Journal of Pharmaceutical and Applied Chemistry
An International Journal

http://dx.doi.org/10.12785/jpac/010102

Rapid and Green Chemistry Catalysis in Synthesis of Hexahydroquinazolinones and Cyclopenta, Cyclohepta[*d*]Pyrimidinones with Prediction of Biological Activity *via* PASS INET.

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Received: 14 Mar. 2015, Revised: 3 Apr. 2015, Accepted: 16 Apr. 2015.
Published online: 1 May 2015

Abstract: Ceric Ammonium Nitrate (CAN), turns out to be commercially available, efficient and mild catalyst for synthesis of polyhydro-2H-cycloalka[*d*]pyrimidinones and hexahydroquinazolinones in few minutes. Accompanied with Predictions of the activity spectra of some selected compounds using *PASS INET*. at Pa > 50%, showing high probability of Protein kinase (CK1) inhibitor and Alpha7 nicotinic receptor agonist. However Cycloheptene systems showed some important targets including, Insulin growth factor agonist, and Acetylcholine nicotinic agonist and Tumour necrosis factor agonist.

Keywords: Ceric Ammonium Nitrate (CAN), cycloalka[d]pyrimidinones hexahydroquinazolinones, Greeen Chemistry, Pass Inet.

1 Introduction

Multi component reactions (MCRs) have a great importance in organic and medicinal chemistry [1]. Biginelli reaction is one of the most important MCRs. Organic reactions carried out under solvent free conditions brought to the attention of scientists as a green chemistry protocol. It was recently found that some fused pyrimidinones carrying an arylidene moiety are potential antitumor agents and drugs (Figure1), besides the broad-spectrum antitumor activity [2], a distinctive pattern of selectivity toward individual cell line such as that of leukemia [3]. It also have pharmacological activity such as anti-inflammatory, anti-microbial, □-1*a*-adrenergic receptor antagonist, and antihypertensives [4], calcium channel modulation, [5] mitotic kinesin inhibition (monastrol) [6a,b], antiviral [7], antibacterial and antifungal activity,[8] anticancer [9], etc [10].

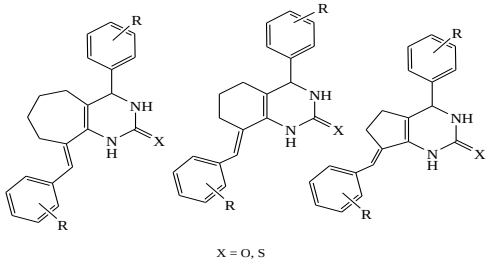

Fig.1: Hexahydroquinazolones and Cyclopenta, Cyclohepta[*d*]pyrimidinones.

Hexahydroquinazolinone derivatives used as anticonvulsant, antimalarial, antimicrobial, antifungal and *HIV-1* integrase by docking [11]. It was reported also that bis(arylmethylene) cyloheptanone possess antifertility and hypocholesterolemic [12].

2 Materials and Method

In the recent years, catalysts, which are capable of performing the reaction under mild conditions have gained particular attention [13]. This gave us the motivation to look for a versatile catalyst to improve the yield and shorten the time of this reaction. Cycloalkanones were used in presence of CAN as catalyst and new derivatives were obtained in moderate to excellent yields, the reaction performed in very short time under solvent free conditions (Scheme 1).

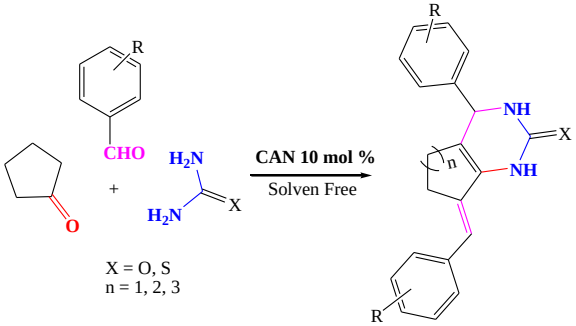

Fig. 2: Synthesis of arylidene heterobicyclic compounds using CAN

As the biological and pharmaceutical importance of hexahydroquinazolinones and cyclopenta, cyclohepta[*d*]-

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pyrimidinones, different reagents were used to synthesize these compounds such as 1,3-cyclohexanedione [14,15], dimedone [16,17] and various catalysts were applied; $BF_3{\cdot}OEt_2$[18], polyphosphate ester [19], $InCl_3$ [20], $ZrCl_4$ [21], $BiCl_3$ [22], NH_2SO_3H [23] and $Cu(OTf)_2$ [24] were applied, but no reactions were observed. Although good results obtained by using NH4VO325, $LaCl_3$ [26],$YbCl_3$ [3] and $(Me)_3SiCl$.[6c].

In this work, cyclopentanone, cyclohexanone and cycloheptanone were used to obtain hexahydroquinazolinones and cyclopenta, cyclohepta[*d*]pyrimidinones. Using CAN as a cheap, mild, and easily available catalyst to the products in moderate to excellent yields (yield based on aromatic aldehyde) under solvent free conditions as a green chemistry protocol. CAN consider an excellent chemical agent which considered as non-hygroscopic solid and can be handled easily. It has a wide use in industry, also in academia and in organic reactions. Representative examples include oxidation, oxidative addition, photo oxidation, nitration, deprotection, graft polymerization, etc. Intermediates formed in these reactions may undergo oxidative fragmentation, rearrangement, or cleavages of C–H and C–C bonds [27]. In recent years, CAN is considered as a powerful one-electron transfer catalyst [28] in many carbon–carbon bond forming reactions. It has also been widely used in carbon–hetero atom bond formation [29]. Since very soon it used in synthesis of 2,4,5-triaryl-1*H*-imidazoles [30a], and polyhydroquinolines [30b].

However, the use of CAN as a catalyst in the synthesis of hexahydroquinazolinones or cyclohepta, cyclopenta[*d*]-pyrimidinones under solvent free conditions has not been reported.

To confirm the activity of CAN to this reaction we began with cyclopentanone, benzaldehyde, Urea. The best molar ratio of cycloalkanone and aldehyde was 1:1 however the molar ratio 2:1 didn't perform smoothly.

To study the catalytic activity and optimize the mol% of CAN, synthesis of 7-benzylidene-4-phenyl-1,3,4,5,6,7-hexahydrocyclo-penta[*d*]pyrimidin-2-one (**4a**) was carried out using cyclopentanone, benzaldehyde, urea and different mol% of CAN (Table1). The title compound (**4a**) was isolated in 90% yield without solvent at 100ºC and 10 mol % CAN, the reaction consumed only four minutes.

Table1: Optimization of CAN mol % and reaction condition for **4a .**

Entry	*Mol% CAN*	*Temperature ° C*	*Reaction time (min.)*	*Yield %*
1	2.5	90	6	75
2	5	100	5	82
3	10	100	4	90
4	15	90	4	90
5	20	100	4	89

In presence of CAN, we noted that the reaction is carried out in very short time about three to five minutes without solvent at 90-100ºC. This in turn gives the economic and industrial importance of this research, also the solvent free condition make this work friendly to the environment because many solvents are toxic or flammable, also the reaction proceed well in the air so no dryness or protection conditions required .separation of products was very simply, only by washing with ice cold water to give sufficient pure compounds .further purification carried out by petroleum ether: $CHCl_3$ (2:1). Using the standardized reaction conditions, a range of arylidine heterobicyclic compounds were synthesized. The results were summarized in tables (2-4).

Cyclopentanone reacted with urea and benzaldehyde **(3a)** in presence of 10 mol% CAN to produce (7*E*)-7-benzylidene-4-phenyl-1,3,4,5,6,7-hexahydro-2H-cyclopenta[*d*]pyrimidin-2-one **(4a)** in 90% yield. Different derivatives of benzaldehyde were used with urea and thiourea to afford benzylidine heterobicyclic pyrimidinones(thiones) (**4a-4k**), (Table 2, Entries 2-11) in yield from 50% to 92% (yield based on aromatic aldehyde).

Table 2: Cyclopenta[d]pyrimidin-2-one products

Entries	*n*	*X*	*R*	*Product No.*	*Reaction Time(min*	*Yield %*
1	1	O	3a H	4a	3	90
2	1	O	3b $2OCH_3$	4b	3	50
3	1	O	3c NO_2	4c	4	92
4	1	O	3d NO_2	4d	4	59
5	1	O	3e 4Br	4e	3	82
6	1	O	3f 	4f	4	93
7	1	S	3g H	4g	3	64
8	1	S	3h $2OCH_3$	4h	3	55
9	1	S	3i $4N(CH_3)_2$	4i	3	50
10	1	S	3j 3-NO_2	4j	3	85
11	1	S	3k 	4k	3	60

Cyclohexanone reacted with urea and benzaldehyde (**3a**) in presence of 10 % mol in absence of solvent to produce (8*E*)-8-benzylidene-4-phenyl-3,4,5,6,7,8-hexahydroquinazolin -2(1*H*)-one (**5a**) in yield 95%. Different aromatic aldehydes were used to afford benzylidine heterobicyclic pyrimidinone (**5a-5o**), (Table 3, Entries 1-15) in 55-98% yield (yield based on aromatic aldehyde).

