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Synthesis, characterization, biological evaluation and docking studies of pyrimidine-imidazole mannich base derivatives as transaminase bioainhibitors

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ABSTRACT

The synthesis, as well as spectroscopic characterization, biological evaluation and docking studies of a novel class of N'-((1-(piperidin/morpholin/ thiomorpholin/ methylpiperazine)-1H-imidazol-4-yl) methylene)-3-(4-substituted phenyl-[1,2,4] triazolo [4,3-c] pyrimidine-8-carbohydrazide derivatives are described. All the synthesized compounds were characterized byelemental analysis FTIR, ^{1}H-NMR, ^{13}C NMR, and Mass spectral data. All the synthesized compounds were exhibits antimicrobial activities. Further the docking studies were carried out based on mycobacterial studies for the model compounds against Transaminase BioA enzyme and the results found are moderate.

Keywords: Pyrimidine, Imidazole, Mannich base, Transaminase BioA

INTRODUCTION

Heterocyclic compounds are abundant in nature and are of great significance to life because their structural subunits exist in many natural products such as vitamins, hormones, and antibiotics **[1,2].** Hence, they have attracted considerable attention in the design of biologically active molecules **[3,4]** and advanced organic chemistry **[5,6].** Also in the family of heterocyclic compounds nitrogen containing Heterocycles are an important class of compounds in the medicinal chemistry and also contributed to the society from biological and industrial point which helps to understand life processes **[7].**A totally unsaturated six membered-ring containing nitrogen is known as azine **[8]**or pyridine, with two nitrogen atoms it is known as diazine **[9]** and with a nitrogen at 1,2-position, it isknown as pyridazine, at 1,3-position as pyrimidine and at 1,4-position as pyrazine. However, the current review intends to focus on the significance of pyrimidines class of antimicrobial agents along with clinical and in-vitro applications of pyrimidine derivatives to facilitate the development of more potent as well as effective antimicrobial agents.
Pyrimidines **[10]** are the heterocyclic aromatic compounds similar to benzene and pyrimidine containing two nitrogen atoms at positions 1 and 3 of the six membered rings. Heterocycles containing pyrimidine moiety are of great interest because they constitute an important class of natural and non-natural products, many of which exhibit useful biological activities and clinical applications **[11]**. Substituted purines and pyrimidines occur very widely in living organisms and were some of the first compounds studied by the organic chemists **[12].**Pyrimidines are biologically very important Heterocycles and represent by far the most important of the diazine family with uracil **[13]** and thymine **[14]** being constituents of ribonucleic acid (RNA) and deoxyribonucleic acid (DNA) and with cytosine **[15].** In addition to this, pyrimidines skeleton is also present in many natural products such as vitamin B_1 (thiamine) and many synthetic compounds, such as barbituric acid **[16]** and Veranal **[17]** which are used as hypnotics **[18]**.

The presence of Pyrimidine base in thymine, cytosine, and uracil, which are the essential building blocks of nucleic acids DNA and RNA, is one possible reason for their widespread therapeutic applications. The Pyrimidines

represent one of the most active classes of compounds possessing wide spectrum of biological activities like signification vitroactivity against unrelated DNA and RNA, viruses including polio herpes viruses, diuretic, antitumor, anti-HIV, and cardiovascular **[19].**

Imidazole is a planer five-member heterocyclic ring with 3C and 2N atom and in ring N is present in 1st and 3rd positions. The imidazole ring is a constituent of several important natural products, including purine, histamine, histidine and nucleic acid.In the field of five membered heterocyclic structures imidazole nucleus shows various properties. The high therapeutic properties of the imidazole related drugs have encouraged the medicinal chemists to synthesize a large number of novel chemotherapeutic agents. Imidazole drugs have broadened scope in remedying various dispositions in clinical medicines. Some imidazole drugs, at high concentrations, could exert direct inhibitory action on membranes, without interference with sterols and sterol esters **[20]**. Imidazole and its derivatives are reported to be physiologically and pharmacologically active and find applications in the treatment of several diseases.

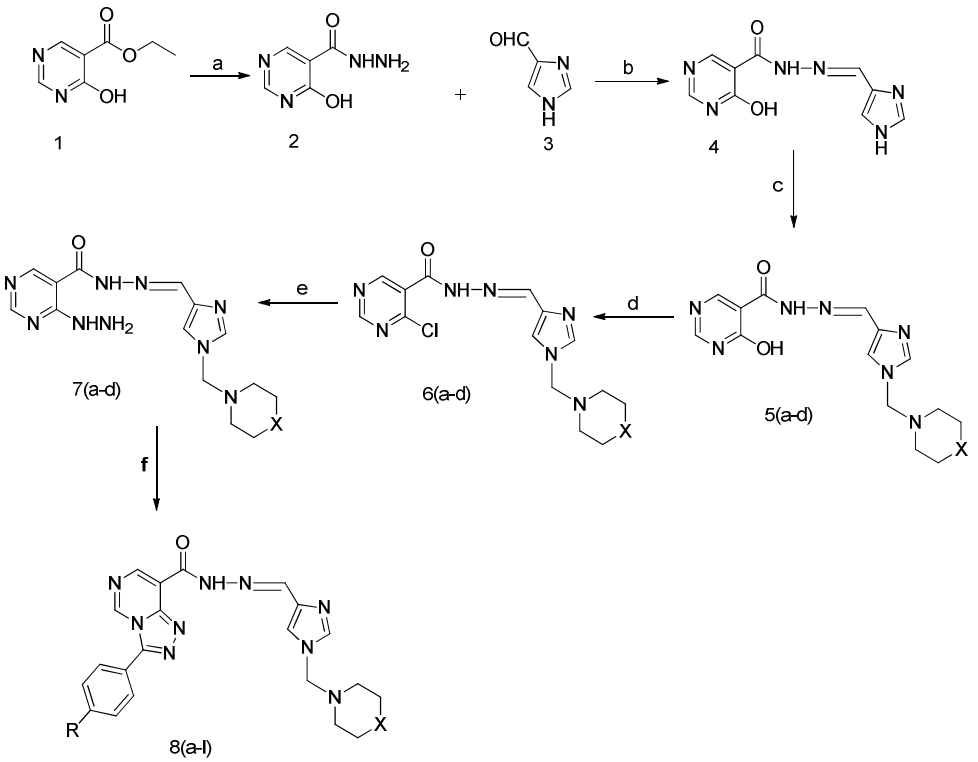
Mannich bases and their derivatives have many attractive applications, in paint and polymer chemistry as hardeners, cross linkers, reaction accelerations **[21]** etc. However, the most important applications are in the field of pharmaceutical products **[22,23].** Studies on anti-neo plastic drugs, analgesic drug, antibiotic drugs **[24,25]**, including labelled molecules **[26]**have received particular attention in the recent past. Mannich bases can either directly be employed or used as intermediates in chemicals synthesis. Literature survey reveals that mannich bases posses a broad spectrum of biological activities **[27].**

