7.29 (t, *J* = 7.4 Hz, 1H), 6.85 (dd, *J* = 8.1, 1.4 Hz, 1H), 6.74 (td, *J* = 7.6, 1.4 Hz, 1H), 6.60 – 6.52 (m, 2H), 5.63 (s, 1H), 4.28 (d, *J* = 2.9 Hz, 2H), 3.83 (s, 3H).

5.2.16 3-Phenyl-5-((pyridin-4-ylamino)methyl)pyrazolo[1,5-*a*]pyrimidine-2,7(1*H*,4*H*)-dione (121)

In a single neck 25 ml RBF, 4-aminopyridine (0.163 gm, 0.00174 M) was dissolved in a mixture of anhydrous K_2CO_3 in dry DMF. This mixture was allowed to stir at room temperature. To this mixture, 5-(chloromethyl)3-phenylpyrazolo[1,5-*a*]pyrimidine-2,7(1*H*,4*H*)-dione (**110**, 0.4 gm, 0.00145 M) was added. The resulting reaction mixture was heated at 80 °C for 5 hours. The reaction was monitored by TLC. Upon, completion, crushed ice was added to the reaction mixture to obtain the desired compound, filtered under vacuum

to obtain crude solid. The crude was further purified by column chromatography using silica gel (10% methanol) afforded white colored compound. (0.35 gm, 89 %); m.p. 230-233 ℃. (**S ix**)

Anal:

TLC : R_f 0.21 (Chloroform: Methanol; 16:4)

IR (KBr, cm^{-1}) : 3338, 3156, 1659, 1586, 1533, 1193, 983, 820, 772.

Mass (m/z) : 334 $[M+1]^+$, 332 $[M-1]^+$.

^{1}H-NMR [400 MHz, DMSO-d_6, δ] : 10.83 (s, 1H), 8.24-8.20 (m, 4H), 8.14-8.10 (s, 2H), 7.24-7.13 (m, 2H), 6.90-6.86 (m, 3H), 5.37 (s, 1H), 5.20 (s, 2H).

5.2.17 3-Phenyl-5-((pyrrolidin-1-yl)methyl)pyrazolo[1,5-*a*]pyrimidine-2,7(1*H*,4*H*)-dione (122)

In a single neck 25 ml RBF, pyrrolidine (0.123 gm, 0.00174 M) was dissolved in a mixture of anhydrous K_2CO_3 in dry DMF. This mixture was allowed to stir at room temperature. To this mixture, 5-(chloromethyl)3-phenylpyrazolo[1,5-*a*]pyrimidine-2,7(1*H*,4*H*)-dione (**110**, 0.4 gm, 0.00145 M) was added. The resulting reaction mixture was heated at 80 °C for 5 hours. The reaction was monitored by TLC. Upon, completion, crushed ice was added to the reaction mixture to obtain the desired compound, filtered under vacuum to obtain crude solid. The crude was further recrystallized by using methanol to afford grey colored needle shaped crystals of compound. (0.36 gm, 90 %); m.p. >250 ℃. (**Sxi**)

Anal:

TLC : R_f 0.21 (Chloroform: Methanol; 18:2)

IR (KBr, cm^{-1}) : 3408, 2617, 1664, 1603, 1446, 1314, 784, 704.

Mass (m/z) : 311 $[M+1]^+$, 309$[M-1]^+$.

^{1}H-NMR [500 MHz, DMSO-d_6, δ] : 10.62 (s, 1H), 8.20-8.19 (d, *J* = 7.8 Hz, 2H), 7.29-7.26 (t, *J* = 7.8, 2H), 7.02-6.99(t, *J* = 7.3, 1H), 5.54 (s, 1H), 4.07, (s, 2H), 3.27-3.24 (t, 4H), 1.94-1.92 (m, 4H).

5.2.18 3-Phenyl-5-((piperazin-1-yl)methyl)pyrazolo[1,5-*a*]pyrimidine-2,7(1*H*,4*H*)-dione (123)

In a single neck 25 ml RBF, piperazine (0.149 gm, 0.00174 M) was dissolved in a mixture of anhydrous K_2CO_3 in dry DMF. This mixture was allowed to stir at room temperature. To this mixture, 5-(chloromethyl)3-phenylpyrazolo[1,5-*a*]pyrimidine-2,7(1*H*,4*H*)-dione (**110**, 0.4 gm, 0.00145 M) was added. The resulting reaction mixture was heated at 80 °C for 5 hours. The reaction was monitored by TLC. Upon, completion, crushed ice was added to the reaction mixture to obtain the desired compound, filtered under vacuum to obtain crude solid. The crude was further purified by column chromatography using silica gel (8% methanol) afforded buff colored compound. (0.34 gm, 86 %); m.p. 215-217 ℃.

Anal:

TLC : R_f 0.50 (Chloroform: Methanol; 19:1)

IR (KBr, cm^{-1}) : 3426, 2923, 1645, 1523, 1441, 1140, 1009 and 771.

Mass (m/z) : 354 $[M+1+28]^+$ (Ethyl adduct)

^{1}H-NMR [400 MHz, DMSO-d_6, δ] : 11.26 (s, 2H), 8.00 (s, 1H), 7.56 (s, 2H), 7.42 (t, *J* = 7.6 Hz, 2H), 7.25 (t, *J* = 7.5 Hz, 1H), 5.74 (s, 1H), 3.50 (s, 2H), 3.41 (m, 5H), 2.45 (d, *J* = 5.2 Hz, 3H).

5.2.19 5-(Morpholinomethyl)-3-phenylpyrazolo[1,5-*a*]pyrimidine-2,7(1*H*,4*H*)-dione (124)

In a single neck 25 ml RBF, morpholine (0.151 gm, 0.00174 M) was dissolved in a mixture of anhydrous K_2CO_3 in dry DMF. This mixture was allowed to stir at room temperature. To this mixture, 5-(chloromethyl)3-phenylpyrazolo[1,5-*a*]pyrimidine-2,7(1*H*,4*H*)-dione (**110**, 0.4 gm, 0.00145 M) was added. The resulting reaction mixture was heated at 80 °C for 5 hours. The reaction was monitored by TLC. Upon, completion, crushed ice was added to the reaction mixture to obtain the desired compound, filtered under vacuum to obtain crude solid. The crude was further purified by recrystallization using methanol to afford dark green colored crystals of pure compound. (0.27 gm, 69 %); m.p. >250 ℃.

Anal:

TLC : R_f 0.50 (Chloroform: Methanol; 19:1)

IR (KBr, cm^{-1}) : 3177, 3098, 2963, 2852, 26331, 1678, 1635, 1526, 1438, 1257, 868.

Mass (m/z) : 327 $[M+1]^+$.

^{1}H-NMR [500 MHz, DMSO-d_6, δ] : 11.30 (s, 2H), 7.56-7.54 (d, *J* = 7.6 Hz, 2H), 7.45-7.42 (t, *J* = 7.8 Hz, 2H), 7.29 – 7.26 (m, 1H), 5.73 (s, 1H), 3.64-3.62 (t, *J* = 4.5 Hz, 4H), 3.48 (s, 2H), 3.18 (s, 1H), 2.51 (m, 4H).

5.2.20 5-((4-Methylpiperazin-1-yl)methyl)-3-phenylpyrazolo[1,5-*a*]pyrimidine-2,7(1*H*,4*H*)-dione (125)

In a single neck 25 ml RBF, 1-methyl piperazine (0.174 gm, 0.00174 M) was dissolved in a mixture of anhydrous K_2CO_3 in dry DMF. This mixture was allowed to stir at room temperature. To this mixture, 5-(chloromethyl)3-phenylpyrazolo[1,5-*a*]pyrimidine-2,7(1*H*,4*H*)-dione (**110**, 0.4 gm, 0.00145 M) was added. The resulting reaction mixture was heated at 80 °C for 5 hours. The reaction was monitored by TLC. Upon, completion, crushed ice was added to the reaction mixture to obtain the desired compound, filtered under vacuum to obtain crude solid. The crude was further purified by column chromatography using silica gel (8% methanol) afforded buff colored compound. (0.30 gm, 76 %); m.p. 245-247 °C.

Anal:

TLC : R_f 0.27 (Chloroform: Methanol; 18:2)

IR (KBr, cm^{-1}) : 3444, 2933, 1620, 1522, 1384, 1283, 1137 and 776.

Mass (m/z) : 340 $[M+1]^+$, 338 $[M-1]^+$.

^{1}H-NMR [500 MHz, DMSO-d_6, δ] : 14.01 (s, 1H), 12.40 (s, 1H), 7.54-7.48 (m, 3H), 7.32-7.29 (m, 2H), 5.52 (s, 1H), 3.45 (s, 2H), 2.77-2.70 (m, 4H), 2.69-2.68 (m, 4H), 2.24 (s, 3H).

5.2.21 Methyl 2-benzyl-2-cyano-3-phenylpropanoate (128)

To a solution of methyl cyanoacetate (**126**) and potassium carbonate in dioxane stirred under nitrogen atmosphere at 0° C was added a solution of benzyl bromide (**127**) in dioxane. The reaction mixture was stirred at 80 °C for overnight. The reaction mixture was diluted with triethylamine and extracted with ethyl acetate (thrice). The combined organic layer was washed with water and brine, dried over anhydrous sodium sulphate and concentrated to dryness in vacuum to obtain buff coloured solid product. This product was directly taken for next step without further purification. m.p. 82-87 °C.

Anal:

TLC : R_f 0.6 (*n*-Hexane: Ethyl acetate; 18:2)

IR (KBr, cm^{-1}) : 2965, 2937, 2264, 1743, 1442, 1011 and 846

5.2.22 3-Amino-4-phenyl-*1H*-pyrazol-5(*4H*)-one (129)

To a solution of methyl 2-benzyl-2-cyano-3-phenylpropanoate (**128**) in methanol stirred under nitrogen environment at room temperature, hydrazine hydrate (99 %) was added drop wise. The reaction mixture was refluxed at 80 °C overnight. After cooling, the reaction mixture was evaporated to dryness in vacuum. The residue was recrystallized using chloroform to provide white coloured solid of 4,4-dibenzyl-5-iminopyrazolidin-3-one having a m.p. of 237-239 °C.

Anal:

TLC : R_f 0.5 (*n*-Hexane: Ethyl acetate; 12:8)

IR (KBr, cm^{-1}):3434, 3061, 2923, 2855, 1686, 1632 and 1448.

Mass (m/z) : 280 $[M+1]^+$.

^{1}H-NMR [400 MHz, DMSO-d_6, δ]: 9.39 (s, 1H), 7.20-7.14 (m, 10H), 6.183 (s, 1H) and 3.07-2.90 (dd, 4H).

5.2.23 3,3-Dibenzyl-5-methylpyrazolo[1,5-*a*]pyrimidine-2,7(1*H*,3*H*)-dione (130)

To a solution of 3-amino-4-phenyl-*1H*-pyrazol-5(*4H*)-one **129**, 0.5 gm, 0.0017 M) in acetic acid, ethyl acetoacetate was added drop wise and stirred at room temperature for 10 minutes. Then, the reaction mixture was heated at 100 °C overnight. The reaction mixture was then diluted with ice cold water to obtain white coloured solid product. m.p.**:** 188-190 °C**.** (**Sxiii**)

Anal:

TLC : R_f 0.3 (*n*-Hexane: Ethyl acetate; 8:12)

IR (KBr, cm^{-1}): 3030, 2970, 2925, 2744, 1739, 1683, 1602, 1549, 1393 and 1265

Mass (m/z) : [M+1]- 346, [M+2]- 347.

^{1}H-NMR [400 MHz, DMSO-d_6, δ]: 12.80 (s, 1H), 7.28-7.19 (m, 6H), 7.04-7.02 (m, 4H), 6.15 (s, 1H), 3.3 (m, 4H), 2.41 (s, 3H).

^{13}C-NMR [126 MHz, DMSO-d_6, δ]: 170.31, 161.99, 151.68, 134.47, 129.21, 128.99, 128.14, 127.99, 127.08, 109.77, 58.65, 41.51, 23.24.

5.2.24 3,3-Dibenzyl-1-bromo-5-methylpyrazolo[1,5-*a*]pyrimidine-2,7(1*H*,3*H*)-dione (131)

In a 10 ml 2-neck RBF was kept on ice-bath wherein 3,3-dibenzyl-5-methylpyrazolo[1,5-a]pyrimidine-2,7(1*H*,3*H*)-dionewas dissolved in chloroform. To this *N*-bromosuccinimide (NBS) was added in portions. Once NBS was added, benzoyl peroxide was added and the reaction mixture was stirred at rt for 10 mins. Reaction was refluxed for 6 hours and the progress was monitored by TLC. Once the reaction was completed, excess chloroform was evaporated using rotary evaporator to obtain brownish residue. To the residue, crushed ice was added to obtain buff coloured solid, which was filtered with aid of vacuum. m.p.**:** 176-179 °C**.**

Anal:

TLC : R_f 0.5 (*n*-Hexane: Ethyl acetate; 8:12)

IR (KBr, cm^{-1}) : 3029, 2967, 2923, 2753, 1741, 1704, 1603, 1549, 1492 and 1385.

Mass (m/z) : 424, [M+1] 425, [M+2] 426.

^{1}H-NMR [400 MHz, DMSO-d_6, δ]: 12.99 (s, 1H), δ 7.96-6.97 (m, 10H), 6.12 (s, 1H) 3.29 (m, 4H), 2.36 (s, 3H).

5.2.25 3,3-Dibenzyl-6-chloro-5-methylpyrazolo[1,5-*a*]pyrimidine-2,7(1*H*,3*H*)-dione (132)

In a single neck RBF containing glacial acetic acid, 3-amino-4-phenyl-*1H*-pyrazol-5(*4H*)-one (**129**, 0.5 gm, 0.0017 M) was added and stirred for 5 mins under cooling conditions. To this, ethyl-2-chloroacetoacetate (0.918 gm, 0.0056 M) was added and stirred for 5 mins. The reaction mixture was refluxed for 3 hours. The progress of the reaction was monitored by TLC. Upon completion, crushed ice was added to the reaction mixture to obtain precipitates. The compound was filtered under vacuum to yield white solid product. (0.45, 90%): m.p. >250 °C**.**

Anal:

TLC : R_f 0.4 (*n*-Hexane: Ethyl acetate; 8:12)

IR (KBr, cm^{-1}): 3061, 3031, 2927, 1740, 1689, 1603, 1496, 1082, 701.

Mass (m/z) : 380 $[M]^+$, 382 $[M+2]^+$

^{1}H-NMR [400 MHz, DMSO-d_6, δ]: 13.16 (s, 1H), 7.36-7.30 (m, 2H), 7.24-7.14 (m, 8H), 3.37-3.21 (m, 4H), 2.53 (s, 3H).

5.2.26 3,3-Dibenzyl-5-(chloromethyl)pyrazolo[1,5-*a*]pyrimidine-2,7(1*H*,3*H*)-dione (133)

In a single neck RBF containing glacial acetic acid, 3-amino-4-phenyl-*1H*-pyrazol-5(*4H*)-one (**129**, 0.5 gm, 0.0017 M) was added and stirred for 5 mins under cooling conditions. To this, ethyl-4-chloroacetoacetate (0.918 gm, 0.0056 M) was added and stirred for 5 mins. The reaction mixture was refluxed for 3 hours. The progress of the reaction was monitored by TLC. Upon completion, crushed ice was added to the reaction mixture to obtain precipitates. The compound was filtered under vacuum to yield white solid product. (0.43, 90%): m.p. 201-203 °C**.** (**Sxv**)

Anal:

TLC : R_f 0.55 (*n*-Hexane: Ethyl acetate; 8:12)

IR (KBr, cm^{-1}) : 3030, 2958, 2927, 1731,1684, 1578, 1274, 1126, 699.

Mass (m/z) : 380 $[M]^+$

^{1}H-NMR [400 MHz, DMSO-d_6, δ]: 8.68 (s, 1H), 7.43-7.30 (m, 4H), 7.29-7.25 (m, 6H), 6.38 (s, 1H), 4.62 (s, 1H), 3.52-3.50 (dd, 2H), 3.02-3.00 (dd, 2H).

5.2.27 3,3-Dibenzyl-5-((benzylamino)methyl)pyrazolo[1,5-*a*]pyrimidine-2,7(1*H*,3*H*)-dione (134)

In a 25 ml 2-neck RBF benzylamine was dissolved in dry DMF and Cs_2CO_3 was added. After stirring at rt for 5-10 mins under the stream of nitrogen, 3,3-dibenzyl-5-(chloromethyl)pyrazolo[1,5-*a*]pyrimidine-2,7(1*H*,3*H*)-dione **(133,** 0.5 gm, 0013 M) was added and the reaction mixture was transferred on oil bath at 80 °C for 5-6 hrs. Progress of the reaction was monitored by TLC. After completion of reaction, crushed ice was added, extracted with chloroform and dried over Na_2SO_4. Solvent was evaporated using rotary evaporator and the sticky material so obtained was purified through column chromatography using petroleum ether and ethyl acetate (60%) as eluents to provide the desired product.

TLC : R_f 0.52 (*n*-Hexane: Ethyl acetate; 8:12)

IR (KBr, cm^{-1}): 3439, 1639,1569, 1125, 699.

Mass (m/z) : 451 $[M+1]^+$

^{1}H-NMR [400 MHz, DMSO-d_6, δ]: 7.73-7.67 (m, 2H), 7.38-7.31 (m, 3H), 7.05-7.01 (m, 11H), 5.86 (s, 1H), 4.17-4.11 (m, 2H), 3.80 (s, 1H), 3.70 (s, 1H), 3.57 (s, 1H), 3.14-3.11 (m, 2H), 3.07-3.04 (m, 2H).

5.2.28 5-((4-Fluorobenzylamino)methyl)-3,3-dibenzylpyrazolo[1,5-*a*]pyrimidine-2,7(1*H*,3*H*)-dione (135)

Compound **(135)** was synthesized using the method as mentioned for compound (**134**) by reacting 4-flourobenzyl amine with 3,3-dibenzyl-5-(chloromethyl)pyrazolo[1,5-*a*]pyrimidine-2,7(1*H*,3*H*)-dione **(133).** Compound **(135)** was obtained as buff coloured solid. m.p.: 173-177 °C**.** (**Sxvi**)

Anal:

TLC : R_f 0.45 (*n*-Hexane: Ethyl acetate; 8:12)

IR (KBr, cm^{-1}) : 3030, 2921, 2853, 1637, 1568, 1511, 1382, 1226, 839 and 699.

Mass (m/z) : 471 [M+3].

^{1}H-NMR [400 MHz, DMSO-d_6, δ]: 7.78 (m, 3H), 7.44-7.21 (m, 4H), 7.04-6.99 (m, 8H), 5.70 (s, 1H), 3.87 (s, 2H), 3.06-3.02 (dd, 4H), 2.21 (s, 2H)

5.2.29 5-((3-Chlorobenzylamino)methyl)-3,3-dibenzylpyrazolo[1,5-*a*]pyrimidine-2,7(1*H*,3*H*)-dione (136)

Compound **(136)** was synthesized using the method as mentioned for compound (**134**) by reacting 3-chlorobenzyl amine with 3,3-dibenzyl-5-(chloromethyl)pyrazolo[1,5-*a*]pyrimidine-2,7(1*H*,3*H*)-dione **(133).** Compound **(136)** was obtained as yellow coloured solid. m.p.: 182-185 °C**.**

Anal:

TLC : R_f 0.5 (*n*-Hexane: Ethyl acetate; 8:12)

IR (KBr, cm^{-1}) : 3026, 2917, 2849, 1614, 1571, 1492, 1202, 1092 and 698.

Mass (m/z) : 482 [M-2].

^{1}H-NMR [400 MHz, DMSO-d_6, δ]: 8.68 (s, 1H), 7.43-7.30 (m, 4H), 7.29-7.18 (m, 10H), 6.26 (s, 1H), 4.07 (s, 2H), 3.98 (s, 2H) 3.52-3.50 (dd, 2H), 3.10-3.00 (dd, 2H), 2.459 (s, 2H)

5.2.30 3,3-Dibenzyl-5-((pyridin-2-ylamino)methyl)pyrazolo[1,5-*a*]pyrimidine-2,7(1*H*,3*H*)-dione (137)

Compound **(137)** was synthesized using the method as mentioned for compound (**134**) by reacting 2-aminopyridine with 3,3-dibenzyl-5-(chloromethyl)pyrazolo[1,5-*a*]pyrimidine-2,7(1*H*,3*H*)-dione **(133).** Compound **(137)** was obtained as brown coloured solid. m.p: 178-181 °C**.**

Anal:

TLC : R_f 0. (*n*-Hexane: Ethyl acetate; 8:12)

IR (KBr, cm^{-1}) : 3063, 3030, 2921, 1742, 1648, 1589, 1223, 1140 and 700.