Cycloheptanone reacted with benzaldehyde and urea to produce (9*E*)-9-benzylidene-4-phenyl-1,3,4,5,6,7,8,9-octahydro-2*H*-cyclohepta[d]pyrimidin-2-one (**6a**). Different aldehydes were used (Entries 1-12) to afford benzilidene heterobicyclic compounds (Table 4, **6a-6k**) in 40-80% yield (yield based on aromatic aldehyde).

Table 3: Hexahydroquinazolinone products

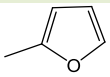
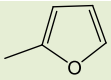
Entries	*N*	*X*	*R*		*Product No.*	*Reaction Time (min.)*	*Yield %*
1	2	O	3a	H	5a	3	90
2	2	O	3b	2-OCH_3	5b	3	92
3	2	O	3c	4-OCH_3	5c	4	58
4	2	O	3d	4-Cl	5d	4	80
5	2	O	3e	3-NO_2	5e	3	86
6	2	O	3f	2-NO_2	5f	5	55
7	2	O	3g	4-F	5g	4	60
8	2	O	3h		5h	3	79
9	2	S	3i	H	5i	3	87
10	2	S	3j	2-OCH_3	5j	3	98
11	2	S	3k	4-OCH_3	5k	3	60
12	2	S	3l	4-Cl	5l	3	93
13	2	S	3m	3-NO_2	5m	4	85
14	2	S	3n	4-$N(CH_3)_2$	5n	4	20
15	2	S	3o		5o	5	65

Table 4: Cyclohepta[d]pyrimidinone products

Entries	*n*	*X*	*R*		*Product No.*	*Reaction Time (min.)*	*Yield %*
1	3	O	3a	H	6a	3	40
2	3	O	3b	2-OH	6b	3	75
3	3	O	3c	4-F	6c	4	66
4	3	O	3d	4-Cl	6d	4	75
5	3	S	3e	H	6e	3	80
6	3	S	3f	2-OCH_3	6e	3	45
7	3	S	3g	4-OCH_3	6f	3	50
8	3	S	3h	4-Br	6g	4	65
9	3	S	3i	2-OH	6h	4	66
10	3	S	3j	4-Cl	6i	3	64
11	3	S	3k	4-$N(CH_3)_2$	6j	5	30
12	3	S	3l	3,4-OH	6k	4	80

In Tables 2,3,4, the effect of electron donating group (EDG) and electron withdrawing group (EWG) can be observed from the yield. It was observed that unsubstituted benzaldehyde (entry 1) gives good yield in case of cyclopentanone and cyclohexanone but low yield with cycloheptanone. EDGs substituted benzaldehydes at *para* position, showed moderate to good yields .Weak and strong EWGs substituted benzaldehydes (*para* or *meta* position) showed increasing yields.

Ortho substituted benzaldehydes, whether it was EDG or EWG afforded the corresponding arylidine heterobicyclic pyrimidinonethiones) in relatively lower yield, due to the steric hindrance effect. Except in case of *ortho* methoxy benzaldehyde and cyclohexanone showed excellent yields 92% and 98% with urea and theorem respectively. Moreover, acid sensitive heterocyclic aldehydes such as furfural furnished good yield 60-93%. Yields in case of cyclohexanone were relatively higher than cyclopentanone and cycloheptanone due to the ring strain effect or the bulky group effect. The behavior of urea was nearly similar to that of thiourea.

3 Reaction Mechanism

From the literature there are three possible mechanisms can be suggested[31]. One of these mechanisms includes the acid catalyzed formation of C=N bond via reaction of aromatic aldehyde with urea or thiourea in presence of CAN to afford the corresponding arylideneurea intermediate followed by nucleophilic attack of cycloalkanone to the arylidine urea then cyclocondensation of intermediates yielding pyrimidinone ring. It was believed that only protic acids proceed with this mechanism but not other metallic salt catalysts. To explain the role of CAN three separated reactions were conducted (*pathways A-C*) under the standard reaction conditions (10 mol% of CAN at 90-100^{o}C and stirring without solvent for 3-5 minutes). (Figure 3) and the reaction mechanism proceed in three steps: Firstly, benzaldehyde (**3a**) was heated with cyclopentanone (**1**) (*pathway A*) to yield diarylidene of cyclopentanone **(7)** (*Knoevenagel reaction*) which in turn cyclized with urea to afford arylidene hetrobicyclic compounds, but this method did not undergo the expected reaction. Secondly, condensation of cyclopentanone and urea which proceeded smoothly to furnish 1-cyclopentylideneurea (**8**) at which addition to benzaldehyde (**3a**) produce heterobicyclic pyrimidinone (**9a**) but not arylidene heterobicyclic pyrimidinone was observed (*pathway B*).

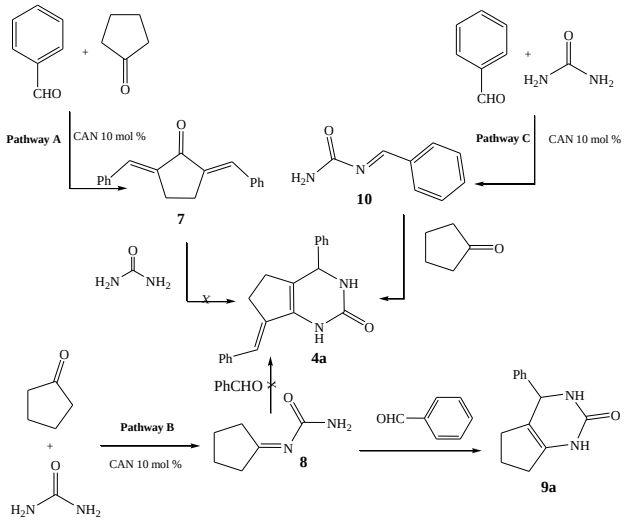


Fig.3. Reaction Pathways

Finally, reaction of benzaldehyde (**3a**) and urea (**2**) to produce the arylidene-urea (**10**), followed by a nucleophilic

attack of the carbon radical of cycloalkanone to the arylidene-urea (**10**) in turn cyclo-condensation to afford arylidine, further attack of benzaldehyde to the second radical of cycloalkanone to afford arylidine heterobicyclic pyrimidinones (**4a**) (*pathway C*). Intermediate (**10**) was separated simply and product **(4a)** was applicable to the three component, one-pot reaction products.

The mechanism of the reaction was assumed to proceed via condensation of aromatic aldehydes with urea or thiourea, followed by losing two protons and two electrons of cycloalkanone forming cycloalkanone diradical which add to the imine bond, further electron transfer forming anion which in turn attacked by proton followed by cyclocondensation to afford arylidine heterobicyclic pyrimidinones (Figure 4) .

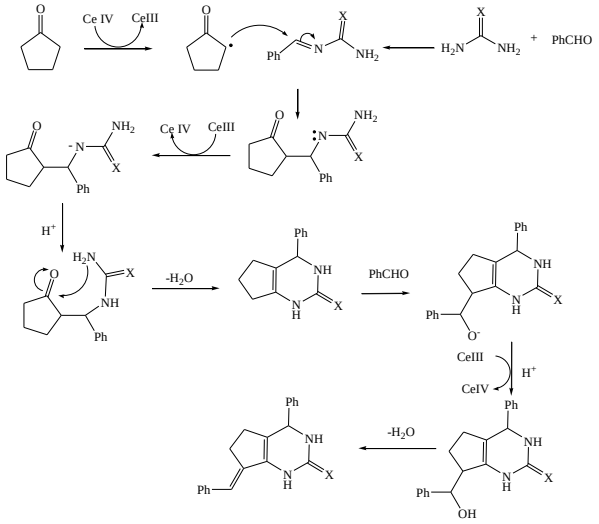


Fig.4: Reaction Mechanism,

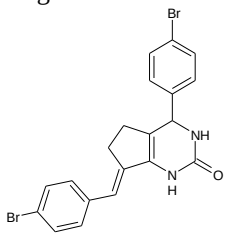
These results proved that Biginelli reaction catalyzed by CAN proceeds through arylidene-urea intermediate **10** as in BrØnsted type catalysis and this respond on the predictions that Biginelli reaction catalyzed by other types of acid catalysts such as metallic salts does not include formation of arylidene-urea intermediate .[32] also BrØnsted acidity of CAN was proved by *T. Caruso et al.*[33]

3.1 Prediction of Biological Activity Spectrum with Pass

Predicted Activity Spectrum of Substances (PASS), is one of the most important programs that used to predict all the biological activity of chemical compounds, on contrast the other methods of SAR/QSAR/QSPR that predict one type of biological activity[34]. It predicts a large number of pharmacotherapeutic effects, biochemical mechanisms of action, adverse effects and toxicities and the list of predicted biological activities available at the web site[35]. It was reported that PASS has the ability to predict carcinogenicity of chemical comounds[36]. Probabilities of presence (*Pa*) and absence (*Pi*) for each particular activity by default, *Pa*>Pi value is provides the mean accuracy of prediction about 90% in leave-one-outcross-validation for all approximately 60,000 compounds and 2500 activities from the PASS training set[37].