MATERIALS AND METHODS

Melting points were determined in open-end capillaries and are uncorrected. Compounds were checked for their purity by TLC on silica gel G plates and spots were located by iodine vapours. ^{1}H NMR spectra were recorded on BRUKER AVANCE II 400 NMR Spectrometer using TMS as internal standard. The mass spectra were obtained on a JEOL 5x102/DA-6000 mass spectrometer. The IR spectra were recorded on Perkin-Elmer spectrum FT-IR System using KBr pellets. Elemental analyses of the newly synthesized compounds were carried out on Perkin Elmer model 2400 C H N analyzer. All the compounds gave satisfactory elemental analysis within ±0.4% of theoretical values.
All reactions were carried out under argon in oven-dried glassware with magnetic stirring. Unless otherwise noted, all materials were obtained from commercial suppliers and were used without further purification. All solvents were reagent grade. THF was distilled from sodium benzophenone ketyl and degassed thoroughly with dry argon directly before use. Unless otherwise noted, organic extracts were dried with anhydrous Na_2SO_4, filtered through a fritted glass funnel, and concentrated with a rotary evaporator (20–30 Torr). Flash chromatography was performed with silica gel (200–300 mesh) by using the mobile phase indicated. The NMR spectra were measured with a 400 MHz Bruker Avance spectrometer at 400.1 and 100.6 MHz, for ^{1}H for ^{13}C, respectively, in $CDCl_3$ solution with tetramethylsilane as internal standard. Chemical shifts are given in ppm (δ) and are referenced to the residual proton resonances of the solvents. Proton and carbon magnetic resonance spectra (^{1}H NMR and ^{13}C NMR) were recorded using tetramethylsilane (TMS) in the solvent of CDCl3-*d* or DMSO-*d*6 as the internal standard (^{1}H NMR: TMS at 0.00 ppm, $CDCl_3$ at 7.26 ppm ,DMSO at 2.50 ppm; ^{13}C NMR: $CDCl_3$ at 77.16 ppm, DMSO at 40.00 ppm.

RESULTS AND DISCUSSION

The pyrimidines containing imidazole mannich bases derivatives were synthesized by following a systematicsynthetic organic procedure depicted in given following scheme **I**



***Scheme - I* :Proposed synthesis route for the synthesis of 7 (a-o)**

Reagents and Conditions: (a) *Ethanol, hydrazine hydrate, Reflux* ***(b)*** *DMF/Toluene& Ethanol* ***(c)*** *HCHO, morpholine/thiomorpholine/piperidine/methylpiperazine, DMF, Ice Cold, Reflux* ***(d)*** *Acetonitrile, $POCl_3$, DEA, Reflux* ***(e)*** *Ethanol, hydrazine hydrate* ***(f)*** *various 4-subtituted benzoic acids, $POCl_3$,Reflux*

Com	8a	8b	8c	8d	8e	8f	8g	8h	8i	8j	8k	8l
X	CH_2	O	O	O	O	O	S	S	S	S	S	NCH_3
R	H	H	CH_3	OCH_3	NO_2	CF_3	H	CH_3	OCH_3	NO_2	CF_3	H

Antibacterial Screening

The antibacterial activity of synthesized compounds 8a-l was studied by the disc diffusion method against *Staphylococcus aureus* NCCS2079 and *Bacillus cereus* NCCS 2106 (gram-positive) and *Escherichia coli* NCCS2065 and *Pseudomonas aeruginosa* NCCS2200 (gram negative) bacteria pathogenic organisms. The synthesized compounds were used at the concentration of 250 µg/ml and 500 µg/ml using DMSO as a solvent. The amoxicillin 10 µg/ml and Streptomycin 10µg/disc were used as a standard. (HimediaLaboratories Ltd, Mumbai). The results were shown in the Table **1** and Fig**1&2**.

Table 1: Antimicrobial activity of compounds

Comp	Zone of inhibition (mm)					
	Antibacterial activity				Antifungal activity	
	Gram +ve		*Gram -ve*		*Gram +ve*	*Gram -ve*
	SA	***BC***	***EC***	***PA***	***AN***	***CA***
8a	8	04	05	06	09	07
8b	14	10	12	13	15	14
8c	13	09	11	12	13	12
8d	12	08	09	10	12	10
8e	18	14	15	17	18	17
8f	16	12	13	15	17	15
8g	13	09	10	12	14	12
8h	12	07	09	10	12	11
8i	11	06	08	09	11	09
8j	16	11	13	14	16	15
8k	15	10	11	13	15	14
8l	09	05	06	08	10	08
amoxicillin	**21**	**27**	**24**	**22**	-	-
ketoconazole	-	-	-	-	**22**	**25**

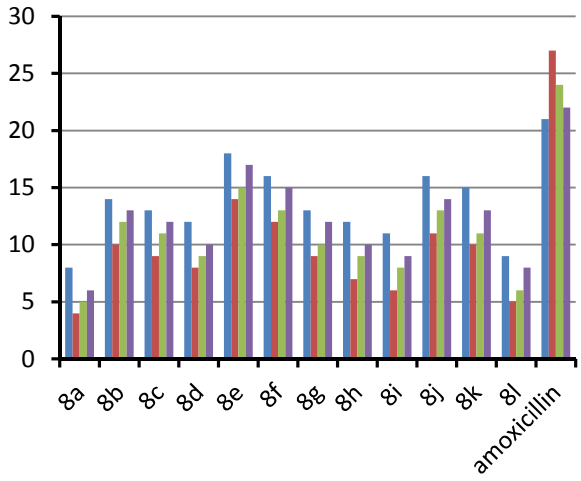


Fig-1

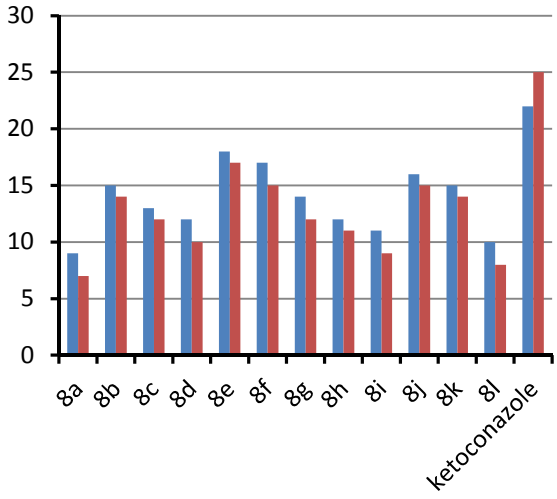


Fig-2

Docking studies

The docking studieswere performed using the binding site of Transaminase BioA. Identification of active site was performed by using CASTP server, a new program which automatically locates and measures the protein pockets and cavities.Human Transaminase BioA protein was chosen as the target protein to screen the synthesized compounds for mycobacterial activity. because Transaminase BioA. and related proteins are key regulators of apoptosis or programmed cell death implicated in human disease including diabetes.

The docking studies of newly synthesised compounds 8e, 8f, 8h, 8i, 8j and 8(l) were carried out as model compounds on **Transaminase BioA** to study the mycobacterial activity of Imidazole Mannich bases bearing pyrimidine-1,2,4-triazole derivatives. Based on protein-ligand interaction GOLD score fitness was evaluated and the Imidazole Mannich bases bearing pyrimidine-1,2,4-triazole derivatives having high GOLD score fitness exhibits high mycobacterial activity. The order of mycobacterial activity based on docking studies are**8i>8h>8e>8f>8j>8(l)**. The model compounds docking conformations images was observed in fig 2 and comparative gold score fitness results were shown in the Table-**2** and Fig-**4**.

