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DEVELOPMENT AND ANTIMICROBIAL ASSESSMENT OF NOVEL IMINE-BASED -PYRAZOLYL-1)-4,5-DIHYDROTHIAZOLYL-2) THIAZOLIDIN-4-ONE AND-PYRAZOLYL-1)-6H-1,3,4-THIADIAZINYL-2)-2-PHENYLTHIAZOLIDIN-4-ONE COMPOUNDS

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ABSTRACT

An efficient and convenient synthesis of thiazolidinone derivatives have a pyrazolyl, dihydrothiazolyl and thiazol ring was achieved, initially prepared by chalcone (Acetophenone and o-nitro benzaldehyde) on reaction with hydrazine hydrate give cyclized product which on further reaction with thiourea and thiosemicarbazide forms II, cyclized derivatives having Schiff's base, the thioglycolic acid and ZnCl2 in trace convert Schiff's base into final products. The chemical structure of the synthesized derivatives has been established by elemental analysis, FT-IR, 1H NMR, and Mass spectral studies. In vitro antibacterial testing against both gram-positive and gram-negative bacteria has also been conducted on the newly synthesized TZ-4-one and PTZ-4-one derivatives using the serial tube dilution method. The newly prepared derivatives demonstrated noticeable antimicrobial properties.

Keywords: Substituted Chalcone, Thiourea, Thiosemicarbazide, Thioglycolic Acid, Substituted Aromatic Aldehyde, Hydrazine Hydrate

1. INTRODUCTION

The present time is witness to the rapid spread and exponentially growth of highly lethal communicable diseases microorganism [1,2]. The destruction of millions of lives in the past three years due to CORONA virus unsurmountable apart from the fact that the clinical damage it has caused to the individual affect various organs is still not fully analyzed and addressed to. It would take another couple of years to estimate the complete damage to the human body brought about by the virus alone [3,4]. In the wake of such aggravating situation the builder of finding novel drugs [5,6] on the

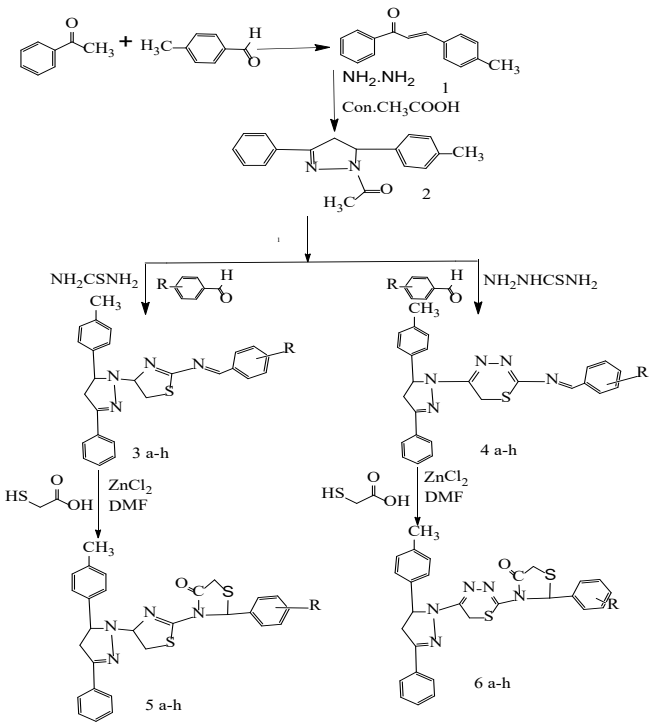
chemist research become all the more intense. Heterocyclic is a class of compounds which has always been the pioneer scaffold addressing the situation [7-13]. These molecules often naturally as well as can be artificially synthesized [14,15]. Amongst one such compound is thiazol ring system which can boast about its presence in some naturally occurring impotent compounds as thiamine vitamin B1. the thiazol ring system is a pharmacologically active molecule manifest various antibacterial [16,17], antibacterial [18,19], anti-fungal [20,21], antiviral [22,23] , anticancer[24,25], antiallergic [26,27], anti-inflammatory [28], antipsychotropic [29], antiarthritic [30] neuroprotective [31], and antidiabetic [32] effects. Its peculiar structure renders Its a formidable scaffold in various commercially available drugs [33].

Another interesting heterocyclic moiety is the pyrazole it is quite popular among chemists/day researchers as it often acts as a key ingredient in the development of drugs, which basically involve the inhibition of protein glycation. These act as antibacterial 1,2 anti-fungal, 3,4, antivirals, anticancer [34], antiallergic [35], anti-inflammatory [36], antipsychotropic [37], antiarthritic [38], neuroprotective [39], and antidiabetic [40,41] effects. The thiazole scaffold is commonly utilized in drug design and is found present in many commercially available drugs. Numerous investigations have focused on the pyrazole moiety because of its wide range of potential microbiological activity. Proteins that are glycation-inhibiting, antiviral, antibacterial, antifungal,anti-tuberculosis, antidepressant, anti-inflammatory, and anticancer [42,43]. we currently describe most relevant preparation and pharmacological properties of pyrazolethiazol heterocyclic derivatives as 2-(substituted-phenyl)-3-(5-(3-(o-NO2-phenyl)-5-phenyl-4,5-dihydro-1H-pyrazolyl-1)-6H-1,3,4-thiadiazin-2-yl)thiazolidin-4-one/2-yl(substituted-phenyl)-3-(4-(3-(2-nitrophenyl)-5-phenyl-4,5-dihydro-1H-pyrazol-1)-4,5-dihydrothiazol-2-yl)thiazolidin-4-one.

Chemistry: The Claisen-Schmidt condensation reaction was used to synthesized chalcone by acetophenone starting 2-nitro benzaldehyde.this α-β unsaturated compound I. which form Dihydropyrazolyl-ethanone.which underwent the condensation of pyrazolyl, by the addition of react with hydrazine hydrate. In the next step thiosemicarbazide/thiourea,substituted aromatic aldehyde substituted pyrazole gives dihydrothiazol-2-amine/thiadiazin-2-amine as schiff base IIIa-h/IVa-h. This imine converted into the cyclized thiazole by the reaction of thioglycolliacidin in trace of ZnCl2. as a (4-(3-(unsubstituted/substituted-phenyl)-5-phenyl-4,5-dihydro-1H-pyrazolyl-1)-4,5-dihydrothiazol-2-yl)-2-phenylthiazolidin-4-one Va-h/ 2-(substituted-phenyl)-3-(5-(3-(2-nitrophenyl)-5-phenyl-4,5-dihydro-1H-pyrazolyl-1)-6H-1,3,4-thiadiazin-2-yl)thiazolidin-4-one VIa-h. The structure of novel synthesized derivatives was determined by their spectral and analytical data (IR, 1HNMR and mass). Tthe characteristic C=O and C=C are 1660 and 1854 cm- for structure I and CH2 for pyrazole ring, C=N band, N-N are 1557,1090 cm- derivatives II, in III/IV derivatives of thiazolyl/thiadiazinyl C=N, C-S-C in the cm-1 region and in the FT-IR spectra of Va-h/VIa-h. The FT-IR spectra of final compounds IVa-h/Va-h. showed the presence of (tert. amide C=O), 710 (C-Cl), in the region cm-1. the 1HNMR compounds of imine proton for CH2 for I and II CH2 substituted pyrazole ring and CH3. whereas in the series of IIIa-h/ IVa-h giving a N=C-H and C-CH2-S ring protons at δ2.78 ppm. and the derivative of Va-h/Va-h were shown the presence 3.55 (s, 2H, S-CH2-C),3.38 (s, 1H, N-CH-R) as a thiazol derivatives. at δ 3.92 ppm. All the newly synthesized derivatives exhibit a good relation between calculated and experimentally.