3.2 Predicted Biological Activity Spectrum Of Cyclopenta[D] Pyrimidinone.

Two selected new derivatives were taken under prediction. First, consider the results of biological activity spectrum predicted for (7*E*)-7-(4-bromobenzylidene)-4-(4-bromo-phenyl)-1,3,4,5,6,7-hexahydro-2*H*-cyclopenta[*d*]-pyrimidin-2-one **4e** (figure 5). It is obvious from the data in figure 5, that 11 possible activities are predicted for **4e** with *Pa*> 50%. Many probable macromolecular targets were observed, *Alpha* 7 nicotinic receptor agonist (*Pa*=93.2%), protein kinase (*CK1*) inhibitor (*Pa*=2%), Antiepileptic (*Pa*=61.9%), sodium / bile acid co-transporter inhibitor (Pa=57.1%), etc. from these activities we notice that *Alpha* 7 nicotinic receptor agonist with *Pa*= 0.932 may be very useful in experimental study. Compound **4e** may be never tested against all these targets. It was observed that cyclopenta[*d*]pyrimidinones have high probability at *Pa* = 93.2%, of Alpha 7 nicotinic receptor agonist. This activity can be applied on a large scale in vitro.



38 Substructure descriptors; 1 new. 11 Possible Activities at *Pa* > 0.500

Pa	***Pi***	***for Activity***
0.932	0.002	Alpha7 nicotinic receptor agonist
0.652	0.026	Protein kinase (CK1) inhibitor
0.619	0.021	Antiepileptic
0.571	0.003	Sodium/bile acid co-transporter inhibitor
0.587	0.037	Lipolytic
0.573	0.054	Proliferative diseases treatment
0.548	0.037	CYP2C19 inducer
0.515	0.036	Anticonvulsant
0.542	0.078	Antianemic
0.558	0.135	Depression
0.538	0.139	Testosterone 17beta-dehydrogenase (NADP+) inhibitor

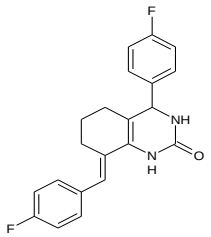
Fig. 5: Structural formula and biological activity spectrum predicted for compound **4e** (known activity given in bold).

Predicted Biological Activity Spectrum of hexahydro-quinazolinone.

Quinazolone and their derivatives are building block for approximately 150 naturally occurring alkaloids and are now

known for a wide range of biological properties including hypnotic, sedative, analgesic, anticonvulsant, antibacterial, ant-diabetic, anti-inflammatory, anti-tumor and several other useful and interesting properties. In addition, some derivatives are calcium antagonists and share the common property of interfering with the influx of extracellular calcium via the calcium L channel. Recently quinozolone chemistry has got new direction due to some resemblance with folic acid .So keeping this fact in mind that quinazolone as very important moiety.

The biological activity spectrum for ((8*E*)-8-(4-fluorobenzylidene)-4-(4-fluorophenyl)-3,4,5,6,7,8-hexahydro-quinazolin-2(1*H*)-one **5g** (Figure 6). Figure 6 revealed 11 possible activities at *Pa* > 50%. We have a probable action on several molecular targets, such as Protein kinase (*CK1*) inhibitor (*Pa* = 96.8%). *Alpha* 7 nicotinic receptor agonist (*Pa*= 91.8%), Ankylosing spondylitis treatment (*Pa* = 68.1%), Apoptosis agonist (*Pa* = 59.8%), Proliferative diseases treatment (*Pa*=59.3%), FMO1 substrate (*Pa* = 58.6%), Sodium/bile acid co-transporter inhibitor (*Pa* = 51.5%), etc. we got a very important targets the can be confirmed with experiments especially the target of Protein kinase (*CK1*) inhibitor which has high probability at (*Pa*=0.964) and Alpha 7 nicotinic receptor agonist at (*Pa*= 0.918).



36 Substructure descriptors; 1 new. 11 Possible activities at *Pa* > 50%

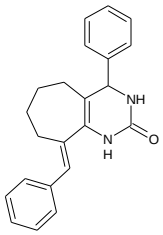
Pa	***Pi***	***for Activity:***
0.964	0.001	Protein kinase (CK1) inhibitor
0.918	0.002	Alpha7 nicotinic receptor agonist
0.681	0.060	Ankylosing spondylitis treatment
0.598	0.012	Apoptosis agonist
0.593	0.046	Proliferative diseases treatment
0.586	0.065	FMO1 substrate
0.515	0.003	Sodium/bile acid co-transporter inhibitor
0.605	0.106	Depression
0.545	0.051	Acute neurologic disorders treatment
0.532	0.046	Adenomatous polyposis treatment
0.508	0.056	G-Quadruplex telomerase inhibitor

Fig. 6. Structural formula and biological activity spectrum predicted for compound **4g**.

Predicted Biological Activity Spectrum of Cyclohepta-[*d*]pyrimidinone.

It was found that bis(arylmethylene) cyloheptanone possess antifertility and hypocholesterolemic and Thiazolone ring fused to a cycloheptene systems possess anticancer activity. The prediction activity of (9*E*)-9-benzylidene-4-phenyl-1,3,4,5,6,7,8,9-octahydro-2*H*-cyclohepta[*d*]pyrimidin -2-one **6a** (Figure 7), afforded 20 Possible activities at *Pa* > 50% including, *Alpha*-7 nicotinic receptor agonist at (93.6%) Testosterone 17 betadehydrogenase (*NADP*$^+$)

Inhibitor (*Pa*=75.5%), Tumour necrosis factor agonist at (*Pa*=54.8%),
Testosterone 17betadehydrogenase (*NADP*+) inhibitor (Pa =75.5%), Tumour necrosis factor agonist (*Pa*=54.8), Acetylcholine nicotinic agonist at (*Pa*=50.3%), Ankylosing spondylitis treatment at (*Pa*=59.3), Insulin growth factor agonist (*Pa* = 52.4%), Steroid 21 – monooxy-genase inhibitor at (*Pa*= 50%). Many important targets were observed with cycloheptene systems that will be effective if they applied in vivo and vitro. But *Alpha 7* nicotinic receptor agonist still has higher probability of prediction (*Pa*=0.936).



32 Substructure descriptors; 1 new.20 Possible activities at ***Pa > 50%***

Pa	***Pi***	***for Activity:***
0.936	0.002	Alpha-7 nicotinic receptor agonist
0.755	0.048	Testosterone 17betadehydrogenase (NADP +) inhibitor
0.711	0.013	Lipolytic
0.694	0.014	CYP2C19 inducer
0.691	0.014	Proliferative diseases treatment
0.592	0.002	Sodium/bile acid cotransporter inhibitor
0.596	0.026	Antiepileptic
0.630	0.091	Depression
0.548	0.024	Tumour necrosis factor agonist
0.557	0.051	Ligase inhibitor
0.585	0.081	Membrane integrity agonist
0.503	0.007	Acetylcholine nicotinic agonist
0.593	0.101	Ankylosing spondylitis treatment
0.540	0.050	Pterin deaminase inhibitor
0.595	0.106	Sialagogue
0.524	0.051	Insulin growth factor agonist
0.524	0.051	Insulin like growth factor 1 agonist
0.516	0.051	Biotinidase inhibitor
0.563	0.128	Transferase inhibitor
0.500	0.171	Steroid 21-monooxygenase inhibitor

Fig.7 Structural formula and biological activity spectrum predicted for compound 6a.

4 Conclusion

CAN (10 mol%) is an efficient catalyst for synthesis of arylidine heterobicyclic pyrimidinones the mechanism proceed through formation of arylidene –urea followed by cyclocondensation to afford the demanded compounds .this mechanism show the BrØnsted acidity of CAN when it used under solvent free conditions. Prediction the biological activity with PASS showed high probability of Alpha-7 nicotinic receptor agonist in all compounds under study. Cycloheptene systems showed some important targets such as Insulin growth factor agonist, Acetylcholine nicotinic agonist and Tumour necrosis factor agonist.