CONCLUSION

In conclusion, a series of novel pyrimidine imidazole mannich base derivatives were synthesized. The anti-bacterial and anti-fungal activities havebeen carried out. Among tested compounds, the derivatives possessing imidazole nucleus found to be more active, some of the compounds are moderately active and some of them are slightly active. The docking studies reveal, among the model compounds tested the pyrimidine derivatives possessing imidazole nucleus(8e, 8f, 8h, 8i, 8j & 8l) is more potent inhibitor against Transaminase BioA.The results were presented in the Table-**2** and docking conformations of 8e, 8f, 8h, 8i, 8j and 8l was shown in the Fig-**3** represents the active site of Transaminase BioA.Protein. SAR studies indicated that the introduction of imidazole group at the 3 and 4 positions pyrimidine ring favored the inhibitory activity against Transaminase BioA. The docking was consistent with the above SAR results.

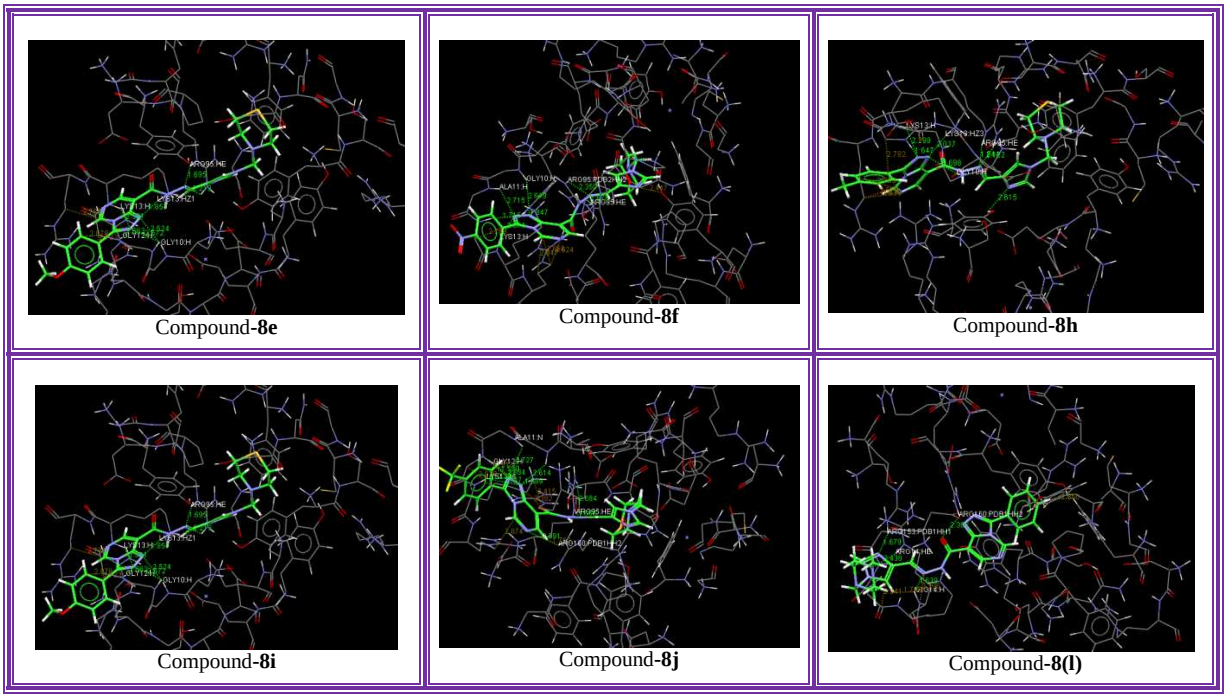


Figure-3: Docking images of model compounds

Table-.2: The docking results of compounds withTransaminase BioA

Comp No	Fitness	S(hb_ext)	S(vdw_ext)	S(hb_int)	S(int)
8e	70.15	10.78	52.92	0.00	-13.38
8f	69.83	10.59	52.72	0.00	-13.25
8h	71.32	9.00	55.70	0.00	-14.26
8i	72.72	9.78	57.06	0.00	-15.53
8j	66.71	12.46	52.53	0.00	-17.99
8l	42.32	5.78	57.92	0.00	-15.60

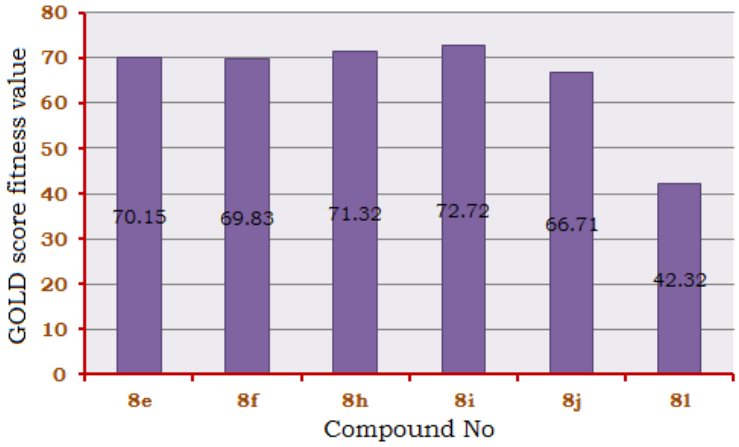


Fig-4 : Comparative Gold score fitness values for model compounds

Experimental

Synthesis of 4-hydroxypyrimidine-5-carbohydrazide[28] (2)

To a mixture of ethyl 4-hydroxy pyrimidine-5-carboxylate **(1)** (0.1 m.mol) and hydrazine hydrate (0.5 m.mol) in ethanol 10 mL was refluxed for a 5 hrs at 100^{o}C. After the reaction mixture was cooled and poured into ice cold water with stirring to get solid compound**(2).IR(KBr,Cm^{-1}):**3550 (-OH str), 3495&3415 (2 bands of -NH_2str), 3202(-NH str),1690(-C=O str).**^{1}H NMR (DMS0-d6,ppm):** 2.24 (s, 2H, -NH_2), 8.65 (s, 1H, -NCH in pyrimidine ring), 8.99(s, 1H, -NCHN in pyrimidine ring), 9.72(s,1H, sec amide), 11.85(s, 1H, -OH). m.p-149-2^{o}C, Yield-71%, **$C_5H_6N_4O_2$**Calculated C-38.96; H-3.92; N-36.35 & found % C, 38.92; H, 3.88; N, 36.30;

Synthesis of N'-((1H-imidazol-4-yl)methylene)-4-hydroxypyrimidine-5-carbohydrazide (4)
Equimolar quantities (0. 1 mmol) of 4-hydroxypyrimidine-5-carbohydrazide **(2)**(0.15m.mol)and 1H-imidazole-4-carbaldehyde **(3)**(0.1m.mol) were dissolved in warm ethanol (5 mL) containing DMF (2 mL). The reaction mixture was refluxed for 3-4hours and then kept at room temperature overnight. The resulting solid was filtered and washed with ethanol, dried and recrystallized from ethanol to afford compound **(4).IR(KBr,Cm^{-1}):**3450cm^{-1} symmetrical stretching of -OH, 3210 cm^{-1} stretching of -NH, 1690cm^{-1} , 1595cm^{-1}, 1555cm^{-1} corresponds to symmetrical stretching of >C=O, -C=N, and -C-N bands respectively.**^{1}H NMR (DMS0-d6,ppm):**7.21 (s, 1H, -NCH imidazole), 7.55 (s, 1H, -N=CH), 7.78 (s, 1H, -NCHN in imidazole), 8.50 (s, 1H, -NHC=O), 8.65 (s, 1H, -NCHN in pyrimidine), 8.90 (s, 1H, -NCH), 11.66 (s, 1H, -OH), 13.52 (s, 1H, -NH). m.p-154-6^{o}C, Yield-69%, **$C_9H_8N_6O_2$**, Calculated: C-46.55,H-3.47, N-36.19 & found C-46.51,H-3.44, N-36.12

General procedures for the synthesis of 4-hydroxy-N'-((1-(piperidin/morpholin/ thiomorpholin/ methylpiperizine)-1H-imidazol-4-yl) methylene) pyrimidine-5-carbohydrazide[29] (5a-d)
A mixture of compound**(4)** (10 m.mol) and piperidine (10 m.mol) and water (8 mL) until a clear solution was obtained. To this solution, HCHO (0.01m.mol) and DMF were added in ice-cold condition and stirred for 2hours in ice-bath and left overnight at room temperature. The obtained white solid was isolated and crystallized from ethanol to give a compound of **(5a).** The reaction procedure leading to 5a was then extended to the synthesis of **5b-d**from morpholine, thiomorpholine, N-methylpiperizine.

