RJC

RASĀYAN *J. Chem.*
Vol. 15 | No. 1 |564-568| January - March | 2022
ISSN: 0974-1496 | e-ISSN: 0976-0083 | CODEN: RJCABP
http://www.rasayanjournal.com
http://www.rasayanjournal.co.in

SYNTHESIS, CHARACTERIZATION AND ANTIMICROBIAL ACTIVITY OF PYRAZOLE-PYRIMIDONE CLUBBED DERIVATIVES

Nikulsinh Sarvaiya[1,✉], Hitesh Samata[1], Sheetal Gulati[1] and H. Patel[2]
[1]Department of Chemistry, Rabindranath Tagore University, Bhopal(M.P.), India
[2]Ex-Head and Professor, Deptartment of Chemistry, S.P. University, VV Nagar, Gujarat, India
✉Corresponding Author: nikul1011@gmail.com

ABSTRACT

4-(2-(1-(4-aryl-3-(furan-2-yl(hydroxy)methyl)-6-methyl-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carbonyl)-3-methyl-5-oxo-1H-pyrazol-4(5H)-ylidene)hydrazinyl)-N-(thiazol-2-yl) benzene sulphonamides (2a-e) were synthesised by condensation of 4-(2-(1-(4-aryl-6-methyl-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carbonyl)-3-methyl-5-oxo-1H-pyrazol-4(5H)-ylidene) hydrazinyl)-N-(thiazol-2-yl) benzene sulphonamide (1a-e) with furfuraldehyde. The structures of all the compounds (2a-e) were characterized duly. The compounds were also monitored for antimicrobial activity.

Keywords: Pyrazole- Pyrimidone Derivatives, Spectral Data Analysis, Antimicrobial Activity, Elemental Analysis.
RASĀYAN *J. Chem.*, Vol. 15, No.1, 2022

INTRODUCTION

Nowadays chemists are doing research to prepare nitrogen-containing heterocyclic compounds due to their various pharmaceuticals and biological activities.[1-3] Presence of pyrazole nucleus in organic compounds exhibit antimicrobial, antipyretic, antidepressant, anticancer, anti-inflammatory, analgesic, antidiabetic, antiulcer and antitubercular activities.[4-9]

Pyrazole fused with pyrimidines nucleus also one of the most important heterocyclic compounds, which also exhibit various pharmacological properties and antimicrobial activities.[10-14] Hence in connection with our previous work[15] here we synthesized pyrazole-pyrimidone clubbed derivatives and studied for their antimicrobial activity. The whole reaction scheme of the present work is shown in Scheme-1.

EXPERIMENTAL

All other chemicals and reagents used were laboratory grade. 4-(2-(1-(4-aryl-6-methyl-2-oxo-1,2,3,4-tetrahydro pyrimidine-5-carbonyl)-3-methyl-5-oxo-1H-pyrazol-4(5H)-ylidene)hydrazinyl)-N-(thiazol-2-yl) benzene sulfonamides (1a-e) were synthesis by reported method.[15-17]

The IR spectra of all compounds were taken in KBr pellets on a Nicolet 400D spectrometer. Proton NMR spectra were recorded on a Bruker (400 MHz) spectrometer. Deuterated DMSO was used as a solvent. LC-MS of selected samples taken on LC-MSD-Trap-SL_01046. All the compounds were checked for their purity by TLC.