4.1 Experimental

All IR spectra were recorded on a Perkin-Elmer Spectrum One spectrophotometer. ^{1}H and ^{13}C-NMR spectra were recorded on a GEMINI-200 MHz "NMR" spectrometer, and shifts are given in ppm downfield from TMS as an internal standard. . MS or HRMS were measured by JEOL JMS-D300 or JEOL JMS-HX110 spectrometer. TLC analyses were performed on E. Merck silica gel 60F glass plates. Kieselgel 60F254. Melting points were determined using an XT-4 apparatus and were uncorrected. Reagents were used without further purifications. Dry conditions were not required.

4.2 General procedure

*Synthesis of benzylidine heterobicyclic products (Table 2-4) compounds **4, 5** and **6:*** Cycloalkanone (**1a-c**, 10 mmol), urea or thiourea (15 mmol), aromatic aldehyde (10 mmol) and CAN (1 mmol) were mixed in a flask (solvent free). The reaction mixture was heated at 90-100 ^{o}C with stirring for 2 min. until the mixture became homogenous. The reaction mixture was left to stand at room temperature with stirring until it solidified. The solid was washed with ice cold water then dried and filtered to give asufficient pure compounds **4,5,6**. Further purification with (Chloroform: Petrolium ether) 1:2 give more pure compounds of purities; 99% (TLC). Analytical results (IR, ^{1}H, ^{13}C-NMR) of known products were identical to those reported in literature. [27,35]

*(7E)-7-benzylidene-4-phenyl-1,3,4,5,6,7-hexahydro-2H-cyclo-penta[d] pyrimidin-2-one **4a**.*

Pale Yellow powder (2.71g, 90%); m. p 234-236^{o}C (lit[27]. m. p. 236-239 ^{o}C); $C_{20}H_{18}N_2O$, found: C, 75.2; H, 5.98; N, 9.2; O, 5.25. requires; C, 75.44; H, 6.00; N, 9.26; O, 5.29. R_f($CHCl_3$:Pet.ether 1:2) 0.35; IR (*KBr*): 3435, 3348, 3030, 2928, 2862, 1657, 1456, 1877, 1224, 1158 cm^{-1}; ^{1}H-NMR(200 MHz, DMSO-d_6): δ_{ppm}; 2,00-2.68 (4H,m,aliph.), 4.40(1H,d,CH), 5.50(1H,S,CH), 6.70(1H,S,NH), 6.90-6.99 (5H,m,arom.), 7.23- 7.31 (5H,m,arom.), 8.79(1H,S,NH); ^{13}C-NMR (200 MHz, DMSO-d_6): δ_{ppm} = 154.7, 142.5, 134.32, 128.4, 122.8, 112.3, 65.9, 24.5; MS(EI, 70 ev): m/z (%)=302 $[M+H]^+$, 226, 150.

*(7E)-7-(2-methoxybenzylidene)-4-(2-methoxyphenyl)-1,3,4,5,6,7-hexahydro-2H-cyclopenta[d] pyrimidin-2-one **4b**.* Yellow powder (1.81g, 50%); m. p. 237-239 ^{o}C (lit.Mp 236-239 ^{o}C [27]); $C_{20}H_{18}N_2O$; found: C, 75.2; H,5.98; N,9.2; O,5.25. requires; C, 75.44; H, 6.00; N, 9.26; O,5.29. R_f ($CHCl_3$:Pet. ether 1:2) 0.35; IR (*KBr*): 3435, 3348, 3030, 2928, 2862, 1657, 1456, 1877, 1224, 1158cm^{-1}; ^{1}H-NMR(200 MHz, DMSO-d_6): δ_{ppm}, 2,00-2.68 (4H,m,aliph), 4.40(1H,d,CH), 5.5 (1H,S,CH), 6.7(1H,S,NH), 8.79(1H,S,NH); ^{13}C-NMR (200 MHz, DMSO-d_6): δ_{ppm}, 159.7, 150, 142.5, 130.32, 126.4, 120.8, 114.3, 58.9, 27; MS(EI, 70 ev):m/z (%)=362 $[M+H]^+$.

(7E)-7-(3-nitrobenzylidene)-4-(3-nitrophenyl)-1,3,4,5,6,7-hexahydro-2H-cyclopenta[d]pyrimidin-2-one **4c**.

Pale brown (3.6g, 92%); m. p. 234-236 ^{o}C (lit[27]. 235-239 ^{o}C); $C_{20}H_{16}N_4O_5$; found: C, 61.1; H,4.0; N,14.1; O,20.25. requires; C, 61.22; H, 4.11; N, 14.28; O,20.39. R_f ($CHCl_3$:Pet.ether 1:2)=0.73; IR (*KBr*): 3445, 3350, 3050, 2978, 1684, 1484, 1224, 1158cm^{-1}; ^{1}H-NMR(200 MHz, DMSO-d_6): δ_{ppm} = 1.60-2.40 (4H,m,aliph.), 4.60(1H,d,CH), 5.6(1H,S,CH), 6.60(1H,S, NH), 8.90(1H,S,NH); ^{13}C-NMR (200 MHz,DMSO-d_6): δ_{ppm}, 148.7, 145, 142.5, 139.42, 136.4, 130, 120, 55, 29; MS(EI, 70 ev): m/z (%) = 392 $[M+H]^+$.

(7E)-7-(2-nitrobenzylidene)-4-(2-nitrophenyl)-1,3,4,5,6,7-hexah ydro-2H-cyclopenta[d]pyrimidin-2-one **4d**.

Yellow powder (2.31g, 59%); m. p. 203 ^{o}C (lit. m. p. not reported[35]); $C_{20}H_{16}N_4O_5$; found: C, 61.12; H,4.05; N,14.13; O,20.28. requires; C, 61.22; H, 4.11; N, 14.28; O,20.39] R_f ($CHCl_3$:Pet.ether 1:2) 0.45; IR (*KBr*): 3455, 3348, 3050, 2990, 1679, 1489,, 1240, 1160 cm^{-1}; ^{1}H-NMR(200 MHz, DMSO-d_6): δ_{ppm}, 1.60-2.40 (4H,m,aliph), 4.60(1H, d, CH), 6.20(1H, S, CH), 6.90-7.50(8H,m,arm.), 6.70(1H,S,NH), 8.90(1H,S, NH);; MS(EI, 70 ev):m/z (%)=392 $[M+H]^+$.

(7E)-7-(4-bromobenzylidene)-4-(4-bromophenyl)-1,3,4,5,6,7-hexahydro-2H-cyclopenta[d]pyrimidin-2-one **4e**.

yYellow powder (3.78g, 82%); m. p 225 ^{o}C, $C_{20}H_{16}Br_2N_2O$; found: C, 52.12; H,3.32; Br,34.52; N,6.02; O,3.28. requires; C, 52.20; H, 3.5; Br,34.73; N, 6.09; O,3.48] R_f($CHCl_3$:Pet.ether 1:2)0.82; IR (*KBr*): 3423, 3315, 3030, 2982, 1693, 1490,, 1240, 1160, 750cm^{-1}; ^{1}H-NMR(200 MHz, DMSO-*d6*): δ; 2.20-2.60(4H,m,aliph.), 4.7(1H,d,CH), 5.90 (1H,S,CH), 6.70-7.30(8H,m,arom.), 6.50(1H,S,NH), 8.50(1H,S,NH); MS(EI, 70 ev):m/z (%) = 460 $[M+H]^+$.

(7E)-4-(2-furyl)-7-(2-furylmethylene)-1,3,4,5,6,7-hexahydro-2H-cyclopenta[d]pyrimidin-2-one **4f**.

Red powder (2.62g , 93%); m. p 225 ^{o}C; $C_{16}H_{14}N_2O_3$; found: C, 52.12; H,3.32; Br,34.52; N,6.02; O,3.28 requires; C, 68.07; H, 5.00; N, 9.92; O,17.00] R_f($CHCl_3$:Pet.ether

1:2)0.93; IR (*KBr*): 3356, 3242, 2994, 1679, 1520,, 1240, 1160, 750cm^{-1}; ^{1}H-NMR(200 MHz, DMSO-d_6): δ; 1.80-2.30 (4H,m,aliph), 4.60(1H,d,CH), 6.20(1H,S,CH), 6.77-6.90 (6H,m,CH_{furyl}), 6.50(1H,S,NH), 8.50(1H,S,NH);; MS(EI, 70 ev):m/z (%)=282 $[M+H]^+$.

(7E)-7-benzylidene-4-phenyl-1,3,4,5,6,7-hexahydro-2H-cyclopenta[d]pyrimidine-2-thione **4g**.