4-hydroxy-N'-((1-(piperidin-1-yl methyl)-1H-imidazol-4-yl) methylene)pyrimidine-5-carbohydrazide (5a)
IR(KBr,Cm^{-1}):3385 (-OH str), 3221(-NH amide), 1688(-C=O), 1599(>C=N); **^{1}H NMR (DMS0-d6,ppm)**1.52-1.60 (m,6H, -$(CH_2)_3$of piperidine), 2.45(t,4H, -N$(CH_2)_2$ of piperidine), 4.79(s,2H, -N-CH_2-N-),6.95 (s, 1H, -CH proton α to one nitrogen atom in imidazole ring), 7.65 (s, 1H,-CHattached to imidazole), 7.79 (s, 1H, -CH proton α to two nitrogen atoms in imidazole ring), 8.55 (s, 1H, -NHC=O), 8.61 (s, 1H, -NCHN in pyrimidine), 8.85(s, 1H, -NCH in pyrimidine), 11.24 (s, 1H, -OH group). m.p-172-5^{o}C, Yield-66%, **$C_{15}H_{19}N_7O_2$**,Calculated (%)C-54.70, H-5.81, N-29.77 & Found (%) C-54.62, H-5.67, N-29.69

4-hydroxy-N'-((1(morpholinomethyl) -1H-imidazol-4-yl)methylene)Pyrimidine-5-carbohydrazide (5b)
IR(KBr,Cm^{-1}): 3350 (-OH str), 3213(-NH amide), 1690(-C=O), 1585(>C=N); **^{1}H NMR (DMS0-d6,ppm**2.50(t,4H, -N$(CH_2)_2$), 3.68 (t, 4H, -O$(CH_2)_2$) 4.78 (s,2H, -N-CH_2-N-),6.95 (s, 1H, -CH), 7.51 (s, 1H, -CH), 7.84 (s, 1H, -CH), 8.55 (s,1H, -NHC=O), 8.61 (s, 1H, -NCHN), 8.85(s, 1H, -NCH in), 11.33 (s, 1H, -OH). m.p -163-5^{o}C, Yield-73%, **$C_{14}H_{17}N_7O_3$,**Calculated (%)C-50.75, H-5.17, N-29.59 &Found (%)C-50.68, H-5.11, N-29.51.

4-hydroxyN'((1(thiomorpholinomethyl) -1H-imidazol-4-yl)methylene) Pyrimidine--5-carbohydrazide (5c)
IR(KBr,Cm^{-1}):3366 (-OH str), 3225(-NH amide), 1685(-C=O), 1603(>C=N); **^{1}H NMR (DMS0-d6,ppm:**2.55(t,4H, -S$(CH_2)_2$), 3.78 (t, 4H, -N$(CH_2)_2$) 4.84 (s,2H, -N-CH_2-N-), 6.93 (s, 1H, - CH), 7.54 (s, 1H, -CH), 7.80 (s, 1H, -CH), 8.55 (s, 1H, -NHC=O), 8.66 (s, 1H, -NCHN), 8.87(s, 1H, -NCH), 11.44 (s, 1H, -OH); m.p-166-8^{o}C, Yield-75%,**$C_{14}H_{17}N_7O_2S$,**Calculated (%)C-48.40, H-4.93, N-28.22 &Found (%) C-48.33,H-4.93, N-28.16.

4-hydroxy-N'-((1- ((4-methylpiperazin-1-yl)methyl)-1H-imidazol-4-yl) methylene) pyrimidine5-carbohydrazide (5d)
IR(KBr,Cm^{-1}):3345 (-OH str), 3228(-NH amide), 1688(-C=O), 1605 (>C=N);**^{1}H NMR (DMS0-d6,ppm:**2.27 (s, 3H, -NCH_3), 2.39(m,8H,-N$(CH_2)_4$), 4.83 (s,2H, -N-CH_2-N-), 6.75 (s, 1H, -CH), 7.49 (s, 1H, -CH), 7.78 (s, 1H, -CH), 8.50 (s, 1H, -NHC=O), 8.60 (s, 1H, -NCHN), 8.77(s, 1H, -NCH), 11.55 (s, 1H, -OH); m.p-170-3^{o}C, Yield-70%,**$C_{15}H_{20}N_8O_2$,**Calculated (%)C-52.32, H-5.85, N-32.54 &Found (%)C-52.70, H-5.79, N-32.46.

General procedures for the synthesis of4-chloro-N'-((1-(piperidin/ morpholin/thiomorpholin/ methylpiperazine)-1H-imidazol-4-yl)methylene) pyrimidine -5-carbohydrazide[30] (6a-d)
A mixture of 4-hydroxy-N'-((1-(piperidin-1-ylmethyl)-1H-imidazol-4-yl) methylene) pyrimidine-5-carbohydrazide **5a** treatment with acetonitrile and $POCl_3$ it were refluxed for 18hrs. After establishing completion of the reaction, the reaction mixture was kept for 2days at room temperature and then treated with cold water. The solid obtained was filtered, washed with water and recrystallized from methanol to yield the desired product **6a.** The reaction procedure leading to 6a was then extended to the synthesis of **6b-d**from **5b-d.**

4-chloro-N'-((1-(piperidin-1-ylmethyl) -1H-imidazol-4-yl)methylene)pyrimidine-5-carbohydrazide (6a)
IR(KBr,Cm^{-1}):3205(-NH amide), 1693(-C=O), 1612 (>C=N);-C-Cl(673); **^{1}H NMR (DMS0-d6,ppm**:1.55-1.66 (m,6H, -$(CH_2)_3$- of piperidine ring), 2.54 (t,4H, -N$(CH_2)_2$ - of piperidine), 4.83 (s,2H, -N-CH_2-N-), 6.93 (s, 1H, -CH proton α to one nitrogen atom in imidazole ring), 7.64 (s, 1H, -CH attached to imidazole ring), 7.88(s, 1H, -CH proton α to two nitrogen atoms in imidazole ring), 8.55 (s, 1H, -NHC=O), 9.26(s, 1H, -NCH in pyrimidine ring).

9.81 (s, 1H, -NCHN in pyrimidine ring), m.p-155-7°C, Yield-69%, **$C_{15}H_{18}ClN_7O$,**Calculated (%)C-51.80, H-5.22, N-28.19 &Found (%)C-51.72, H-5.17, N-28.11.