Experimental Section: The using of the open capillaries approach, the melting points (m.p.) were investigated without any corrections. Precoated TLC plates (Merk, 60F-254) were used to assess the produced compounds' purity and structure. The eluent 5:2hexane/ethyl acetate contains iodine vapor as a visualizing medium. The 1HNMR spectra were recorded at 300 MHz using a Bruker NMR spectrophotometer in CDCl3 and DMSO. TMS was used as the internal standard, and the chemical shift value (δ) was expressed in parts per million (ppm). These tools were employed: The diffuse reflectance method of the Jasco FTIR-470 spectrophotometer (KBr); MS-JEOL SX102 mass spectroscopy using m-nitrobenzyl alcohol (NBA) as the matrix and xenon and argon (6Kv, 10mA) as the FAB gas. Using a twin beam UV spectrophotometer, the sample's UV spectrum was examined.

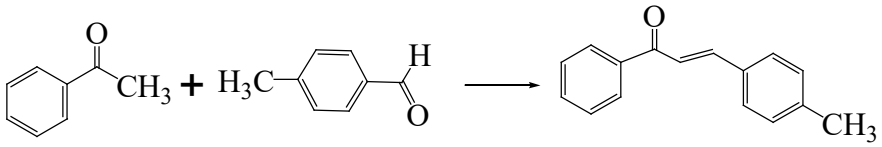
SCHEME-I



1) (E)-1-phenyl-3-p-tolylprop-2-enone-1: In 30 ml

absolute alcohol mixed with 0.1 mole of both p-methylbenzaldehyde, phenolethanone and 30% of aqueous KOH was added than refluxed For 10 hr in a water bath. Using methanol and chloroform, thin-layer chromatography was used to check the progress of the process. the reaction was put into crushed ice and weak HCl was added to acidify it. Chalcone crystallizes as a solid. After that, the ethanol is filtered out and recrystallized.

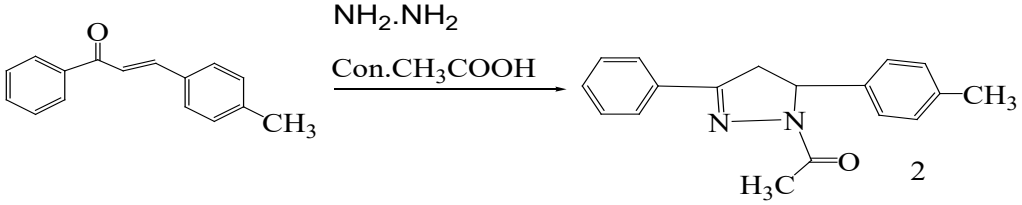
Chemical formula: C16H14O, Mol. Wt.: 222.3, Elemental analysis: C, 86.45; O, 7.20, Yield:67%, melting point:107-108 °C.



2) Synthesis of 1-(3-phenyl-5- p-CH3-phenyl-4,5-dihydropyrazolyl-1) ethanone:

On a water bath, 0.02 moles of the reactants chalcone in 20 milliliters of acetic acid and hydrazine hydrate in 30 milliliters of pure EtOH were refluxed for 8 to 10 hours. Once the reaction is complete. then use low-pressure distillation to concentrate the solution. A solid mass was produced by cooling, and methanol recrystallization was used to purify and dry it.

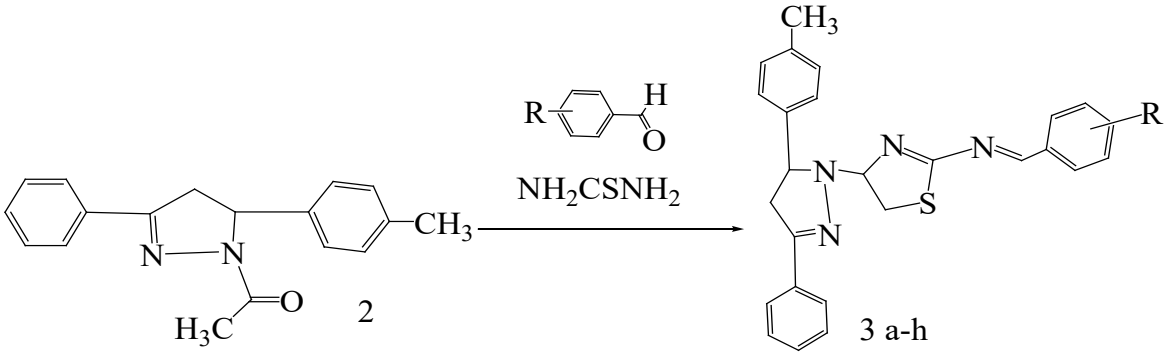
Chemical formula: C18H18N2O, Molecular Weight: 278.3, Yield 72 %; m.p. 111-112 °C.



3) **Synthesis of (E)-N-substituted/substitutedbenzylidene-4-(3-phenyl-5-p-CH3-phenyl -4,5-dihydropyrazolyl-1)-4,5-dihydrothiazol-2-amine:** A 0.1 moles of three reactant (E)-N-benzylidene-4-(3-phenyl-5-p-CH3-phenyl-4,5-dihydropyrazolyl-1)-4,5-dihydrothiazol-2-amine and substituted/substituted aromatic aldehydes, thiourea were mixed with 25 ml of dimethyl carbonate (solvent) and NH4OAc as a catalyst. For 7-8 hours, the reaction was refluxed in a water bath. After the reaction was finished, cold water was used to repeatedly wash the leftover residue and recrystallized in ethanol.

3a.(E)-N-benzylidene-4-(3-phenyl-5-p-CH3-phenyl-4,5-dihydropyrazolyl-1)-4,5-dihydrothiazol-2-amine: Chemical Formula: C26H24N4S,Mol. Wt.: 424.6, Yield 70 %; m.p. 144-145 °C, elemental ana.: C, 73.55; N, 13.20; S, 7.55,found: : C, 73.52; N, 13. 18; S, 7.52, FT- infrared-νmax per cm-KBr: 1634 (C=C, for aro.), 3082(aro.C-H str.), 3093(C-H, stretching-aro.), Hydrogen-1 nuclear magnetic resonance-CDCl3-300 MHz δ in ppm : 6.69-7.87 (m,9H, Ar-H), 6.62(1H,d, Ph-CH=C),6.32(1H, C=CH-toluene), 8.71 (1H, s, replaceable m-hydroxypheny, 3.23 (d,2H, -CH2).

1-(3-phenyl-5-p-CH3-phenyl-4,5-dihydropyrazolyl-1)ethenone, Chemical Formula: C18H18N2O, Mol. Wt.: 278.3,yield:69.45%,melting point:187.5°C, elemental ana.: 77.67; N, 10.06; O, 5.75,found: 77.63; N, 10.02; O, 5.73.



3a.(E)-N-benzylidene-4-(3-phenyl-5-p-CH3-phenyl -4,5-dihydropyrazolyl)-4,5-dihydrothiazol-2-amine, Chemical formula:C26H24N4S,Mol. Wt.: 424.6, elemental ana.: C, 73.55; N, 13.20; S, 7.55,found: C, 73.52; N, 13.18; S, 7.52, infrared-νmax per cm-KBr: 1634 (C=C, for aro.), 3082(aro.C-H str.), 2993(C-H, streching), 1550(C=N),1025(C-S), 1485(N-N), Hydrogen-1 nuclear magnetic resonance-CDCl3-300 MHz δ- in ppm : 6.70-7.10 (m,14H, Ar-H), 4(t,1H,-CH-N-N),3.6(d,2H,CH2-CH-N),4.8(s,1H,N=CH),2.7(t,2H,N-CH-N),2.2(d,2H,-CH2S),1.7(s,3H,-CH3).

3b.(E)-4-((4-(3-phenyl-5-p-CH3-phenyl-4,5-dihydropyrazolyl-1)-4,5-dihydrothiazol-2 ylimino)methyl)phenol, Chemical formula:C26H24N4OS,Mol. Wt.: 440.6, Yield 69 %; m.p. 137.5-138 °C, elemental ana.: C, 70.88; N, 12.72; S, 7.28,found: C, 70.86; N, 12.70; S, 7.25, infrared-νmax per cm-KBr: 1644 (C=C, for aro.), 3080(aro.C-H str.), 2996(C-H, streching), 1555(C=N),1025(C-S), 1480(N-N), 1739(-CO), Hydrogen-1 nuclear magnetic resonance-CDCl3-300 MHz δ- in ppm : : 6.78-7.12 (m,13H, Ar-H), 4.34(t,1H,-CH-N-N),3.43(d,2H,CH2-CH-N),4.76(s,1H,N=CH),2.78(t,2H,N-CH-N),2.29(d,2H,-CH2S),1.72(s,3H,-CH3),5.4(s,1H,-OH).