Yellow powder (2.03g ,64%); m. p. 218-220 ºC (lit[27]. m. p 219-223ºC), $C_{20}H_{18}N_2S$; found: C, 75.12; H,5.42; ; N, 6.00; S,10.00. requires; C, 75.44; H, 5.70; N, 6.09; S,10.07] R_f ($CHCl_3$: Pet.ether 1:2)=0.82; IR (*KBr*): 3448, 3365, 3030, 2982, 1689, 1490,, 1240, 1170 cm^{-1}; ^{1}H-NMR(200 MHz, DMSO-d_6): δ_{ppm}, 2.10-2.0 (4H,m,aliph), 4.70(1H,d,CH), 5.90(1H,S,CH), 6.70-7.40(10H,m,arm), 6.60(1H,S,NH), 8.40(1H,S,NH); MS(EI, 70 ev):m/z (%)=318 $[M+H]^+$.

(7E)-7-(2-methoxybenzylidene)-4-(2-methoxyphenyl)-1,3,4, 5,6,7-hexahydro-2H-cyclopenta[d]pyrimidine-2-thione **4h**. Yellow powder (2.07g , 55%); m. p 205-207ºC; $C_{22}H_{22}N_2O_2S$; found: C, 69.72; H,5.62; ; N,7.20;O,8.15 S,8.30 .requires; C, 69.81; H, 5.86; N, 7.40; O,8.45; S,8.47] R_f ($CHCl_3$:Pet.ether 1:2)=0.82; IR (*KBr*): 3450, 3347, 3040, 2993, 1664, 1456, 1224, 1158 cm^{-1}; ^{1}H-NMR(200 MHz, DMSO-d_6): δ_{ppm}, 2.00-2.40 (4H,m,aliph.), 3.80(6H,S,CH_3), 4.50(1H,d,CH), 5.80(1H,S,CH), 6.90-7.60(8H,m,arom.), 6.60(1H,S,NH), 8.40(1H,S,NH);; MS(EI, 70 ev): m/z (%) =378 $[M+H]^+$.

(E)-7-(2-(dimethylamino)benzylidene)-4-(2-(dimethylamino-)phenyl)-3,4,6,7-tetrahydro-1H-cyclopenta[d]pyrimidine-2-(5H)thione **4i**.

Green crystal (2.02g, 50%); m. p 202-204 ºC; $C_{24}H_{28}N_4S$, found: C, 71.12; H,6.62; N,13.70; S,7.85. requires; C, 71.25; H, 6.98; N, 13.85; S,7.93. R_f ($CHCl_3$:Pet.ether 1:2) = 0.54; ν_{max} (*KBr*) 3420, 3247, 2926, 1599, 1522, 1355, 1158 cm^{-1}; ^{1}H-NMR (200 MHz, DMSO-d_6) : δ_{ppm}, 1.8-2.3 (4H,m,aliph.), 3.20(6H,S,CH_3), 4.30(1H,d,CH), 5.70(1H,S,CH), 6.90-7.70(8H,m, arom.), 6.70(1H,S,NH), 9.60(1H,S,NH);; MS(EI, 70 ev): m/z (%) = 404 $[M+H]^+$.

(7E)-7-(3-nitrobenzylidene)-4-(3-nitrophenyl)-1,3,4,5,6,7-hexah ydro-2H-cyclopenta[d]pyrimidine-2-thione **4j**.

Yellow powder (3.46g, 85%); m. p 213-214 ºC· $C_{20}H_{16}N_4O_4S$; found; C, 58.75; H, 3.84;N,13.70; S,7.72. Requires C, 58.81; H, 3.95; N, 13.72; O, 15.67; S, 7.85. R_f ($CHCl_3$:Pet.ether 1:2) = 0.32; ν_{max} (*KBr*) 3450, 3257, 2966, 1589, 1542,, 1355, 1149 cm^{-1}; ^{1}H-NMR (200 MHz, DMSO-d_6) 1.90-2.30(4H,m,aliph), 4.40(1H,d,CH), 5.80(1H, S, CH), 6.90-7.70(8H,m,arom.), 6.80(1H,S,NH), 9.80(1H,S,NH); MS(EI, 70 ev):m/z (%) = 408$[M+H]^+$.

(7E)-4-(2-furyl)-7-(2-furylmethylene)-1,3,4,5,6,7-hexahydro-2H-cyclopenta[d]pyrimidine-2-thione **4k**.

Yellow powder (1.78g, 60%); m. p 265-267 ºC; $C_{16}H_{14}N_2O_2S$; found: C, 64.39; H,4.71; N,9.34; O, 10.69; S,10.72. requires; C, 64.41; H, 4.73; N, 9.39 ;O, 10.72; S,10.75] R_f ($CHCl_3$:Pet.ether 1:2)= 0.64; ν_{max} (*KBr*) 3390, 3257, 3020, 2975, 1586, 1542, 1355, 1149 cm^{-1}; 1HNMR(200 MHz, DMSO-d6):δ= 2.0-2.3 (4H,m,aliph), 4.5 (1H,d,CH), 5.7 (1H,S,CH), 6.9-7.7 (6H,m,arom.), 6.6 (1H,S,NH), 8.7 (1H, S,NH);; MS(EI, 70 ev): m/z (%)=298 $[M+H]^+$.

(8E)-8-benzylidene-4-phenyl-3,4,5,6,7,8-hexahydro-quinazolin-2(1H)-one ***5a***.

Yellow powder (2.84g, 90%); m. p. 196-198 ºC; $C_{21}H_{20}N_2O$ found: C, 79.6; H,6.34; N,8.9; O,5.1. requires; C, 79.72; H, 6.37; N, 8.85; O,5.06] R_f ($CHCl_3$:Pet.ether 1:2)=0.84; IR (*KBr*): 3378, 3248, 3043, 2933, 2862, 1669, 1467, 1377, 1256, 1145cm^{-1}; ^{1}H-NMR(200 MHz, DMSO-d_6):δ_{ppm} 2.10-2.70(6H,m,aliph.), 4.30(1H,d,CH), 5.60(1H,S,CH), 6.70(1H, S,NH), 8.79(1H,S,NH); ^{13}C-NMR (200 MHz, DMSO-d_6):δ_{ppm},154.7, 142.5, 134.32, 128.4, 122.8, 112.3, 65.9, 24.5; MS(EI, 70 ev):m/z (%)=316 $[M+H]^+$, 240, 164, 96.

(E)-8-(2-methoxybenzylidene)-4-(2-methoxyphenyl)-3,4,5,6, 7,8-hexahydroquinazolin-2(1H)-one **5b**.

Yellow powder (3.45g, 92%); m. p 200-202 ºC; $C_{23}H_{24}N_2O_3$, found: C, 73.20; H,6.24; N,7.35; O,12.64. requires; C, 73.38; H, 6.43; N, 7.44; O,12.75. R_f ($CHCl_3$:Pet.ether 1:2)=0.92; IR (*KBr*): 3369, 3245, 3037, 2985, 2862, 1678, 1467, 1387, 1237, 1145 cm^{-1}; ^{1}H-NMR(200 MHz, DMSO-d_6):δ_{ppm}, 1.80-2.30(6H,m,aliph.), 4.50(1H,d,CH), 5.70(1H,S,CH),6.90-7.50(8H,m,arom.), 6.80(1H,S,NH), 8.85(1H,S,NH); ^{13}C-NMR (200 MHz,DMSO-d_6):δ_{ppm}, 154.7,142.5, 134.32, 128.4, 122.8, 112.3, 65.9, 24.5; MS(EI, 70 ev):m/z (%)=376 $[M+H]^+$.

(E)-8-(4-methoxybenzylidene)-4-(4-methoxyphenyl)-3,4,5,6,7,8-hexahydroquinazolin-2(1H)-one **5c**.

Red crystals (2.18g, 58%); m. p., 204-205 ºC. $C_{23}H_{24}N_2O_3$; found: C, 73.25; H, 6.33; N, 7.39; O, 12.68. requires; C, 73.38; H, 6.43; N, 7.44; O,12.75] R_f ($CHCl_3$:Pet.ether 1:2)=0.92; IR (*KBr*): 3412, 3318, 3050, 2960, 2862, 1669, 1467, 1377, 1256, 1145 cm^{-1}; ^{1}H-NMR(200 MHz,DMSO-d6); δ_{ppm}, 20-2.60(6H,m,aliph), 4.40(1H,d,CH), 5.50(1H,S,CH), 6.70(1H,S, NH), 8.79(1H,S,NH); ^{13}C-NMR (200 MHz,DMSO-d_6): δ_{ppm}, 154.7, 142.5, 134.32, 128.4, 122.8, 112.3, 65.9, 24.5; MS(EI, 70 ev):m/z (%)=376 $[M+H]^+$.