4-chloro-N'-((1-(morpholinomethyl) -1H-imidazol-4-yl) methylene)pyrimidine-5-carbohydrazide (6b)
IR(KBr,Cm^{-1}):3222(-NH amide), 1687(-C=O), 1612 (>C=N),-C-Cl(695),**^{1}H NMR (DMS0-d6,ppm:** 2.58 (t,4H, -$N(CH_2)_2$), 3.69 (t,4H, - $O(CH_2)_2$), 4.83 (s,2H, -N-CH_2-N-), 6.93 (s, 1H, -CH), 7.64 (s, 1H, -CH), 7.88 (s, 1H, - CH), 8.55 (s, 1H, -NHC=O), 9.26(s, 1H, -NCH).9.81 (s, 1H, -NCHN); m.p-167-9°C, Yield-83%,**$C_{14}H_{16}ClN_7O_2$,**Calculated (%)C-48.07, H-4.61, N-28.03 &Found (%)C-48.00, H-4.55, N-27.96.

4-chloro-N'-((1(thiomorpholinomethyl)-1H-imidazol-4-yl)methylene)pyrimidine-5-carbohydrazide (6c)
IR(KBr,Cm^{-1}):3219(-NH amide), 1690C=O), 1598 (>C=N);-C-Cl(682); **^{1}H NMR (DMS0-d6,ppm:** 2.58 (t,4H, -$S(CH_2)_2$), 2.79 (t,4H, - $N(CH_2)_2$), 4.83 (s,2H, -N-CH_2-N-), 6.93 (s, 1H, -CH), 7.64 (s, 1H, -CH), 7.88 (s, 1H, -CH imidazole ring), 8.55 (s, 1H, -NHC=O), 9.15(s, 1H, -NCH in), 9.79 (s, 1H, -NCHN); m.p-173-5°C, Yield-75%,**$C_{14}H_{16}ClN_7OS$,** Calculated (%)C-45.96, H-4.41, N-26.80 &Found (%)C-45.89, H-4.36, N-26.71.

4-chloro-N'-((1-((4-methylpiperazin-1-yl)methyl)-1H-imidazol-4-yl)methylene) pyrimidine-5-carbohydrazide (6d)
IR(KBr,Cm^{-1}):3212(-NH amide), 1695(-C=O), 1609 (>C=N);-C-Cl(669); **^{1}H NMR (DMS0-d6,ppm:** 2.25 (s, 3H, -N-CH_3)2.37 (m,8H, -$N(CH_2)_4$), 4.83 (s, 2H, -N-CH_2-N-), 6.93 (s, 1H, -CH), 7.74 (s, 1H, -CH), 7.88 (s, 1H, -CH), 9.15(s, 1H, -NCH), 8.55 (s, 1H, -NHC=O), 9.79 (s, 1H, -NCHN); m.p-160-2°C, Yield-65%, **$C_{15}H_{19}ClN_8O$**,Calculated (%)C-49.66, H-5.28, N-30.88 &Found (%)C-49.58, H-5.22, N-30.81.

General procedures for the synthesis of 4-hydrazinyl-N'-((1-(piperidin/morpholin /thiomorpholin/methylpiperazine)-1H-imidazol-4-yl)methylene) pyrimidine -5-carbohydrazide[30] (7a-d)
A mixture of 4-chloro-N'-((1-(piperidin-1-ylmethyl)-1H-imidazol-4-yl) methylene) pyrimidine-5-carbohydrazide **6a** and hydrazine hydrate in ethanol was refluxed for a 5-6 hrs at 100°C. After the reaction mixture was cooled and poured into ice cold water with stirring. The separated solid was filtered, washed with water and recrystallized from ethanol to afford 4-hydrazinyl-N'-((1-(piperidin-1-ylmethyl)-1H-imidazol-4-yl) methylene) pyrimidine-5-carbohydrazide**7a.** The reaction procedure leading to 7a was then extended to the synthesis of **7b-d**from **6b-d**.

4-hydrazinyl-N'-((1-(piperidine-1-ylmethyl)- 1H-imidazol-4-yl) methylene) pyrimidine-5-carbohydrazide (7a)
IR(KBr,Cm^{-1}):3498 & 3411(-NH_2), 3217(-NH), 1691(-C=O), 1573(>C=N);
^{1}H NMR (DMS0-d6,ppm: 11.53-1.64 (m,6H, -$(CH_2)_3$of piperidine ring),2.41 (t,4H, -$N(CH_2)_2$ of piperidine), 4.24 (s, 2H, hydrazine -NH_2), 4.81 (s,2H, -N-CH_2-N-), 6.89 (s, 1H, -CH proton α to one nitrogen atom in imidazole ring), 7.54 (s, 1H, -CH attached to imidazole ring), 7.92 (s, 1H, -CH proton α to two nitrogen atoms in imidazole ring), 8.08 (s, 1H, hydrazine -NH), 8.26(s, 1H, -NCH in pyrimidine ring), 8.47 (s, 1H, -NHC=O), 8.77 (s, 1H, -NCHN in pyrimidine ring), m.p-182-4°C, Yield-69%, **$C_{15}H_{21}N_9O$,**Calculated (%)C-52.47, H-6.16, N-36.71 &Found (%)C-52.39, H-6.11,N-36.64.

4-hydrazinyl-N'-((1-(morpholinomethyl)-1H-imidazol-4-yl)methylene)pyrimidine -5-carbohydrazide (7b)
IR(KBr,Cm^{-1}):3490 & 3409(-NH_2), 3211(-NH), 1688(-C=O), 1599(>C=N); **^{1}H NMR (DMS0-d6,ppm:** 2.55 (t,4H, -$N(CH_2)_2$), 3.67 (t,4H, -$O(CH_2)_2$),4.24 (s, 2H,-NH_2), 4.81 (s,2H, -N-CH_2-N-), 6.89 (s, 1H, -CH), 7.51 (s, 1H, -CH), 7.84 (s, 1H, -CH), 8.08 (s, 1H, hydrazine -NH), 8.21(s, 1H, -NCH). 8.55 (s, 1H, -NHC=O), 8.70 (s, 1H, -NCHN), m.p-191-4°C, Yield-65%, **$C_{14}H_{19}N_9O_2$,**Calculated (%)C-48.69, H-5.55, N-36.50 &Found (%)C-48.61,H-5.49, N-36.41.

4-hydrazinyl-N'-((1-(thio morpholinomethyl) -1H-imidazol-4-yl)methylene)pyrimidine-5-carbohydrazide (7c)
IR(KBr,Cm^{-1}):3487 & 3406(-NH_2), 3210(-NH), 1695(-C=O), 1605(>C=N);**^{1}H NMR (DMS0-d6,ppm:** 2.59 (m,4H, -$S(CH_2)_2$), 2.80 (t,4H, -$N(CH_2)$), 4.24 (s, 2H, -NH_2), 4.81 (s,2H, -N-CH_2-N-), 6.89 (s, 1H, - CH), 7.51 (s, 1H, -CH), 7.84 (s, 1H, -CH), 8.08 (s, 1H, -NH), 8.21(s, 1H, -NCH).8.47 (s, 1H, -NHC=O), 8.70 (s, 1H, -NCHN); m.p-177-9°C, Yield-76%, **$C_{14}H_{19}N_9OS$,** Calculated (%)C-46.52, H-5.30, N-34.88 &Found (%)C-46.44, H-5.24, N-34.77.