Mass (m/z) : 436 [M^+]

^{1}H-NMR [400 MHz, DMSO-d_6, δ]: 8.68 (s, 1H), 8.07-8.05 (m, 1H), 7.43-7.30 (m, 5H), 7.29-7.25 (m, 6H), 6.92-6.90 (m, 1H), 6.40 (dd, 1H), 6.31 (s, 1H), 6.24 (s, 1H), 4.69 (s, 2H), 3.52-3.50 (dd, 2H) and 3.02-3.00 (dd, 2H).

5.2.31 3,3-Dibenzyl-5-((4-methylbenzylamino)methyl)-pyrazolo[1,5-*a*]pyrimidine-2,7(1*H*, 3*H*)-dione (138)

Compound **(138)** was synthesized using the method as mentioned for compound (**134**) by reacting 4-methylbenzyl amine with 3,3-dibenzyl-5-(chloromethyl)pyrazolo[1,5-*a*]pyrimidine-2,7(1*H*,3*H*)-dione **(133).** Compound **(138)** was obtained as buff coloured solid. m.p.: 180-184 °C**.**

Anal:

TLC : R_f 0. 47 (*n*-Hexane: Ethyl acetate; 8:12)

IR (KBr, cm^{-1}) : 3060, 3030, 2922, 2853, 1739, 1687, 1579, 1085 and 701.

Mass (m/z) : 467 [M+3]

^{1}H-NMR [400 MHz, DMSO-d_6, δ]: 8.68 (s, 1H), 8.07-8.05 (m, 1H), 7.43-7.30 (m, 5H), 7.29-7.25 (m, 6H), 6.92-6.90 (m, 1H), 6.40 (dd, 1H), 6.31 (s, 1H), 6.24 (s, 1H), 4.69 (s, 2H), 3.52-3.50 (dd, 2H), 3.02-3.00 (dd, 2H).

5.2.32 5-((2,4-Dichlorobenzylamino)methyl)-3,3-dibenzylpyrazolo[1,5-*a*]pyrimidine-2,7(1*H*,3*H*)-dione (139)

Compound **(139)** was synthesized using the method as mentioned for compound (**134**) by reacting 3, 4-dichlorobenzyl amine with 3,3-dibenzyl-5-(chloromethyl)pyrazolo[1,5-

a]pyrimidine-2,7(1*H*,3*H*)-dione **(133).** Compound **(139)** was obtained as orange coloured solid. m.p.: 190-192 °C**.**

Anal:

TLC : R_f 0. 54 (*n*-Hexane: Ethyl acetate; 8:12)

IR (KBr, cm^{-1}) : 3179, 3064, 3024, 2872, 1587, 1484, 1100 and 821.

Mass (m/z) : 521 [M+2]

^{1}H-NMR [400 MHz, DMSO-d_6, δ]: 8.68 (s, 1H), 7.43-7.30 (m, 4H), 7.29-7.25 (m, 6H), 7.16-7.14 (s, 2H), 7.04-7.02 (d, 2H), 6.26 (s, 1H), 4.07 (s, 2H), 3.98 (s, 2H), 3.52-3.50 (dd, 2H), 3.02-3.00 (dd, 2H), 2.38 (s, 3H).

5.2.33 5-((4-Methoxybenzylamino)methyl)-3,3-dibenzylpyrazolo[1,5-*a*]pyrimidine-2,7(1*H*,3*H*)-dione (140)

Compound **(140)** was synthesized using the method as mentioned for compound (**134**) by reacting 4-methoxybenzyl amine with 3,3-dibenzyl-5-(chloromethyl)pyrazolo[1,5-*a*]pyrimidine-2,7(1*H*,3*H*)-dione **(133).** Compound **(140)** was obtained as white solid. m.p. 230-232 °C**.** (**Sxviii**)

Anal:

TLC : R_f 0.61 (*n*-Hexane: Ethyl acetate; 8:12)

IR (KBr, cm^{-1}) : 3424, 1573, 1420, 1030, 702.

Mass (m/z) : 481 $[M+1]^+$

^{1}H-NMR [400 MHz, DMSO-d_6, δ]: 7.71-7.69 (m, 2H), 7.37-7.31 (m, 2H), 7.07-7.02 (m, 9H) and 6.96-6.93 (m, 2H), 6.02 (s, 1H) 4.14-4.13 (m, 3H), 3.76 (s, 3H), 3.65 (s, 2H), 3.19-3.10 (m, 4H).

5.2.34 3,3-Dibenzyl-5-(morpholinomethyl)pyrazolo[1,5-*a*]pyrimidine-2,7(1*H*,3*H*)-dione (141)

Compound **(141)** was synthesized using the method as mentioned for compound (**134**) by reacting morpholine with 3,3-dibenzyl-5-(chloromethyl)pyrazolo[1,5-*a*]pyrimidine-2,7(1*H*,3*H*)-dione **(133).** Compound **(141)** was obtained as greenish solid. m.p. 194-197 °C**.**

Anal:

TLC : R_f 0.65 (*n*-Hexane: Ethyl acetate; 8:12)

IR (KBr, cm^{-1}): 3432, 3308, 3192, 1683, 1645, 1403, 1293, 702.

Mass (m/z) : 431 $[M+1]^+$

^{1}H-NMR [400 MHz, DMSO-d_6, δ]: 8.65 (s, 1H), 7.43-7.39 (m, 4H), 7.30-7.25 (m, 6H), 6.30 (s, 1H), 3.77 (s, 2 H), 3.56-3.50 (m, 6H), 3.02-3.00 (d, 2H), 2.93-2.91 (m, 4H).

5.2.35 Methyl-2-cyano-3-phenylpropanoate (142)

To a solution of methyl cyanoacetate (**126**) and potassium carbonate in THF stirred under nitrogen atmosphere at 0° C, benzyl bromide (**127**) was added. The reaction mixture was then stirred at room temperature for overnight. The reaction mixture was diluted with triethylamine and extracted with ethyl acetate (thrice). The combined organic layer was washed with water and brine, dried over anhydrous sodium sulphate and concentrated to dryness in vacuum to obtain clear liquid product. This product was directly taken for next step without further purification. b.p. 156-158°C.

Anal:

IR (KBr cm^{-1}) : 3063, 3032, 2956, 2252, 1748, 1445, 1235.

5.2.36 5-Amino-4-benzyl-1,2-dihydropyrazol-3-one (143)

To a solution of methyl-2-cyano-3-phenylpropanoate (**142**) in methanol stirred under nitrogen environment at room temperature, hydrazine hydrate (99 %) was added drop wise. The reaction mixture was stirred at room temperature for 15 minutes. Sodium hydroxide pellets were added to the reaction and the mixture was allowed to stir for further 3 hours. The mixture was diluted with water, which was then filtered to obtain white coloured solid. m.p. 178-180 °C.

Anal:

IR (KBr, cm^{-1}) :3169, 3067, 2925, 2802, 1676, 1608, 1494 and 1002.

^{1}H-NMR [400 MHz, DMSO-d_6, δ]: 11.36 (s, 1H), 9.56 (s, 1H), 7.26-7.19 (m, 5H), 7.13 (m, 1H) and 3.58 (s, 2H).

5.2.37 3-Benzyl-5-methylpyrazolo[1,5-*a*]pyrimidine-2,7(1*H*,4*H*)-dione (144)

To a solution of 5-amino-4-benzyl-1,2-dihydropyrazol-3-one (**143**) in acetic acid, ethyl acetoacetate was added drop wise and stirred at room temperature for 10 minutes. The reaction mixture was heated at 100 °C overnight. The reaction mixture was then diluted with ice cold water to obtain white coloured solid product. m.p.**:** 178-180 °C**. (Sxx)**

Anal:

TLC : R_f 0.3 (*n*-Hexane: Ethyl acetate; 8: 12)

IR (KBr, cm^{-1}) : 3354, 3250, 3071, 3071, 2918, 1707, 1622, 1526 and 1306

Mass (m/z) : 256 $[M+1]^+$ and 254 $[M-2]^+$

^{1}H-NMR [400 MHz, DMSO-d_6, δ]: 12.69 (s, 1H), 9.53 (s, 1H), 7.29-7.20 (m, 5H), 5.18 (s, 1H), 3.36 (s, 2H) and 2.10 (s, 3H).

5.2.38 3-Benzyl-6-chloro-5-methylpyrazolo[1,5-*a*]pyrimidine-2,7(1*H*,4*H*)-dione (145)

To a solution of 5-amino-4-benzyl-1,2-dihydropyrazol-3-one (**143**) in acetic acid, ethyl 2-chloro acetoacetate was added drop wise and stirred at room temperature for 10 minutes. The reaction mixture was heated at 100 °C overnight. The reaction mixture was then diluted with ice cold water to obtain white coloured solid product. m.p.**:** 201-203 °C**.**

Anal:

TLC : R_f 0.36 (*n*-Hexane: Ethyl acetate; 8: 12)

IR (KBr, cm^{-1}) : 3234, 2920, 1742, 1640, 1543 and 1103

^{1}H-NMR [400 MHz, DMSO-d_6, δ]: 13.30 (s, 1H), 7.91 (s, 1H), 7.29-7.20 (m, 5H), 3.75 (s, 2H) and 2.37 (s, 3H)

5.2.39 3-Benzyl-5-(chloromethyl)pyrazolo[1,5-*a*]pyrimidine-2,7(1*H*,4*H*)-dione (146)

To a solution of 5-amino-4-benzyl-1,2-dihydropyrazol-3-one (**143**) in acetic acid, ethyl 4-chloro acetoacetate was added drop wise and stirred at room temperature for 10 minutes. The reaction mixture was heated at 100 °C overnight. The reaction mixture was then diluted with ice cold water to obtain white coloured solid product. m.p.**:** 195-197 °C**.**

Anal:

TLC : R_f 0.4 (*n*-Hexane: Ethyl acetate; 8: 12)

IR (KBr, cm^{-1}) : 3224, 3098, 2922, 1701, 1619, 1554, 1365 and 1035

Mass (m/z) : 288 [M-1]

^{1}H-NMR [400 MHz, DMSO-d_6, δ]: 13.30 (s, 1H), 8.57 (s, 1H), 7.29-7.20 (m, 5H), 6.12 (s, 1H), 4.63 (s, 2H), 3.75 (s, 2H)

5.2.40 5-((Benzylamino)methyl)-3-benzylpyrazolo[1,5-*a*]pyrimidine-2,7(1*H*,4*H*)-dione (147)

In a 25 ml 2-neck RBF benzylamine was dissolved in dry DMF and Cs_2CO_3 was added. After stirring at rt for 5-10 mins under the stream of nitrogen, 3-benzyl-5-(chloromethyl)pyrazolo[1,5-*a*]pyrimidine-2,7(1*H*,4*H*)-dione **(146)** was added and the reaction mixture was transferred on oil bath at 80 °C for 5-6 hrs. Progress of the reaction was monitored by TLC. After completion of reaction, crushed ice was added, extracted with chloroform and dried over Na_2SO_4. Solvent was evaporated using rotary evaporator and the sticky material so obtained was purified through column chromatography using petroleum ether and ethyl acetate (60%) as eluents to provide the desired product. m.p.**:** 202-205 °C**.**

Anal:

TLC : R_f 0.2 (*n*-Hexane: Ethyl acetate; 8: 12)

IR (KBr, cm^{-1}) : 3430, 3066, 2920, 2861, 1685, 1632 and 1448.

^{1}H-NMR [400 MHz, DMSO-d_6, δ]: 9.53 (s, 1H, -OH), 7.35-7.20 (m, 10H), 5.48 (s, 1H), 3.98 (s, 2H), 3.68 (s, 2H), 3.53 (s, 1H), 3.36 (s, 2H).

5.2.41 5-((4-Flourobenzylamino)methyl)-3-benzylpyrazolo[1,5-*a*]pyrimidine-2,7(1*H*,4*H*)-dione (148)

Compound **(148)** was synthesized using the method as mentioned for compound (**147**) by reacting 4-flourobenzyl amine with 3-benzyl-5-(chloromethyl)pyrazolo[1,5-*a*]pyrimidine-2,7(1*H*,4*H*)-dione **(146).** Compound **(148)** was obtained as white solid. m.p.**:** 215-217 °C**.**

Anal:

TLC : R_f 0.26 (*n*-Hexane: Ethyl acetate; 8: 12)

IR (KBr, cm^{-1}) : 3066, 3022,2948, 1688, 1690, 1606, 1500, 1442

^{1}H-NMR [400 MHz, DMSO-d_6, δ]: 9.65, 7.41-7.32 (m, 9H), t 5.60 (s, 1H), 4.15 (s, 2H), 3.80 (s, 2H), 3.65 (s, 1H), 3.48 (s, 2H)

5.2.42 5-((4-Chlorobenzylamino)methyl)-3-benzylpyrazolo[1,5-*a*]pyrimidine-2,7(1*H*,4*H*)-dione (149)

Compound **(149)** was synthesized using the method as mentioned for compound (**147**) by reacting 4-chlorobenzyl amine with 3-benzyl-5-(chloromethyl)pyrazolo[1,5-*a*]pyrimidine-2,7(1*H*,4*H*)-dione **(146).** Compound **(149)** was obtained as buff solid. m.p.**:** 245-247 °C**.** (**Sxxii**)

Anal:

TLC : R_f 0.3 (*n*-Hexane: Ethyl acetate; 8:12)

IR (KBr, cm^{-1}) : 3114, 2961, 174, 1655, 1514 and 1027

Mass (m/z) : 397 $[M+2]^+$

^{1}H-NMR [400 MHz, DMSO-d_6, δ]: 9.53 (s, 1H, -OH), 7.29-7.20 (m, 9H), 5.48 (s, 1H), 4.03 (s, 2H), 3.68 (s, 2H), 3.53 (s, 1H), 3.36 (s, 2H)

5.2.43 5-((3,4-Dichlorobenzylamino)methyl)-3-benzylpyrazolo[1,5-*a*]pyrimidine-2,7(1*H*,4*H*)-dione (150)

Compound **(150)** was synthesized using the method as mentioned for compound (**147**) by reacting 3, 4-dicholorobenzyl amine with 3-benzyl-5-(chloromethyl)pyrazolo[1,5-*a*]pyrimidine-2,7(1*H*,4*H*)-dione **(146).** Compound **(150)** was obtained as brownish solid. m.p.**:** >250 °C**.**

Anal:

TLC : R_f 0.25 (*n*-Hexane: Ethyl acetate; 18:2)

IR (KBr, cm^{-1}): 3224, 3098, 2922, 1701, 1679, 1554, 1365 and 1035

Mass (m/z) : 427 $[M-2]^+$

^{1}H-NMR [400 MHz, DMSO-d_6, δ]: 9.53 (s, 1H), 7.36-7.34 (m, 2H), 7.29-7.15 (m, 6H), 5.48 (s, 1H), 4.08 (s, 2H), 3.78 (s, 1H), 3.68 (s, 2H), 3.36 (s, 2H)

5.2.44 5-(Pyridin-4-ylamino)methyl)-3-benzylpyrazolo[1,5-*a*]pyrimidine-2,7(1*H*,4*H*)-dione (151)

Compound **(151)** was synthesized using the method as mentioned for compound (**147**) by reacting 4-amino pyridine with 3-benzyl-5-(chloromethyl)pyrazolo[1,5-*a*]pyrimidine-2,7(1*H*,4*H*)-dione **(146).** Compound **(151)** was obtained as white solid. m.p.**:** 240-242 °C**.**

Anal:

TLC : R_f 0.34 (*n*-Hexane: Ethyl acetate; 18:2)

IR (KBr, cm^{-1}) : 3325, 3083, 3025, 1689, 1597, 1454

^{1}H-NMR [400 MHz, DMSO-d_6, δ]: 9.53 (s, 1H), 8.07-8.05 (d, 2H), 7.29-7.20 (m, 5H), 6.73 (s, 1H), 6.45-6.43 (d, 2H), 5.53 (s, 1H), 4.26 (s, 2H), 3.36 (s, 2H).

5.2.45 5-((4-Methylbenzylamino)methyl)-3-benzylpyrazolo[1,5-*a*]pyrimidine-2,7(1*H*,4*H*)-dione (152)

Compound **(152)** was synthesized using the method as mentioned for compound (**147**) by reacting 4-methylbenzyl amine with 3-benzyl-5-(chloromethyl)pyrazolo[1,5-*a*]pyrimidine-2,7(1*H*,4*H*)-dione **(146).** Compound **(152)** was obtained as white solid. m.p.**:** 239-241 °C**.**

Anal:

TLC : R_f 0.32 (*n*-Hexane: Ethyl acetate; 18:2)

IR (KBr, cm^{-1}): 3342, 3029, 2967, 2923, 1741, 1704, 1686, 1549, 1492 and 1385

Mass (m/z) : 374 $[M]^+$

^{1}H-NMR [400 MHz, DMSO-d_6, δ]: 13.30 (s, 1H), 7.29-7.14 (m, 8H), 7.04-7.02 (m, 2H), 6.00 (s, 1H), 4.07 (s, 2H), 3.99 (s, 2H), 3.75 (s, 2H), 2.38 (s, 3H).

SECTION II

5.2.46 (*E*)-1,3-Diphenylprop-2-en-1-one (174)

In a 25ml-RBF containing ethanol (2 ml), aqueous NaOH solution (4 ml) was added and allowed to stir on ice-bath. To this mixture, acetophenone (**153**, 0.308 ml, 0.0026 M) was added and allowed to stir for another 5 mins. To this mixture benzaldehyde (**161**, 0.5gm, 0.0047 M) was added and was brought to RT and stirred vigorously for 3 hours. The reaction was monitored by TLC. Upon completion, crushed ice was added to reaction mixture to obtain desired compound **(174)** which was filtered under vacuum to obtain white solid. The compound (**174**) was taken for further reaction without purification (0.495 gm, 99%); m.p. 54-58°C (Lit. 57.5°C)[1-3].

Anal:

TLC : R_f 0.42(*n*-hexane: ethyl acetate; 18:2)

IR (KBr, cm^{-1}) : 3051, 1661, 1604, 1445, 1209, 991, 749.

5.2.47 (*E*)-3-(4- Chlorophenyl)-1-phenylprop-2-en-1-one (175)

Compound (**175**) was synthesized by reacting 4- chlorobenzaldehyde (**162**, 0.5 gm, 0.0035 M) under similar reaction conditions as described for compound (**174**) to get buff solid (**175)** (0.5 gm, 100%); m.p. 113- 117 ºC (Lit.114-116 ºC) [1-3].

Anal:

TLC : R_f 0.5 (*n*-hexane: ethyl acetate; 18:2)

IR (KBr, cm^{-1}) : 3053, 2923, 2850, 1659, 1602, 1332, 1215, 870, 762.

5.2.48 (*E*)-1-Phenyl-3-*p*-tolylprop-2-en-1-one (176)

Compound (**176**) was synthesized by reacting 4- methylbenzaldehyde (**163**, 0.5 gm, 0.0041 M) under similar reaction conditions as described for compound (**174**) to get reddish brown solid (**176**), (0.49 gm, 99 %); m.p. 94-98 ºC (Lit. 87-91 ºC) [1-3].

Anal:

TLC : R_f 0.5 (*n*-hexane: ethyl acetate; 18:2)

IR (KBr, cm^{-1}) : 3050, 3020, 2859, 1654, 1596, 1216, 981, 813.

5.2.49 (*E*)-3-(4- Fluorophenyl)-1-phenylprop-2-en-1-one (177)

Compound (**177**) was synthesized by reacting 4-fluorobenzaldehyde (**164**, 0.5 gm, 0.0040 M) under similar reaction conditions as described for compound (**174**) to get buff solid (**177**), (0.49 gm, 98%); m.p. 84-86 ºC (Lit. 86-87 ºC) [1-3].