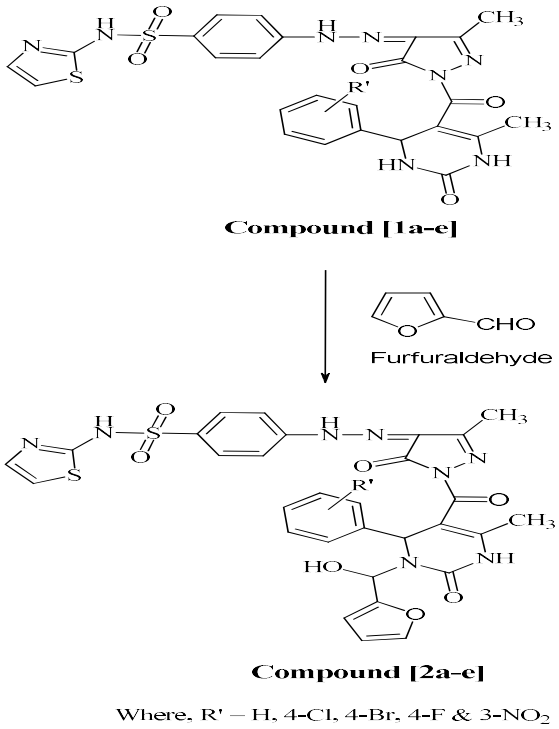
The antibacterial activities of both the series of compounds (2a-e) were studied against gram +Ve and -Ve bacteria shown in Table-1. The activity was measured at a conc, 50µg/ml by the agar-cup plate method.[18] The percentage inhibition of growth of bacteria by the compounds is shown in Table-2. The antifungal activities of both the series of compounds (2a-e) were measured at 1000ppm concentration in vitro Plant pathogen shown in Table-2 have been selected for the study.[19]

Synthesis of 4-(2-(1-(4-aryl-3-(furan-2-yl(hydroxy)methyl)-6-methyl-2-oxo-1,2,3,4-tetra hydropyrimidine-5-carbonyl)-3-methyl-5-oxo-1H-pyrazol-4(5H)-ylidene) hydrazinyl)-N-(thiazol-2-yl) benzene sulfonamide (2a-e)

A solution of 4-(2-(1-(4-aryl-6-methyl-2-oxo-1,2,3,4-tetrahydro pyrimidine-5-carbonyl)-3-methyl-5-oxo-1H-pyrazole-4(5H)-ylidene) hydrazinyl)-N-(thiazol-2-yl) benzene sulfonamide (1a-e) (40 mmol) in dimethyl sulfoxide (25 mL) was heated gently until (1a-e) dissolved, and then potassium carbonate (20

http://dx.doi.org/10.31788/RJC.2022.1516656

mmol) was added with stirring. Furfuraldehyde (40 mmol) was added one time and the mixture was stirred at room temperature for 5 h. Water (40 mL) was added and cooled in an icebox for several hours. The formed precipitate was collected by filtration, washed with water, dried in the oven at 80 °C, and crystallized from methanol to give a crystalline precipitate of (2a-e). The product was checked by TLC frequently.



Reaction Map of Compounds (2a-e)
Scheme-1

4-(2-(1-(3-(furan-2-yl(hydroxy)methyl)-6-methyl-2-oxo-4-phenyl-1,2,3,4-tetrahydro pyrimidine-5-carbonyl)-3-methyl-5-oxo-1H-pyrazol-4(5H)-ylidene)hydrazinyl)-N-(thiazol -2-yl)benzenesulfonamide (2a)

Light yellow solid; Yield: 56%; Elemental Analysis for $C_{30}H_{26}N_8O_7S_2$(674.71) ,Calc.(Found): %C,53.40(53.40),%H,3.88(3.90),%N 16.61 (16.60) and %S 9.50(9.50);IR (KBr,vmax,cm^{-1}): 3465(OH),2960,1600,1500 (Aromatic C-H stretching),3200(-NH of amine) and 1690(C=O),1138,1045(C-O); 1H-NMR (400 MHz, DMSO-d6) δ7.10-8.10 (multiplet, aromatic C-H protons & C-H of furan),1.4(3H Triplet, CH_3), 2.53-2.56(3H,Singlet,CH_3),3.56 (1H singlet, OH);M^+:675.9

4-(2-(1-(4-(4-chlorophenyl)-3-(furan-2-yl(hydroxy)methyl)-6-methyl-2-oxo-1,2,3,4-tetra hydropyrimidine-5-carbonyl)-3-methyl-5-oxo-1H-pyrazol-4(5H)-ylidene) hydrazinyl)-N-(thiazol-2-yl)benzenesulfonamide (2b)