4-hydrazinyl-N'-((1-((4-methylpiperazin-1-yl)methyl)-1H-imidazol-4-yl) methylene) pyrimidine-5-carbohydrazide (7d)
IR(KBr,Cm^{-1}):3488& 3412(-NH_2), 3219(-NH), 1678(-C=O), 1605(>C=N); **^{1}H NMR (DMS0-d6,ppm:** 2.23 (s, 3H, -N-CH_3) 2.38(m,8H, N$(CH_2)_4$), 4.24 (s, 2H, -NH_2), 4.81(s,2H, -N-CH_2-N-), 6.89 (s, 1H, -CH), 7.51 (s, 1H, -CH), 7.84 (s, 1H, -CH), 8.08 (s, 1H, -NH), 8.21(s, 1H, -NCH). 8.47 (s, 1H, -NHC=O), 8.70 (s, 1H, -NCHN), m.p-186-8°C, Yield-74%, **$C_{15}H_{22}N_{10}O$,** Calculated (%)C-50.27, H-6.19, N-39.08 &Found (%)C-50.25, H-6.12, N-39.02.

Synthesis of N'-((1-(piperidin/morpholin/ thiomorpholin/ methylpiperazine)-1H-imidazol-4-yl)methylene)-3-(4-substituted phenyl-[1,2,4]triazolo[4,3-c]pyrimidine-8-carbohydrazide[31] (8a-l)

A mixture of 4-hydrazinyl-N'-((1-(piperidin-1-ylmethyl)-1H-imidazol-4-yl) methylene) pyrimidine-5-carbohydrazide **7a** and substituted benzoic acid were taken in POCl3 and heated to reflux for 6hrs. The reaction mass was concentrated under reduced pressure and then quenched in ice. The solid obtained **(8a)** was filtered off, washed with water, dried and recrystallized from ethanol solvent. The same reaction procedure was adopted for the synthesis of compounds (**8b-l).**

3-phenyl-N'-((1-(piperidine-1-ylmethyl)-1H-imidazol-4-yl)methylene)-[1,2,4] triazolo[4,3-c]pyrimidine-8-carbohydrazide(8a)

IR(KBr,Cm^{-1}):3205(-NH str), 3084 (Ar-CH str), 1689 (-C=O str), 1610(>C=N);**^{1}H NMR (DMS0-d6,ppm:** 1.51-1.61 (m,6H, –$(CH_2)_3$- of piperidine ring), 2.49 (t,4H, -N-$(CH_2)_2$- of piperidine), 4.79 (s,2H, -N-CH_2-N-), 6.91 (s, 1H, - CH proton α to one nitrogen atom in imidazole ring), 7.40-7.55 (m, 3H, Ar-H), 7.48 (s, 1H, –CH attached to imidazole ring), 7.90 (s, 1H, -CH proton α to two nitrogen atoms in imidazole ring), 8.30(d, 2H, Ar-H),8.75 (s, 1H, -NHC=O), 9.38 (s, 1H, -NCH in pyrimidine ring), 9.65 (s, 1H, -NCHN in pyrimidine ring).**^{13}C NMR (DMSO-d6,75 MHz,&ppm):**141.4, 158.9, 129.1, 152.3, 164.5, 141.7, 123.9, 124.2, 139.1, 76.2, 55.7, 26.4, 25.3, 153.7, 133.4, 128.6, 131.4 and 132.5 corresponds to C_1, C_2, C_3, C_4, C_5, C_6, C_7, C_8, C_9, C_{10}, C_{11}, C_{12}, C_{13}, $C_{14,}$ C_{15}, C_{16}, C_{17}, and C_{18} respectively; m.p-196-9^{o}C, Yield-65%, **$C_{22}H_{23}N_9O$;** Calculated (%)C-61.52, H-5.40, N-29.35 &Found (%)C-61.46, H-5.36, N-29.27.

N'-((1(morpholinomethyl)-1H-imidazol-4-yl)methylene)-3-phenyl-[1,2,4]triazolo[4,3-c]pyrimidine-8-carbohydrazide(8b)

IR(KBr,Cm^{-1}):3215(-NH str), 3095 (Ar-CH str), 1690 (-C=O str), 1600 (>C=N); **^{1}H NMR (DMS0-d6,ppm:** 2.53 (t, 4H, -N$(CH_2)_2$-), 3.68 (t,4H, -O$(CH_2)_2$), 4.79 (s,2H, -N-CH_2-N-), 6.91 (s, 1H, -CH), 7.40-7.55 (m, 3H, Ar-H), 7.48 (s, 1H, -CH), 7.90 (s, 1H, -CH), 8.30(d, 2H, Ar-H), 8.75 (s, 1H, -NHC=O), 9.38 (s, 1H, -NCH), 9.65 (s, 1H, -NCHN).**^{13}C NMR (DMSO-d6,75 MHz,&ppm):**140.4, 157.5, 127.5, 151.3, 163.6, 139.2, 122.9, 123.2, 137.3, 75.3, 53.7, 66.4, 152.8, 131.4, 125.5, 129.6 and 130.5 corresponds to C_1, C_2, C_3, C_4, C_5, C_6, C_7, C_8, C_9, C_{10}, C_{11}, C_{12}, C_{13}, $C_{14,}$ C_{15}, C_{16} and C_{17}respectively. m.p-201-3 ^{o}C, Yield-70%,**$C_{21}H_{21}N_9O_2$,**Calculated (%)C-58.46, H-4.91, N-29.22 &Found (%)C-58.39, H-4.87, N-29.16.

N'-((1(morpholinomethyl)-1H-imidazol-4-yl)methylene)-3-(p-tolyl)-[1,2,4]triazolo[4,3-c]pyrimidine-8-carbohydrazide (8c)

IR(KBr,Cm^{-1}):3200(-NH str), 3100 (Ar-CH str), 1689 (-C=O str), 1590 (>C=N);**^{1}H NMR (DMS0-d6,ppm:** 2.27 (s, 3H, -CH_3), 2.53(t, 4H, -N$(CH_2)_2$-), 3.68 (t,4H, -O$(CH_2)_2$-), 4.79(s,2H, -N-CH_2-N-), 6.91(s, 1H, -CH), 7.30 (2H, Ar-H), 7.52 (s, 1H, -CH), 7.90 (s, 1H, -CH), 8.55(d, 2H, Ar-H), 8.75 (s, 1H,-NHC=O), 9.38 (s, 1H, -NCH), 9.57 (s, 1H, -NCHN).**^{13}C NMR (DMSO-d6,75 MHz,&ppm):**139.7, 156.8, 126.6, 150.2, 162.5, 138.1, 121.4, 122.6, 136.5, 75.8, 54.2, 65.4, 151.8, 133.4, 127.5, 128.6, 132.5 and 22.3 corresponds to C_1, C_2, C_3, C_4, C_5, C_6, C_7, C_8, C_9, C_{10}, C_{11}, C_{12}, C_{13}, $C_{14,}$ C_{15}, C_{16}, C_{17} and C_{18}respectively. m.p-187-9^{o}C, Yield-73%, **$C_{22}H_{23}N_9O_2$,**Calculated (%)C-59.32, H-5.20, N-28.30 &Found (%)C-59.27, H-5.14, N-28.22.