Anal:

TLC : R_f 0.5 (*n*-hexane: ethyl acetate; 18:2)

IR (KBr, cm^{-1}) : 3065, 2801, 1659, 1597, 1216, 835.

5.2.50 (*E*)-3-(4- Bromophenyl)-1-phenylprop-2-en-1-one (178)

Compound (**178**) was synthesized by reacting 4-bromobenzaldehyde (**165**, 0.5 gm, 0.0027 M) under similar reaction conditions as described for compound (**174**) to get buff solid (**178**), (0.49 gm, 99 %); m.p. 120-124 ºC (Lit. 112-114 ºC) [1-3] .

Anal:

TLC : R_f 0.5 (*n*-hexane: ethyl acetate; 18:2)

IR (KBr, cm^{-1}) : 3057, 2992, 1657, 1601, 1485, 1329, 1218, 821, 689.

5.2.51 (*E*)-3-(4- Nitrophenyl)-1-phenylprop-2-en-1-one (179)

Compound (**179**) was synthesized by reacting 4-nitrobenzaldehyde (**166**, 0.5 gm, 0.0033 M) under similar reaction conditions as described for compound (**174**) to get pale yellow solid (**179**), (0.33 gm, 67%); m.p. 160-164 ºC (Lit. 162-166 ºC)[1-3].

Anal:

TLC : R_f 0.36 (*n*-hexane: ethyl acetate; 18:2)

IR (KBr, cm^{-1}) : 3073, 2929, 2840, 2441, 1660, 1602, 1218, 893.

5.2.52 (*E)*-3-(4-Methoxyphenyl)-1-phenylprop-2-en-1-one (180)

Compound (**180**) was synthesized by reacting 4-methoxybenzaldehyde (**167**, 0.5 gm, 0.0036 M) under similar reaction conditions as described for compound (**174**) to get pale yellow solid (**180**), (0.49 gm, 99%); m.p. 118-120 ºC (Lit. 120 ºC)[1-3] .

Anal:

TLC : R_f 0.38 (*n*-hexane: ethyl acetate; 18:2)

IR (KBr, cm^{-1}) : 3058, 3008, 2933, 2844, 1654, 1598, 1509, 1304, 1015, 820.

5.2.53 (*E*)-3-(3- Chlorophenyl)-1-phenylprop-2-en-1-one (181)

Compound (**181**) was synthesized by reacting 3- chlorobenzaldehyde (**168**, 0.5 gm, 0.0027 M) under similar reaction conditions as described for compound (**174**) to get buff solid (**181**), (0.30 gm, 60.47%); m.p. 72-74 ^{o}C (Lit. 73-75 ^{o}C) [1-3].

Anal:

TLC : R_f 0.29 (*n*-hexane: ethyl acetate; 18:2)

IR (KBr, cm^{-1}) : 3060, 1657, 1602, 1305, 1213, 771, 670.

5.2.54 (*E*)-3-(3- Fluorophenyl)-1-phenylprop-2-en-1-one (182)

Compound (**182**) was synthesized by reacting 3- fluorobenzaldehyde (**169**, 0.5 gm, 0.0040 M) under similar reaction conditions as described for compound (**174**) to get light green solid (**182**), (0.48 gm, 97 %); m.p. 85-90 ^{o}C (Lit. 87-89 ^{o}C) [1-3] .

Anal:

TLC : R_f 0.5 (*n*-hexane: ethyl acetate; 19:1)

IR (KBr, cm^{-1}) : 3058, 1663, 1604, 1480, 1443, 1142, 850.

5.2.55 (*E*)-3-(3- Bromophenyl)-1-phenylprop-2-en-1-one (183)

Compound (**183**) was synthesized by reacting 3- bromobenzaldehyde (**170**, 0.5 gm, 0.0035 M) under similar reaction conditions as described for compound (**174**) to get pale yellow solid (**183**), (0.79 gm, 59 %); m.p. 85-90 ^{o}C (Lit. 83-86 ^{o}C) [1-3].

Anal:

TLC : R_f 0.5 (*n*-hexane: ethyl acetate; 18:2)

IR (KBr, cm^{-1}) : 3061, 2835, 1689, 1602, 1216.

5.2.56 (*E*)-3-(3- Nitrophenyl)-1-phenylprop-2-en-1-one (184)

Compound (**184**) was synthesized by reacting 3- nitrobenzaldehyde (**171**, 0.5 gm, 0.0033 M) under similar reaction conditions as described for compound (**174**) to get buff solid (**184**), (0.24 gm, 48 %); m.p. 140-141 ^{o}C (Lit. 145-146 ^{o}C)[1-3].

Anal:

TLC : R_f 0.16 (*n*-hexane: ethyl acetate; 18:2)

IR (KBr, cm^{-1}) : 3070, 2867, 1662, 1607, 1529, 1349, 1221, 780.

5.2.57 (*E*)-3-(3-Methoxyphenyl)-1-phenylprop-2-en-1-one (185)

Compound (**185**) was synthesized by reacting 3-methoxybenzaldehyde (**172**, 0.5 gm, 0.0036 M) under similar reaction conditions as described for compound (**174**) to get yellow solid (**185**), (0.44 gm, 88.93 %); m.p. 64-67 ^{o}C (Lit. 60 ^{o}C) [1-3].

Anal:

TLC : R_f 0.33 (*n*-hexane: ethyl acetate; 18:2)

IR (KBr, cm^{-1}) : 3061, 2955, 2830, 1654, 1599, 1209, 1044 and 766.

5.2.58 (*E*)-3-(2- Nitrophenyl)-1-phenylprop-2-en-1-one (186)

Compound (**186**) was synthesized by reacting 2-nitrobenzaldehyde (**173**, 0.5 gm, 0.0033 M) under similar reaction conditions as described for compound (**174**) to get pale black solid (**186**), (0.24 gm, 48 %); m.p. 124-126 ^{o}C (Lit. 124-128 ^{o}C)[1-3].

Anal:

TLC : R_f 0.2 (*n*-hexane: ethyl acetate; 18:2)

IR (KBr, cm^{-1}) : 3058, 2920, 2857, 1662, 1622, 1396, 1071, 690.

5.2.59 (*E*)-1-(2-Bromophenyl)-3-phenylprop-2-en-1-one (187)

In a 25ml-RBF containing ethanol (2 ml), aqueous NaOH solution (4 ml) was added and allowed to stir on ice-bath. To this mixture, 1-(2-bromophenyl)ethanone (**154**, 0.308 ml, 0.0037 M) was added and allowed to stir for another 5 mins. To this mixture benzaldehyde (**161**, 0.5gm, 0.0047 M) was added and was brought to RT and stirred vigorously for 3 hours. The reaction was monitored by TLC. Upon completion, crushed ice was added to reaction mixture to obtain desired compound which was filtered under vacuum to obtain black solid. The compound (**187**) was taken for further reaction without purification, (0.8gm, 60%); m.p. 99-101 ^{o}C.

Anal:

TLC : R_f 0.37(*n*-hexane: ethyl acetate; 18:2)

IR (KBr, cm^{-1}) : 3023, 2917, 1652, 1601, 1400, 1325, 1176 and 809

5.2.60 *(E)*-3-(3-Chlorophenyl)-1-(4- chlorophenyl)prop-2-en-1 one (188)

In a 25ml-RBF containing ethanol (2 ml), aqueous NaOH solution (4 ml) was added and allowed to stir on ice-bath. To this mixture,4-chloroacetophenone (**155**, 0.5 ml, 0.0035 M) was added and allowed to stir for another 5 mins. To this mixture 3-chlorobenzaldehyde

(**168**, 0.5gm, 0.0035 M) was added and was brought to RT and stirred vigorously for 3 hours. The reaction was monitored by TLC. Upon completion, crushed ice was added to reaction mixture to obtain desired compound which was filtered under vacuum to obtain white solid (**188**). The compound (**188**) was taken for further reaction without purification, (0.495 gm, 99%); m.p. 96-100 ℃.

Anal:

TLC : R_f 0.41 (*n*-hexane: ethyl acetate; 18:2)

IR (KBr, cm^{-1}) : 3023, 2918, 1663, 1604, 1310, 980, 789.

5.2.61 (*E*)-3-(3-Chlorophenyl)-1-*p*-tolylprop-2-en-1-one (189)

In a 25ml-RBF containing ethanol (2 ml), aqueous NaOH solution (4 ml) was added and allowed to stir on ice-bath. To this mixture, 4-methylacetophenone (**156**, 0.379 ml, 0.0028 M) was added and allowed to stir for another 5 mins. To this mixture 3-chlorobenzaldehyde (**168**, 0.5gm, 0.0035 M) was added and was brought to RT and stirred vigorously for 3 hours. The reaction was monitored by TLC. Upon completion, crushed ice was added to reaction mixture to obtain desired compound which was filtered under vacuum to obtain white solid. The compound (**189**) was taken for further reaction without purification, (0.293 gm, 58.63 %); m.p. 101-105 ºC (Lit. 107-109 ºC) [1-3].

Anal:

TLC : R_f 0.41 (*n*-hexane: ethyl acetate; 18:2)

IR (KBr, cm^{-1}) : 3026, 2920, 1664, 1604, 1415, 1082, 981, 790.

5.2.62 (*E*)-1-(4-Chlorophenyl)-3-(3-nitrophenyl)prop-2-en-1-one (190)

Compound (**190**) was synthesized by reacting 3-nitrobenzaldehyde (**171**, 0.5 gm, 0.0033 M) under similar reaction conditions as described for compound (**188**) to get light brown solid (**190**), (0.55 gm, 110%); m.p. 115-120 ℃.

Anal:

TLC : R_f 0.43 (*n*-hexane: ethyl acetate; 18:2)

IR (KBr, cm^{-1}) : 3065, 3034, 1667, 1609, 1527, 1289, 1090, 738.

5.2.63 (*E*)-1-(4-Chlorophenyl)-3-(3-methoxyphenyl)prop-2-en-1-one (191)

Compound (**191**) was synthesized by reacting 3-methoxybenzaldehyde (**172**, 0.5 gm, 0.0036 M) under similar reaction conditions as described for compound (**188**) to get brown sticky solid (**191**), (0.403 gm, 80.65%); m.p. 115-120 ℃.

Anal:

TLC : R_f 0.51 (*n*-hexane: ethyl acetate; 16:4)

IR (KBr, cm^{-1}) : 2928, 2843, 1658, 1598, 1211, 1092, 825 and 790.

5.2.64 (*E*)-1-(4-Bromophenyl)-3-phenylprop-2-en-1-one (192)

Compound (**192**) was synthesized by reacting 1-(4-bromophenyl)ethanone (**154**, 0.308 ml, 0.0037 M) under similar reaction conditions as described for compound (**187**) to get buff solid (**192**), (0.495 gm, 99%); m.p. 104-106℃ (Lit. 103.26℃)[1-3].

Anal:

TLC : R_f 0.40(*n*-hexane: ethyl acetate; 18:2)

IR (KBr, cm^{-1}) : 3057, 2916, 1654, 1601, 1394, 1106, 826 and 792.

5.2.65 (*E*)-3-(4-Bromophenyl)-1-p-tolylprop-2-en-1-one (193)

Compound (**193**) was synthesized by reacting 4-bromobenzaldehyde (**165**, 0.5 gm, 0.0027 M) under similar reaction conditions as described for compound (**189**) to get white solid (**193**), (0.272 gm, 54.75%); m.p. 155-160℃ (Lit. 153-155℃)[1-3].

Anal:

TLC : R_f 0.37(*n*-hexane: ethyl acetate; 18:2)

IR (KBr, cm^{-1}) : 3023, 2917, 1652, 1601, 1400, 1325, 1176 and 809

5.2.66 (*E*)-3-(4-Bromophenyl)-1-(4-chlorophenyl)prop-2-en-1 one (194)

Compound (**194**) was synthesized by reacting 4-bromobenzaldehyde (**165,** 0.5 gm, 0.0027 M) under similar reaction conditions as described for compound (**188**) to get white solid (**194**), (0.485 gm, 97%); m.p. 165-170 ℃ (lit. 167-168℃)[1-3].

Anal:

TLC : R_f 0.72(*n*-hexane: ethyl acetate; 18:2)

IR (KBr, cm^{-1}) : 3084, 2945, 1659, 1598, 1402, 1218, 1090 and 738.

5.2.67 (E)-1-(4-Chlorophenyl)-3-phenylprop-2-en-1-one (195)

Compound (**195**) was synthesized by reacting benzaldehyde (**161,** 0.5gm, 0.0035 M) under similar reaction conditions as described for compound (**188**) to get white solid (**195**), (0.48 gm, 97%); m.p. 161-163 ℃ (lit. 161-163℃)[1-3].

Anal:

TLC : R_f 0.72(*n*-hexane: ethyl acetate; 18:2)

IR (KBr, cm^{-1}) : 3079, 2985, 1660, 1556, 1413. 1030, 780.

5.2.68 (*E*)-3-(4-Chlorophenyl)-1-p-tolylprop-2-en-1-one (196)

Compound (**196**) was synthesized by reacting 4-chlorobenzaldehyde (**162,** 0.5 gm, 0.0035 M) under similar reaction conditions as described for compound (**189**) to get orange solid (**196**), (0.3735 gm, 74.7%); m.p. 120-123℃ (lit. 122-125℃)[1-3].

Anal:

TLC : R_f 0.44 (*n*-hexane: ethyl acetate; 18:2)

IR (KBr, cm^{-1}) : 3026, 2920, 1664, 1604, 1415, 1311, 1031 and 790.

5.2.69 (*E*)-1,3-*bis*(4-chlorophenyl)prop-2-en-1-one (197)

Compound (**197**) was synthesized by reacting 4-chlorobenzaldehyde (**162,** 0.5 gm, 0.0035 M) under similar reaction conditions as described for compound (**188**) to get yellow solid (**197**), (0.495 gm, 99%); m.p. 152-155℃ (lit. 156-160℃)[1-3].

Anal:

TLC : R_f 0.42(*n*-hexane: ethyl acetate; 18:2)

IR (KBr, cm^{-1}) : 3085, 1653, 1593, 1327, 1213, 1091, 817.

5.2.70 (*E*)-1-(4-Chlorophenyl)-3-(4-methoxyphenyl)prop-2-en-1-one (198)

Compound (**198**) was synthesized by reacting 4-methoxybenzaldehyde (**167,** 0.5 gm, 0.0036 M) under similar reaction conditions as described for compound (**188**) to get sticky solid (**198**), (0.45 gm, 90%); m.p. 128-130℃.

Anal:

TLC : R_f 0.52(*n*-hexane: ethyl acetate; 16:4)

IR (KBr, cm^{-1}) : 3000, 2970, 2934, 2840, 1654, 1592, 1508, 1302, 1114 and 817.

5.2.71 (*E*)-1-(4-Nitrophenyl)-3-phenylprop-2-en-1-one (199)

Compound (**199**) was synthesized by reacting benzaldehyde (**161,** 0.5 gm, 0.0047 M) under similar reaction conditions as described for compound (**174**) to get Pale yellow solid (**199**), (0.495 gm, 99%); m.p. 188-191℃ (it. 190-192℃)[1-3].

Anal:

TLC : R_f 0.48(*n*-hexane: ethyl acetate; 18:2)

IR (KBr, cm^{-1}) : 3053, 2841, 1659, 1596, 1512, 1329, 1204, 847, 740.

5.2.72 (*E*)-1-(4-Chlorophenyl)-3-(4-nitrophenyl)prop-2-en-1-one (200)

Compound (**200**) was synthesized by reacting 4-nitrobenzaldehyde (**166,** 0.5 gm, 0.0033 M) under similar reaction conditions as described for compound (**188**) to get yellow solid (**200**), (0.57 gm, 114%); m.p. 140-145℃.

Anal:

TLC : R_f 0.6(*n*-hexane: ethyl acetate; 18:2)

IR (KBr, cm^{-1}) : 3109, 2856, 1662, 1603, 1534, 1347, 1178, 794.

5.2.73 (*E*)-1,3-Di*p*-tolylprop-2-en-1-one (201)

Compound (**201**) was synthesized by reacting 4-methylbenzaldehyde (**163,** 0.5 gm, 0.0041 M) under similar reaction conditions as described for compound (**190**) to get white solid (**201**), (0.3735 gm, 74.7%); m.p. 132-136℃ (lit. 127-130℃)[1-3].

Anal:

TLC : R_f 0.56(*n*-hexane: ethyl acetate; 18:2)

IR (KBr, cm^{-1}) : 3023, 2916, 2860, 1651, 1596, 1327, 1176, 813 and 729.

5.2.74 (*E*)-3-Phenyl-1-*p*-tolylprop-2-en-1-one (202)

Compound (**202**) was synthesized by reacting benzaldehyde (**161,** 0.5 gm, 0.0047 M) under similar reaction conditions as described for compound (**189**) to get brown solid (**202**), (0.495 gm, 99%); m.p. 70-73℃ (lit. 73.7-75.1℃)[1-3].

Anal:

TLC : R_f 0.39(*n*-hexane: ethyl acetate; 18:2)

IR (KBr, cm^{-1}) : 3031, 2921, 1654, 1599, 1210, 1113, 977, 759.

5.2.75 (*E*)-3-(4-Fluorophenyl)-1-*p*-tolylprop-2-en-1-one (203)

Compound (**203)** was synthesized by reacting 4-fluorobenzaldehyde (**164,** 0.5 gm, 0.0040 M) under similar reaction conditions as described for compound (**189**) to get orange solid (**203**), (0.312 gm, 62.55%); m.p. 120-124℃ (lit. 117-119℃)[1-3].

Anal:

TLC : R_f 0.56 (*n*-hexane: ethyl acetate; 18:2)

IR (KBr, cm^{-1}) : 3036, 2919, 2843, 1657, 1601, 1505, 1414, 1218 and 819.

5.2.76 (*E*)-3-(4-Chlorophenyl)-1-(4-fluorophenyl)prop-2-en-1-one (204)

Compound (**204)** was synthesized by reacting 4-chloro benzaldehyde (**162,** 0.5g, 0.0028 mM) with 4-fluoro acetophenone (**159,** 0.453 mL, 0.00633 M) under similar conditions as described for compound **(188)** to get white solid (**204),** (0.30, 80%)**;** m.p. 88-89 °C (lit. 85-86 °C) [1-3].

Anal:

TLC : R_f 0.76 (*n*-hexane: ethyl acetate; 18:2)

IR (KBr, cm^{-1}) : 3074, 1666, 1602, 1265, 874 and 811.

5.2.77 (*E*)-1-(3-Chlorophenyl)-3-phenylprop-2-en-1-one (205)

In a 25ml-RBF containing ethanol (2 ml), aqueous NaOH solution (4 ml) was added and allowed to stir on ice-bath. To this mixture,3-chloroacetophenone (**160,** 0.5 ml, 0.0035 M) was added and allowed to stir for another 5 mins. To this mixture benzaldehyde (**161,** 0.5gm, 0.0035 M) was added and was brought to RT and stirred vigorously for 3 hours. The reaction was monitored by TLC. Upon completion, crushed ice was added to reaction mixture to obtain desired compound which was filtered under vacuum to obtain white solid (**188**). The compound (**188**) was taken for further reaction without purification, (0.495 gm, 99%); m.p. 96-100 ℃.

Anal:

TLC : R_f 0.41 (*n*-hexane: ethyl acetate; 18:2)

IR (KBr, cm^{-1}) : 3023, 2986, 1632, 1280, 1001, 756.

5.2.78 (*E*)-1-(4-Fluorophenyl)-3-*p*-tolylprop-2-en-1-one (206)

Compound (**206**) was synthesized by reacting 4-flourobenzaldehyde (**164,** 0.5 gm, 0.0041 M) under similar reaction conditions as described for compound (**189**) to get White solid (**206**), (0.475 gm, 95%); m.p. 128-132°C.

Anal:

TLC : R_f 0.6(*n*-hexane: ethyl acetate; 18:2)

IR (KBr, cm^{-1}) : 2917, 1658, 1600, 1504, 1222, 1031, 838.

5.2.79 (*E*)-3-(3-Fluorophenyl)-1-(4-fluorophenyl)prop-2-en-1-one (207)

Compound (**207)** was synthesized by reacting 3-fluoro benzaldehyde (**169,** 0.5g, 0.0028 mM) with 4-fluoro acetophenone (**159,** 0.453 mL, 0.00633 M) under similar conditions as described for compound **(188)** to get white solid (**207),** (0.38, 85%)**;** m.p. 115-118°C (lit. 117-119°C) [1-3].