Light blue solid; Yield: 58%; Elemental Analysis for $C_{30}H_{25}N_8O_7S_2Cl$ (709.15),Calc.(Found): %C,50.81(50.80),%H,3.55(3.50),%N15.80 (15.80) and %S 9.04(9.00);IR (KBr, vmax, cm^{-1}): 3460(OH),2962,1610,1500 (Aromatic C-H stretching),3210(-NH of amine) and 1692(C=O) 1140,1047(C-O); 1H-NMR (400 MHz, DMSO-d6) δ7.10-8.10(multiplet, aromatic C-H protons & C-H of furan),1.50(3H Triplet, CH_3), 2.53-2.58(3H,Singlet,CH_3),3.57(1H singlet, OH).

4-(2-(1-(4-(4-bromophenyl)-3-(furan-2-yl(hydroxy)methyl)-6-methyl-2-oxo-1,2,3,4-tetra hydropyrimidine-5-carbonyl)-3-methyl-5-oxo-1H-pyrazol-4(5H)-ylidene) hydrazinyl)-N-(thiazol-2-yl)benzenesulfonamide(2c)

Light brown solid; Yield: 57%; Elemental Analysis for $C_{30}H_{25}N_8O_7S_2Br$ (753.60) ,Calc.(Found):%C,47.81(47.80),%H,3.34(3.30),%N14.87 (14.90) and %S10.60(10.60); IR (KBr, vmax,

cm^{-1}): 3460(OH),2960,1610,1500 (Aromatic C-H stretching), 3210(NH of amine) and 1693(C=O) 1139,1045(C-O); 1H-NMR (400 MHz, DMSO-d6) δ7.10- 8.14 (multiplet,aromatic C-H protons & C-H of furan),1.52(3H Triplet,CH_3),2.53-2.55(3H , Singlet, CH_3), 3.56(1H singlet, OH);M^+: 755.

4-(2-(1-(4-(4-fluorophenyl)-3-(furan-2-yl(hydroxy)methyl)-6-methyl-2-oxo-1,2,3,4-tetra hydro pyrimidine-5-carbonyl)-3-methyl-5-oxo-1H-pyrazol-4(5H)-ylidene)hydrazinyl)-N-(thiazol -2-yl)benzenesulfonamide(2d)

Light white solid; Yield: 58%; Elemental Analysis for $C_{30}H_{25}N_8O_7S_2F$(692.70),Calc.(Found):%C,52.02(52.00),%H,3.54(3.50),%N16.18(16.20) and %S9.26(9.30);IR (KBr,vmax, cm^{-1}): 3470(OH), 2960,1600,1510 (Aromatic C-H stretching), 3213(NH of amine) and 1693(C=O) 1140,1044(C-O); 1H-NMR(400 MHz, DMSO-d6) δ7.10- 8.10 (multiplet, aromatic C-H protons & C-H of furan),1.47(3H Triplet,CH_3),2.50-2.55(3H , Singlet, CH_3), 3.55(1H singlet, OH).

4-(2-(1-(4-(3-nitrophenyl)-3-(furan-2-yl(hydroxy)methyl)-6-methyl-2-oxo-1,2,3,4-tetra hydropyrimidine-5-carbonyl)-3-methyl-5-oxo-1H-pyrazol-4(5H)-ylidene)hydrazinyl)-N-(thiazol-2-yl)benzenesulfonamide (2e)

Yellowish white solid; Yield: 58%; Elemental Analysis for $C_{30}H_{25}N_9O_9S_2$(719.70),Calc.(Found):%C,50.07(50.00),%H,3.50(3.50),%N 17.52 (17.50) and %S8.91(8.90); IR (KBr, vmax, cm^{-1}):3460(OH),2965,1600, 1510 (Aromatic C-H stretching), 3215(NH of amine) and 1690(C=O) 1138,1048(C-O);1H-NMR(400 MHz, DMSO-d6) δ7.10- 8.15 (multiplet,aromatic C-H protons & C-H of furan),1.50(3H Triplet,CH_3),2.50-2.50(3H , Singlet, CH_3), 3.52(1H singlet, OH).