(8E)-8-(4-chlorobenzylidene)-4-(4-chlorophenyl)-3,4,5,6,7,8-hexahydroquinazolin-2(1H)-one **5d**.

Pale yellow crystals (2.18g, 80%); m. p. 204-205 ºC; $C_{21}H_{18}Cl_2N_2O$, found: C, 65.25; H, 4.65; Cl, 18.2; N, 7.11; O, 4.00. requires; C, 65.46; H, 4.71; Cl,18.4; N, 7.27; O,4.15] R_f ($CHCl_3$:Pet.ether 1:2)=0.64; IR (*KBr*): 3314, 3246, 3060, 2980, 2862, 1687, 1448, 1369, 1256, 1153cm^{-1}; ^{1}H-NMR(200 MHz, DMSO-d_6):δ= 2.10-2.70(6H,m,aliph.), 4.60(1H,d,CH), 5.60(1H,S,CH), 6.40(1H,S,NH), 6.60-7.40(8H,m,arm); 8.79(1H,S,NH); MS(EI, 70 ev):m/z

(%)=385 $[M+H]^+$.

(8E)-8-(3-nitrobenzylidene)-4-(3-nitrophenyl)-3,4,5,6,7,8-hexahydroquinazolin-2(1H)-one **5e** .

Yellow crystals (3.49g, 86%); m. p. 205-207 °C; $C_{21}H_{18}N_4O_5$, found: C, 61.98; H, 4.25; N, 13.54; O, 19.54. requires; C, 62.06; H, 4.46; C; N, 13.79; O,19.68] R_f ($CHCl_3$:Pet.ether 1:2)=0.73; IR (*KBr*): 3435, 3315, 3046, 2990, 2885, 1690, 1456, 1336, 1242, 1165 cm^{-1}; ^{1}H-NMR(200 MHz, DMSO-d_6) : δ_{ppm} 2.20-2.70 (6H,m,aliph.), 4.50(1H,d,CH), 5.40(1H,S, CH), 6.60(1H,S,NH), 6.80-7.50(8H,m,arom.); 8.79 (1H,S,NH); MS(EI, 70 ev):m/z (%)=406 $[M+H]^+$.

(8E)-8-(2-nitrobenzylidene)-4-(2-nitrophenyl)-3,4,5,6,7,8-hexahydroquinazolin-2(1H)-one **5f**.

Yellow crystals (2.23g, 55%); Mp 205-207 °C; $C_{21}H_{18}N_4O_5$ found: C, 62.00; H,4.23; N,13.58; O,19.46 . requires; C, 62.06; H, 4.46; N, 13.79; O,19.68] R_f ($CHCl_3$:Pet.ether 1:2)=0.53; IR (*KBr*): 3515, 3346, 3056, 2975, 2896, 1687, 1512, 1423, 1235, 1146cm^{-1}; ^{1}H-NMR(200 MHz, DMSO-d_6):δ_{ppm}, 2.00-2.40 (6H,m,aliph.), 4.40(1H,d,CH), 5.50(1H,S, CH), 6.40(1H,S,NH),6.60-7.20(8H,m,arm); 9.11(1H,S,NH); MS(EI, 70 ev):m/z (%)=406 $[M+H]^+$.

(8E)-8-(4-fluorobenzylidene)-4-(4-fluorophenyl)-3,4,5,6,7,8-hexahydroquinazolin-2(1H)-one **5g**.

Yellow powder (2.23g, 60%); m. p. 205-207°C; $C_{21}H_{18}F_2N_2O$, found: C, 71.26; H, 5.01; F, 10.64; N, 7.73; O, 4.35. requires; C, 71.58; H, 5.15; F,10.78; N, 7.95; O,4.54] Rf ($CHCl_3$:Pet.ether 1:2)=0.53; IR (*KBr*): 3445, 3348, 2929, 2867, 1657, 1456, 1377, 1224, 1157cm^{-1}; ^{1}H-NMR(200 MHz, DMSO-d_6):δ_{ppm}, 1.50-2.80(6H,m,aliph.), 4.66(1H,d, CH), 5.73(1H,S,CH), 6.70(1H, S, NH), 7.00-7.50(8H,m,arom.); 10.22(1H,S,NH); MS(EI, 70 ev) :m/z (%)=352 $[M+H]^+$.

(8E)-4-(2-furyl)-8-(2-furylmethylene)-3,4,5,6,7,8-hexahydro quinazolin-2(1H)-one **5h**.

Brownish red powder (2.33g, 79%); m. p. 205-207 °C; $C_{17}H_{16}N_2O_3$, found: C, 68.65; H, 5.1; N, 9.35; O, 16.01. requires; C,68.91; H,5.44; N,9.45; O,16.20] R_f ($CHCl_3$:Pet.ether 1:2) = 0.49; IR (*KBr*): 3390, 3186, 2931, 1687, 1597, 1485, 1235, 1134 cm^{-1}; ^{1}H-NMR(200 MHz, DMSO-d_6): δ_{ppm}, 1.50-2.80(6H,m,aliph.), 4.57(1H,d,CH), 5.64(1H,S,CH), 6.60(1H,S,NH), 6.90-7.40(6H,m,furyl); 9.20(1H,S,NH); MS(EI, 70 ev):m/z (%)=296 $[M+H]^+$.

(E)-8-benzylidene-4-phenyl-3,4,5,6,7,8-hexahydroquinazolin-2(1H)-thione **5i**.

Pale Yellow powder (2.88g, 87%); m. p. 196-197°C; $C_{21}H_{20}N_2S$, found: C, 79.6; H, 6.06; N, 8.90; S, 5.10. requires; C, 75.87; H, 6.06; N, 8.43; S,9.64] *Rf* ($CHCl_3$:Pet.ether 1:2)=0.87; IR (*KBr*): 3419, 3235, 3080, 2852, 1684, 1434, 1276, 1145 cm^{-1}; ^{1}H-NMR(200 MHz, DMSO-d_6): δ_{ppm}, 1.20-1.70(6H,m,aliph.), 4.65(1H,d,CH), 5.10(1H,S,CH),7.02(1H, S,NH), 7.15-7.36(10H,m,arm), 9.10(1H,S,NH); ^{13}C-NMR (200 MHz,DMSO-d_6): δ_{ppm}, 172, 142.5, 134.32, 128.4, 124.8, 115.3, 64, 23; MS(EI, 70 ev):m/z (%)=332 $[M+H]^+$, 256, 180, 168.

(E)-8-(2-methoxybenzylidene)-4-(2-methoxyphenyl)-3,4,5,6,7, 8 -hexahydroquinazolin-2(1H)-thione **5j**.

Yellow powder (2.88g, 98%); m. p. 196-197 °C; $C_{23}H_{24}N_2O_2S$, found: C, 79.6; H, 6.06; N,8.9; S,8.11. requires; C, 70.38; H, 6.16; N, 7.14; O,8.15; S,8.17] R_f ($CHCl_3$:Pet.ether 1:2) = 0.73; IR (*KBr*): 3435, 3233, 3070, 2934, 1674, 1454, 1256, 1165cm^{-1}; ^{1}H-NMR(200 MHz, DMSO-d_6):δ_{ppm}, 1.20-1.70 (6H,m,aliph.), 4.65(1H,d,CH), 5.10(1H,S,CH), 7.02(1H,S, NH),7.15-7.36(10H,m,arom.), 9.10(1H,S,NH); MS(EI, 70 ev):m/z (%)=392 $[M+H]^+$.

(E)-8-(4-methoxybenzylidene)-4-(4-methoxyphenyl)-3,4,5,6,7,8-hexahydroquinazolin-2(1H)-thione **5k**.

Yellow powder (2.35g, 60%); m. p. 184-185 °C (lit. mp 185 °C[27]); $C_{23}H_{24}N_2O_2S$, found: C, 79.5; H, 6.00; N, 8.86; S, 8.14. requires; C, 70.38; H, 6.16; N, 7.14; O,8.15; S,8.17] Rf ($CHCl_3$:Pet.ether 1:2)=0.73; IR (*KBr*): 3423, 3215, 3054, 2918, 1650, 1462, 1268, 1165cm^{-1}; ^{1}H-NMR(200 MHz, DMSO-d_6): δ_{ppm} 1.40-1.80(6H,m,aliph.), 4.70(1H,d,CH), 5.30(1H,S,CH),7.02(1H,S,NH),7.20-7.50(10H,m,arom.), 9.30 (1H,S,NH); MS(EI, 70 ev):m/z (%)=392 $[M+H]^+$.

(E)-8-(4-chlorobenzylidene)-4-(4-chlorophenyl)-3,4,5,6,7,8-hexahydroquinazolin-2(1H)-thione **5l**.