Anal:

TLC : R_f 0.46 (*n*-hexane: ethyl acetate; 18:2)

IR (KBr, cm^{-1}) : 3181, 3072, 1660, 1599

5.2.80 Methyl-2,2-bis(4-methylbenzyl)-2-cyano-ethanoate (209)

In a 25 ml 1-neck RBF methyl 2-cynoacetate (**126**, 0.2 gm, 0.002 M) was dissolved in dry dioxane and anhydrous K_2CO_3 (0.552 gm, 0.004 M) was added. After stirring at room temperature for 5-10 mins, 1-(bromomethyl)-4-methylbenzene (**208**, 0.36 ml, 0.003 M) was added and the reaction mixture was refluxed for overnight. Progress of the reaction was monitored by TLC. After completion of reaction, crushed ice was added in reaction mixture. This reaction mixture was then extracted with ethyl acetate (thrice). The combined organic layer was washed with water and brine, dried over anhydrous sodium sulphate and concentrated to dryness in vacuum to obtain colourless liquid product (0.15 ml, 73%); b.p. 89-91 °C.

Anal:

TLC : R_f 0.71 (*n*-hexane: ethyl acetate; 18:2)

IR (KBr, cm^{-1}) : 3021, 2951, 2926, 2863, 2245, 1744, 1443, 1116 and 816.

5.2.81 3-Amino-4,4-*bis*(4-methylbenzyl)-1*H*-pyrazol-5(4*H*)-one (210)

In a 10 ml RBF methyl-2,2-*bis*(4-methylbenzyl)-2-cyano-ethanoate (**209,** 0.2 gm, 0.00065 M) was dissolved in methanol, to this mixture of hydrazine hydrate (0.063 ml, 0.0013 M) in methanol was added drop-wise. Reaction mixture was refluxed at 80 °C for 5-6 hours. Progress of the reaction was monitored by TLC. After completion of reaction, excess of methanol was evaporated with the aid of rotary evaporator. To the residue, crushed ice was added to obtain white solid (0.16 gm, 80%); m.p. 89-91 °C.

Anal:

TLC : R_f 0.71 (*n*-hexane: ethyl acetate; 12:8)

IR (KBr, cm^{-1}) : 3426, 3296, 3251, 3174, 3051, 3022, 2915, 2856, 1685, 1632, 1512, 1446, and 817.

Mass (m/z) : 308 $[M+1]^+$

5.2.82 3-(3-Oxo-1,3-diphenylpropylamino)-4,4-dibenzyl-1*H*-pyrazol-5(4*H*)-one (211)

In a single neck 25-ml RBF, 3-amino-4,4-dibenzyl-1*H*-pyrazol-5(4*H*)-one (**129**, 0.4 gm, 0.0014 M) was dissolved in a mixture of Cs_2CO_3 in dry DMF. This mixture was allowed to stir at room temperature. To this mixture, (*E*)-1,3-diphenylprop-2-en-1-one (**174,** 0.23gm, 0.0011 M) was added portion-wise. The reaction mixture was heated at 80 °C for 6 hours. The reaction was monitored by TLC. Upon completion, crushed ice was added to the reaction mixture to obtain the precipitates, filtered under vacuum to obtain crude yellow solid. Further purification of the compound was done by column chromatography using silica gel (25% ethyl acetate) afforded a pure white solid (0.34 gm, 81 %); m.p. 222-224°C. (**Sxxii**)

Anal:

TLC : R_f 0.62 (*n*-hexane: ethyl acetate; 12:8)

IR (KBr, cm^{-1}) : 3438, 3305, 03187, 3030, 2921, 1682, 1643, 1595, 1450 and 696.

Mass (m/z) : 487 $[M]^+$, 488 $[M+1]^+$.

^{1}H-NMR [500 MHz, DMSO-d_6, δ] : 7.79 (dd, *J* = 8.4, 1.3 Hz, 2H), 7.74 – 7.62 (m, 1H), 7.58 (dd, *J* = 8.3, 7.2 Hz, 2H), 7.24 (m, 5H), 7.19 – 7.14 (m, 4H), 7.13 – 7.08 (m, 1H), 7.04 (dd, *J* = 8.2, 6.7 Hz, 2H), 6.96 (tt, *J* = 7.3, 1.3 Hz, 1H), 6.55 (dd, *J* = 9.7, 2.7 Hz, 3H), 5.58 (dd, *J* = 8.7, 3.8 Hz, 1H),

3.38 (dd, *J* = 18.4, 8.7 Hz, 1H), 3.18 (dd, *J* = 25.0, 13.1 Hz, 2H), 3.07 (dd, *J* = 18.6, 13.1 Hz, 2H), 2.31 (ddd, *J* = 22.2, 18.4, 4.0 Hz, 1H).

^{13}C-NMR [126 MHz, DMSO-d6, δ] : 196.33, 170.20, 159.44, 139.42, 135.80, 135.50, 133.29, 129.68, 129.50, 128.70, 128.59, 127.74, 127.57, 126.28, 58.09, 49.30, 41.59, 40.80, 37.97.

5.2.83 3-(1-(4-Chlorophenyl)-3-oxo-3-phenylpropylamino)-4,4-dibenzyl-1*H*-pyrazol-5(4*H*)-one (212)

In a single neck 25-ml RBF, 3-amino-4,4-dibenzyl-1*H*-pyrazol-5(4*H*)-one (**129**, str no., 0.4 gm, 0.0014 M) was dissolved in a mixture of Cs_2CO_3 in dry DMF. This mixture was allowed to stir at room temperature. To this mixture, (*E*)-3-(4-chlorophenyl)-1-phenylprop-2-en-1-one (**175,** 0.33 gm, 0.0013 M) was added portion-wise. The reaction mixture was heated at 80 °C for 6 hours. The reaction was monitored by TLC. Upon completion, crushed ice was added to the reaction mixture to obtain the precipitates, filtered under vacuum to obtain crude yellow solid. Further purification of the compound was done by column chromatography using silica gel (25% ethyl acetate) afforded a pure light-yellow compound (0.345gms, 86%); m.p. 218-220 °C.

Anal:

TLC : R_f 0.62 (*n*-hexane: ethyl acetate; 12:8)

IR (KBr, cm^{-1}) : 3437, 3313, 3183, 3059, 2917, 1686, 1644, 725.

MS (m/z) : 523 $[M+1]^+$, 525 $[M+2]^+$.

^{1}H-NMR [500 MHz, DMSO-d_6, δ] **:** 7.73-7.71 (d, 2H), 7.67-7.63 (t, 1H), 7.54-7.51 (t, 2H), 7.21-7.18 (m, 4H), 7.17-7.14 (t, 4H), 7.13-7.09 (t, 2H), 7.07-7.01 (d, 2H), 6.93-6.90 (t, 1H), 6.53-6.50 (m, 3H), 5.48-5.45 (dd, 1H), 3.34-3.31 (m, 1H), 3.15-3.08 (dd, 2H), 3.02-2.98 (dd, 2H), 2.34-2.29 (dd, 1H).

5.2.84 3-(3-Oxo-3-phenyl-1-p-tolylpropylamino)-4,4-dibenzyl-1*H*-pyrazol-5(4*H*)-one (213)

3-Amino-4,4-dibenzyl-1*H*-pyrazol-5(4*H*)-one (**129,** 0.4 gm, 0.0014 M) was reacted with (*E*)-1-phenyl-3-*p*-tolylprop-2-en-1-one (**129,** 0.31 gm, 0.0013 M) under the same conditions as described for compound (**211**). The titled compound was obtained as white solid (0.268 gm, 67%); m.p. 223-225°C.

Anal:

TLC : R_f 0.81 (*n*-hexane: ethyl acetate; 12:8)

IR (KBr, cm^{-1}) : 3462, 3293, 3178, 2960, 2851, 1689, 1641, 1403, 1357.

Mass (m/z) : 502 $[M+1]^+$, 503 $[M+2]^+$.

^{1}H-NMR [500 MHz, DMSO-d_6, δ] **:** 7.82 – 7.75 (m, 2H), 7.78 – 7.69 (m, 1H), 7.63 – 7.56 (m, 2H), 7.30 – 7.13 (m, 14H), 7.02 – 6.95 (m, 2H), 6.85 (d, *J* = 8.1 Hz, 3H), 6.56 (s, 3H), 6.45 – 6.39 (m, 3H), 5.53 (dd, *J* = 8.9, 3.7 Hz, 1H), 3.38 (d, *J* = 3.8 Hz, 1H), 3.39 – 3.31 (m, 1H), 3.23 – 3.16 (m, 2H), 3.07 (dd, *J* = 20.5, 13.1 Hz, 2H), 2.22 (s, 3H), 2.19 (d, *J* = 3.7 Hz, 1H).

5.2.85 3-(1-(4-Fluorophenyl)-3-oxo-3-phenylpropylamino)-4,4-dibenzyl-1*H*-pyrazol 5(4*H*)-one (214)

3-Amino-4,4-dibenzyl-1*H*-pyrazol-5(4*H*)-one (**129,** 0.4 gm, 0.0014 M) was reacted with (*E*)-3-(4-fluorophenyl)-1-phenylprop-2-en-1-one (**177,** 0.31 gm, 0.0013 M) under the same conditions as described for compound (**211**). The titled compound was obtained as white solid (0.356 gm, 88%); m.p. 216-218 °C.

Anal:

TLC : R_f 0.81 (*n*-hexane: ethyl acetate; 12:8)

IR (KBr, cm^{-1}) : 3404, 3188, 3059, 2918, 1686, 1644, 1450, 1359 and 450.

Mass (m/z) : 506 $[M+1]^+$

^{1}H-NMR [500 MHz, DMSO-d_6, δ] **:** 7.77 – 7.71 (m, 2H), 7.70 – 7.63 (m, 1H), 7.57 – 7.51 (m, 2H), 7.21 – 7.18 (m, 2H), 7.15 (d, *J* = 1.8 Hz, 3H), 7.14 – 7.09 (m, 3H), 6.97 – 6.90 (m, 1H), 6.81 (t, *J* = 8.9 Hz, 2H), 6.57 – 6.50 (m, 4H), 5.49 (dd, *J* = 8.8, 3.9 Hz, 1H), 3.32 (d, *J* = 8.6 Hz, 1H), 3.12 (dd, *J* = 23.8, 13.1 Hz, 2H), 3.01 (dd, *J* = 13.2, 10.7 Hz, 2H), 2.29 (dd, *J* = 18.4, 3.9 Hz, 1H).

5.2.86 3-(1-(4-Bromophenyl)-3-oxo-3-phenylpropylamino)-4,4-dibenzyl-1*H*-pyrazol-5(4*H*)-one (215)

3-Amino-4,4-dibenzyl-1*H*-pyrazol-5(4*H*)-one (**129,** 0.4 gm, 0.0014 M) was reacted with (*E*)-3-(4-bromophenyl)-1-phenylprop-2-en-1-one (**178,** 0.31 gm, 0.0013 M) under the same conditions as described for compound (**211**). The titled compound was obtained as white solid (0.298 gm,74 %); m.p. 242-244°C. (**Sxxv**)

Anal:

TLC : R_f 0.62 (*n*-hexane: ethyl acetate; 12:8)

IR (KBr, cm^{-1}) : 3442, 3299, 3189, 3059, 2915, 2855, 1685, 1641, 695.

Mass (m/z) : 565, $[M-1]^+$, 566 $[M]^+$, 568 $[M+2]^+$.

^{1}H-NMR [500 MHz, DMSO-d_6, δ] : 7.82 – 7.76 (m, 2H), 7.76 – 7.69 (m, 1H), 7.63 – 7.56 (m, 2H), 7.23 (dd, *J* = 7.8, 6.0 Hz, 4H), 7.21 – 7.19 (m, 4H), 7.15 (d, *J* = 7.8 Hz, 1H), 7.02 – 6.95 (m, 1H), 6.62 (d, *J* = 3.5 Hz, 2H), 6.52 (s, 1H), 6.50 (s, 1H), 5.51 (dd, *J* = 8.5, 4.0 Hz, 1H), 3.39 – 3.34 (m, 1H), 3.18 (dd, *J* = 23.5, 13.1 Hz, 2H), 3.06 (dd, *J* = 13.1, 8.6 Hz, 2H), 2.36 (dd, *J* = 18.5, 4.0 Hz, 1H)

5.2.87 3-(1-(4-Nitrophenyl)-3-oxo-3-phenylpropylamino)-4,4-dibenzyl-1*H*-pyrazol-5(4*H*)-one (216)

3-Amino-4,4-dibenzyl-1*H*-pyrazol-5(4*H*)-one (**129,** 0.4 gm, 0.0014 M) was reacted with (*E*)-3-(4-nitrophenyl)-1-phenylprop-2-en-1-one (**179,** 0.33 gm, 0.0014 M) under the same conditions as described for compound (**211**). The titled compound was obtained as bright yellow solid (0.392 gm, 98%); m.p. 226-228°C.

Anal:

TLC : R_f 0.7 (*n*-hexane: ethyl acetate; 12:8)

IR (KBr, cm^{-1}) : 3433, 3306, 3197, 3060, 2921, 2853, 1686, 1643, 1524, 1494, 1347.

Mass (m/z) : 533.24 $[M+1]^+$, 534.28 $[M+2]^+$

^{1}H-NMR [500 MHz, DMSO-d_6, δ] : 7.90 (d, *J* = 8.8 Hz, 2H), 7.83 – 7.78 (m, 2H), 7.76 – 7.69 (m, 1H), 7.60 (t, *J* = 7.8 Hz, 2H), 7.27 – 7.22 (m, 2H), 7.21 (d, *J* = 1.0 Hz, 3H), 7.16 (t, *J* = 7.7 Hz, 2H), 7.03 – 6.96 (m, 1H), 6.83 (d, *J* = 8.8 Hz, 2H), 6.69 (s, 2H), 5.64 (dd, *J* = 8.1, 4.3 Hz, 1H), 3.46 (dd, *J* =

18.7, 8.2 Hz, 1H), 3.19 (dd, *J* = 25.5, 13.1 Hz, 2H), 3.08 (dd, *J* = 13.0, 1.6 Hz, 2H), 2.52 (dd, *J* = 18.7, 4.3 Hz, 1H).

5.2.88 3-(1-(4-Methoxyphenyl)-3-oxo-3-phenylpropylamino)-4,4-dibenzyl-1*H*-pyrazol-5(4*H*)-one (217)

3-Amino-4,4-dibenzyl-1*H*-pyrazol-5(4*H*)-one (**129,** 0.4 gm, 0.0014 M) was reacted with (*E*)-3-(4-methoxyphenyl)-1-phenylprop-2-en-1-one (**180,** 0.26 gm, 0.0010 M) under the same conditions as described for compound (**211**). The titled compound was obtained as white solid (0.272 gm, 68 %); m.p. 220-222℃.

Anal:

TLC : R_f 0.42 (*n*-hexane: ethyl acetate; 12:8)

IR (KBr, cm^{-1}) : 3442, 3312, 3180, 3060, 2918, 1684, 1643, 1450, 1246, 697.

Mass (m/z) : 517 $[M]^+$, 518 $[M+1]^+$, 519 $[M+2]^+$.

^{1}H NMR [500 MHz, DMSO-d_6, δ] : 7.91-7.89 (d, 2H), 7.81-7.79 (d, 2H), 7.74-7.71 (t, 1H), 7.61-7.58 (t, 2H) 7.25-7.14 (m, 8H), 7.01-6.97 (t, 1H), 6.83-6.81 (d, 2H), 6.68 (s, 2H), 5.63-5.62 (dd, 1H), 3.48-3.42 (m, 1H), 3.37 (s, 3H, *merged with H_2O peak*). 3.18-3.15 (dd, 2H), 3.09-3.06 (dd, 2H), 2.49-2.50 (dd, 1H)

5.2.89 3-(1-(3-Chlorophenyl)-3-oxo-3-phenylpropylamino)-4,4-dibenzyl-1*H*-pyrazol-5(4*H*)-one (218)

3-Amino-4,4-dibenzyl-1*H*-pyrazol-5(4*H*)-one (**129,** 0.4 gm, 0.0014 M) was reacted with (*E*)-3-(3-chlorophenyl)-1-phenylprop-2-en-1-one (**181,** 0.31 gm, 0.0013 M) under the same conditions as described for compound (**211**). The titled compound was obtained as white solid (0.39gm, 87%); m.p. 214-214℃.

Anal:

TLC : R_f 0.62 (*n*-hexane: ethyl acetate; 12:8)

IR (KBr, cm^{-1}) : 3439, 3315, 3185, 3060, 2923, 1681, 1640, 1497, 1230, 832 and 725.

^{1}H-NMR [500 MHz, DMSO-d_6, δ]: 7.75 (d, *J* = 8.2 Hz, 2H), 7.61 (d, *J* = 8.2 Hz, 2H), 7.19 (dd, *J* = 15.3, 7.4 Hz, 5H), 7.15 – 7.08 (m, 4H), 7.07 – 6.97 (m, 3H), 6.94 (t, *J* = 7.4 Hz, 1H), 6.51 (d, *J* = 6.8 Hz, 3H), 5.52 (dd, *J* = 8.4, 4.1

Hz, 1H), 3.35 – 3.28 (m, 1H), 3.18-3.10 (dd, 2H), 3.05-3.02 (dd, 2H), 2.30 (dd, *J* = 18.5, 4.2 Hz, 1H).

5.2.90 3-(1-(3-Fluorophenyl)-3-oxo-3-phenylpropylamino)-4,4-dibenzyl-1*H*-pyrazol-5(4*H*)-one (219)

3-Amino-4,4-dibenzyl-1*H*-pyrazol-5(4*H*)-one (**129,** 0.4 gm, 0.0014 M) was reacted with (*E*)-3-(3-fluorophenyl)-1-phenylprop-2-en-1-one (**182,** 0.31 gm, 0.0013 M) under the same conditions as described for compound (**211**). The titled compound was obtained as white solid (0.276 gm, 69.34 %); m.p. 212-214 ℃.

Anal:

TLC : R_f 0.68 (*n*-hexane: ethyl acetate; 12:8)

IR (KBr, cm^{-1}) : 3420, 3297, 3191, 3028, 2912, 2856, 1689, 1643, 1591, 1393, 650.

^{1}H-NMR [500 MHz, DMSO-d_6, δ] **:** 7.77 – 7.72 (m, 2H), 7.70 – 7.63 (m, 1H), 7.54 (t, *J* = 7.8 Hz, 2H), 7.21 – 7.17 (m, 2H), 7.16 – 7.13 (m, 2H), 7.11 (d, *J* = 7.4 Hz, 4H), 7.04 (dd, *J* = 8.0, 6.2 Hz, 1H), 6.91 (m, *J* = 6.9, 2.0 Hz, 2H), 6.57 (s, 2H), 6.42 (dt, *J* = 10.3, 2.2 Hz, 1H), 6.38 (d, *J* = 7.8 Hz, 1H), 5.52 (dd, *J* = 8.4, 4.1 Hz, 1H), 4.04 (m, 1H), 3.35 – 3.31 (m, 1H), 3.12 (dd, *J* = 22.5, 13.1 Hz, 2H), 3.02 (t, *J* = 13.1 Hz, 2H), 2.30 (dd, *J* = 18.5, 4.1 Hz, 1H).

5.2.91 3-(1-(3-Bromophenyl)-3-oxo-3-phenylpropylamino)-4,4-dibenzyl-1*H*-pyrazol-5(4*H*)-one (220)

3-Amino-4,4-dibenzyl-1*H*-pyrazol-5(4*H*)-one (**129,** 0.4 gm, 0.0014 M) was reacted with (*E*)-3-(3-bromophenyl)-1-phenylprop-2-en-1-one (**183,** 0.402 gm, 0.0013 M) under the same conditions as described for compound (**211**). The titled compound was obtained as white solid (0.320 gm, 80 %); m.p. 194-196℃.

Anal:

TLC : R_f 0.72 (*n*-hexane: ethyl acetate; 12:8)

IR (KBr, cm^{-1}) : 3433, 3305, 3190, 3028, 2920, 1686, 1642, 1449, 1394, 722.