3c.(E)-N-(4-chlorobenzylidene)-4-(3-phenyl-5-p-CH3-phenyl-4,5-dihydropyrazolyl-1)-4,5-dihydrothiazol-2-amine,Elemental: C26H23ClN4S, Mol. Wt.: 459, Yield 67 %; m.p. 117.5 °C, elemental ana.: C, 68.03; Cl, 7.72; N, 12.21; S, 6.99,found: C, 68.03; Cl, 7.72; N, 12.21; S, 6.99, infrared-νmax per cm-KBr: 1639 (C=C, for aro.), 3087(aro. C-H str.), 2998(C-H, streching), 1552(C=N),1029(C-S), 1480(N-N),657 (C-Cl), Hydrogen-1 nuclear magnetic resonance-CDCl3-300 MHz δ- in ppm : : 6.71-7.15 (m,13H, Ar-H), 4(t,1H,-CH-N-N),3.57(d,2H,CH2-CH-N),4.67(s,1H,N=CH),2.67(t,2H,N-CH-N),2.26(d,2H,-CH2S),1.72(s,3H,-CH3).

3d.(E)-N-(4-nitrobenzylidene)-4-(3-phenyl-5-p-CH3-phenyl-4,5-dihydropyrazolyl-1)-4,5-dihydrothiazol-2-amine,Chemical formula:C26H23N5O2S, Mol. Wt.: 469.6, Yield 63 %; m.p. 129-130 °C, elemental ana.: C, 66.50; N, 14.91; S, 6.83,found: C, 66.48; N, 14.87; S, 6.80, infrared-νmax per cm-KBr: 1639 (C=C, for aro.), 3087(aro. C-H str.), 2996(C-H, streching), 1554(C=N),1027(C-S), 1485(N-N), 1365, 1467(-NO2), Hydrogen-1 nuclear magnetic resonance-CDCl3-300 MHz δ- in ppm : : 6.53-7.18 (m,13H, Ar-H), 4.15 (t,1H,-CH-N-N),3.56(d,2H,CH2-CH-N),4.76(s,1H,N=CH),2.73(t,2H,N-CH-N),2.34(d,2H,-CH2S),1.93(s,3H,-CH3).

3e.(E)-2-((4-(3-phenyl-5-p-CH3-phenyl-4,5-dihydropyrazolyl-1)-4,5-dihydrothiazol-2-ylimino)methyl)phenol, elemental ana.:C26H24N4OS,Mol. Wt.: 440.6, Yield 61%; m.p. 109-110 °C,elemental ana.: C, 70.88; N, 12.72; S, 7.28,found:

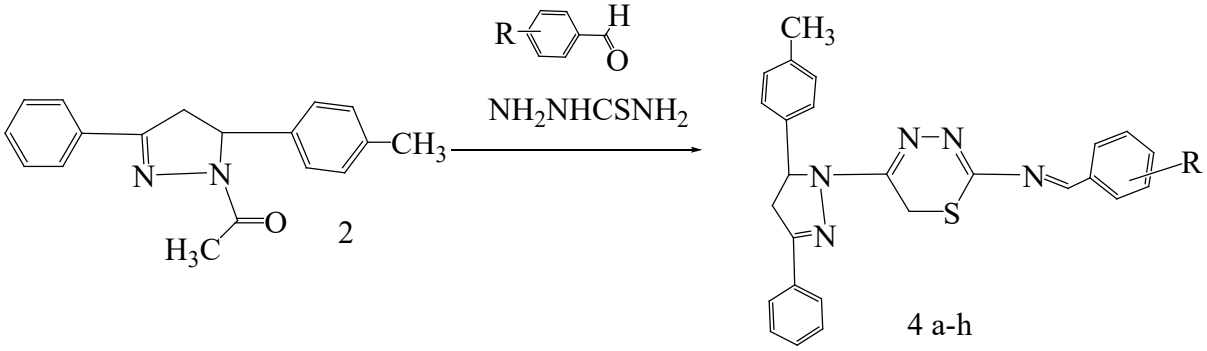
C, 70.84; N, 12.70; S, 7.23, infrared-νmax per cm-KBr: 1639 (C=C, for aro.3072(aro.C-H str.), 2983(C-H, streching), 1542(C=N),1024(C-S), 1485(N-N), 1688 (C-O) Hydrogen-1 nuclear magnetic resonance-CDCl3-300 MHz δ- in ppm : : 6.55-7.34 (m,13H, Ar-H), 4.09 (t,1H,-CH-N-N),3.54 (d,2H,CH2-CH-N),4.82 (s,1H,N=CH),2.67 (t,2H,N-CH-N),2.43 (d,2H,-CH2S),1.88(s,3H,-CH3),5.56(s,1H,-OH).

3f.(E)-N-(2-chlorobenzylidene)-4-(3-phenyl-5-p-CH3-phenyl-4,5-dihydropyrazolyl-1)-4,5-dihydrothiazol-2-amine, Chemical formula: C26H23ClN4S, Mol. Wt.: 459, Yield 75 %; m.p. 104-105 °C, elemental ana.: C, 68.03; Cl, 7.72; N, 12.21; S, 6.99,found: C, 68.0; Cl, 7.68; N, 12.17; S, 6.93, infrared-νmax per cm-KBr: 1645 (C=C, for aro.), 3089(aro. C-H str.), 2997(C-H, stretching), 1542(C=N),1028(C-S), 1488(N-N),670(C-Cl), Hydrogen-1 nuclear magnetic resonance-CDCl3-300 MHz δ- in ppm : 6.67-7.22 (m,13H, Ar-H), 4.12(t,1H,-CH-N-N),3.67(d,2H,CH2-CH-N),4.89(s,1H,N=CH),2.72(t,2H,N-CH-N),2.29(d,2H,-CH2S),1.87(s,3H,-CH3).

3g.(E)-2-methoxy-5-((4-(3-phenyl-5-p-CH3-phenyl-4,5-dihydropyrazolyl-1)-4,5-dihydrothiazol-2-ylimino)methyl)phenol,elemetal ana.:C27H26N4O2S, Mol. Wt.: 470.6, , Yield 67 %; m.p. 118-119 °C, elemental ana.: C, 68.91; N, 11.91; S, 6.81,found: C, 68.91; N, 11.91; S, 6.81, infrared-νmax per cm-KBr: 1637 (C=C, for aro.), 3089(aro.C-H str.), 2990(C-H, streching), 1553(C=N),1020(C-S), 1482(N-N),3380(-OH),3022(-OCH3), Hydrogen-1 nuclear magnetic resonance-CDCl3-300 MHz δ- in ppm : 6.73-7.17 (m,12H, Ar-H), 4.13(t,1H,-CH-N-N),3.76(d,2H,CH2-CH-N),4.83(s,1H,N=CH),2.77(t,2H,N-CH-N),2.34(d,2H,-CH2S),1.85(s,3H,-CH3),5.67(s,1H,-OH),2.45(s,3H,-OCH3).

3h.(E)-N-(2-bromobenzylidene)-4-(3-phenyl-5-pp-CH3-phenyl-4,5-dihydropyrazolyl-1)-4,5-dihydrothiazol-2-amine, Chemical formula: C26H23BrN4S,Mol. Wt.: 503.5, Yield 64 %; m.p. 174-175 °C, elemental ana.: C, 62.03; Br, 15.87; N, 11.13; S, 6.37,found: C, 62.0; Br, 15.82; N, 11.10; S, 6.32, infrared-νmax per cm-KBr: 1634 (C=C, for aro.), 3082(aro. C-H str.), 2993(C-H, streching), 1550(C=N),1025(C-S), 1485(N-N),615(C-Br),Hydrogen-1 nuclear magnetic resonance-CDCl3-300 MHz δ- in ppm : : 6.56-7.23 (m,12H, Ar-H), 4.07(t,1H,-CH-N-N),3.64(d,2H,CH2-CH-N),4.83(s,1H,N=CH),2.79(t,2H,N-CH-N),2.18(d,2H,-CH2S),1.(s,3H,-CH3), 5.62(s,1H,-OH),2.43(s,3H,-OCH3)..