3-(4-methoxyphenyl)-N'-((1-(morpholinomethyl)-1H-imidazol-4-yl)methylene)-[1,2,4]triazolo[4,3-c]pyrimidine-8-carbohydrazide (8d)

IR(KBr,Cm^{-1}):3215(-NH str), 3089 (Ar-CH str), 1699 (-C=O str), 1609 (>C=N);1127 (C-O-C)**; ^{1}H NMR (DMS0-d6,ppm:** 2.53 (t, 4H, -N$(CH_2)_2$-), 3.68 (t,4H, -O$(CH_2)_2$-), 3.81 (s, 3H, -OCH_3), 4.79 (s,2H, -N-CH_2-N-), 6.91 (s, 1H, -CH), 7.07 (d, 2H, Ar-H), 7.52(s, 1H, -CH), 7.90 (s, 1H, -CH), 7.99 (d, 2H, Ar-H), 8.75 (s, 1H, -NHC=O), 9.35 (s, 1H, -NCH), 9.60 (s, 1H, -NCHN).**^{13}C NMR (DMSO-d6,75 MHz,&ppm):** 140.4, 157.5, 127.5, 151.3, 163.6, 139.2, 122.9, 123.2, 137.3, 75.3, 53.7, 66.4, 152.8, 127.4, 131.5, 115.6, 161.5 and 56.4 corresponds to C_1, C_2, C_3, C_4, C_5, C_6, C_7, C_8, C_9, C_{10}, C_{11}, C_{12}, C_{13}, $C_{14,}$ C_{15}, C_{16}, $C_{17}$and C_{18}respectively. m.p-193-5 ^{o}C, Yield-65%, **$C_{22}H_{23}N_9O_3$,**Calculated (%)C-57.26, H-5.02, N-27.32 &Found (%)C-57.20, H-4.94, N-27.26.

N'-((1(morpholinomethyl)-1H-imidazol-4-yl)methylene)-3-(4-(trifluoromethyl) phenyl)-[1,2,4]triazolo[4,3-c]pyrimidine-8-carbohydrazide (8e)

IR(KBr,Cm^{-1}):3202(-NH str), 3099 (Ar-CH str), 1689 (-C=O str), 1617 (>C=N);**^{1}H NMR (DMS0-d6,ppm:** 2.53 (t, 4H, -N$(CH_2)_2$-), 3.68 (t,4H, -O$(CH_2)_2$-), 4.79 (s,2H, -N-CH_2-N-), 6.87 (s, 1H, - CH), 7.50 (s, 1H, -CH), 7.70(d, 2H, Ar-H), 7.83 (s, 1H, -CH), 8.57 (d, 2H, Ar-H), 8.75 (s, 1H, -NHC=O), 9.38 (s, 1H, -NCH), 9.69 (s, 1H, -NCHN).**^{13}C NMR (DMSO-d6,75 MHz,&ppm):** 140.4, 157.5, 127.5, 151.3, 163.6, 139.2, 122.9, 123.2, 137.3, 75.3, 53.7, 66.4, 152.8, 137.4, 126.5, 125.6, 131.5 and 125.4 corresponds to C_1, C_2, C_3, C_4, C_5, C_6, C_7, C_8, C_9, C_{10}, C_{11}, C_{12}, C_{13}, $C_{14,}$ C_{15}, C_{16}, $C_{17}$and C_{18}respectively. m.p-166-9 ^{o}C, Yield-69%, **$C_{22}H_{20}F_3N_9O_2$,**Calculated (%)C-52.91, H-4.04, N-25.24 &Found (%)C-52.84, H-3.99, N-25.15.

N'-((1(morpholinomethyl)-1H-imidazol-4-yl)methylene)-3-(4-nitrophenyl)-[1,2,4]triazolo[4,3-c]pyrimidine-8-carbohydrazide (8f)

IR(KBr,Cm^{-1}):3220(-NH str), 3095 (Ar-CH str), 1692 (-C=O str), 1599 (>C=N);**^{1}H NMR (DMS0-d6,ppm:** 2.50 (t, 4H, -N(CH_2)$_2$-), 3.65 (t,4H, -O(CH_2)$_2$-), 4.80 (s,2H, -N-CH_2-N-), 6.87 (s, 1H, CH), 7.53 (s, 1H, -CH), 7.79 (s, 1H, -CH), 8.06-8.37(m, 4H, Ar-H), 8.75 (s, 1H, -NHC=O), 9.38 (s, 1H, -NCH),9.57 (s, 1H, -NCHN).**^{13}C NMR (DMSO-d6,75 MHz,&ppm):** 140.4, 157.5, 127.5, 151.3, 163.6, 139.2, 122.9, 123.2, 137.3, 75.3, 53.7, 66.4, 152.5, 140.4, 127.2, 124.6 and 148.5 corresponds to C_1, C_2, C_3, C_4, C_5, C_6, C_7, C_8, C_9, C_{10}, C_{11}, C_{12}, C_{13}, $C_{14,}$ C_{15}, C_{16} and C_{17}respectively. m.p-202-5^{o}C, Yield-82%, **$C_{21}H_{20}N_{10}O_4$,**Calculated (%)C-52.94, H-4.23, N-29.40 &Found (%)C-52.87, H-4.18, N-29.31.

3-phenyl-N'-((1-(thio-morpholinomethyl)-1H-imidazol-4-yl)methylene)-[1,2,4] Triazolo[4,3-c]pyrimidine-8-carbohydrazide (8g)

IR(KBr,Cm^{-1}):3225(-NH str), 3084 (Ar-CH str), 1689 (-C=O str), 1592 (>C=N);**^{1}H NMR (DMS0-d6,ppm:** 2.55 (t,4H, -N-CH_2)$_2$-), 2.72 (t, 4H, -S(CH_2)$_2$-), 4.83 (s,2H, -N-CH_2-N-), 6.84 (s, 1H, -CH), 7.40-7.55 (m, 3H, Ar-H), 7.51(s, 1H, -CH), 7.79 (s, 1H, -CH), 8.30 (d, 2H, Ar-H), 8.75 (s, 1H, -NHC=O), 9.36 (s, 1H, -NCH),9.57 (s, 1H, -NCHN).**^{13}C NMR (DMSO-d6,75 MHz,&ppm):** 140.3, 157.7, 127.4, 151.1, 163.2, 139.2, 122.6, 123.2, 137.8, 75.1, 58.1, 28.0, 152.5, 134.4, 127.5, 129.6 and 131.5 corresponds to C_1, C_2, C_3, C_4, C_5, C_6, C_7, C_8, C_9, C_{10}, C_{11}, C_{12}, C_{13}, $C_{14,}$ C_{15}, C_{16} and C_{17}respectively. m.p-200-4 ^{o}C -, Yield-80%, **$C_{21}H_{21}N_9OS$:**Calculated (%)C-56.36, H-4.73, N-28.17 &Found (%)C-56.29, H-4.67, N-28.09.

N'-((1-(thio morpholinomethyl) -1H-imidazol-4-yl) methylene)-3- (p-tolyl)-[1,2,4]triazolo[4,3-c]pyrimidine-8-carbohydrazide (8h)

IR(KBr,Cm^{-1}):3208(-NH str), 3073 (Ar-CH str), 1691 (-C=O str), 1621 (>C=N);**^{1}H NMR (DMS0-d6,ppm:** 2.29 (s, 3H, -CH_3), 2.55 (t,4H, -N(CH_2)$_2$-), 2.73 (t, 4H, -S(CH_2)$_2$-), 4.80 (s,2H, -N-CH_2-N-), 6.88 (s, 1H, -CH), 7.32 (m, 3H, Ar-H), 7.50(s, 1H, -CH), 7.86 (s, 1H, - CH), 8.56(d, 2H, Ar-H), 8.71 (s, 1H, -NHC=O), 9.38 (s, 1H, -NCH),9.69 (s, 1H, -NCHN).**^{13}C NMR (DMSO-d6,75 MHz,&ppm):** 141.4, 156.5, 128.2, 150.7, 164.6, 138.4, 123.5, 122.7, 138.2, 74.6, 57.8, 29.4, 151.6, 130.8, 126.1, 128.2, 132.7 and 22.6 corresponds to C_1, C_2, C_3, C_4, C_5, C_6, C_7, C_8, C_9, C_{10}, C_{11}, C_{12}, C_{13}, $C_{14,}$ C_{15}, $C_{16,}$ C_{17} and C_{18}respectively. m.p-197-9^{o}C, Yield-85%, **$C_{22}H_{23}N_9OS$,**Calculated (%)C-57.25, H-5.02, N-27.31 &Found (%) C-57.18, H-4.98, N-27.22.