^{1}H-NMR [500 MHz, DMSO-d_6, δ] **:** 7.75 – 7.70 (m, 2H), 7.69 – 7.62 (m, 1H), 7.53 (t, *J* = 7.7 Hz, 2H), 7.31 – 7.25 (m, 1H), 7.18 (d, *J* = 8.0 Hz, 2H), 7.13 – 7.06 (m, 6H), 7.01 – 6.91 (m, 2H), 6.91 (dd, *J* = 8.1, 6.5 Hz, 1H), 6.55 (s, 2H),

6.51 (d, *J* = 7.8 Hz, 1H), 5.47 (dd, *J* = 8.6, 4.1 Hz, 1H), 3.41 – 3.33 (m, 1H), 3.10 (dd, *J* = 15.6, 13.1 Hz, 2H), 3.00 (dd, *J* = 15.1, 13.2 Hz, 2H), 2.27 (dd, *J* = 18.5, 4.1 Hz, 1H).

5.2.92 3-(1-(3-Nitrophenyl)-3-oxo-3-phenylpropylamino)-4,4-dibenzyl-1*H*-pyrazol-5(4*H*)-one (221)

3-Amino-4,4-dibenzyl-1*H*-pyrazol-5(4*H*)-one (**129,** 0.4 gm, 0.0014 M) was reacted with (*E*)-3-(3-nitrophenyl)-1-phenylprop-2-en-1-one (**184,** 0.35 gm, 0.0013 M) under the same conditions as described for compound (**211**). The titled compound was obtained as yellow solid (0.32 gm, 80 %); m.p. 214-220 °C.

Anal:

TLC : R_f 0.71 (*n*-hexane: ethyl acetate; 12:8)

IR (KBr, cm^{-1}) : 3436, 3375, 3185, 2916, 2854, 1688, 1641, 1525, 1349.

^{1}H-NMR [500 MHz, DMSO-d_6, δ] : 8.03 (dd, *J* = 8.2, 2.4, 1.0 Hz, 1H), 7.80 (dd, *J* = 8.4, 1.4 Hz, 2H), 7.75 – 7.68 (m, 2H), 7.59 (t, *J* = 7.7 Hz, 2H), 7.38 (t, *J* = 8.0 Hz, 1H), 7.27 – 7.22 (m, 2H), 7.17 (t, *J* = 7.7 Hz, 2H), 7.13 (d, *J* = 3.8 Hz, 1H), 7.07 – 7.04 (m, 1H), 7.03 – 7.01 (m, 3H), 6.67 (s, 2H), 5.63 (dd, *J* = 8.1, 4.6 Hz, 1H), 3.49 (dd, *J* = 18.5, 8.2 Hz, 1H), 3.16 (dd, *J* = 13.2, 11.2 Hz, 2H), 3.06 (t, *J* = 12.6 Hz, 2H), 2.61 (dd, *J* = 18.4, 4.7 Hz, 1H)

5.2.93 3-(1-(3-Methoxyphenyl)-3-oxo-3-phenylpropylamino)-4,4-dibenzyl-1*H*-pyrazol-5(4*H*)-one (222)

3-Amino-4,4-dibenzyl-1*H*-pyrazol-5(4*H*)-one (**129,** 0.4 gm, 0.0014 M) was reacted with (*E*)-3-(3-methoxyphenyl)-1-phenylprop-2-en-1-one (**185,** 0.26 gm, 0.0010 M) under the same conditions as described for compound (**211**). The titled compound was obtained as white solid (0.296 gm,74 %); m.p. 172-174°C.

Anal:

TLC : R_f 0.47 (*n*-hexane: ethyl acetate; 12:8)

IR (KBr, cm^{-1}) : 3452, 3297, 3190, 2906, 2839, 1684, 1640, 1445, 1255, 1165 and 1037.

Mass (m/z) : 518$[M+1]^+$, 519$[M+2]^+$.

^{1}H NMR [500 MHz, DMSO-d_6, δ] : 7.80 – 7.74 (m, 2H), 7.73 – 7.65 (m, 1H), 7.60 – 7.53 (m, 2H), 7.30 – 7.22 (m, 2H), 7.22 – 7.07 (m, 7H), 6.99 – 6.90 (m, 2H), 6.69 (ddd, *J* = 8.3, 2.6, 0.9 Hz, 1H), 6.53 (s, 2H), 6.42 (t, *J* = 2.1 Hz, 1H), 6.14 – 6.08 (m, 1H), 5.55 (dd, *J* = 8.7, 4.1 Hz, 1H), 3.61 (s, 3H), 3.37 (dd, *J* = 18.2, 8.7 Hz, 2H), 3.15 (dd, *J* = 17.0, 13.2 Hz, 2H), 3.06 (dd, *J* = 23.2, 13.2 Hz, 2H), 2.28 (dd, *J* = 18.2, 4.1 Hz, 1H).

^{13}C NMR (126 MHz, DMSO, δ) : 196.28, 170.26, 159.39, 158.67, 141.08, 135.81, 135.51, 133.26, 129.70, 129.33, 128.69, 128.60, 127.69, 127.54, 126.31, 119.08, 112.64, 111.40, 57.93, 54.67, 49.65, 41.41, 40.88, 39.63, 39.14.

5.2.94 3-(1-(2-Nitrophenyl)-3-oxo-3-phenylpropylamino)-4,4-dibenzyl-1*H*-pyrazol-5(4*H*)-one (223)

3-Amino-4,4-dibenzyl-1*H*-pyrazol-5(4*H*)-one (**129,** 0.4 gm, 0.0014 M) was reacted with (*E*)-3-(2-nitrophenyl)-1-phenylprop-2-en-1-one (**186,** 0.68 gm, 0.0011 M) under the same conditions as described for compound (**211**). The titled compound was obtained as white solid (0.304 gm, 76 %); m.p. 218-220 ℃.

Anal:

TLC : R_f 0.7 (*n*-hexane: ethyl acetate; 12:8)

IR (KBr, cm^{-1}) : 3442, 3169, 2921, 1689, 1643, 1347, 1090.

^{1}H-NMR [500 MHz, DMSO-d_6, δ] : 8.03 (dd, *J* = 8.3, 2.3 Hz, 1H), 7.83 – 7.77 (m, 2H), 7.74 – 7.68 (m, 2H), 7.59 (t, *J* = 7.7 Hz, 2H), 7.38 (t, *J* = 8.0 Hz, 1H), 7.27 – 7.22 (m, 2H), 7.20 – 7.10 (m, 4H), 7.09 – 7.00 (m, 5H), 6.67 (s, 2H), 5.63 (dd, *J* = 8.2, 4.7 Hz, 1H), 3.49 (dd, *J* = 18.5, 8.2 Hz, 1H), 3.16 (dd, *J* = 13.2, 11.3 Hz, 2H), 3.06 (t, *J* = 12.6 Hz, 2H), 2.61 (dd, *J* = 18.5, 4.7

5.2.95 3-(3-(2-Bromophenyl)-3-oxo-1-phenylpropylamino)-4,4-dibenzyl-1*H*-pyrazol-5(4*H*)-one (224)

3-Amino-4,4-dibenzyl-1*H*-pyrazol-5(4*H*)-one (**129,** 0.4 gm, 0.0014 M) was reacted with (*E*)-1-(2-bromophenyl)-3-phenylprop-2-en-1-one (**187,** 0.311 gm, 0.0011 M) under the same conditions as described for compound (**211**). The titled compound was obtained as white solid (gm, 75%); m.p. 226-229 °C**.**

Anal:

TLC : R_f 0.72 (*n*-hexane: ethyl acetate; 12:8)

IR (KBr, cm^{-1}) : 3461, 3294, 3179, 3028, 2919, 1686, 1640, 1449, 1221 and 804.

^{1}H NMR [500 MHz, DMSO-d_6, δ] : 7.79 (dd, *J* = 8.4, 1.3 Hz, 2H), 7.76 – 7.69 (m, 1H), 7.59 (dd, *J* = 8.3, 7.3 Hz, 2H), 7.23 (dd, *J* = 7.8, 5.9 Hz, 5H), 7.21 – 7.18 (m, 4H), 7.16 (t, *J* = 7.7 Hz, 2H), 7.02 – 6.95 (m, 1H), 6.62 (s, 2H), 6.51 (d, *J* = 8.5 Hz, 2H), 5.54 – 5.48 (m, 1H), 3.39 – 3.29 (m, 1H), 3.18 (dd, *J* = 23.5, 13.1 Hz, 2H), 3.06 (dd, *J* = 13.1, 8.6 Hz, 2H), 2.36 (dd, *J* = 18.5, 4.0 Hz, 1H).

5.2.96 3-(1-(3-Chlorophenyl)-3-(4-chlorophenyl)-3-oxopropylamino)-4,4-dibenzyl-1*H*-pyrazol-5(4*H*)-one (225)

3-Amino-4,4-dibenzyl-1*H*-pyrazol-5(4*H*)-one (**129,** 0.4 gm, 0.0014 M) was reacted with (*E*)-3-(3-chlorophenyl)-1-(4-chlorophenyl)prop-2-en-1-one (**188,** 0.317gm, 0.0011 M)under the same conditions as described for compound (**211**). The titled compound was obtained as white solid (gm, 72%); m.p. 236-239 °C.

Anal:

TLC : R_f 0.7 (*n*-hexane: ethyl acetate; 12:8)

IR (KBr, cm^{-1}) : 3437, 3308, 3199, 3030, 2918, 2857, 1685, 1641, 1088 and 704.

^{1}H NMR [500 MHz, DMSO-d_6, δ] : 7.70 – 7.65 (m, 2H), 7.37 (d, *J* = 8.0 Hz, 2H), 7.30 – 7.21 (m, 2H), 7.21 – 7.04 (m, 9H), 7.02 – 6.95 (m, 1H), 6.84 (t, *J* = 2.0 Hz, 1H), 6.59 (s, 2H), 6.54 (m, 1H), 5.53 (dd, *J* = 8.8, 3.9 Hz, 1H), 3.37 (dd, *J* = 18.3, 8.9 Hz, 1H), 3.16 (dd, *J* = 14.9, 13.1 Hz, 2H), 3.06 (dd, *J* = 14.9, 13.1 Hz, 2H), 2.27 (dd, *J* = 18.3, 4.0 Hz, 1H).

5.2.97 3-(1-(3-Chlorophenyl)-3-oxo-3-*p*-tolylpropylamino)-4,4-dibenzyl-1*H*-pyrazol-5(4*H*)-one (226)

3-Amino-4,4-dibenzyl-1*H*-pyrazol-5(4*H*)-one (**129,** 0.4 gm, 0.0014 M) was reacted with (*E*)-3-(3-chlorophenyl)-1-*p*-tolylprop-2-en-1-one (**189,** 0.26gm, 0.0011 M) under the same conditions as described for compound (**211**). The titled compound was obtained as buff solid (gm, 77%); m.p. 231-234 °C.

Anal:

TLC : R_f 0.64 (*n*-hexane: ethyl acetate; 12:8)

IR (KBr, cm^{-1}) : 3437, 3319, 3199, 2921, 1684, 1641, 1444, 881 and 701.

Mass (m/z) : 536 $[M]^+$, 538 $[M+2]^+$.

^{1}H NMR [500 MHz, DMSO-d_6, δ] : 7.69 (d, *J* = 8.3 Hz, 2H), 7.42 – 7.34 (m, 2H), 7.27 – 7.23 (m, 2H), 7.21 – 7.12 (m, 8H), 7.09 (t, *J* = 7.9 Hz, 1H), 7.04 – 6.97 (m, 1H), 6.85 (s, 1H), 6.59 (s, 2H), 6.56 – 6.51 (m, 1H), 5.53 (dd, *J* = 8.8, 3.9 Hz, 1H), 3.40 (d, *J* = 8.9 Hz, 1H), 3.16 (dd, *J* = 14.8, 13.1 Hz, 2H), 3.06 (dd, *J* = 14.6, 13.2 Hz, 2H), 2.44 (s, 3H), 2.27 (dd, *J* = 18.4, 3.9 Hz, 1H).

^{13}C NMR (126 MHz, DMSO, δ) : 195.63, 170.29, 159.55, 143.77, 142.00, 135.62, 135.46, 133.20, 132.42, 129.66, 129.49, 129.26, 129.10, 127.88, 127.59, 126.64, 125.42, 58.03, 49.23, 41.17, 40.68, 21.05.

5.2.98 3-(3-(4-Chlorophenyl)-1-(3-nitrophenyl)-3-oxopropylamino)-4,4-dibenzyl-1*H*-pyrazol-5(4*H*)-one (227)

3-Amino-4,4-dibenzyl-1*H*-pyrazol-5(4*H*)-one (**129,** 0.4 gm, 0.0014 M) was reacted with (*E*)-1-(4-chlorophenyl)-3-(3-nitrophenyl) prop-2-en-1-one (**190,** 0.32 gm, 0.0011 M) under the same conditions as described for compound (**211**). The titled compound was obtained as yellow solid (gm, 82%); m.p. 200-204 °C.

Anal:

TLC : R_f 0.5 (*n*-hexane: ethyl acetate; 12:8)

IR (KBr, cm^{-1}) : 3448, 3292, 3170, 2916, 1690, 1642, 1490, 1294, 1091 and 696.

^{1}H NMR [500 MHz, DMSO-d_6, δ] : 7.85 (d, *J* = 8.8 Hz, 1H), 7.76 (d, *J* = 8.7 Hz, 2H), 7.62 (d, *J* = 8.4 Hz, 2H), 7.25 – 7.07 (m, 10H), 7.04 – 6.93 (m, 1H), 6.78 (d, *J* = 8.7 Hz, 2H), 6.63 (s, 2H), 5.57 (dd, *J* = 7.7, 4.7 Hz, 1H), 3.37 (s, 1H), 3.13 (dd, *J* = 26.8, 13.1 Hz, 2H), 3.01 (dd, *J* = 13.0, 2.1 Hz, 2H), 2.50 (d, *J* = 3.9 Hz, 1H).

5.2.99 3-(3-(4-Chlorophenyl)-1-(3-methoxyphenyl)-3-oxopropylamino)-4,4-dibenzyl-1*H*-pyrazol-5(4*H*)-one (228)

3-Amino-4,4-dibenzyl-1*H*-pyrazol-5(4*H*)-one (**129,** 0.4 gm, 0.0014 M) was reacted with (*E*)-1-(4-chlorophenyl)-3-(3-methoxyphenyl) prop-2-en-1-one (**191,** 0.3gm, 0.0010M)

under the same conditions as described for compound (**211**). The titled compound was obtained as white solid (gm, 71 %); m.p. 195-198℃.

Anal:

TLC : R_f 0.60 (*n*-hexane: ethyl acetate; 12:8)

IR (KBr, cm^{-1}) **:** 3429, 3303, 3200, 3060, 3029, 2920, 2840, 1685, 1642, 1593, 1254, and 698.

^{1}H NMR [500 MHz, DMSO-d_6, δ] : 7.80 (d, *J* = 8.6 Hz, 2H), 7.65 (d, *J* = 8.6 Hz, 2H), 7.28 – 7.20 (m, 2H), 7.20 – 7.07 (m, 7H), 7.02 – 6.92 (m, 2H), 6.71 (m, 1H), 6.52 (s, 2H), 6.44 (s, 1H), 6.15 – 6.09 (m, 1H), 5.52 (dd, *J* = 8.2, 4.5 Hz, 1H), 3.64 (s, 3H), 3.37 – 3.30 (m, 1H), 3.15 (dd, *J* = 18.3, 13.2 Hz, 2H), 3.05 (dd, *J* = 22.6, 13.2 Hz, 2H), 2.35 (dd, *J* = 18.3, 4.5 Hz, 1H).

5.2.100 3-(3-(4-Bromophenyl)-3-oxo-1-phenylpropylamino)-4,4-dibenzyl-1*H*-pyrazol-5(4*H*)-one (229)

3-Amino-4,4-dibenzyl-1*H*-pyrazol-5(4*H*)-one (**129,** 0.4 gm, 0.0014 M) was reacted with (*E*)-1-(4-bromophenyl)-3-phenylprop-2-en-1-one (**192,** 0.32gm, 0.0011 M) under the same conditions as described for compound (**211**). The titled compound was obtained as white solid (0.316 gm,79 %); m.p. 230-232℃.

Anal:

TLC : R_f 0.7 (*n*-hexane: ethyl acetate; 12:8)

IR (KBr, cm^{-1}) : 3422, 3303, 3191, 3059, 3028, 2922, 1686, 1643, 1287 and 698.

Mass (m/z) : 566$[M]^+$, 568 $[M+2]^+$

^{1}H NMR [500 MHz, DMSO-d_6, δ] : 7.79 – 7.60 (m, 5H), 7.25 – 7.14 (m, 10H), 7.00-7.97 (t, 1H), 6.62 (s, 2H), 6.52-6.50 (d, 2H), 5.52 (dd, *J* = 8.3, 4.2 Hz, 1H), 3.39-35 (dd, *J* = 18.4, 8.3 Hz, 1H), 3.21-3.14 (d, *J* = 13.4 Hz, 2H), 3.09-3.04 (dd, *J* = 19.0, 13.2 Hz, 2H), 2.38-2.34 (dd, *J* = 18.5, 4.2 Hz, 1H).

^{13}C NMR (126 MHz, DMSO, δ): 131.65, 129.72, 129.49, 127.77, 127.58, 127.36, 126.29, 58.08, 49.31, 41.61, 40.78, 39.13.

5.2.101 3-(1-(4-Bromophenyl)-3-oxo-3-*p*-tolylpropylamino)-4,4-dibenzyl-1*H*-pyrazol-5(4*H*)-one (230)

3-Amino-4,4-dibenzyl-1*H*-pyrazol-5(4*H*)-one (**129,** 0.4 gm, 0.0014 M) was reacted with (*E*)-3-(4-bromophenyl)-1-*p*-tolylprop-2-en-1-one (**193,** 0.34gm, 0.0011 M) under the same conditions as described for compound (**226**). The titled compound was obtained as white solid (0.4 gm, 82%); m.p. 233-235℃.

Anal:

TLC : R_f 0.67 (*n*-hexane: ethyl acetate; 12:8)

IR (KBr, cm^{-1}) : 3435, 3305, 3185, 3029, 2920, 2855, 1685, 1642, 1442, 1006, 697.

Mass (m/z) : 579 $[M]^+$, 581 $[M+2]^+$.

^{1}H NMR [500 MHz, DMSO-d_6, δ] : 7.69 (d, *J* = 8.2 Hz, 2H), 7.39 (d, *J* = 8.0 Hz, 2H), 7.30 (t, *J* = 7.3 Hz, 1H), 7.27 – 7.20 (m, 5H), 7.20 – 7.14 (m, 5H), 7.04 – 6.98 (m, 1H), 6.59 (s, 2H), 6.51 (d, *J* = 8.5 Hz, 2H), 5.50 (dd, *J* = 8.7, 3.8 Hz, 1H), 3.37 – 3.30 (m, 1H), 3.18 (dd, *J* = 21.5, 13.1 Hz, 2H), 3.12 – 3.03 (m, 2H), 2.45 (s, 1H), 2.30 (s, 3H).

^{13}C NMR (126 MHz, DMSO, δ): 195.65, 170.16, 159.53, 143.78, 138.91, 135.74, 135.49, 133.21, 130.43, 129.65, 129.47, 129.12, 129.01, 128.70, 128.06, 127.81, 127.55, 126.83, 126.34, 119.47, 58.13, 48.93, 41.21, 40.63, 21.05.

5.2.102 3-(1-(4-Bromophenyl)-3-(4-chlorophenyl)-3-oxopropylamino)-4,4-dibenzyl-1*H*-pyrazol-5(4*H*)-one (231)

3-Amino-4,4-dibenzyl-1*H*-pyrazol-5(4*H*)-one (**129,** 0.4 gm, 0.0014 M) was reacted with (*E*)-3-(4-bromophenyl)-1-(4-chlorophenyl) prop-2-en-1-one (**194,** 0.36 gm, 0.0011 M) under the same conditions as described for compound (**211**). The titled compound was obtained as white solid (0.31gm, 67 %); m.p. 200-202℃.

Anal:

TLC : R_f 0.66 (*n*-hexane: ethyl acetate; 12:8)

IR (KBr, cm^{-1}) : 3441, 3310, 3185, 2960, 2926, 1684, 1643, 1589, 1450, 1091 and 809.

Mass (m/z) : 600 [M^+], 602 [M+2]$^+$.