4.Synthesis of (E)-N-substituted/unsubstitutedbenzylidene-5-(3-phenyl-5-p-CH3-phenyl-4,5-dihydropyrazolyl-1)-6H-1,3,4-thiadiazin-2-amine:4.A 0.1 moles of three reactant (E)-N-substituted/unsubstitutedbenzylidene-5-(3-phenyl-5-p-CH3-phenyl-4,5-dihydropyrazolyl-1)-6H-1,3,4-thiadiazin-2-amine and substituted/unsubstituted araldehydes, thiosemicarazide were mixed with 25 ml of dimethyl carbonate and NH4OAc as a catalyst. The reaction was refluxed for 9-10 hr on a water bath. After the reaction has finished, cold water was used to repeatedly wash the leftover residue and crystallized in ethanol.



4a.(E)-N-benzylidene-5-(3-phenyl-5-p-CH3-phenyl-4,5-dihydropyrazolyl-1)-6H-1,3,4-thiadiazin-2-amine, Chemical formula: C26H23N5S,Mol. Wt.: 437.6, Yield 68.5 %; m.p. 172-173 °C,elemental ana.: C, 71.37; N, 16.01; S, 7.33,found: C, 71.27; N, 15.97; S, 7.30, infrared-νmax per cm-KBr: 1644 (C=C, for aro), 3092(aro. C-H str.), 2998(C-H, streching), 1558(C=N),1029(C-S), 1480(N-N), 1233(C-N),Hydrogen-1 nuclear magnetic resonance-CDCl3-300 MHz δ- in ppm : 6.93-7.12 (m,14H, Ar-H),6.6(s,1H,N=CH),3.1(t,1H,CH-N-N),2.7(d,2H,CH2-S),5.4(d,2H,-CH2-CH-N),1.4(s,3H,-CH3).

4b.(E)-4-((5-(3-phenyl-5-p-CH3-phenyl-4,5-dihydropyrazolyl-1)-6H-1,3,4-thiadiazin-2-ylimino)methyl)phenol,Chemical analysis:C26H23N5OS,Mol. Wt.: 453.6, Yield 61 %; m.p. 154-155 °C, elemental ana.: C, 68.85; N, 15.44; S, 7.07,found: C, 68.82; N, 15.40; S, 7.03, infrared-νmax per cm-KBr: 1634 (C=C, for aro.), 3082(aro. C-H str.), 2993(C-H, streching), 1550(C=N),1025(C-S), 1485(N-N), Hydrogen-1 nuclear magnetic resonance-CDCl3-300

MHz δ- in ppm : 6.63-7.19 (m,13H, Ar-H),6.47(s,1H,N=CH),3.18(t,1H,CH-N-N),2.56(d,2H,CH2-S),5.35(d,2H,-CH2-CH-N),1.34(s,3H,-CH3),5.35(s,1H,-OH).

4c.(E)-N-(4-chlorobenzylidene)-5-(3-phenyl-5-p-CH3-phenyl-4,5-dihydropyrazolyl-1)-6H-1,3,4-thiadiazin-2-amine,Chemical analysis:C26H22ClN5S, Mol. Wt.: 472, Yield 67 %; m.p. 159-159.5 °C, elemental ana.: C, 66.16; Cl, 7.51; N, 14.84; S, 6.79,found: C, 66.12; Cl, 7.46; N, 14.82; S, 6.74, infrared-νmax per cm-KBr: 1640 (C=C, for aro.), 3085(aro. C-H str.), 2997(C-H, streching), 1558(C=N),1028(C-S), 1487(N-N), 1230(C-N),667(C-Cl) Hydrogen-1 nuclear magnetic resonance-CDCl3-300 MHz δ- in ppm : 6.67-7.34 (m,13H, Ar-H),6.45(s,1H,N=CH),3.89(t,1H,CH-N-N),2.56(d,2H,CH2-S),5.34(d,2H,-CH2-CH-N),1.45(s,3H,-CH3).

4d.(E)-N-(4-nitrobenzylidene)-5-(3-phenyl-5-p-CH3-phenyl-4,5-dihydropyrazol-1-yl)-6H-1,3,4-thiadiazin-2-amine,Chemical formula:C26H22N6O2S, Mol. Wt.: 482.6, Yield 59 %; m.p. 107.5 °C, elemental ana.: C, 64.71; N, 17.42; S, 6.64,found: C, 64.67; N, 17.37; S, 6.60, infrared-νmax per cm-KBr: 1638 (C=C, for aro.), 3089(aro. C-H str.), 2997(C-H, streching), 1556(C=N),1029(C-S), 1480(N-N), 1377, 1455(-NO2),Hydrogen-1 nuclear magnetic resonance-CDCl3-300 MHz δ- in ppm : 6.45-7.56(m,13H, Ar-H),6.34(s,1H,N=CH),3.23(t,1H,CH-N-N),2.58(d,2H,CH2-S),5.32(d,2H,-CH2-CH-N),1.26(s,3H,-CH3).

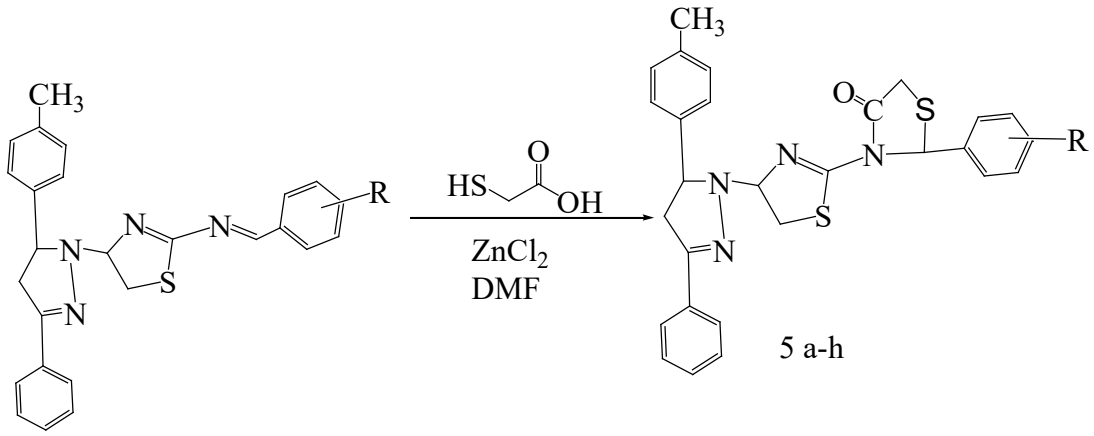
4e.(E)-2-((5-(3-phenyl-5-p-CH3-phenyl-4,5-dihydropyrazolyl-1)-6H-1,3,4-thiadiazin-2-ylimino)methyl)phenol,Chemical formula:C26H23N5OS,Mol. Wt.: 453.6, Yield 66 %; m.p. 127.5 °C, elemental ana.: C, 68.85; N, 15.44; S, 7.07,found: C, 68.83; N, 15.42; S, 7.02, infrared-νmax per cm-KBr: 1632 (C=C, for aro.), 3085 (aro. C-H str.), 2998(C-H, streching), 1555(C=N),1023(C-S), 1484(N-N),1225(C-O) Hydrogen-1 nuclear magnetic resonance-CDCl3-300 MHz δ- in ppm : 6.77-7.45 (m,13H, Ar-H),6.57(s,1H,N=CH),3.23(t,1H,CH-N-N),2.90(d,2H,CH2-S),5.67(d,2H,-CH2-CH-N),1.78(s,3H,-CH3),5.35(s,1H,-OH).