Yellow powder (2.35g, 60%); Mp 217-219 °C; $C_{21}H_{18}Cl_2N_2S$; found: C, 79.5; H,6.00; N,8.86; S,8.14. requires; C, 62.84; H, 4.52; Cl,17.67; N, 6.98; S,7.99] Rf ($CHCl_3$:Pet.ether 1:2)=0.83; IR (*KBr*): 3449, 3267, 3033, 2929, 1622, 1525, 1462, 1284, 1184 cm^{-1}; ^{1}H-NMR(200 MHz, DMSO-d_6): δ_{ppm} ,1.40-2.70(6H,m,aliph.), 4.58(1H,d,CH), 6.30(1H,S, CH), 6.8 (1H,S,NH),7.10-7.40(8H,m,arom), 8.67(1H,S,NH); MS(EI, 70 ev):m/z (%)=401 $[M+H]^+$.

(8E)-8-(3-nitrobenzylidene)-4-(3-nitrophenyl)-3,4,5,6,7,8-hexahydroquinazolin-2(1H)-thione **5m**.

Yellow powder (2.35g, 85%); m. p. 102-104 °C; $C_{21}H_{18}N_4O_4S$, found: C, 59.60; H, 4.11; N, 13.06; O, 15.00; S, 7.36. Requires; C, 59.70; H, 4.29; N, 13.26; O, 15.15; S, 7.59. R_f ($CHCl_3$:Pet.ether 1:2)=0.65; IR (*KBr*): 3459, 3290, 3049, 2989, 1635, 1545, 1456, 1287, 1192 cm^{-1}; ^{1}H-NMR(200 MHz, DMSO-d_6): δ_{ppm} 1.80-2.90(6H,m,aliph.), 4.40(1H,d, CH), 5.90(1H,S,CH), 6.50(1H,S, NH),7.1-7.4(8H, m, arm), 8.9(1H, S, NH); MS(EI, 70 ev):m/z (%)=422 $[M+H]^+$.

(E)-8-(4-(dimethylamino)benzylidene)-4-(4-(dimethylamino)-phenyl)-3,4,5,6,7,8-tetrahydro quinazoline-2(1H)- thione **5n**.

Yellow powder (2.35g, 85%); m. p. 185-186 °C; $C_{25}H_{30}N_4S$ found: C, 71.57; H, 7.02; N, 13.15; S, 7.57. Requires; C, 71.73; H, 7.22; N, 13.38; S, 7.66. R_f ($CHCl_3$:Pet.ether

1:2)=0.84; IR (*KBr*): 3421, 3216, 2919,2887, 1599, 1525, 1356, 1169cm^{-1}; ^{1}H-NMR (200 MHz, DMSO-d_6):δ_{ppm}, 1.30-1.90(6H,m,aliph.), 4.50(1H,d,CH), 5.6(1H,S,CH), 4.90(1H,S, NH), 6.80-7.50(8H,m,arom), 10.50(1H,S,NH); MS(EI, 70 ev): m/z (%)=418 $[M+H]^+$.

(E)-4-(2-furyl)-8-(furan-2-ylmethylene)-3,4,5,6,7,8-hexa-hydroquinazolin-2(1H)-thione **5o**.

Black crystal (2.35g, 85%); m. p. 157-158^{o}C; $C_{17}H_{16}N_2O_2S$ found: C, 65.15; H, 5.02; N, 8.83; O, 10.15; S, 10.18. requires; C, 65.36; H, 5.16; N, 8.97;O,10.24; S,10.26] Rf ($CHCl_3$:Pet.ether 1:2) = 0.56; IR (*KBr*): 3421, 3216, 2919, 2887, 1599, 1525, 1356, 1169 cm^{-1}; ^{1}H-NMR(200 MHz, DMSO-d_6): δ_{ppm}, 1.50-2.70(6H,m,aliph.), 4.40(1H,d, CH), 6.40 (1H,S,CH), 4.90(1H,S,NH), 6.70-7.40(6H,m,furyl), 9.40 (1H,S,NH); MS(EI, 70 ev):m/z (%)=312 $[M+H]^+$.

(E)-9-benzylidene-4-phenyl-3,4,6,7,8,9-hexahydro-1H-cyclohepta[d]pyrimidin-2(5H)-one **6a**.

Pale yellow powder (1.32g, 40%); m. p. 130-132 ^{o}C; $C_{22}H_{22}N_2O$, found: C, 79.76; H, 6.59; N, 8.23; O,4.32. requires; C, 79.97; H, 6.71; N, 8.48; O,4.84] R_f ($CHCl_3$:Pet.ether 1:2)=0.92; IR (*KBr*): 3432, 3348, 3928, 2852, 1669, 1458, 1375, 1224, 1153 cm^{-1}; ^{1}H-NMR(200 MHz, DMSO-d_6):δ= 1.40-1.90 (8H, m, aliph.), 4.90(1H,d, CH), 6.60(1H,S,CH), 6.20(1H,S,NH),7.00-7.65(10H,m, arom.), 11.20(1H,S,NH); ^{13}C-NMR (200 MHz,DMSO-d_6): δ_{ppm}, 162, 145.5, 134.32, 128.4, 124.8, 115.3, 65, 22; MS(EI, 70 ev):m/z (%)=330 $[M+H]^+$, 256, 180, 168.

(E)-9-(2-hydroxybenzylidene)-4-(2-hydroxyphenyl)-3,4,6,7,8, 9-hexahydro-1H-cyclohepta[d] pyrimidin-2(5H)-one **6b**.

Yellow powder (1.32g, 40%); m. p. 273-275 ^{o}C; $C_{22}H_{22}N_2O_3$, found: C, 79.76; H,6.59; N,8.23; O,4.32. requires; C, 79.97; H, 6.71; N, 8.48; O,4.84] Rf ($CHCl_3$:Pet.ether 1:2)=0.92; IR (*KBr*): 3432, 3348, 3928, 2852, 1669, 1458, 1375, 1224, 1153 cm^{-1}; ^{1}H-NMR(200 MHz, DMSO-*d6*): δ_{ppm}, 1.60-2.00 (8H,m,aliph.), 4.90(1H,d,CH), 5.30(2H,S,OH), 6.12(1H,S, CH), 6.40(1H,S,NH), 7.00-7.65(8H,m,arm), 8.22(1H,S,NH); MS(EI, 70 ev):m/z (%)=362 $[M+H]^+$.

(E)-9-(4-fluorobenzylidene)-4-(4-fluorophenyl)-3,4,6,7,8,9-hexahydro-1H-cyclohepta[d]pyrimidin-2(5H)-one **6c**.

Yellow powder (3.29g, 90%); m.p. 235-237 ^{o}C; $C_{22}H_{20}F_2N_2O$ found: C, 79.76; H, 6.59; N, 8.23; O, 4.32. requires; C72.12; H, 5.50; F,10.37; N, 7.65; O, 4.37] Rf ($CHCl_3$:Pet.ether 1:2) = 0.49; IR (*KBr*): 3447, 3350, 3930, 1652, 1458, 1381, 1160 cm^{-1}; ^{1}H-NMR(200 MHz, DMSO-d_6): δ_{ppm}, 1.3-2.05 (8H,m, aliph), 5.20(1H,d,CH), 6.20(1H,S,NH), 6.50(1H,S,CH), 7.00 -7.85 (8H,m,arm), 8.86(1H,S,NH); MS(EI, 70 ev):m/z (%)=366 $[M+H]^+$.

(E)-9-(4-chlorobenzylidene)-4-(4-chlorophenyl)-3,4,6,7,8,9-hexahydro-1H-cyclohepta[d]pyrimidin-2(5H)-one **6d**.

Yellow powder (3.29g, 75%); Mp 245-247 ^{o}C; $C_{22}H_{22}N_2O_3$, found: C, 79.76; H,6.59; N,8.23; O,4.32. requires; C72.12; H, 5.50; F,10.37; N, 7.65; O, 4.37] Rf ($CHCl_3$:Pet.ether 1:2)=0.49; IR (*KBr*): 3454, 3360, 2937, 1652, 1474, 1389, 1135 cm^{-1}; ^{1}H-NMR(200 MHz, DMSO-d_6): δ_{ppm}, 1.4-2.5(8H, m, aliph.), 5.40(1H,d,CH), 6.70(1H,S,NH), 6.90(1H,S,CH), 7.00-7.7 (8H,m,arm), 9.20(1H,S,NH); MS(EI, 70 ev):m/z (%)=398 $[M+H]^+$.

(E)-9-benzylidene-4-phenyl-3,4,6,7,8,9-hexahydro-1H-cyclo-hepta[d]pyrimidin-2(5H)-thione **6e**.