^{1}H-NMR [500 MHz, DMSO-d_6, δ] : 7.82 – 7.72 (m, 2H), 7.67 (d, *J* = 8.6 Hz, 2H), 7.24 – 7.21 (m, 5H), 7.19 (s, 3H), 7.16 (d, *J* = 7.5 Hz, 2H), 7.03 – 6.96 (m, 1H), 6.61 (s, 2H), 6.55 – 6.49 (m, 2H), 5.49 (dd, *J* = 8.1, 4.4 Hz, 1H), 3.36 (dd, *J* = 18.6, 8.2 Hz, 1H), 3.17 (dd, *J* = 25.0, 13.1 Hz, 2H), 3.06 (dd, *J* = 13.1, 8.6 Hz, 2H), 2.41 (dd, *J* = 18.6, 4.4 Hz, 1H).

5.2.103 3-(3-(4-Chlorophenyl)-3-oxo-1-phenylpropylamino)-4,4-dibenzyl-1*H*-pyrazol-5(4*H*)-one (232)

3-Amino-4,4-dibenzyl-1*H*-pyrazol-5(4*H*)-one (**129,** 0.4 gm, 0.0014 M) was reacted with (*E*)-1-(4-chlorophenyl)-3-phenylprop-2-en-1-one (**195,** 0.27gm, 0.0011 M) under the same conditions as described for compound (**211**). The titled compound was obtained as white solid (0.42 gm, 90%); m.p. 239-241°C.

Anal:

TLC : R_f 0.63 (*n*-hexane: ethyl acetate; 12:8)

IR (KBr, cm^{-1}) : 3419, 3305, 3191, 3060, 3029, 1685, 1645, 1450, 1092 and 729.

Mass (m/z) : 521[M+1]$^+$, 522[M+2]$^+$

^{1}H NMR [500 MHz, DMSO-d_6, δ] : 7.75 (d, *J* = 8.2 Hz, 2H), 7.61 (d, *J* = 8.2 Hz, 2H), 7.19 (dd, *J* = 15.3, 7.4 Hz, 6H), 7.14 – 7.04 (m, 5H), 7.00 (t, *J* = 7.3 Hz, 2H), 6.94 (t, *J* = 7.4 Hz, 1H), 6.52 (s, 4H), 5.52 (dd, *J* = 8.3, 4.1 Hz, 1H), 3.34 – 3.28 (m, 1H), 3.14 (dd, *J* = 26.4, 13.1 Hz, 2H), 3.02 (dd, *J* = 18.9, 13.1 Hz, 2H), 2.30 (dd, *J* = 18.5, 4.2 Hz, 1H).

^{13}C-NMR (126 MHz, DMSO, δ): 195.30, 170.22, 159.43, 139.40, 138.19, 135.81, 135.49, 134.43, 129.68, 129.50, 128.70, 127.78, 127.58, 126.30, 58.09, 49.31, 41.59, 40.78, 40.20.

5.2.104 3-(1-(4-Chlorophenyl)-3-oxo-3-*p*-tolylpropylamino)-4,4-dibenzyl-1*H*-pyrazol-5(4*H*)-one (233)

3-Amino-4,4-dibenzyl-1*H*-pyrazol-5(4*H*)-one (**129,** 0.4 gm, 0.0014 M) was reacted with (*E*)-3-(4-chlorophenyl)-1-*p*-tolylprop-2-en-1-one (**196,** 0.26gm, 0.0011 M) under the same conditions as described for compound (**211**). The titled compound was obtained as white solid (0.31 gm, 69%); m.p. 226-229°C.

Anal:

TLC : R_f 0.6 (*n*-hexane: ethyl acetate; 12:8).

IR (KBr, cm^{-1}) : 3442, 3300, 3185, 3031, 1684, 1643, 1450, 1089 and 767.

Mass (m/z) : 535 $[M]^+$ and 537 $[M+2]^+$

^{1}H NMR [500 MHz, DMSO-d_6, δ] : 7.68 (d, *J* = 8.3 Hz, 2H), 7.41 – 7.35 (m, 2H), 7.27 – 7.23 (m, 3H), 7.23 – 7.20 (m, 1H), 7.20 – 7.18 (m, 2H), 7.18 – 7.13 (m, 3H), 7.10 – 7.05 (m, 2H), 7.03 – 6.96 (m, 1H), 6.61 – 6.52 (m, 4H), 5.52 (dd, *J* = 8.8, 3.8 Hz, 1H), 3.34 (dd, *J* = 18.4, 8.8 Hz, 1H), 3.18 (dd, *J* = 22.1, 13.1 Hz, 2H), 3.06 (dd, *J* = 13.1, 9.1 Hz, 2H), 2.43 (s, 3H), 2.29 (dd, *J* = 18.3, 3.9 Hz, 1H).

^{13}C-NMR (126 MHz, DMSO, δ): 129.66, 129.48, 128.67, 128.33, 127.77, 127.54, 126.34, 58.16, 48.88, 41.42, 40.62, 39.68.

5.2.105 3-(1,3-*bis*(4-chlorophenyl)-3-oxopropylamino)-4,4-dibenzyl-1*H*-pyrazol-5(4*H*)-one (234)

3-Amino-4,4-dibenzyl-1*H*-pyrazol-5(4*H*)-one (**129,** 0.4 gm, 0.0014 M) was reacted with (*E*)-1,3-bis(4-chlorophenyl) prop-2-en-1-one (**197,** 0.31gm, 0.0011 M) under the same conditions as described for compound (**211**). The titled compound was obtained as pale yellow solid (0.35 gm, 69%); m.p. 238-240°C.

Anal:

TLC : R_f 0.58 (*n*-hexane: ethyl acetate; 12:8)

IR (KBr, cm^{-1}) : 3441, 3311, 3188, 3030, 2920, 1684, 1642, 1400, 1092, 824 and 701.

Mass (m/z) : 556 $[M]^+$, 558 $[M+2]^+$.

^{1}H NMR [500 MHz, DMSO-d_6, δ] : 7.78 (d, *J* = 8.6 Hz, 2H), 7.64 (d, *J* = 8.6 Hz, 2H), 7.24 – 7.21 (m, 3H), 7.20 (q, *J* = 1.5 Hz, 1H), 7.19 – 7.17 (m, 2H), 7.17 – 7.12 (m, 3H), 7.09 – 7.06 (m, 2H), 7.02 – 6.94 (m, 1H), 6.61 – 6.53 (m, 4H), 5.51 (dd, *J* = 8.1, 4.4 Hz, 1H), 3.35 (dd, *J* = 18.5, 8.1 Hz, 1H), 3.17 (dd, *J* = 24.9, 13.1 Hz, 2H), 3.05 (dd, *J* = 13.2, 8.5 Hz, 2H), 2.42 (dd, *J* = 18.5, 4.4 Hz, 1H).

^{13}C NMR (126 MHz, DMSO, δ) : 129.66, 129.48, 128.67, 128.33, 127.77, 127.54, 126.34, 58.16, 48.88, 41.42, 40.62, 39.68.

5.2.106 3-(3-(4-Chlorophenyl)-1-(4-methoxyphenyl)-3-oxopropylamino)-4,4-dibenzyl-1*H*-pyrazol-5(4*H*)-one (235)

3-Amino-4,4-dibenzyl-1*H*-pyrazol-5(4*H*)-one (**129,** 0.4 gm, 0.0014 M) was reacted with (*E*)-1-(4-chlorophenyl)-3-(3-methoxyphenyl) prop-2-en-1-one (**198,** 0.3gm, 0.0010M) under the same conditions as described for compound (**211**). The titled compound was obtained as white solid (0.36 gm, 78 %); m.p. 195-198℃.

TLC : R_f 0.56 (*n*-hexane: ethyl acetate; 12:8).

IR (KBr, δ) : 3442, 3314, 3029, 2923, 1683, 1642, 1291, 826

Mass (m/z) : 552 $[M]^+$

^{1}H NMR [500 MHz, DMSO-d_6, δ] : 7.80-7.78 (dd, 2H), 7.67-7.65 (dd, 2H), 7.25-7.14 (m, 9H), 7.02-6.99 (t, 1H), 6.61-6.59 (m, 2H), 6.52-6.50 (m, 4H), 5.50-5.48 (m, 1H), 3.71 (s, 3H), 3.36-3.31 (m, 1H), 3.19-3.12 (m, 2H), 3.08-3.02 (m, 2H), 2.33-2.28 (dd, 1H).

5.2.107 3-(3-(4-Nitrophenyl)-3-oxo-1-phenylpropylamino)-4,4-dibenzyl-*1H*-pyrazol-5(*4H*)-one (236)

3-Amino-4,4-dibenzyl-1*H*-pyrazol-5(4*H*)-one (**129,** 0.4 gm, 0.0014 M) was reacted with (*E*)-1-(4-nitrophenyl)-3-phenylprop-2-en-1-one (**199,** 0.28gm, 0.0011 M) under the same conditions as described for compound (**211**). The titled compound was obtained as maroon solid (0.312 gm, 78 %); m.p. 234-238℃.

Anal:

TLC : R_f 0.65 (*n*-hexane: ethyl acetate; 12:8)

IR (KBr, cm^{-1}) : 3432, 3307, 3192, 2920, 1683, 1643, 1519, 1229, 839, 701.

^{1}H NMR [500 MHz, DMSO-d_6, δ] : 7.91-7.89 (d, 2H), 7.81 (d, 2H), 7.74-7.71 (t, 1H), 7.61-7.58 (t, 2H), 7.25-7.14 (m, 9H), 7.01-6.97 (t, 1H), 6.83-6.81 (d, *J*= 8.8, 2H), 6.68 (s, 2H), 5.65-6.62 (m, 1H), 3.48-3.42 (q, 1H), 3.23-3.15 (m, 2H), 3.09-3.06 (m, 2H), 2.54-2.49 (dd, 1H).

5.2.108 3-(3-(4-Chlorophenyl)-1-(4-nitrophenyl)-3-oxopropylamino)-4,4-dibenzyl-1*H*-pyrazol-5(4*H*)-one (237)

3-Amino-4,4-dibenzyl-1*H*-pyrazol-5(4*H*)-one (**129,** 0.4 gm, 0.0014 M) was reacted with (*E*)-1-(4-chlorophenyl)-3-(4-nitrophenyl)prop-2-en-1-one (**200,** 0.32 gm, 0.0011 M)

under the same conditions as described for compound (**211**). The titled compound was obtained as brown solid (0.40 gm, 68%); m.p. 134-138°C

Anal:

TLC : R_f 0.62 (*n*-hexane: ethyl acetate; 12:8)

IR (KBr, cm^{-1}) : 3455, 3314, 3240, 3203, 3029, 2919, 1683, 1636, 1299, 702.

Mass (m/z) : $[M^+]$ 567, $[M+2]^+$ 569

^{1}H NMR [500 MHz, DMSO-d_6, δ] : 7.86-7.83 (d, 2H), 7.76-7.64 (d, 2H), 7.62-7.61 (d, 2H), 7.19-7.09 (m, 8H), 6.97-6.94 (m, 1H), 6.79-6.77 (d, 2H), 6.62 (s, 2H), 5.57-5.55 (m, 1H), 3.40-3.36 (m, 1H), 3.31-3.09 (m, 2H), 3.02-2.99 (m, 2H), 2.4 (m, 1H).

5.2.109 3-(3-Oxo-1,3-di*p*-tolylpropylamino)-4,4-dibenzyl-1*H*-pyrazol-5(4*H*)-one (238)

3-Amino-4,4-dibenzyl-1*H*-pyrazol-5(4*H*)-one (**129,** 0.4 gm, 0.0014 M) was reacted with (*E*)-1,3-di*p*-tolylprop-2-en-1-one (**201,** 0.24 gm, 0.0010 M) under the same conditions as described for compound (**211**). The titled compound was obtained as white solid (0.319 gm, 80 %); m.p. 240-243°C.

TLC : R_f 0.73 (*n*-hexane: ethyl acetate; 12:8).

IR (KBr, cm^{-1}) : 3459, 3293, 3180, 2919, 1685, 1640, 1451, 809.

^{1}H-NMR [500 MHz, DMSO-d_6, δ]: 7.84-7.81 (d, 2H), 7.73-7.71 (t, 1H), 7.61-7.58 (t, 2H), 7.15-7.09 (m, 5H), 7.05-7.04 (t, 2H), 7.03-6.99 (dd, 2H), 6.93-6.91 (dd, 2H), 6.58-6.56 (d, 2H), 6.49 (s, 2H), 5.65-5.62 (m, 1H), 3.43-3.39 (t, 1H), 3.15-3.06 (dd, 2H), 3.03-2.97 (dd, 2H), 2.37-2.32 (dd, 1H), 2.30 (s, 3H), 1.92 (s, 3H).

5.2.110 3-(3-Oxo-1-phenyl-3-p-tolylpropylamino)-4,4-dibenzyl-1*H*-pyrazol-5(4*H*)-one (239)

3-Amino-4,4-dibenzyl-1*H*-pyrazol-5(4*H*)-one (**129,** 0.4 gm, 0.0014 M) was reacted with (*E*)-3-phenyl-1-p-tolylprop-2-en-1-one (**202,** 0.24 gm, 0.0010 M) under the same conditions as described for compound (**211**). The titled compound was obtained as white solid (0.328 gm, 82 %); m.p. 240-243°C.

Anal:

TLC : R_f 0.73 (*n*-hexane: ethyl acetate; 12:8)

IR (KBr, cm^{-1}) : 3443, 3303, 3195, 3058, 2922, 1684, 1642, 1450, 698.

MS (m/z) : 502 $[M]^+$ and 503 $[M+2]^+$.

^{1}H NMR [500 MHz, DMSO-d_6, δ] : 7.69-7.67 (d, 2H), 7.39-7.37 (d, 2H), 7.26-7.25 (d, 2H), 7.22-7.14 (m, 7H), 7.10-7.09 (m, 1H), 7.03-6.98 (m, 3H), 6.55-6.52 (m, 4H) 5.58-5.55 (m, 1H), 3.36-3.32 (m, 1H), 3.22-3.14 (m, 2H) 3.10-3.03 (m, 2H), 2.43 (s, 3H), 2.22-2.18 (dd, 1H).

5.2.111 3-(1-(4-Fluorophenyl)-3-oxo-3-p-tolylpropylamino)-4,4-dibenzyl-1*H*-pyrazol-5(4*H*)-one (240)

3-Amino-4,4-dibenzyl-1*H*-pyrazol-5(4*H*)-one (**129,** 0.4 gm, 0.0014 M) was reacted with (*E*)-3-(4-fluorophenyl)-1-p-tolylprop-2-en-1-one (**203,** 0.26gm, 0.0011 M) under the same conditions as described for compound (**211**). The titled compound was obtained as pale yellow solid (0.42 gm, 82%); m.p. 233-235°C

Anal:

TLC : R_f 0.64 (*n*-hexane: ethyl acetate; 12:8)

IR (KBr, cm^{-1}) : 3440, 3305, 3185, 3029, 2920, 2855, 1684, 1642, 1442, 1006 and 697.

Mass (m/z) : 520 $[M+1]^+$.

^{1}H NMR [500 MHz, DMSO-d_6, δ] : 7.88-7.85 (m, 2H), 7.43-7.40 (t, 2H), 7.25-7.14 (m, 9H), 7.01-7.00 (t, 1H), 6.85-6.84 (d, 2H), 6.53 (s, 2H), 6.44-6.43 (d, 2H). 5.53-5.50 (m, 1H), 3.36-3.31 (q, 1H), 3.21-3.13 (m, 2H), 3.09-3.02 (m, 2H), 2.28-2.24 (dd, 1H), 2.22 (s, 3H).

5.2.112 3-(1-(4-Chlorophenyl)-3-(4-fluorophenyl)-3-oxopropylamino)-4,4-dibenzyl-1*H*-pyrazol-5(4*H*)-one (241)

3-Amino-4,4-dibenzyl-1*H*-pyrazol-5(4*H*)-one (**129,** 0.4 gm, 0.0014 M) was reacted with (*E*)-3-(4-chlorophenyl)-1-(4-fluorophenyl)prop-2-en-1-one (**204,** 0.28 gm, 0.0011 M) under the same conditions as described for compound (**211**). The titled compound was obtained as buff solid (0.36 gm, 87%); m.p. 244-246°C.

Anal:

TLC : R_f 0.66 (*n*-hexane: ethyl acetate; 12:8)

IR (KBr, cm^{-1}) : 3437, 3300, 3185, 3031, 2917, 1682, 1642, 1293, 1089, 815 and 702.

^{1}H NMR [500 MHz, DMSO-d_6, δ] : 7.75-7.73 (d, 2H), 7.62-7.60 (d, 2H), 7.18-7.08 (m, 9H), 6.96-6.92 (t, 1H), 6.82-6.79 (t, 1H), 6.55-6.53 (m, 4H), 5.47-5.45 (m, 1H), 4.16-4.11 (m, 1H), 3.34-3.32 (q, 1H), 3.15-3.07 (dd, 2H), 3.02-2.97 (m, 2H), 2.35-2.30 (dd, 1H).

5.2.113 3-(3-(3-Chlorophenyl)-3-oxo-1-phenylpropylamino)-4,4-dibenzyl-1*H*-pyrazol-5(4*H*)-one (242)

3-Amino-4,4-dibenzyl-1*H*-pyrazol-5(4*H*)-one (**129,** 0.4 gm, 0.0014 M) was reacted with (*E*)-1-(3-chlorophenyl)-3-phenylprop-2-en-1-one (**205,** 0.27gm, 0.0011 M) under the same conditions as described for compound (**211**). The titled compound was obtained as white solid (0.42 gm, 90%); m.p. 245-247°C.

Anal:

TLC : R_f 0.69 (*n*-hexane: ethyl acetate; 12:8).

IR (KBr, cm^{-1}) : 3419, 3307, 3184, 2922, 1685, 1645, 1227, 830

^{1}H NMR [500 MHz, DMSO-d_6, δ] : 7.75 (d, 2H), 7.62-7.60 (d, 2H), 7.21-7.17 (m, 6H), 7.14-7.05 (m, 5H), 7.06-6.99 (t, 2H), 6.95-6.92 (t, 1H), 6.52-6.51 (d, 4H), 5.53-5.51 (m, 1H), 3.33-3.30 (m, 1H), 3.18-3.10 (m, 2H), 3.05-2.99 (m, 2H), 2.32-2.27 (dd, 1H).

5.2.114 3-(3-(3-Fluorophenyl)-3-oxo-1-*p*-tolylpropylamino)-4,4-dibenzyl-1*H*-pyrazol-5(4*H*)-one (243)

3-Amino-4,4-dibenzyl-1*H*-pyrazol-5(4*H*)-one (**129,** 0.4 gm, 0.0014 M) was reacted with (*E*)-1-(4-fluorophenyl)-3-*p*-tolylprop-2-en-1-one (2**06,** 0.26gm, 0.0011 M) under the same conditions as described for compound (**211**). The titled compound was obtained as white solid (0.39 gm, 78 %); m.p. 226-230°C.

Anal:

TLC : R_f 0.62 (*n*-hexane: ethyl acetate; 12:8)

IR (KBr, cm^{-1}): 3440, 3313, 3062, 2919, 1684, 1641, 1230, 1155 and 702.

Mass (m/z) : 520 $[M+1]^+$

^{1}H NMR [500 MHz, DMSO-d_6, δ] : 7.89-7.85 (q, 2H), 7.43-7.40 (t, 2H), 7.25-7.14 (m, 9H), 7.01-6.98 (m, 1H), 6.85-6.84 (d, 2H), 6.53 (s, 2H), 6.44-6.43 (d, 2H), 5.53-5.50 (m, 1H), 3.38-3.31 (q, 1H), 3.21-3.13 (m, 2H), 3.09-3.02 (m, 2H), 2.28-2.24 (dd, 1H), 2.22 (s, 3H).

5.2.115 3-(1-(3-Fluorophenyl)-3-(4-fluorophenyl)-3-oxopropylamino)-4,4-dibenzyl-1*H*-pyrazol-5(4*H*)-one (244)

3-Amino-4,4-dibenzyl-1*H*-pyrazol-5(4*H*)-one (**129,** 0.4 gm, 0.0014 M) was reacted with (*E*)-1-(3-fluorophenyl)-3-(4-fluorophenyl)prop-2-en-1-one (**207,** 0.25gm, 0.0011 M) under the same conditions as described for compound (**211**). The titled compound was obtained as cream solid (0.41 gm, 82%); m.p. 229-231°C.