Table-1: Antibacterial Activity of Compounds (2a-e)

Comp. No.	Zone of Inhibition(mm)				
	Gram +ve		*Gram –ve*		
	Bacillus Subtilis	*Staphylococcus aureus*	*Kllebsiella promioe*	*Salmonella Typhl*	*E.coil*
2a	58	44	62	55	59
2b	67	47	67	63	65
2c	60	46	67	56	61
2d	66	45	69	60	63
2e	71	50	79	70	67
Tetracycline	79	55	87	76	72

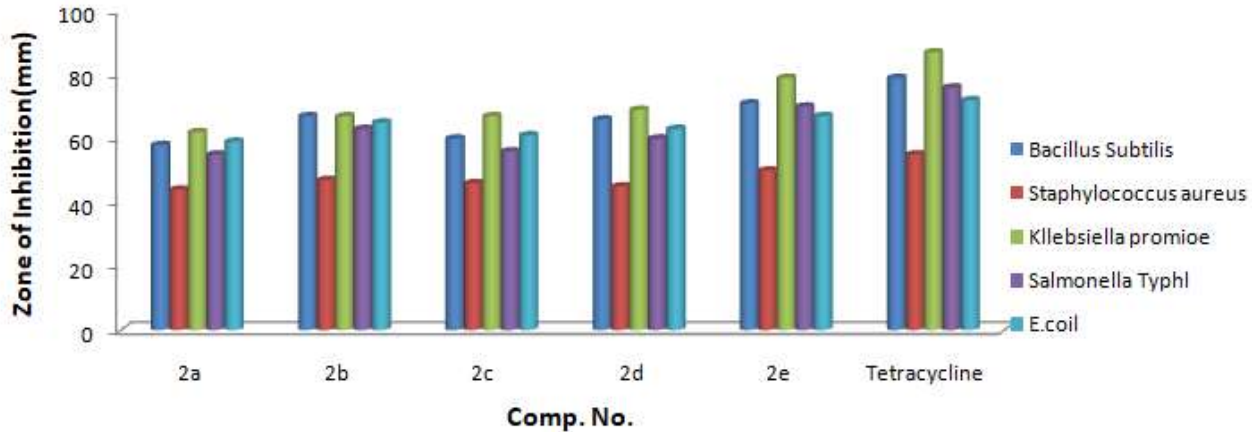


Fig.-1: Antibacterial Activity of Compounds (2a-e)

Table-2: Antifungal Activity of Compounds (2a-e)

Comp. No.	Zone of Inhibition at 1000 ppm (%)			
	Botrydepladia Thiobromine	*Nigrosspora Sp.*	*Penicillium Expansum*	*Rhizopus Nigricuns*
2a	66	69	65	65
2b	76	75	72	74