4f.(E)-N-(2-chlorobenzylidene)-5-(3-phenyl-5-p-CH3-phenyl-4,5-dihydropyrazolyl-1)-6H-1,3,4-thiadiazin-2-amine,Chemical analysis:C26H22ClN5S,Mol. Wt.: 472, Yield 68 %; m.p. 184-185 °C,elemental ana.: C, 66.16; Cl, 7.51; N, 14.84; S, 6.79,found: C, 66.12; Cl, 7.46; N, 14.82; S, 6.75 infrared-νmax per cm-KBr: 1630 (C=C, for aro.), 3087(aro. C-H str.), 2992(C-H, streching), 1556(C=N),1020(C-S), 1482(N-N), 1256 (C-O),618(C-Br), Hydrogen-1 nuclear magnetic resonance-CDCl3-300 MHz δ- in ppm : 6.53-7.24 (m,13H, Ar-H),6.47(s,1H,N=CH),3.34(t,1H,CH-N-N),2.69(d,2H,CH2-S),5.34(d,2H,-CH2-CH-N),1.34(s,3H,-CH3).

4g.(E)-2-methoxy-4-((5-(3-phenyl-5-p-CH3-phenyl-4,5-dihydropyrazolyl-1)-6H-1,3,4-thiadiazin-2-ylimino)methyl)phenol,Chemical formula: C27H25N5O2S, Mol. Wt.: 483.6, Yield 70 %; m.p. 161-162 °C ,elemetal ana.: C, 67.06; N, 14.48; S, 6.63,found: C, 67.02; N, 14.44; S, 6.60 infrared-νmax per cm-KBr: 1634 (C=C, for aro.), 3082(aro. C-H str.), 2993(C-H, streching), 1550(C=N),1025(C-S), 1485(N-N), Hydrogen-1 nuclear magnetic resonance-CDCl3-300 MHz δ- in ppm 6.56-7.23 (m,12H, Ar-H),6.47(s,1H,N=CH),3.45(t,1H,CH-N-N),2.45(d,2H,CH2-S),5.32(d,2H,-CH2-CH-N),1.34(s,3H,-CH3),5.07(1H,s,-OH),2.65(3H,s,-OCH3).

4h.(E)-N-(2-bromobenzylidene)-5-(3-phenyl-5-p-CH3-phenyl-4,5-dihydropyrazolyl-1)-6H-1,3,4-thiadiazin-2-amine,Chemical formula:C26H22BrN5S,Mol. Wt.: 516.5, Yield 68 %; m.p. 127-128 °C,elemental ana.: C, 60.47; Br, 15.47; N, 13.56; S, 6.21,found: C, 60.42; Br, 15.42; N, 13.53; S, 6.18, infrared-νmax per cm-KBr: 1632 (C=C, for aro.), 3080(aro. C-H str.), 2997(C-H, streching), 1557(C=N),1023(C-S), 1487(N-N),690(C-Br), Hydrogen-1 nuclear magnetic resonance-CDCl3-300 MHz δ- in ppm : 6.58-7.32 (m,12H, Ar-H),6.43(s,1H,N=CH),3.41(t,1H,CH-N-N),2.35(d,2H,CH2-S),5.38(d,2H,-CH2-CH-N),1.30(s,3H,-CH3),4.87(1H,s,-OH),2.69(3H,s,-OCH3).

Synthesis of 2-(substituted/unsubstitutedphenyl)-3-(4-(3-phenyl-5-p-CH3-phenyl-4,5-dihydropyrazolyl-1)-4,5-dihydrothiazol-2-yl)thiazolidin-4-one: 0.01 mole of both 2-(4-hydroxyphenyl)-3-(4-(3-phenyl-5-p-CH3-phenyl-4,5-dihydropyrazolyl-1)-4,5-dihydrothiazol-2-yl)thiazolidin-4-one and thioglycollic acid containing anhydrous ZnCl2 (0.1 g) in dimethylformamide was refluxed on heating mental for 10-12 hours. It was poured into crushed ice and stirred vigorously. Solidification occurred after fifteen minutes. It was filtered off than washed with cold water and recrystallized in ethanol.



5a. 2-phenyl-3-(4-(3-phenyl-5-p-CH3-phenyl-4,5-dihydropyrazolyl-1)-4,5-dihydrothiazol-2-yl)thiazolidin-4-one,Chemical formula: C28H26N4OS2,Mol. Wt.: 498.7, Yield 71 %; m.p. 109-110 °C, elemental ana.: C, 67.44; N, 11.24; S, 12.86,found: C, 67.42; N, 11.20; S, 12.82, infrared-νmax per cm-KBr:3225(-CH , aro.),3185(CH, Aliphatic),3063(-CH-N), 1606 (Amide), 1251(C-N), 1157(C=S), 1054(N-N), 969(C-S),Hydrogen-1 nuclear magnetic resonance-CDCl3-300 MHz δ- in ppm : 6.8-7.1(m,14H,aro.),4.9(s,1H,N-CH-S),4.5(t,1H,-CH-N-N),3.6(d,2H,CH2-CH-N-N),3.3(s,1H,N-CH-N),2.4(d,2H,-CH2S),1.1(s,3H,-CH3).

5b.2-(4-hydroxyphenyl)-3-(4-(3-phenyl-5- p-CH3-phenyl -4,5-dihydropyrazolyl-1)-4,5-dihydrothiazol-2-yl)thiazolidin-4-one,Chemical formula:C28H26N4O2S2,Mol. Wt.: 514.7, Yield 64 %; m.p. 117-118 °C,elemental ana.: C, 65.34; N, 10.89; S, 12.46,found: C, 65.30; N, 10.84; S, 12.42, infrared-νmax per cm-KBr:3387(-OH), 3230(-CH , aro.),2982(CH, Aliphatic),2690(-CH-N), 1647(Amide), 1247(C-N), 1165(C=S), 1086(N-N), 1034(C-S), Hydrogen-1 nuclear magnetic resonance-CDCl3-300 MHz δ- in ppm : 6.77-7.56(m,13H,aro.),4.76(s,1H,N-CH-S),4.48(t,1H,-CH-N-N),3.34(d,2H,CH2-CH-N-N),3.15(s,1H,N-CH-N),2.34(d,2H,-CH2S),1.23(s,3H,-CH3),5.15(s,1H,-OH).

5c.2-(4-chlorophenyl)-3-(4-(3-phenyl-5-p-CH3-phenyl-4,5-dihydropyrazol-1-yl)-4,5-dihydrothiazol-2-yl)thiazolidin-4-one,Chemical formula:C35H33ClN4OS2,Mol. Wt.: 625.2, Yield 65 %; m.p. 102-103 °C,elemental ana.: C, 67.23; Cl, 5.67; N, 8.96; S, 10.26,found: C, 67.20; Cl, 5.62; N, 8.93; S, 10.22, infrared-νmax per cm-KBr: 3226(-CH , aro.),2980(CH, Aliphatic),2693(-CH-N), 1648(Amide),1255(C-N), 1167(C=S), 1092(N-N), 1027(C-S), Hydrogen-1 nuclear magnetic resonance-CDCl3-300 MHz δ- in ppm : 6.5-7.67(m,13H,Aromatic),4.87(s,1H,N-CH-S),4.43(t,1H,-CH-N-N),3.54(d,2H,CH2-CH-N-N),3.36(s,1H,N-CH-N),2.56(d,2H,-CH2S),1.23(s,3H,-CH3).

5d.2-(4-nitrophenyl)-3-(4-(3-phenyl-5-p-CH3-phenyl-4,5-dihydropyrazolyl-1)-4,5-dihydrothiazol-2-yl)thiazolidin-4-one,Chemical formula:C28H25N5O3S2,Mol. Wt.: 543.7, ,Yield 62 %; m.p. 174.5 °C, elemental ana.: C, 61.86; N, 12.88; S, 11.80,found: C, 61.82; N, 12.83; S, 11.78, infrared-νmax per cm-KBr:3234(-CH , aro.),2989(CH, Aliphatic),2698(-CH-N), 1655(Amide), 1245(C-N), 1160(C=S), 1099(N-N), 1026(C-S), 1435, 1366(-NO2), Hydrogen-1 nuclear magnetic resonance-CDCl3-300 MHz δ- in ppm : 6.24-7.34(m,13H,aro.),4.81(s,1H,N-CH-S),4.36(t,1H,-CH-N-N),3.54(d,2H,CH2-CH-N-N),3.23(s,1H,N-CH-N),2.49(d,2H,-CH2S),1.34(s,3H,-CH3).