Anal:

TLC : R_f 0.5 (*n*-hexane: ethyl acetate; 12:8)

IR (KBr, cm^{-1}) : 3414, 3299, 3185, 3029, 2924, 1685, 1645, 1450, 1229, 1154 and 697.

Mass (m/z) : 524 $[M+1]^+$

^{1}H NMR [500 MHz, DMSO-d_6, δ] : 7.43-7.39 (t, 2H), 7.27- 7.19 (m, 7H), 7.17-7.13 (m, 3H), 7.02 – 6.98 (t, 1H), 6.87-6.84 (t, 2H), 6.62– 6.57 (m, 4H), 5.54-5.52 (m, 1H), 3.36-3.34 (d, 1H), 3.21-3.13 (dd, 2H), 3.08-3.03 (dd, 2H), 2.41-2.36 (dd, 1H).

5.2.116 3-(1-Phenyl-3-oxo-3-phenylpropylamino)-4,4-*bis*(4-methylbenzyl)-1*H*-pyrazol-5(4*H*)-one (245)

4,4-*bis*(4-methylbenzyl)-3-amino-1*H*-pyrazol-5(4*H*)-one (**210,** 0.4 gm, 0.0013 M) was (*E*)-1,3-diphenylprop-2-en-1-one (**174,** 0.27gm, 0.0010 M) under the same conditions as described for compound (**211**). The titled compound was obtained as white solid (0.4 gm, 82%); m.p. 207-210°C. (**Sxxvi**)

Anal:

TLC : R_f 0.7 (*n*-hexane: ethyl acetate; 12:8)

IR (KBr, cm^{-1}) : 3442, 3315, 3192, 2919, 2858, 1684, 1642, 1447, 1289 and 695.

Mass (m/z) : 516 $[M+1]^+$

^{1}H NMR [500 MHz, DMSO-d_6, δ] : 7.85 – 7.79 (m, 2H), 7.76 – 7.68 (m, 1H), 7.63 – 7.56 (m, 2H), 7.11 (dt, *J* = 7.9, 6.0 Hz, 5H), 7.04 (dd, *J* = 8.4, 7.0 Hz, 2H), 6.98 (d, *J* = 7.8 Hz, 2H), 6.92 (d, *J* = 7.7 Hz, 2H), 6.57 (dd, *J* = 7.3, 1.0 Hz, 2H), 6.49 (s, 2H), 5.63 (dd, *J* = 8.4, 3.8 Hz, 1H), 3.44 – 3.38 (m, 1H), 3.11 (dd, *J* = 28.8, 13.1 Hz, 2H), 3.00 (dd, *J* = 16.0, 13.1 Hz, 2H), 2.35 (dd, *J* = 18.6, 3.8 Hz, 1H), 2.30 (s, 3H), 1.92 (s, 3H).

5.2.117 3-(1-(4-Chlorophenyl)-3-oxo-3-phenylpropylamino)-4,4-*bis*(4-methylbenzyl)-1*H*-pyrazol-5(4*H*)-one (246)

4,4-*bis*(4-methylbenzyl)-3-amino-1*H*-pyrazol-5(4*H*)-one (**210,** 0.4 gm, 0.0013 M) was reacted (*E*)-3-(4-chlorophenyl)-1-phenylprop-2-en-1-one (**175,** 0.25gm, 0.0010 M) under the same conditions as described for compound (**211**). The titled compound was obtained as buff solid (0.42 gm, 89 %); m.p. 242-245°C. (**Sxxviii**)

Anal:

TLC : R_f 0.63 (*n*-hexane: ethyl acetate; 12:8)

IR (KBr, cm^{-1}) : 3437, 3301, 3187, 2922, 1685, 1644, 1402, 1288 and 818.

Mass (m/z) **:** 550 $[M]^+$, 552 $[M+2]^+$.

^{1}H NMR [500 MHz, DMSO-d_6, δ] : 7.79 – 7.74 (m, 2H), 7.66 (t, *J* = 7.4 Hz, 1H), 7.53 (t, *J* = 7.6 Hz, 2H), 7.08 – 6.99 (m, 6H), 6.88 (dd, *J* = 12.9, 7.7 Hz, 4H), 6.61 (d, *J* = 8.2 Hz, 2H), 6.47 (s, 2H), 5.55 (dd, *J* = 8.0, 4.3 Hz, 1H), 3.31 (d, *J* = 8.0 Hz, 1H), 3.05 (dd, *J* = 25.8, 13.1 Hz, 2H), 2.95 (d, *J* = 13.0 Hz, 2H), 2.50 – 2.43 (m, 1H), 2.24 (s, 3H), 1.90 (s, 3H).

^{13}C-NMR (126 MHz, DMSO-d_6) : δ 195.98, 170.31, 159.64, 138.74, 135.75, 135.28, 135.21, 133.28, 132.67, 132.47, 130.88, 129.44, 129.33, 128.64, 128.43, 128.29, 128.23, 128.11, 127.63, 127.39, 58.32, 48.66, 41.57, 40.15, 39.13, 20.55, 20.19.

5.2.118 3-(1-(4-Fluorophenyl)-3-oxo-3-phenylpropylamino)-4,4-bis(4-methylbenzyl)-1*H*-pyrazol-5(4*H*)-one (247)

4,4-*bis*(4-methylbenzyl)-3-amino-1*H*-pyrazol-5(4*H*)-one (**210,** 0.4 gm, 0.0013 M) was reacted (*E*)-3-(4-fluorophenyl)-1-phenylprop-2-en-1-one (**177,** 0.23gm, 0.0010 M) under

the same conditions as described for compound (**211**). The titled compound was obtained as buff solid (0.41 gm, 90%); m.p. 231-235°C.

Anal:

TLC : R_f 0.68 (*n*-hexane: ethyl acetate; 12:8)

IR (KBr, cm^{-1}) : 3438, 3307, 3189, 2920, 1689, 1643, 1510, 1224 and 821.

Mass (m/z) : 534 $[M+1]^+$

^{1}H NMR [500 MHz, DMSO-d_6, δ] : 7.85 – 7.78 (m, 2H), 7.73 – 7.69 (m, 1H), 7.58 (t, *J* = 7.7 Hz, 2H), 7.08 (dd, *J* = 17.7, 7.9 Hz, 5H), 6.93 (dd, *J* = 14.6, 7.9 Hz, 4H), 6.85 (t, *J* = 8.9 Hz, 2H), 6.67 (dd, *J* = 8.6, 5.6 Hz, 2H), 6.50 (s, 2H), 5.60 (dd, *J* = 8.2, 4.2 Hz, 1H), 3.41 (d, *J* = 8.3 Hz, 1H), 3.09 (dd, *J* = 25.2, 13.1 Hz, 2H), 2.99 (dd, *J* = 13.2, 4.9 Hz, 2H), 2.47 (dd, *J* = 18.6, 4.2 Hz, 1H), 2.28 (s, 3H), 1.95 (s, 3H).

5.2.119 3-(1-(4-Tolyl)-3-oxo-3-phenylpropylamino)-4,4-*bis*(4-methylbenzyl)-1*H*-pyrazol-5(4*H*)-one (248)

4,4-*bis*(4-methylbenzyl)-3-amino-1*H*-pyrazol-5(4*H*)-one (**210,** 0.4 gm, 0.0013 M) was reacted (*E*)-1-phenyl-3-*p*-tolylprop-2-en-1-one (**176,** 0.23gm, 0.0010 M) under the same conditions as described for compound (**211**). The titled compound was obtained as buff solid (gm, 77%); m.p. **:** 233-236°C.

Anal:

TLC : R_f 0.72 (*n*-hexane: ethyl acetate; 12:8)

IR (KBr, cm^{-1}) : 3457, 3291, 3184, 2921, 1687, 1638, 1512, 1288 and 811.

Mass (m/z) : 530 $[M+1]^+$

^{1}H NMR [500 MHz, DMSO-d_6, δ] : 7.84 – 7.78 (m, 2H), 7.74 – 7.68 (m, 1H), 7.59 (t, *J* = 7.7 Hz, 2H), 7.09 (dd, *J* = 10.7, 7.9 Hz, 4H), 6.94 (dd, *J* = 20.6, 7.7 Hz, 4H), 6.84 (d, *J* = 7.9 Hz, 2H), 6.51 – 6.44 (m, 4H), 5.59 (dd, *J* = 8.5, 3.8 Hz, 1H), 3.35 (d, *J* = 8.5 Hz, 1H), 3.09 (dd, *J* = 25.9, 13.1 Hz, 2H), 2.99 (dd, *J* = 15.7, 13.1 Hz, 2H), 2.34 (dd, *J* = 18.5, 3.9 Hz, 1H), 2.30 (s, 3H), 2.24 (s, 3H), 1.94 (s, 3H).

5.2.120 3-(1-(4-Nitrophenyl)-3-oxo-3-phenylpropylamino)-4,4-bis(4-methylbenzyl)-1*H*-pyrazol-5(4*H*)-one (249)

4,4-*bis*(4-methylbenzyl)-3-amino-1*H*-pyrazol-5(4*H*)-one (**210,** 0.4 gm, 0.0013 M) was reacted (*E*)-3-(4-nitrophenyl)-1-phenylprop-2-en-1-one (**179,** 0.26gm, 0.0010 M) under the same conditions as described for compound (**211**). The titled compound was obtained as orange solid (gm, 72 %); m.p. 249-251°C.

Anal:

TLC : R_f 0.56 (*n*-hexane: ethyl acetate; 12:8)

IR (KBr, cm^{-1}) : 3435, 3308, 3195, 2919, 1684, 1642, 1519, 1292 and 1109

Mass (m/z) **:** 561 $[M+1]^+$

^{1}H NMR [500 MHz, DMSO-d_6, δ] : 7.90 (d, *J* = 8.9 Hz, 2H), 7.86 – 7.80 (m, 2H), 7.76 – 7.68 (m, 1H), 7.62 – 7.56 (m, 2H), 7.08 (dd, *J* = 10.4, 8.0 Hz, 5H), 6.99 – 6.84 (m, 6H), 6.59 (s, 2H), 5.70 (dd, *J* = 7.6, 4.6 Hz, 1H), 3.45 (dd, *J* = 18.8, 7.6 Hz, 1H), 3.11 (dd, *J* = 32.1, 13.2 Hz, 2H), 3.00 (dd, *J* = 13.2, 10.3 Hz, 2H), 2.69 (dd, *J* = 18.8, 4.6 Hz, 1H), 2.27 (s, 3H), 1.97 (s, 3H).

5.2.121 3,3-Dibenzyl-3,3a-dihydro-5,7-diphenylpyrazolo[1,5-*a*]pyrimidin-2(1*H*)-one (250)

In a single neck 25-ml RBF, 3-amino-4,4-dibenzyl-1*H*-pyrazol-5(4*H*)-one (**129,** 0.5 gm, 0.0017 M) was dissolved in a mixture of KOH in *n*-propanol. This mixture was allowed to stir at room temperature. To this mixture, 1,3-diphenylprop-2-en-1-one (**174,** 0.35gm, 0.0017 M) was added portion-wise. The reaction mixture was refluxed at 100-110 °C for 2 hours. Reaction was monitored by TLC. Upon completion of the reaction, crushed ice was added to the reaction mixture and pH was neutralized, to obtain the desired compound which was filtered under vacuum to obtain crude white solid. Further purification of compound by column chromatography using silica gel (25% ethyl acetate) afforded pure white compound (0. 7 gm, 86%); m.p. 179-182°C.

Anal:

TLC : R_f 0.42 (*n*-hexane: ethyl acetate (10:10)

IR (KBr, cm^{-1}) : 3062, 3028, 2923, 2857, 1728, 1641, 1555, 1121and 692.

Mass (m/z) : 468 $[M]^+$

^{1}H-NMR [400 MHz, $CDCl_3$, δ] : 8.22 – 8.13 (m, 2H), 7.64 – 7.41 (m, 9H), 7.15 – 7.05 (m, 10H), 3.64 – 3.60 (m, 2H), 3.44-3.39 (dd, *J* = 12.9, 6.8 Hz, 2H).

5.2.122 3,3-Dibenzyl-5-(4-chlorophenyl)-3,3*a*-dihydro-7-phenylpyrazolo[1,5-*a*]pyrimidin-2(1*H*)-one (251)

The desired compound (**251**) obtained by reacting 3-amino-4,4-dibenzyl-1*H*-pyrazol-5(4*H*)-one (**129,** 0.5 gm, 0.0017 M) with (*E*)-3-(4-chlorophenyl)-1-phenylprop-2-en-1-one (**175,** 0.43 gm, 0.0017 M) using the same method as described for compound (**250**). The title compound (**251**) was obtained as white solid (0.76 gm, 89%); m.p. 227-230 °C. (**Sxxix**)

Anal:

TLC **:** R_f 0.45 (*n*-hexane: ethyl acetate (10:10)

IR (KBr, cm^{-1}) : 3030, 2920, 2855, 1717, 1635, 1555, 1271, 1019 and 697.

Mass (m/z) : 502 $[M]^+$

^{1}H-NMR [400 MHz, $CDCl_3$, δ] : 8.21-8.19 (m, 2H), 7.64-7.63 (m, 3H), 7.50-7.46 (m, 3H), 7.34-7.32 (d, 2H), 7.13-7.12 (m,4H), 7.08-7.04 (m, 6H), 3.63-3.40 (dd, 4H).

^{13}C-NMR [126 MHz, DMSO-d_6, δ] : 182.47, 161.59, 156.25, 144.39, 138.13, 135.02, 134.73, 134.54, 131.99, 130.75, 129.81, 129.74, 129.53, 128.87, 128.40, 127.75, 127.32, 127.05, 126.96, 114.16, 58.96, 42.69, 41.01.

5.2.123 3,3-Dibenzyl-3,3*a*-dihydro-5-(4-nitrophenyl)-7-phenylpyrazolo[1,5-*a*]pyrimidin-2(1*H*)-one (252)

The desired compound (**252**) obtained by reacting 3-amino-4,4-dibenzyl-1*H*-pyrazol-5(4*H*)-one (**129,** 0.5 gm, 0.0017 M) with (*E*)-3-(4-nitrophenyl)-1-phenylprop-2-en-1-one (**179,** 0.43gm, 0.0017 M) using the same method as described for compound (**250**). The title compound (**252**) was obtained as crimson red compound. (0.66 gm, 76%); m.p. 220-223°C.

Anal:

TLC : R_f 0.42 (*n*-hexane: ethyl acetate (10:10)

IR (KBr, cm^{-1}) : 3327, 3196, 3062, 3030, 2925, 1636, 1515, 1450, 1339 and 764.

^{1}H-NMR [400 MHz, $CDCl_3$, δ] : 8.14 (d, *J* = 8.7 Hz, 1H), 7.60 – 7.58 (m, 2H), 7.50 – 7.32 (m, 2H), 7.16 – 7.10 (m, 4H), 7.06 (dd, *J* = 5.0, 2.1 Hz, 5H), 3.62 (d, *J* = 12.9 Hz, 2H), 3.40 (d, *J* = 12.9 Hz, 2H).

5.2.124 3,3-Dibenzyl-3,3*a*-dihydro-7-phenyl-5-*p*-tolylpyrazolo[1,5-*a*]pyrimidin-2(1*H*)-one (253)

The desired compound (**253**) obtained by reacting 3-amino-4,4-dibenzyl-1*H*-pyrazol-5(4*H*)-one (**129,** 0.5 gm, 0.0017 M) with (*E*)-1-phenyl-3-*p*-tolylprop-2-en-1-one (**176,** 0.37gm, 0.0017 M) using the same method as described for compound (**250**). The title compound (**253**) was obtained as white compound. (0.56 gm, 69%); m.p. 160-162°C.

Anal:

TLC **:** R_f 0.44 (*n*-hexane: ethyl acetate (10:10)

IR (KBr, cm^{-1}) : 3066, 2914, 1643, 1596, 1500, 1365, 1158, 844 and 694.

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

^{1}H-NMR [400 MHz, $CDCl_3$, δ] **:** 8.21 – 8.20 (m, 1H), 7.64 – 7.62 (m, 3H), 7.52 (s, 1H), 7.45-7.43 (d, *J* = 8.3 Hz, 2H), 7.37 (d, *J* = 1.8 Hz, 1H), 7.17 – 7.12 (m, 6H), 7.06-7.04 (m, 5H), 3.61 (d, *J* = 12.9 Hz, 2H), 3.40 (d, *J* = 12.9 Hz, 2H), 2.34 (s, 3H).

5.2.125 3,3-Dibenzyl-5-(4-fluorophenyl)-3,3*a*-dihydro-7-phenylpyrazolo[1,5-*a*]pyrimidin -2(1*H*)-one (254)

The desired compound (**254**) obtained by reacting 3-amino-4,4-dibenzyl-1*H*-pyrazol-5(4*H*)-one (**129,** 0.5 gm, 0.0017 M) with (*E*)-3-(4-fluorophenyl)-1-phenylprop-2-en-1-one (**177,** 0.38gm, 0.0017 M) using the same method as described for compound (**250**). The title compound (**254**) was obtained as white compound. (0.74 gm, 90%); m.p. 201-204°C. (**Sxxiv**)

Anal:

TLC : R_f 0.57 (*n*-hexane: ethyl acetate (10:10)

IR (KBr, cm^{-1}) : 3056, 2912, 1669, 1601, 1504, 1356, 1115 and 696.

Mass (m/z) : 486 $[M]^+$

^{1}H-NMR [400 MHz, $CDCl_3$, δ]: 8.21-8.18 (m, 2H), 7.64-7.62 (t, 3H), 7.56-7.53 (m, 2H), 7.78 (s, 1H), 7.14-7.12 (m, 4H), 7.08-7.03 (m, 8H), 3.63-3.60 (dd, 2H), 3.43-3.39 (dd, 2H).

5.2.126 3,3-Dibenzyl-5-(3-chlorophenyl)-3,3*a*-dihydro-7-phenylpyrazolo[1,5-*a*]pyrimidin-2(1*H*)-one (255)

The desired compound (**255**) obtained by reacting 3-amino-4,4-dibenzyl-1*H*-pyrazol-5(4*H*)-one (**129,** 0.5 gm, 0.0017 M) with (*E*)-3-(3-chlorophenyl)-1-phenylprop-2-en-1-one (**181,** 0.41gm, 0.0017 M) using the same method as described for compound (**250**). The title compound (**255**) was obtained as white compound. (0.76 gm, 89%); m.p. 237-240°C.

Anal:

TLC **:** R_f 0.52 (*n*-hexane: ethyl acetate (10:10)

IR (KBr, cm^{-1}) : 3440, 3315, 3189, 2918, 2855, 1642, 1598 1449, 1120 and 698.

Mass (m/z) : 502 $[M]^+$

^{1}H-NMR [400 MHz, $CDCl_3$, δ] : 8.21-8.19 (t, 2H), 7.64-7.63 (t, 3H), 7.50-7.46 (m, 3H), 7.47 (s, 1H), 7.41-7.37 (m, 3H), 7.31-7.29 (d, 1H), 7.24-7.22 (m, 1H), 7.13-7.10 (m, 4H), 7.07-7.06 (m, 6H), 4.28 (s, 1H), 3.64-3.61 (dd, 2H), 3.43-3.40 (dd, 2H).

5.2.127 3,3-Dibenzyl-5-(3-fluorophenyl)-3,3*a*-dihydro-7-phenylpyrazolo[1,5-*a*]pyrimidin-2(1*H*)-one (256)

The desired compound (**256**) obtained by reacting 3-amino-4,4-dibenzyl-1*H*-pyrazol-5(4*H*)-one (**129,** 0.5 gm, 0.0017 M) with (*E*)-3-(3-fluorophenyl)-1-phenylprop-2-en-1-one (**182,** 0.38 gm, 0.0017 M) using the same method as described for compound (**250**). The title compound (**256**) was obtained as white solid.

Anal:

TLC **:** R_f 0.55 (*n*-hexane: ethyl acetate (10:10)

IR (KBr, cm^{-1}) : 3449, 3066, 2915, 1652, 1500, 1365, 1158, 803 and 694.

^{1}H-NMR [400 MHz, $CDCl_3$, δ]**:** 8.21-8.18 (m, 2H) 7.64-7.62 (t, 3H). 7.56-7.53 (m, 2H) 7.78 (s, 1H). 7.14-7.12 (m, 4H), 7.08-7.03 (m, 8H), 3.63-3.60 (d, 2H), 3.43-3.39 (d, 2H).