2c	61	66	65	69
2d	73	72	67	68
2e	79	78	74	79

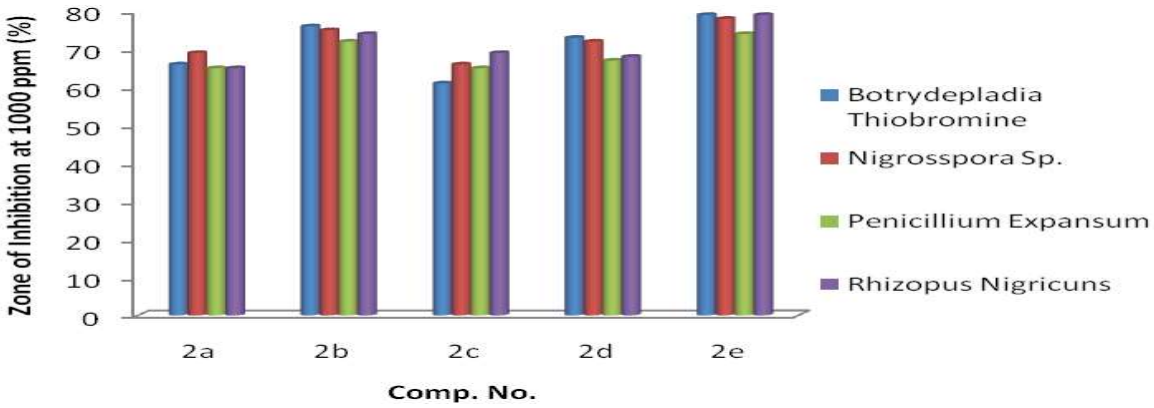


Fig.-2: Antifungal Activities of Compounds (2a-e)

RESULTS AND DISCUSSION

The reaction of 4-(2-(1-(4-aryl-6-methyl-2-oxo-1,2,3,4-tetrahydro pyrimidine-5-carbonyl)-3-methyl-5-oxo-1H-pyrazol-4(5H)-ylidene)hydrazinyl)-N-(thiazol-2-yl) benzene sulfonamide (1a-e) with Furfuraldehyde yielded 4-(2-(1-(4-aryl-3-(furan-2-yl(hydroxy) methyl)-6-methyl-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carbonyl)-3-methyl-5-oxo-1H-pyrazol-4(5H)-ylidene) hydrazinyl)-N-(thiazol-2-yl) benzene sulfonamide (2a-e).

The structures of **(2a-e)** were confirmed by elemental analysis and IR spectra showing characteristic absorption bands at 3460-3470 cm^{-1}(OH) and 1138-1140,1045-1048(C-O), additional IR bands than **(1a-e)** i.e. 2960,1610,1500(Aromatic C-H stretching),3210(NH of amine), 1693(C=O),1620-1630 cm^{-1}(C=N), 680(C-S), 1160(SO_2),1695-1750cm^{-1}(C=O), 1070 (C=S),1080(-Cl),1555,1375(-NO_2),1070(C-Br),1150(C-F).Similarly ^{1}H NMR data shows 3.56 (1H singlet, OH) and 9.95-11.9(s,3H,NH) which is one less NH peak than **(1a-e)**.The C, H, N analysis data of all compounds are presented.

All the elemental and spectral features suggest that the data are consistent with the predicted structure shown in Scheme-1. The LC-MS of compounds shows the peak of M^+ ion which is consistent with their molecular weight. All these facts confirm the structures 2a-e.

The examination of antibacterial activity data reveals that all compounds are toxic against microbes and the compounds **2e** found more active against the gram-positive and gram-negative bacteria.

CONCLUSION

The novel heterocyclic compounds, 4-(2-(1-(4-aryl-3-(furan-2-yl(hydroxy) methyl)-6-methyl-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carbonyl)-3-methyl-5-oxo-1H-pyrazol-4(5H)-ylidene) hydrazinyl)-N-(thiazol-2-yl) benzene sulfonamide (2a-e) synthesised from reaction of 4-(2-(1-(4-aryl-6-methyl-2-oxo-1,2,3,4-tetrahydro pyrimidine-5-carbonyl)-3-methyl-5-oxo-1H-pyrazol-4(5H)-ylidene)hydrazinyl)-N-(thiazol-2-yl) benzene sulfonamide (1a-e) and Furfuraldehyde. The predicted structures were confirmed with elemental and spectral features. Antibacterial activity data reveals that all compounds toxic against microbes.

ACKNOWLEDGEMENT

We are very thankful to the Department of Chemistry, Rabindranath Tagore University for providing a research facility.