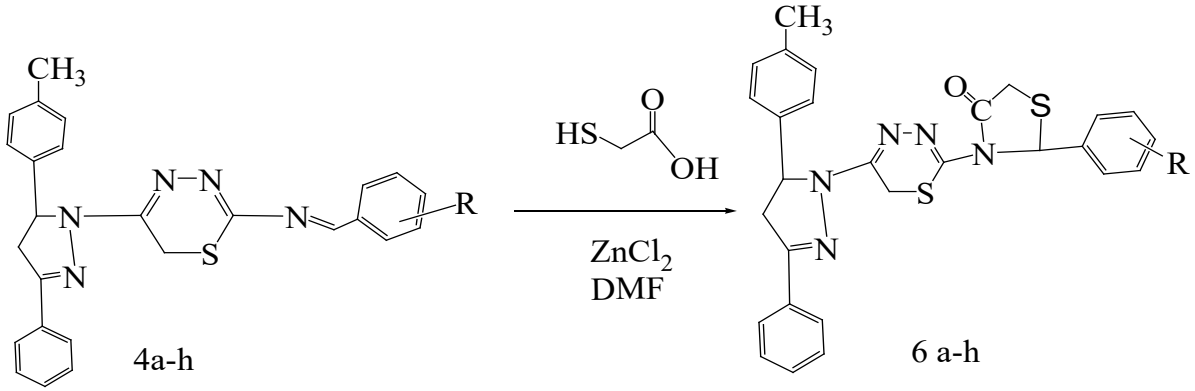
5e.2-(2-hydroxyphenyl)-3-(4-(3-phenyl-5-p-CH3-phenyl-4,5-dihydropyrazolyl-1)-4,5-dihydrothiazol-2-yl)thiazolidin-4-one,Chemical formula:C28H26N4O2S2,Mol. Wt.: 514.7, Yield 68 %; m.p. 158-157 °C ,elemental ana.: C, 65.34; N, 10.89;S, 12.46,found: C, 65.32; N, 10.85;S, 12.43, infrared-νmax per cm-KBr: 3398(-OH), 3234(-CH , aro.),2998(CH, Aliphatic),2678(-CH-N), 1664(Amide), 1267(C-N), 1165(C=S), 1086(N-N), 1028(C-S), Hydrogen-1 nuclear magnetic resonance-CDCl3-300 MHz δ- in ppm : 6.67-7.43(m,13H,aro.),4.77(s,1H,N-CH-S),4.49(t,1H,-CH-N-N),3.53(d,2H,CH2-CH-N-N),3.45(s,1H,N-CH-N),2.38(d,2H,-CH2S),1.18(s,3H,-CH3),5.23(s,1H,-OH).

5f.2-(2-chlorophenyl)-3-(4-(3-phenyl-5-p-CH3-phenyl-4,5-dihydropyrazolyl-1)-4,5-dihydrothiazol-2-yl)thiazolidin-4-one,Chemical formula:C28H25ClN4OS2, Mol. Wt.: 533.1, Yield 74 %; m.p. 198.5 °C ,elemental ana.: C, 63.08; Cl, 6.65; N, 10.51; S, 12.03,found: C, 63.05; Cl, 6.62; N, 10.46; S, 12.02, infrared-νmax per cm-KBr: 3243(-CH , aro.),2989(CH, Aliphatic),2692(-CH-N), 1653(Amide), 1260(C-N), 1165(C=S), 1085(N-N), 1028(C-S), Hydrogen-1 nuclear magnetic resonance-CDCl3-300 MHz δ- in ppm : 6.45-7.54(m,13H,aro.),4.78(s,1H,N-CH-S),4.58(t,1H,-CH-N-N),3.63(d,2H,CH2-CH-N-N),3.38(s,1H,N-CH-N),2.32(d,2H,-CH2S),1.24(s,3H,-CH3).

5g.2-(4-hydroxy-3-methoxyphenyl)-3-(4-(3-phenyl-5-p-CH3-phenyl-4,5-dihydropyrazolyl-1)-4,5-dihydrothiazol-2-yl)thiazolidin-4-one,Chemical formula:C29H28N4O3S2,Mol. Wt.: 544.7, Yield 59 %; m.p. 181.5 °C,elemental ana.: C, 63.95; N, 10.29; S, 11.77,found: C, 63.92; N, 10.24; S, 11.72, infrared-νmax per cm-KBr: 3046(CH, aro), 3023(CH, Aliphatic), 1900(C=C), 1786(C=N), 1623(Amide), 1487(C-N), 1168(CS), 1092(-N-N-), Hydrogen-1 nuclear magnetic resonance-CDCl3-300 MHz δ- in ppm : 6.67-7.89(m,13H,aro.),4.86(s,1H,N-CH-S),4.45(t,1H,-CH-N-N),3.57(d,2H,CH2-CH-N-N),3.39(s,1H,N-CH-N),2.47(d,2H,-CH2S),1.34(s,3H,-CH3), 5.33(s,1H,-OH),2.60(s,3H,-OCH3).

5h.2-(2-bromophenyl)-3-(4-(3-phenyl-5-p-CH3-phenyl-4,5-dihydropyrazolyl-1)-4,5-dihydrothiazol-2-yl)thiazolidin-4-one,Chemical formula:C28H25BrN4OS2,Mol. Wt.: 577.6, Yield 66.5 %; m.p. 147-148 °C, elemental ana.: C, 58.23; Br, 13.83; N, 9.70; S, 11.10,found: C, 58.23; Br, 13.83; N, 9.70; S, 11.10,, 6a.2-phenyl-3-(5-(3-phenyl-5-p-tolyl-4,5-dihydropyrazol-1-yl)-6H-1,3,4-thiadiazin-2-yl)thiazolidin-4-one,Chemical formula:C28H25N5OS2,Mol. Wt.: 511.7, Yield 68 %; m.p. 168.5 °C, elemental ana.: C, 65.73; N, 13.69; S, 12.53,found: C, 65.70; N, 13.64; S, 12.50, infrared-νmax per cm-KBr: 3397(-OH), 3228(-CH , aro.),2986.02(CH, Aliphatic),2696(-CH-N), 1648(Amide),1255(C-N), 1159 (C=S), 1096.78(N-N), 1022.47(C-S) ,614 (C-Br),Hydrogen-1 nuclear magnetic resonance-CDCl3-300 MHz δ- in ppm : 6.56-7.27(m,13H,aro.),4.87(s,1H,N-CH-S),4.59(t,1H,-CH-N-N),3.56(d,2H,CH2-CH-N-N),3.45(s,1H,N-CH-N),2.35(d,2H,-CH2S),1.56(s,3H,-CH3),5.45(s,1H,-OH),2.38(s,3H,-OCH3)..

6.Synthesis of 2-(substituted/unsubstitutedphenyl)-3-(5-(3-phenyl-5-p-CH3-phenyl-4,5-dihydropyrazolyl-1)-6H-1,3,4-thiadiazin-2-yl)thiazolidin-4-one:0.01 mole of both 2-(4-hydroxyphenyl)-3-(4-(3-phenyl-5- p-CH3-phenyl-4,5-dihydropyrazolyl-1)-4,5-dihydrothiazol-2-yl)thiazolidin-4-one and thioglycollic acid containing anhydrous trace amount of ZnCl2 in dimethylformamide was refluxed in heating mental for 15-18 hours. It was poured into crushed ice and stirred vigorously. Solidification occurred after fifteen minutes. It was filtered off than washed with cold water and recrystallized in ethanol.