5.2.128 3,3-Dibenzyl-7-(4-fluorophenyl)-3,3*a*-dihydro-5-phenylpyrazolo[1,5-*a*]pyrimidin-2(1*H*)-one (257)

The desired compound (**257**) obtained by reacting 3-amino-4,4-dibenzyl-1*H*-pyrazol-5(4*H*)-one (**129,** 0.5 gm, 0.0017 M) with (*E*)-1-(4-fluorophenyl)-3-phenylprop-2-en-1-one (0.38gm, 0.0017 M) using the same method as described for compound (**250**). The title compound (**257**) was obtained as white compound. (0.76 gm, 92%); m.p. 237-239°C.

Anal:

TLC **:** R_f 0.55 (*n*-hexane: ethyl acetate (10:10)

IR (KBr, cm^{-1}) : 3449, 3066, 2915, 1643, 1500, 1365, 1158, 803 and 694.

Mass (m/z) : 486 $[M]^+$

^{1}H-NMR [400 MHz, $CDCl_3$, δ]**:** 8.21-8.18 (m, 2H), 7.50-7.48 (m, 2H), 7.48 (s, 1H), 7.46-7.41 (d, 1H), 7.38-7.36 (d, 2H), 7.34-7.28 (t, 2H), 7.14-7.11 (m, 4H), 7.08-7.04 (m, 6H), 3.63-3.60 (dd, 2H), 3.41-3.38 (dd, 2H).

5.2.129 3,3-Dibenzyl-3,3*a*-dihydro-5,7-di*p*-tolylpyrazolo[1,5-*a*]pyrimidin-2(1*H*)-one (258)

The desired compound (**258**) obtained by reacting 3-amino-4,4-dibenzyl-1*H*-pyrazol-5(4*H*)-one (**129,** 0.5 gm, 0.0017 M) with (*E*)-1,3-di*p*-tolylprop-2-en-1-one (**201,** 0.401gm, 0.0017 M) using the same method as described for compound (**250**). The title compound (**258**) was obtained as white compound. (0.71 gm, 84%); m.p. 221-224°C.

Anal:

TLC **:** R_f 0.42 (*n*-hexane: ethyl acetate (10:10)

IR (KBr, cm^{-1}) : 3434, 3297, 3181, 3029, 2918, 1646, 1603, 1446, 1275, 1116 and 701.

Mass (m/z) : 496 $[M]^+$

^{1}H-NMR [400 MHz, $CDCl_3$, δ] : 8.11-8.09 (d, *J*= 8.4, 2H), 7.47 (s, 1H), 7.45-7.41 (t, *J*=8.4 and *J*=7.2, 4H), 7.17 (s, 1H) 7.15-7.12 (m, 5H), 7.06-7.02 (6H), 3.62-3.59 (dd, *J*=12.8, 2H), 3.41-3.38 (dd, *J*=12.8, 2H), 2.50 (s, 3H), 2.34 (s, 3H).

5.2.130 3,3-Dibenzyl-5-(4-fluorophenyl)-3,3a-dihydro-7-*p*-tolylpyrazolo[1,5-*a*]pyrimidin-2(1*H*)-one (259)

The desired compound (**259**) obtained by reacting 3-amino-4,4-dibenzyl-1*H*-pyrazol-5(4*H*)-one (0.5 gm, 0.0017 M) with (*E*)-3-(4-fluorophenyl)-1-*p*-tolylprop-2-en-1-one (**206**, 0.40 gm, 0.0017 M) using the same method as described for compound (**250**). The title compound (**259**) was obtained as white compound. (0.75 gm, 89%); m.p. 201-203°C.

Anal:

TLC : R_f 0.3 (*n*-hexane: ethyl acetate (10:10)

IR (KBr, cm^{-1}) : 3434, 3313, 3065, 2919, 2857, 1683, 1636, 1447, 1123 and 700.

Mass (m/z) : 500 $[M]^+$

^{1}H-NMR [400 MHz, $CDCl_3$, δ]: 8.11 (d, *J* = 8.2 Hz, 1H), 7.53 (dd, *J* = 8.8, 5.0 Hz, 1H), 7.48 – 7.40 (m, 1H), 7.22 (d, *J* = 9.4 Hz, 1H), 7.13 (dd, *J* = 6.9, 2.8 Hz, 2H), 7.09 – 7.01 (m, 3H), 3.23 (d, *J* = 13.5 Hz, 2H), 2.97 (d, *J* = 13.5 Hz, 2H), 2.55 (s, 3H).

5.2.131 3,3-Dibenzyl-3,3*a*-dihydro-5-phenyl-7-*p*-tolylpyrazolo[1,5-*a*]pyrimidin-2(1*H*) one (260)

The desired compound (**257**) obtained by reacting 3-amino-4,4-dibenzyl-1*H*-pyrazol-5(4*H*)-one (**129,** 0.5 gm, 0.0017 M) with (*E*)-3-phenyl-1-*p*-tolylprop-2-en-1-one (**202**, 0.377gm, 0.0017 M) using the same method as described for compound (**250**). The title compound (**257**) was obtained as white compound. (0.68 gm, 84%); m.p. 144-147°C. (**Sxxxii**)

Anal:

TLC **:** R_f 0.45 (*n*-hexane: ethyl acetate (10:10)

IR (KBr, cm^{-1}) : 3064, 3029, 2913, 2857, 1725, 1638, 1494, 1362, 1119 and 692.

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

^{1}H-NMR [400 MHz, $CDCl_3$, δ] : 8.11-8.09 (d, *J*=8.0, 2H), 7.49-7.47 (m, 3H), 7.42-7.40 (m, 3H), 7.37-7.33 (m, 2H), 7.14-7.12 (m, 4H), 7.07-7.03 (m, 6H), 3.62-3.59 (d, *J*=12.8, 2H), 3.41-3.38 (d, *J*=12.8, 2H), 2.50 (s, 3H).

5.2.132 3,3-Dibenzyl-7-(4-chlorophenyl)-3,3*a*-dihydro-5-phenylpyrazolo[1,5-*a*]pyrimidin-2(1*H*)-one (261)

The desired compound (**257**) obtained by reacting 3-amino-4,4-dibenzyl-1*H*-pyrazol-5(4*H*)-one (**129,** 0.5 gm, 0.0017 M) with (*E*)-1-(4-chlorophenyl)-3-phenylprop-2-en-1-one (**195**, 0.41gm, 0.0017 M) using the same method as described for compound (**250**). The title compound (**257**) was obtained as white compound. (0.78 gm, 91%); m.p. 229-231 °C

Anal:

TLC **:** R_f 0.48 (*n*-hexane: ethyl acetate (10:10)

IR (KBr, cm^{-1}) : 3433, 3298, 3179, 2915, 2853, 1685, 1632, 1598, 1447, 1289, 1126 and 700.

Mass (m/z) : 502 $[M]^+$

^{1}H-NMR [400 MHz, $CDCl_3$, δ] : 8.15-8.12 (m, 2H), 7.60-7.58 (m, 2H), 7.49-7.47 (m, 3H), 7.43-7.41 (m, 1H), 7.37-7.34 (m, 2H), 7.13-7.11 (m, 4H), 7.07-7.05 (m, 6H), 3.63-3.60 (dd, *J*=12.8, 2H), 3.41-3.38 (dd, *J*=12.8, 2H).

5.3 Biological screening

5.3.1 MABA

There are various techniques used for test drug sensitivity against Mycobacterium. But most of the techniques have on or the other drawbacks. The determination of colony forming units (CFU) make take up to 2 months to obtain results. The BACTEC systems, the growth indicator tubes and Etest are simple and rapid methods but are high-cost methods. So, its impractical to use these methods for HTS discovery applications or for clinical use in resource-poor settings. The Microplate Alamar Blue Assay (MABA) uses a 4-week incubation in 96 well plates followed by addition of the resazurin that is dark blue in colour. This resazurin is blue when blue in colour when present in its oxidized form, but it turns pink after reduction to resorufin as a result of cellular metabolism. The read out for MABA can be visual, colorimetric or fluorometric. Thus, MABA can be used for determinations of inhibition of actively growing Mycobacteria.

5.3.2 Principle

The alamar blue oxidation-reduction (redox) indicator is one of the most commonly used for measuring cell viability, toxicity and cellular growth. The dye in oxidized state

imparts blue colour which is changed to pink when reduced, which can be easily differentiated visually, thus proving to be the simplest measure of viability

5.3.3 Assay procedure

The *Mycobacterium bovis* BCG (BCG) was grown to logarithmic phase (OD595 ~0.5) in Middlebrook 7H9 broth (Himedia) supplemented with 10% (v/v) OADC (Oleic acid, albumin dextrose and catalase), 0.05% glycerol (v/v) and 0.05% (v/v) Tween 80 and were grown in shaker incubator at 150rpm and 37°C till the optical density of the BCG culture reaches 0.5 at 595nm. The bacterial stocks were stored in aliquots using cryovials at -80°C and used within a month. The bacterial culture was resuspended by passaging it 10–15 times through a 26½ gauge needle to avoid clumps and dilute in growth medium till the OD595~0.001.

Percentage inhibition against BCG were determined by MABA. Drug susceptibility testing using Alamar blue of the compounds on BCG was done in aerobic condition following the method described by Palomino *et al.* with slight modification. Rifampicin and isoniazid were used as positive control. Rifampicin and isoniazid were solubilized according to manufacturer's recommendation and the test compounds were dissolved in DMSO and water respectively. Stock solutions were filter sterilized using 0.22 µm filters and stored at -20°C. 0.02% Resazurin sodium salt (SRL) solution was prepared in sterile distilled water, filter sterilized and stored at 4°C for not more than 10 days.

Compound stock solutions were prepared in DMSO and serially diluted in two-fold. The final testing solution was 50 and 10 µg/ml. Assay was performed using clear bottom transparent 96 well plate. The outer perimeter wells were filled with sterile distilled to avoid dehydration during the experiment. The Bacterial culture was grown till OD 0.5 and diluted with the growth medium till the OD reaches 0.05

100 µl of the bacterial culture was added in each well along with the test compounds and the positive and negative controls. All the experiments were performed in triplicates. and the plates were incubated at 37 °C for 7 days. On days 7, Resazurin was added at the concentration of 0.02% in each well. After incubation for another 24 hours, the colours of all wells were recorded and reading were taken at 570nm and 600nm. Theoretically, the compound wells with lesser reduction of resazurin are considered to be have higher inhibition of Mycobacterium. Typically, a colour change from the blue to pink indicates bacterial growth.

5.3.4 Cell viability assay

A cell viability assay on human lung adenocarcinoma cell line A549 was performed for compound (**118**). All the procedures were carried out in a sterile environment using biological safety cabinet. Stock of resazurin sodium salt (0.6 mM) was prepared in PBS, filtered using 0.22 µM syringe filter. A549 cells were plated in 96-well clear flat-bottom microplates at a density of 0.5×10^3 cells per well in 100 µl DMEM supplemented with 10 % FBS and cultured for 24 hours at 37 °C and 5 % CO_2. Cells were treated either with DMSO alone or with compounds at final concentrations of 1.5 µg/ml, 3.125 µg/ml and 6.25 µg/ml, and incubated further for 7 days. Cell viability was assessed by addition of 20 µl resazurin stock solution followed by further incubation for 16-18 hours at 37 °C. The absorbance at 570 nm and 600 nm was measured with BioTek Synergy H1 Multimode Reader. The amount of reduced resazurin was calculated by using the formula:

$$AR_{570} = A_{570} – (A_{600} \text{ x } R_O),$$

where A_{570} and A_{600} are sample absorbance, and R_o is a correction factor which is calculated by the formula, absorbance of oxidized form at lower wavelength (570nm)/ absorbance of oxidized form at higher wavelength (600nm).

Further, the absorbance values of the media only were subtracted from the absorbance values of Resazurin in media. The correction factor R_o was calculated by dividing absorbance of the oxidized form of lower wavelength (570 nm) by absorbance of the oxidized form at higher wavelength (600 nm). Finally, the percentage difference in reduction was calculated by using the formula:

$$\text{Percent difference in reduction} = \frac{A570 - (A600\ x\ Ro) for\ test\ well}{A570 - (A600\ x\ Ro)\ \ positive\ control} X\ 100$$

Statistical analysis was performed by using Prism 8 software.

5.4 References:

(1) Dixon, S. L.; Smondyrev, A. M.; Knoll, E. H. *et al.* PHASE: A New Engine for Pharmacophore Perception, 3D QSAR Model Development, and 3D Database Screening: 1. Methodology and Preliminary Results. *J. Comput. Aided. Mol. Des.* **2006**, *20* (10), 647–671. https://doi.org/10.1007/s10822-006-9087-6.

(2) Dixon, S. L.; Smondyrev, A. M.; Rao, S. N. PHASE: A Novel Approach to Pharmacophore Modeling and 3D Database Searching. *Chem. Biol. Drug Des.* **2006**, *67* (5), 370–372. https://doi.org/https://doi.org/10.1111/j.1747-0285.2006.00384.x.

(3) Halgren, T. A.; Murphy, R. B.; Friesner, R. A. *et al.* Glide: A New Approach for Rapid, Accurate Docking and Scoring. 2. Enrichment Factors in Database Screening. *J. Med. Chem.* **2004**, *47* (7), 1750–1759. https://doi.org/10.1021/jm030644s.

(4) Eberhardt, J.; Santos-Martins, D.; Tillack, A. F. *et al.* AutoDock Vina 1.2.0: New Docking Methods, Expanded Force Field, and Python Bindings. *J. Chem. Inf. Model.* **2021**, *61* (8), 3891–3898. https://doi.org/10.1021/acs.jcim.1c00203.

(5) Trott, O.; Olson, A. J. AutoDock Vina: Improving the Speed and Accuracy of Docking with a New Scoring Function, Efficient Optimization, and Multithreading. *J. Comput. Chem.* **2010**, *31* (2), 455–461. https://doi.org/https://doi.org/10.1002/jcc.21334.

(6) QikProp, Schrödinger, LLC, New York, NY, 2009.

(7) Daina, A.; Michielin, O.; Zoete, V. SwissADME: A Free Web Tool to Evaluate Pharmacokinetics, Drug-Likeness and Medicinal Chemistry Friendliness of Small Molecules. *Sci. Rep.* **2017**, *7* (March), 1–13. https://doi.org/10.1038/srep42717.

(8) Makarov, V.; Manina, G.; Mikusova, K. *et al.* Benzothiazinones Kill Mycobacterium Tuberculosis by Blocking Arabinan Synthesis. *Sci.* **2009**, *324* (5928), 801–804. https://doi.org/10.1126/science.1171583.Benzothiazinones.

(9) Greene, N.; Judson, P. N.; Langowski, J. J.; Marchant, C. A. Knowledge-Based Expert Systems for Toxicity and Metabolism Prediction: DEREK, StAR and METEOR. *SAR QSAR Environ. Res.* **1999**, *10* (2–3), 299–314. https://doi.org/10.1080/10629369908039182.

(10) Landge, S.; Mullick, A. B.; Nagalapur, K. *et al.* Discovery of Benzothiazoles as Antimycobacterial Agents: Synthesis, Structure-Activity Relationships and Binding

Studies with Mycobacterium Tuberculosis Decaprenylphosphoryl-β-d-Ribose 2′-Oxidase. *Bioorganic Med. Chem.* **2015**, *23* (24), 7694–7710. https://doi.org/10.1016/j.bmc.2015.11.017.

(11) Shirude, P. S.; Shandil, R. K.; Manjunatha, M. R. *et al.* Lead Optimization of 1,4-Azaindoles as Antimycobacterial Agents. *J. Med. Chem.* **2014**, 57 (13), 5728-37. https://doi.org/10.1021/jm500571f.

(12) Shirude, P. S.; Shandil, R.; Sadler, C. *et al.* Azaindoles: Noncovalent DprE1 Inhibitors from Scaffold Morphing Efforts, Kill Mycobacterium Tuberculosis and Are Efficacious in Vivo. *J. Med. Chem.* **2013**, 56 (23), 9701-8. **2013**. https://doi.org/10.1021/jm401382v.

(13) Naik, M.; Humnabadkar, V.; Tantry, S. J. *et al.* 4-Aminoquinolone Piperidine Amides: Noncovalent Inhibitors of DprE1 with Long Residence Time and Potent Antimycobacterial Activity. *J. Med. Chem.* **2014**, 57(12), 5419-34. https://doi.org/10.1021/jm5005978.

(14) Neres, J. O.; Hartkoorn, R. C.; Chiarelli, L. R. *et al.* 2-Carboxyquinoxalines Kill Mycobacterium Tuberculosis through Noncovalent Inhibition of DprE1 More Medicines for Tuberculosis (MM4TB) Consortium (Www.Mm4tb.Org). **2014**. https://doi.org/10.1021/cb5007163.

(15) Stanley, S. A.; Schmidt Grant, S.; Kawate, T.; Iwase, N.; Shimizu, M.; Wivagg, C.; Silvis, M.; Kazyanskaya, E.; Aquadro, J.; Golas, A.; Fitzgerald, M.; Dai, H.; Zhang, L.; Hung, D. T. Identification of Novel Inhibitors of M. Tuberculosis Growth Using Whole Cell Based High-Throughput Screening. *ACS Chem. Biol* **2012**, *7*, 2022. https://doi.org/10.1021/cb300151m.

(16) Karabanovich, G.; Dušek, J.; Savková, K. *et al.* Development of 3,5-Dinitrophenyl-Containing 1,2,4-Triazoles and Their Trifluoromethyl Analogues as Highly Efficient Antitubercular Agents Inhibiting Decaprenylphosphoryl-β- d -Ribofuranose 2′-Oxidase. *J. Med. Chem.* **2019**, *62* (17), 8115–8139. https://doi.org/10.1021/acs.jmedchem.9b00912.

(17) Maestro 9.4, Schrödinger, LLC, New York, NY, 2013.

(18) LigPrep, Schrödinger, LLC, New York, NY, 2013.

(19) Https://Zinc.Docking.Org/.

(20) Maestro, Schrödinger, LLC, New York, NY, 2013.

(21) Friesner, R. A.; Murphy, R. B.; Repasky, M. P. *et al.* Extra Precision Glide: Docking and Scoring Incorporating a Model of Hydrophobic Enclosure for Protein−Ligand Complexes. *J. Med. Chem.* **2006**, *49* (21), 6177–6196. https://doi.org/10.1021/jm051256o.

(22) SYSTÈMES, D. BIOVIA Discovery Studio Dassault Syst Mes BIOVIA, Discovery Studio Modeling Environment. *Release*.

(23) RSCB PDB https://www.rcsb.org/

(24) Murumkar, P. R.; Sharma, M. K.; Gupta, P. *et al.* Selection of Suitable Protein Structure from Protein Data Bank: An Important Step in Structure Based Drug Design Studies. *Mini Rev. Med. Chem.* **2022**. https://doi.org/10.2174/1389557522666220512151454.

(25) Allouche, A.; Lyon, D.; Lyon, F.-. Software News and Updates Gabedit — A Graphical User Interface for Computational Chemistry Softwares. **2010**. https://doi.org/10.1002/jcc.

(26) Van Der Spoel, D.; Lindahl, E.; Hess, B. *et al.* GROMACS: Fast, Flexible, and Free. *J. Comput. Chem.* **2005**, *26* (16), 1701–1718. https://doi.org/10.1002/jcc.20291.

(27) Vanommeslaeghe, K., Hatcher, E., Acharya, C. *et al.* CHARMM General Force Field: A Force Field for Drug-like Molecules Compatible with the CHARMM All-Atom Additive Biological Force Fields. *J. Comput. Chem.* **2010**, 31 (4), 671-90. https://doi.org/https://doi.org/10.1002/jcc.21367.

(28) Jorgensen, W. L.; Chandrasekhar, J.; Madura, J. D. *et al.* Comparison of Simple Potential Functions for Simulating Liquid Water. *J. Chem. Phys.* **1983**, *79* (2), 926–935. https://doi.org/10.1063/1.445869.

(29) Bianco, A.; Chen, Y.; Frackowiak, E. *et al.* Carbon Science Perspective in 2020 : Current Research and Future Challenges. *Mat. today.* **2020**, 4–17.