Yellow powder (3.29g, 80%); m. p. 286-288 ^{o}C ; $C_{22}H_{22}N_2S$; found: C, 79.76; H,6.59; N,8.23; S, 9.25; requires C,76.26; H, 6.40; N, 8.08; S, 9.25] R_f ($CHCl_3$:Pet.ether 1:2)=0.36; IR (*KBr*): 3428, 3260, 2927, 1612, 1474, 1393, 1165 cm^{-1}; ^{1}H-NMR(200 MHz, DMSO-d_6): δ_{ppm}, 1.40-2.50(8H,m,aliph.), 5.20(1H,d,CH), 6.54(1H,S,NH), 6.80(1H,S,CH), 7.20-7.80 (10H,m,arom.), 9.20(1H,S,NH); MS(EI, 70 ev):m/z (%) = 346 $[M+H]^+$.

(E)-9-(2-methoxybenzylidene)-4-(2-methoxyphenyl)-3,4,6,7,8, 9-hexahydro-1H-cyclohepta[d]pyrimidin-2(5H)-thione **6f**.

Yellow powder (1.75g, 45%); m. p., 228-230 ^{o}C; $C_{24}H_{26}N_2O_2S$; found: C, 70.76; H, 6.39; N, 6.65; O, 7.69; S, 7.73. requires C,70.90; H, 6.45; N, 6.89; O,7.87; S, 7.89] R_f ($CHCl_3$: Pet. ether 1:2)=0.55; IR (*KBr*): 3415, 3233, 2934,2850, 1674, 1454, 1243, 1164,1029 cm^{-1}; ^{1}H-NMR(200 MHz, DMSO-d_6) : δ_{ppm}; 1.20-2.20 (8H,m,aliph), 3.90(6H,S, CH_3), 4.40(1H,d,CH), 4.70(1H,S,NH), 6.60(1H,S,CH), 6.90-7.80 (8H,m,arom.), 10.50(1H,S,NH); MS(EI, 70 ev):m/z (%)=406 $[M+H]^+$.

(E)-9-(4-methoxybenzylidene)-4-(4-methoxyphenyl)-3,4,6,7,8, 9-hexahydro-1H-cyclohepta[d]pyrimidin-2(5H)-thione **6g** .

Yellow powder (1.75g, 45%); m.p. 235-237 ^{o}C; $C_{24}H_{26}N_2O_2S$; Found: C, 70.74; H, 6.28; N, 6.63; O, 7.71; S, 7.64. Requires C, 70.90; H, 6.45; N, 6.89; O, 7.87; S, 7.89. R_f($CHCl_3$:Pet.ether 1:2) = 0.55; IR (*KBr*): 3432, 3250, 2965, 2823, 1653, 1474, 1259, 1168,1050 cm^{-1}; ^{1}H-NMR(200 MHz, DMSO-d_6):δ_{ppm}, 1.20-2.20 (8H,m,aliph), 3.80(6H,S,CH_3), 4.20(1H,d,CH), 4.70(1H,S,NH), 6.50(1H,S,CH), 7.10-7.90 (8H,m,arom), 9.40(1H,S,NH); MS(EI, 70 ev):m/z (%) = 406 $[M+H]^+$.

(E)-9-(4-bromobenzylidene)-4-(4-bromophenyl)-3,4,6,7,8,9-hexahydro-1H-cyclohepta[d]pyrimidin-2(5H)-thione 6h .

Yellow powder (1.75g, 45%); Mp 235-237 ^{o}C ; $C_{22}H_{20}Br_2N_2S$; found: C, 52.15; H,3.89; Br, 31.52; N,6.63; S, 6.25, requires C,52.40; H, 4.00; Br, 31.69; N, 5.56; S, 6.36] R_f ($CHCl_3$:Pet.ether 1:2)=0.72; IR (*KBr*): 3365, 3143, 2943, 2850, 1614, 1554, 1474, 1236, 1154,1060 cm^{-1}; ^{1}H-NMR(200 MHz, DMSO-d_6): δ_{ppm}; 1.40-2.50(8H,m,aliph.),

4.20(1H,d, CH), 6.20(1H,S,NH), 6.70(1H,S,CH), 7.10-7.90 (8H,m,arom.), 8.90(1H,S,NH); MS(EI, 70 ev) : m/z (%)=504 $[M+H]^+$.

(E)-9-(2-hydroxybenzylidene)-4-(2-hydroxyphenyl)-3,4,6,7,8, 9-hexahydro-1H-cyclohepta[d]pyrimidin-2(5H)-thione **6i**.

Brown powder (2.49g, 66%); m. p. 223-225 ^oC; $C_{22}H_{22}N_2O_2S$; found: C, 52.15; H, 3.89; Br, 31.52; N, 6.63; S, 6.25. Requires; C, 69.81; H, 5.86; N, 7.40; O, 8.45; S, 8.47. R_f ($CHCl_3$:Pet.ether 1:2)=0.84; IR (*KBr*): 3418, 3265, 2934, 1563, 1465, 1396, 1267, 1146,1070 cm^{-1}; ^{1}H-NMR(200 MHz, DMSO-d_6):δ_{ppm}, 1.60-2.40 (8H,m,aliph.), 4.30(1H,d,CH), 6.20(1H,S,NH), 6.60(1H,S,CH), 6.90-7.50 (8H,m,arom), 8.70(1H,S,NH); MS(EI, 70 ev) : m/z (%)=378$[M+H]^+$.

(E)-9-(4-chlorobenzylidene)-4-(4-chlorophenyl)-3,4,6,7,8,9-hexahydro-1H-cyclohepta[d]pyrimidin-2(5H)-thione 6j .

Yellow powder (2.65g, 64%); m. p. 243-245 ^oC; $C_{22}H_{20}Cl_2N_2S$; found: C, 52.15; H,3.89; Br, 31.52; N,6.63; S, 6.25. requires; C,63.61; H, 4.85; Cl, 17.07; N, 6.74; S, 7.72] R_f ($CHCl_3$:Pet.ether 1:2)=0.72; IR (*KBr*): 3374, 3168, 2915, 1597, 1474, 1354, 1275, 1162,1058 cm^{-1}; ^{1}H-NMR(200 MHz, DMSO-d_6): δ_{ppm}' 1.60-2.70 (8H,m,aliph.), 4.60(1H,d,CH), 6.40(1H,S,NH), 6.80(1H,S,CH), 7.00-8.10 (8H,m,arom.), 9.40(1H,S,NH); MS(EI, 70 ev) :m/z (%) = 415 $[M+H]^+$.

(E)-9-(4-(4-dimethylamino)benzylidene)-4-(4-dimethylamino)-phenyl)-3,4,6,7,8,9-hexahydro-1H-cyclohepta[d]pyrimidin-2(5H)-thione **6k**.

Green crystals (2.38g, 55%); m. p.; 256-257 ^oC; $C_{26}H_{32}N_4S$; found; C, 71.98; H,7.27; N,12.84; S, 7.32. requires; C,72.18; H,7.46; N,12.95; S,7.41] *Rf* ($CHCl_3$: Pet. ether 1:2)=0.55; IR(*KBr*): 3420, 3212, 2918, 2855, 1599,1522, 1355, 1197, 1168,1061 cm^{-1}; ^{1}H-NMR(200 MHz, DMSO-d_6): δ_{ppm}, 1.20-2.10 (8H,m,aliph.), 3.20(12H,S,CH_3), 4.30(1H,d,CH), 4.50(1H,S,NH), 6.40(1H,S,CH), 6.80-7.90 (8H,m,arom.), 11.50(1H,S,NH); MS(EI, 70 ev) :m/z (%)=434$[M+H]^+$.

(E)-9-(3,4-dihydroxybenzylidene)-4-(3,4-dihydroxyphenyl)-3,4,6,7,8,9-hexahydro-1H-cyclohepta[d]pyrimidin-2(5H)-thione **6l** .

Pale yellow powder (2.49g, 86%); m. p. 223-225^oC; $C_{22}H_{22}N_2O_4S$; found: C, 64.12; H,5.23; N,6.67; S, 7.70 . requires; C,64.37; H, 5.40; N, 6.82; O,15.59; S, 7.81] R_f ($CHCl_3$:Pet.ether 1:2) = 0.39; IR (*KBr*): 3359, 3240, 2990, 1615, 1564, 1473, 1328, 1172,1064 cm^{-1}; ^{1}H-NMR(200 MHz, DMSO-d_6); δ_{ppm}, 1.30-2.50 (8H,m,aliph.), 4.20(1H,d,CH), 5.9(1H,S,NH), 6.4(1H,S,CH), 6.7-7.4 (8H,m,arom.), 8.20 (1H,S,NH); MS(EI,70 ev) :m/z (%) = 410 $[M+H]^+$.

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