6a.2-phenyl-3-(5-(3-phenyl-5-p-CH3-phenyl-4,5-dihydropyrazolyl-1)-6H-1,3,4-thiadiazin-2-yl)thiazolidin-4-one,Chemical formula:C28H25N5OS2,Mol. Wt.: 511.7,elemental ana.:C, 65.73; N, 13.69; S, 12.53,found: C, 65.70; N, 13.63; S, 12.51, infrared-νmax per cm-KBr: 3392(CH, aro.), 2986(CH, Aliphatic), 1718(C=C), 1645(C=N), 1630(Amide), 1420(C-N), 1245(CS), 1094(-N-N-), Hydrogen-1 nuclear magnetic resonance-CDCl3-300 MHz δ- in ppm : 7.15-7.90 (m, 13H, aro.),1.8(s,2H,-CH2S),4.0(t,1H,CH-N-N),3.2(d,2H,-CH2-CH-N-N),5(s,1H,N-CH-S),2.9(s,2H,CO-CH2-S).

6b.2-(4-hydroxyphenyl)-3-(5-(3-phenyl-5-p-CH3-phenyl-4,5-dihydropyrazolyl-1)-6H-1,3,4-thiadiazin-2-yl)thiazolidin-4-one,Chemical formula:C28H25N5O2S2,Mol. Wt.: 527.7, Yield 68.5 %; m.p. 177.5 °C, elemental ana.: C, 63.73; N, 13.27; S, 12.15,found: C, 63.70; N, 13.23; S, 12.12, infrared-νmax per cm-KBr: 3364(-OH), 3068(CH, aro.), 3018(CH, Aliphatic), 1906(C=C), 1785(C=N), 1656(Amide), 1475(C-N), 1167(CS), 1089(-N-N-), Hydrogen-1 nuclear magnetic resonance-CDCl3-300 MHz δ- in ppm : 7.22-7.98 (m, 13H, aro.),1.87(s,2H,-CH2S),4.22(t,1H,CH-N-N),3.27(d,2H,-CH2-CH-N-N),5.1(s,1H,N-CH-S),2.8(s,2H,CO-CH2-S), 5.32(s,1H,-OH).

6c. 2-(4-chlorophenyl)-3-(5-(3-phenyl-5-p-CH3-phenyl-4,5-dihydropyrazolyl-1)-6H-1,3,4-thiadiazin-2-yl)thiazolidin-4-one,Chemical formula:C28H24ClN5OS2,Mol. Wt.: 546.1, Yield 65 %; m.p. 101.5 °C, elemental ana.: C, 61.58; Cl, 6.49; N, 12.82; S, 11.74,found: C, 61.53; Cl, 6.43; N, 12.80; S, 11.72, infrared-νmax per cm-KBr: 3350.72(-OH), 3063.19(CH, aro.), 3015.93(CH, Aliphatic), 1902.90(C=C), 1778.46(C=N), 1606.80(Amide), 1479.29(C-N), 1447.73,

1301.52(-NO2), 1157.57(CS), 1084.52(-N-N-), Hydrogen-1 nuclear magnetic resonance-CDCl3-300 MHz δ- in ppm :7.23-7.98 (m, 13H, aro.),1.8(s,2H,-CH2S),4.3(t,1H,CH-N-N),3.14(d,2H,-CH2-CH-N-N),5.6(s,1H,N-CH-S),2.78(s,2H,CO-CH2-S).

6d.2-(4-nitrophenyl)-3-(5-(3-phenyl-5-p-CH3-phenyl-4,5-dihydropyrazolyl-1)-6H-1,3,4-thiadiazin-2-yl)thiazolidin-4-one,Chemical formula:C28H24N6O3S2, Mol. Wt.: 556.7, Yield 70 %; m.p. 192.5 °C,elemental ana.: C, 60.41; N, 15.10; S, 11.52,found: C, 60.38; N, 15.09; S, 11.50, infrared-νmax per cm-KBr:3086(CH, aro.), 3035(CH, Aliphatic), 1923(C=C), 1783(C=N), 1608(Amide), 1489(C-N), 1446, 1301(-NO2), 1153(CS), 1087(-N-N-), Hydrogen-1 nuclear magnetic resonance-CDCl3-300 MHz δ- in ppm : 7.22-7.98 (m, 13H, aro.),1.76(s,2H,-CH2S),4.23(t,1H,CH-N-N),3.28(d,2H,-CH2-CH-N-N),5.10(s,1H,N-CH-S),2.98(s,2H,CO-CH2-S).

6e.2-(2-hydroxyphenyl)-3-(5-(3-phenyl-5-p-CH3-phenyl-4,5-dihydropyrazolyl-1)-6H-1,3,4-thiadiazin-2-yl)thiazolidin-4-one,Chemical formula :C28H25N5O2S2,Mol. Wt.: 527.7,C, Yield 70 %; m.p. 178.5 °C, elemental ana.: 63.73; N, 13.27; S, 12.15,found: 63.72; N, 13.23; S, 12.13, infrared-νmax per cm-KBr: 3354(-OH), 3076(CH, aro.), 3023(CH, Aliphatic), 1923(C=C), 1780(C=N), 1623(Amide), 1483(C-N), 1167(CS), 1096(-N-N-), Hydrogen-1 nuclear magnetic resonance-CDCl3-300 MHz δ- in ppm : 7.08-7.99 (m, 13H, aro.),1.67(s,2H,-CH2S),4.34(t,1H,CH-N-N),3.37(d,2H,-CH2-CH-N-N),5.24(s,1H,N-CH-S),2.78(s,2H,CO-CH2-S), 5.42(s,1H,-OH).

6f.2-(2-chlorophenyl)-3-(5-(3-phenyl-5-p-CH3-phenyl-4,5-dihydropyrazolyl-1)-6H-1,3,4-thiadiazin-2-yl)thiazolidin-4-one,Chemical formula:C28H24ClN5OS2,Mol. Wt.: 546.1, Yield 71 %; m.p. 145.7 °C, elemental ana.: C, 61.58; Cl, 6.49; N, 12.82; S, 11.74,found: C, 61.53; Cl, 6.44; N, 12.80; S, 11.72, infrared-νmax per cm-KBr: 3076(CH, aro.), 3023(CH, Aliphatic), 1902.90(C=C), 1787(C=N), 1620(Amide), 1483(C-N), 1163(CS), 1090(-N-N-), Hydrogen-1 nuclear magnetic resonance-CDCl3-300 MHz δ- in ppm: 7.22-7.99 (m, 13H, aro.),1.82(s,2H,-CH2S),4.12(t,1H,CH-N-N),3.29(d,2H,-CH2-CH-N-N),5.22(s,1H,N-CH-S),2.86(s,2H,CO-CH2-S).

6g.2-(4-hydroxy-3-methoxyphenyl)-3-(5-(3-phenyl-5-p-CH3-phenyl-4,5-dihydropyrazolyl-1)-6H-1,3,4-thiadiazin-2-yl)thiazolidin-4-one,Chemical formula:C29H27N5O3S2,Mol. Wt.: 557.7

Yield 60 %; m.p. 155.5 °C, elemental ana.: C, 62.46; N, 12.56; S, 11.50, found: C, 62.42; N, 12.54; S, 11.48, infrared-νmax per cm-KBr: 3350.72(-OH), 3063.19(CH,aro.), 3015.93(CH, Aliphatic), 1902.90(C=C), 1778.46(C=N), 1606.80(Amide), 1479.29(C-N), 1447.73, 1301.52(-NO2), 1157.57(CS), 1084.52(-N-N-), Hydrogen-1 nuclear magnetic resonance-CDCl3-300 MHz δ- in ppm: 7.35-7.93 (m, 13H, aro.),1.82(s,2H,-CH2S),4.23(t,1H,CH-N-N),3.29(d,2H,-CH2-CH-N-N),5.03(s,1H,N-CH-S),2.86(s,2H,CO-CH2-S),5.44(s,1H,-OH),2.67(s,3H,-OCH3)..