3-(4-methoxyphenyl)-N'-((1(thio morpholinomethyl)-1H-imidazol-4-yl)methylene)-[1,2,4]triazolo[4,3-c] pyrimidine-8-carbohydrazide (8i)

IR(KBr,Cm^{-1}):3200(-NH str), 3115 (Ar-CH str), 1689 (-C=O str), 1599 (>C=N);1134 (C-O-C)**; ^{1}H NMR (DMS0-d6,ppm:** 2.56 (t,4H, -N(CH_2)$_2$-), 2.77 (t, 4H, -S(CH_2)$_2$-), 3.82 (s, 3H, -OCH3), 4.84 (s,2H, -N-CH_2-N-), 6.92 (s, 1H, -CH), 7.09 (d, 2H, Ar-H), 7.55(s, 1H, -CH), 7.89 (s, 1H, -CH), 7.99(d,2H, Ar-H), 8.75 (s, 1H, -NHC=O), 9.33 (s, 1H, -NCH in),9.54 (s, 1H, -NCHN).**^{13}C NMR (DMSO-d6,75 MHz,&ppm):** 140.3, 157.7, 127.4, 151.1, 163.2, 139.2, 122.6, 123.2, 137.8, 75.1, 58.1, 28.5, 152.5, 126.4, 130.5, 115.6 160.4 and 131.5 corresponds to C_1, C_2, C_3, C_4, C_5, C_6, C_7, C_8, C_9, C_{10}, C_{11}, C_{12}, C_{13}, $C_{14,}$ C_{15}, C_{16} C_{17} and C_{18}respectively. m.p-181-2^{o}C, Yield-75%, **$C_{22}H_{23}N_9O_2S$,**Calculated (%)C-55.33, H-4.85, N-26.40 &Found (%) C-55.28, H-4.80, N-26.33.

N'-((1-(thio-morpholinomethyl)-1H-imidazol-4-yl)methylene)-3-(4-(trifluoromethyl)phenyl)-[1,2,4]triazolo [4,3-c]pyrimidine-8-carbohydrazide (8j)

IR(KBr,Cm^{-1}):3225(-NH str), 3067 (Ar-CH str), 1690 (-C=O str), 1589 (>C=N);**^{1}H NMR (DMS0-d6,ppm:** 2.54 (t,4H, -N(CH_2)$_2$-), 2.73 (t, 4H, -S(CH_2)$_2$-), 4.81 (s,2H, -N-CH_2-N-), 6.90 (s, 1H, -CH), 7.50(s, 1H, -CH), 7.71 (d, 2H, Ar-H), 7.82 (s, 1H, -CH), 8.56 (d, Ar-H), 8.78 (s, 1H, -NHC=O), 9.33 (s, 1H, -NCH),9.54 (s, 1H, -NCHN).**^{13}C NMR (DMSO-d6,75 MHz,&ppm):** 141.4, 157.5, 127.2, 151.7, 164.6, 138.4, 123.5, 122.7, 138.2, 75.6, 57.8, 28.4, 152.6, 137.8, 126.9, 125.2, 132.7 and 125.6 corresponds to C_1, C_2, C_3, C_4, C_5, C_6, C_7, C_8, C_9, C_{10}, C_{11}, C_{12}, C_{13}, $C_{14,}$ C_{15}, $C_{16,}$ C_{17} and C_{18}respectively. m.p-192-5^{o}C, Yield-65%,**$C_{22}H_{20}F_3N_9OS$,**Calculated (%)C-51.26, H-3.91, N-24.45 &Found (%) C-51.17, H-3.84, N-24.39.

3-(4-nitrophenyl)-N'-((1-(thio-morpholinomethyl)-1H-imidazol-4-yl)methylene)-[1,2,4]triazolo[4,3-c] pyrimidine-8-carbohydrazide (8k)

IR(KBr,Cm^{-1}):3222(-NH str), 3095 (Ar-CH str), 1689 (-C=O str), 1596 (>C=N);**^{1}H NMR (DMS0-d6,ppm:** 2.54 (t,4H, -N(CH_2)$_2$-), 2.73 (t, 4H, -S(CH_2)$_2$-), 4.80 (s,2H, -N-CH_2-N-), 6.86 (s, 1H, -CH), 7.50(s, 1H, -CH), 7.82 (s, 1H, -CH), 8.06-8.33 (m, 4H, Ar-H), 8.76 (s, 1H, -CO-NH), 9.35(s, 1H, -NCH), 9.51 (s, 1H, -NCHN).**^{13}C NMR (DMSO-d6,75 MHz,&ppm):** 140.3, 157.7, 127.4, 151.1, 163.2, 139.2, 122.6, 123.2, 137.8, 75.1, 58.1, 28.5, 152.5, 141.4, 128.5, 125.6 and 148.5 corresponds to C_1, C_2, C_3, C_4, C_5, C_6, C_7, C_8, C_9, C_{10}, C_{11}, C_{12}, C_{13}, $C_{14,}$ C_{15}, C_{16} and C_{17}respectively. m.p-193-5^{o}C, Yield-75%, **$C_{21}H_{20}N_{10}O_3S$**, Calculated (%)C-51.21, H-4.09, N-28.44 &Found (%)C-51.14, H-4.01, N-28.38.

N'-((1-((4methylpiperazin-1-yl)methyl)-1H-imidazol-4-yl)methylene)-3-phenyl-[1,2,4]triazolo[4,3-c]pyrimidine-8-carbohydrazide (8l)

IR(KBr,Cm^{-1}):3230(-NH str), 3090 (Ar-CH str), 1690 (-C=O str), 1592 (>C=N);**^{1}H NMR (DMS0-d6,ppm:** 2.26 (s, 3H, -N-CH_3), 2.34 (m,8H, -N$(CH_2)_4$-), 4.80 (s,2H, -N-CH_2-N-), 6.88 (s, 1H, -CH), 7.40-7.55 (m, 3H, Ar-H), 7.50(s, 1H, -CH), 7.83 (s, 1H, -CH), 8.30(d, 2H, Ar-H), 8.72 (s, 1H, -CO-NH), 9.35(s, 1H, -NCH), 9.51 (s, 1H, -NCHN).**^{13}C NMR (DMSO-d6,75 MHz,&ppm):** 141.5, 158.7, 127.5, 151.7, 163.4, 139.8, 122.7, 124.2, 138.8, 75.5, 52.9, 57.5, 46.5, 153.2 134.4, 127.5, 129.6 and 131.5 corresponds to C_1, C_2, C_3, C_4, C_5, C_6, C_7, C_8, C_9, C_{10}, C_{11}, C_{12}, C_{13}, $C_{14,}$ C_{15}, $C_{16,}$ C_{17} and C_{18}respectively. m.p-185-7^{o}C, Yield-79%, **$C_{22}H_{24}N_{10}O$,**Calculated (%)C-59.45, H-5.44, N-31.51 &Found (%) C-59.39, H-5.39, N-31.44.

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