REFERENCES

1. K. Karrouchi, S. Radi, Y. Ramli, J. Taoufik, Y. N. Mabkhot, F. A. Al-aizari, and M. Ansar, *Molecules*, **23**,134(2018), https://doi.org/10.3390/molecules23010134
2. M. G. El-Gazzar, and H. M. Aly, *Current Organic Synthesis*, **15**, 414(2018), https://doi.org/10.2174/2211556006666170927155809

3. H. S. Lin, Y. L. Huang, Y. S. Wang, E. Hsiao, T. A. Hsu, H. Y. Shiao, *Cancers,* **11**, E739(2019), https://doi.org/10.3390/cancers11060739
4. A. Ansari, A. Ali, and M. Asif, *New Journal of Chemistry,* **41(1)**, 16(2017), https://doi.org/10.1039/C6NJ03181A
5. S. M. Gomha, M. M. Edrees, R. A. Faty, Z. A. Muhammad, Y. N. Mabkhot, *Chemistry Central Journal,* **11(1)**, 37(2017), https://doi.org/10.1186/s13065-017-0266-4
6. R. Aggarwal, A. Bansal, I. Rozas, B. Kelly, P. Kaushik, D. Kaushik, *European Journal of Medicinal Chemistry,* **1(70)**, 350(2013), https://doi.org/10.1016/j.ejmech.2013.09.052
7. R. Aggarwal, S. Kumar, P. Kaushik, D. Kaushik, G. K. Gupta, *European Journal of Medicinal Chemistry,* **1(62)**, 508(2013), https://doi.org/10.1016/j.ejmech.2012.11.046
8. S. Mukarram, B. P. Bandgar, R. U. Shaikh, S. D. Ganapure, H.V. Chavan, *Medicinal Chemistry Research*, **26(1)**, 262(2017), https://doi.org/10.1007/s00044-016-1744-2
9. R. Aggarwal, R. Kumar, S. Kumar, G. Garg, R. Mahajan, J. Sharma, *Journal of Fluorine Chemistry,* **132(11)**, 965(2011), https://doi.org/10.1016/j.jfluchem.2011.07.029
10. N. Abunada, H. Hassaneen, N. Kandile, and O. Miqdad, *Molecules,***13**,1501(2008), https://doi.org/10.3390/molecules13071501
11. R. Kumar, J. Arora, S. Ruhil, N. Phougat, A. K. Chhillar, A. K. Prasad, *Advances in Chemistry*, **2014**, 1(2014), https://doi.org/10.1155/2014/329681
12. J. B. Shi, W. J. Tang, R. Li, X. H. Liu, *European Journal of Medicinal Chemistry,* **201**, 90, 889(2014), https://doi.org/10.1016/j.ejmech.2014.12.013
13. E. C. Nossier, H. Fahmy, N. Khalifa, W. El-Eraky, M. Baset, *Molecules,* **22**, 512(2017), https://doi.org/10.3390/molecules22040512
14. A. A. Hadi, Z. Y. Kadhim, A. N. Seewan, M. G. Munahi, and M. Q. Waheeb, *Medico-legal Update*, **20(2)**, 326(2020).
15. N. Sarvaiya, H. S. Patel, S. Gulati, *International Advanced Research Journal in Science, Engineering and Technology*, **06(1)**, 49(2019), https://doi.org/10.17148/IARJSET.2019.6108
16. I. M. Shaban, and M. S. Al-Ajely, *Journal of Scientific & Technical Research*, **22 (1)**, 16293(2019), DOI: 10.26717/BJSTR.2019.22.003684
17. P. J. Shah, H. S. Patel, and B. P. Patel, Synthesis, *Journal of Saudi Chemical Society*, **17**, 307(2013), https://doi.org/10.1016/j.jscs.2011.04.016
18. E. I. Nweze, P. K. Mukherjee, and M. A. Ohannoum, *Journal of Clinical Microbiology*, **48(10)**, 3750(2019), https://doi.org/10.1128/JCM.01357-10
19. US-FDA Office of Regulatory Affairs Pharmaceutical Microbiology Manual Doc.No. ORA 007, Revised Aug.2020.

[RJC-6656/2021]