6h.2-(2-bromophenyl)-3-(5-(3-phenyl-5-p-CH3-phenyl-4,5-dihydropyrazolyl-1)-6H-1,3,4-thiadiazin-2-yl)thiazolidin-4-one,Chemial formula:C28H24BrN5OS2,Mol. Wt.: 590.6, Yield 59 %; m.p. 194-195 °C, elemental ana.: C, 56.95;Br, 13.53; N, 11.86; S, 10.86,found: C, 56.90;Br, 13.52; N, 11.83; S, 10.84, infrared-νmax per cm-KBr: 3359(-OH), 3072(CH, aro.), 3023(CH, Aliphatic), 1922(C=C), 1780(C=N), 1623(Amide), 1467(C-N), 1160(CS), 1090(-N-N-),628(C-Br),Hydrogen-1 nuclear magnetic resonance-CDCl3-300 MHz δ- in ppm : 7.23-7.67 (m, 13H, aro.),1.78(s,2H,-CH2S),4.16(t,1H,CH-N-N),3.34(d,2H,-CH2-CH-N-N),5.04(s,1H,N-CH-S),2.88(s,2H,CO-CH2-S), 5.88(s,1H,-OH),2.73(s,3H,-OCH3)..

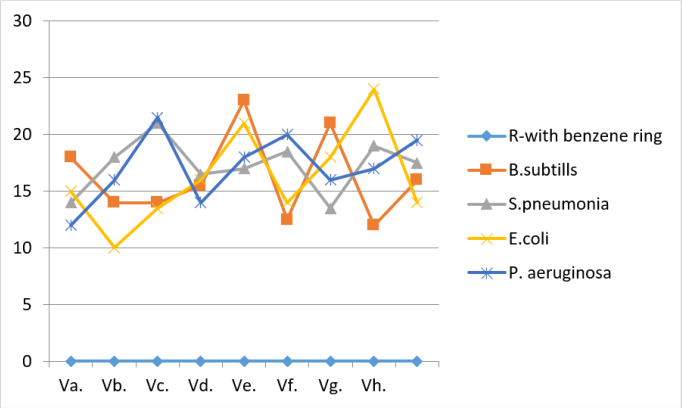
Table 2 In Anti-microbial activity in vitro

The zone of Inhibition of the synthesized compounds V a-h and VI a-h :

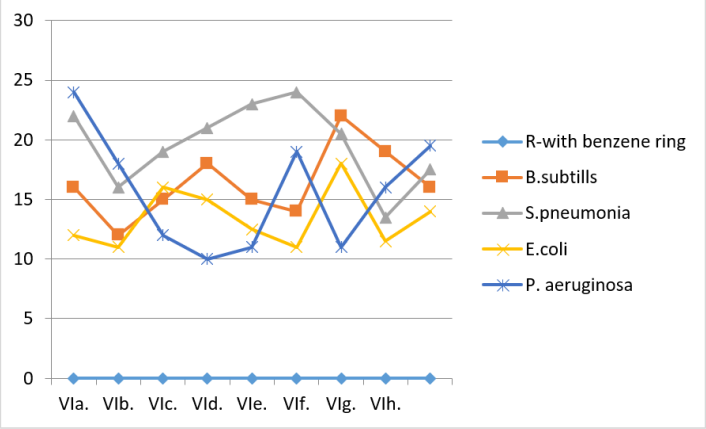
S.No.		Zone of Inhibition (zoi)(in mm)			
	R-with benzene ring	*B.subtills*	*S.pneumonia*	*E.coli*	*P. aeruginosa*
Va.	Phenyl	18	14	15	12
Vb.	p-OH- phenyl	14	18	10	16
Vc.	p-Cl-phenyl	14	21	13.5	21.5
Vd.	p-NO2- henyl	15.5	16.5	16	14
Ve.	o-OH-phenyl	23	17	21	18
Vf.	o-Cl-phenyl	12.5	18.5	14	20
Vg.	4-OH,3-OCH3-phenyl	21	13.5	18	16
Vh.	o-Br-phenyl	12	19	24	17
VIa.	Phenyl	16	22	12	24
VIb.	p-OH- phenyl	12	16	11	18
VIc.	p-Cl-phenyl	15	19	16	12
VId.	p-NO2- henyl	18	21	15	10

VIe.	o-OH-phenyl	15	23	12.5	11
VIf.	o-Cl-phenyl	14	24	11	19
VIg.	4-OH,3-OCH3-phenyl	22	20.5	18	11
VIh.	o-Br-phenyl	19	13.5	11.5	16
	Ciprofloxacin	16	17.5	14	19.5

Graphical Representation of V(a-h):



Graphical Representation of VI(a-h):



Gram-negative (-) Bacteria strain (E. coli, Escherichia coli), Pseudomonas aeruginosa, and Gram-positive (+) Bacteria strain (S.pneumonia, Bacillus subtilis) were raised in various uniform sets of liquid media(LB media) having different concentrations of synthesized derivatives V(a-h) and VI(a-h). keeping track of the optical density, all the bacterial strains within conical flask containing 10 ml of LB separately and incubated for 8 hr at 37°C. Then, 100 µl of the bacterial suspension is added to each conical tube containing the test compound, which has a final experimental substance concentration of 1000-0.244 µg ml −1 in 10 ml of LB media. The identical 100 µl of the clear solution was taken in to a conical flask, having 10 ml of LB media separately in the other side control experiment.

The increase in the expansion of all the bacterial strains for all set was checked by noting the OD of the solution at 600 nm after twenty four time. Then the OD versus synthesized derivatives concentration was plotted for every set to achieve the minimum inhibitory concentration (MIC) for all the bacterial strains. The minimum inhibition of all strains was determined by measuring the decrease in OD at the appropriate dose of antibacterial compounds.

A test for antibiotic sensitivity was conducted to evaluate the effectiveness of various compounds against infections. AST is typically performed for the determination of in vivo effectiveness of the antibiotics against bacterial infections. This exercise was done in vitro by following the Disc Diffusion method. In this method, the nutrient agar was prepared

and poured into sterile petri plates for solidification. Then spreading was done all bacterial strains (E. coli, Pseudomonas aeruginosa, S.pneumonia and Bacillus subtilis). Antibacterial disc were kept at the upper layer of the nutrient agar medium with bacterial lawn. All these plates were incubated at 37°C overnight.

Agar well diffusion method: The Nutrient agar medium was prepared and poured into sterile petri plates.

For solidification. Spreading was done for all bacterial strains (E. coli, Pseudomonas aeruginosa, S.pneumonia and Bacillus subtilis). wells were made using a conventional technique, and 100 µl of antibiotics wre placed into each well of nutrient agar with bacterial lawn. Every plate in this set was incubated at 37°C for overnight. The average zone of inhibition was taken into consideration of antibiotic sensitivity test in mm.

Results and Discussion: The screening data revealed that the synthesized derivatives V(a-h) and VI(a-h) exhibit significant antimicrobial activity. The compounds no Va, Vg, Vh, and VIa, VId, Vif shown outstanding antimicrobial activity of Bacillus subtilis having R=unsubstituted pheny, 4-hydroxy-3-methoxy,o-bromo, p-nitro and o-chloro groups. The compounds Vb and VIg showed excellent activity against S.pneumonia having R p-hydroxy. and 4-hydroxy groups. The compounds Vc, Vd,Vg, and VId has exhibited higher antimicrobial efficacy than references against E. coli having R=p-chloro, p-nitro,4-hydroxy-3-methoxy, and p-nitro, respectively. The compounds Vc, Vf, and VIa, Vif have higher activity than the reference against Pseudomonas aeruginosa, having R=p/o-chloro, unsubstituted pheny and o-chloro group. All the other prepared derivatives have shown moderate antimicrobial activity. This reveals that the different functions at various arrangements are responsible for significant antimicrobial activity in the synthesized compounds. The maximum ZOI (Table II) and the lowest MIC value (Table I) indicated the potency of synthesized compounds. The initial observations in structure structure-activity relationship (SAR) study revealed that the antimicrobial activity was affected by altering the substituent groups attached to the scaffold.

2. CONCLUSION

In the present work synthesized novel heterocyclic products were synthesized under very simple conditions without using expensive/toxic reagents. The intermediate Schiff base has been directly transformed into heterocycles by using suitable cyclizing agents.

CONFLICT OF INTERESTS

None.

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