Journal of Chemical, Biological and Physical Sciences

An International Peer Review E-3 Journal of Sciences

*Available online at*www.jcbsc.org

Section A: Chemical Sciences

CODEN (USA): JCBPAT Research Article

An efficient one-pot multi Component Synthesis of pyrimidine and their Antimicrobial activity

Mohammad Ashid and Ajit Joshi*

Synthesis Organic & Medicinal Chemistry lab, Dept of Chemistry, Mewar University, Gangrar, Rajasthan, India (312901)

Received: 28 November 2016**; Revised:** 16 December 2016**; Accepted:** 23 December 2016

Abstract: One pot three component synthesis of 4-amino/mercapto-6-(3-nitrophenyl)-2-sulfanylpyrimidine-5-carbonitrile (IVa-b) in moderate to high yield is achieved via a one pot synthesis reaction of malononitrile, substituted aromatic aldehyde & Guanidine/thiourea in ethanol. Which is further treated with formic acid via Cyclization gives 7-Substituted-5-(3-nitrophenyl) pyrimido [4,5-*d*]pyrimidin-4(3*H*)-one (V a-b) in condensation process. Which was further treated with Bromoethoxyphthallimide to give 2-(2-{[4-(3-nitrophenyl)-5-oxo-5,6-dihydropyrimido[4,5-*d*]pyrimidin-2-yl]sulfanyl/ amino} ethoxy)-1*H*-isoindole-1,3(2*H*)-dione (VIIIa-b). All the synthesized compoundso give were supported by spectral and analytical analysis. Also the synthesized compounds were tested for their antimicrobial activity.

Keywords: Malononitrile, Thiourea, Guanidine, Pyrimidine, Tetrazolopyrimidine, s-Triazolopyrimidine.

INTRODUCTION

Heterocyclic chemistry evolved Medicinal chemistry is a scientific discipline at the intersection of chemistry and pharmacy involved with designing, synthesizing and developing pharmaceutical drugs. It also includes the study of existing drugs, their biological properties, and their quantitative structure

activity relationships (QSAR). New drugs are necessitated, to cure new diseases, to find harmless drugs (no side effects) and to cure diseases whose drugs have become ineffective due to resistant strains of micro-organisms. Besides these causes, new drug discovery and research in medicinal chemistry is required to identify pharmacophore present in effective drugs (as a little modification in the structure of a durg may cause abrupt change in its pharmacology). Research is necessary to replace the broad-spectrum medicines by narrow spectrum drugs, which can be achieved by designing the drug in the light of pharmacogenomics. Also, the global population of different physical and climatic conditions may not tolerate a single drug. Thus there is a growing need of research in the field of synthetic chemistry.

Pyrimidine ring as Tetrazolo pyrimidine play an important role as potent analgesic, anti-inflammatory, antipyretic, antimicrobial, anticonvulsant, fungicidal, antiplatelet activities, and central nervous system (CNS) affecting activities. In addition, pyrimidine nucleus can be found in a broad variety of antibacterial, anticancer and anti-tumor agents as well as in agrochemicals and veterinary products, Pyrimidine derivatives serve both as biomimetic and reactive pharmacophores due to their diverse medicinal properties such as antitumor, anticancer (lungs, breast and CNS cancer), immunodilator, antiviral etc. Pyrimidine derivatives have activities like tyrosine kinase inhibitors, COX-2 inhibitor, calcium channel blockers plus antihypertensive and also activity against Y181C HIV-1 mutant strain, etc. Diverse biological activities like: anticonvulsant, diuretic, fungicidal and trypanocidal. Pyrimidine derivatives possess several interesting biological activities such as antimicrobial, antitumour and antifungal activities[1-5].

RESULT & DISCUSSION

Our continuous research directed to synthesise biologically active compounds, we report here a new synthesis for 2-amino-, 2-mercapto- and 2-benzylmercaptopyrimidine derivatives *via* the reaction of aromatic aldehydes, malononitrile and each of Thiourea, Guanidine and S-benzylisothiourea respectively. The reaction products were utilised for the synthesis of other new azolopyrimidines bearing latent functional substituents. Thus, when a ternary mixture of the appropriate aromatic aldehyde, malononitrile and thiourea or guanidine was refluxed in ethanol in the presence of sodium acetate, the 2-mercapto and 2,4- diamino-5-cyano-6-phenyl pyrimidine (IVa-b) were obtained. Structure (IVa-b) was inferred from the following facts: The H NMR spectrum of IVa showed signals at 3.32 (s, 1H, SH), 4.14 (s, 2H, NH2), 7.61-7.96 (m, 4H, Ar-H) and IVb showed signals at 4.48 (s, 4H, NH2) 7.63-7.96 (m, 4H, Ar-H) led to the disappearance of the first and the last signals. The IR spectra of IVa-b displayed characteristic bands for NH2, CN and SH. **Compound VIa** showed the H NMR signals at 2.42 (s, 2H, CH2), 4.14 (s, 2H, NH2), 7.61-7.96 (m, 9H, Ar-H). The IR spectra of VIa displayed characteristic bands for NH2, CN and CH2. **Compound Va** showed the H NMR signals at 1.56 (s, 1H, CH) 3.32 (s, 1H, SH) 8.56 (s, 1H, NH), 7.63-7.96 (m, 4H, Ar-H), The IR spectra of Va displayed characteristic bands for NH, CN, CO, CH and SH. Whereas **Compound Vb** showed the H NMR signals at 1.48 (s, 1H, CH) 4.56 (s, 2H, NH2) 8.41 (s, 1H, NH), 7.26-7.91 (m, 4H, Ar-H). The IR spectra of Vb displayed characteristic bands for NH2, NH, CN, SH, CO and CH.

All the synthesized compounds are tested for antibacterial and anti fungal activity. In these compounds **IVb, Va & Vb** shows good activity against bacterial and **Va** & **Vb** gave good activity against fungal and rest of compounds show moderate activity.

MATERIAL & METHOD

All the chemicals and solvents (analytical grade) were purchased from commercial sources and used without further purification. All melting points were determined in open capillary tube and are uncorrected. TLC aluminum sheets were used for thin-layer chromatography (TLC) and spots were visualized under UV light. Melting points were taken in open capillary tubes and therefore uncorrected. Purity of the compounds was checked on silica gel G TLC plates of 2 mm thickness using n-hexane and ethyl acetate as solvent system. The visualization of spots was carried out in an UV/Iodine chamber. The IR spectra of the compounds were recorded in the 4000-450 cm^{-1} ranges using KBr discs on FTIR Perkin Elmer spectrometers and 1H NMR were recorded on a Bruker DRX-300 MHz spectrometer (DMSO) using TMS as an internal standard. The mass spectra were recorded on a Jeol SX-102 (FAB) mass spectrometer. Structure of all the synthesized compounds was assigned on basis of their analytical Data and spectral data.

EXPERIMENTAL SECTION

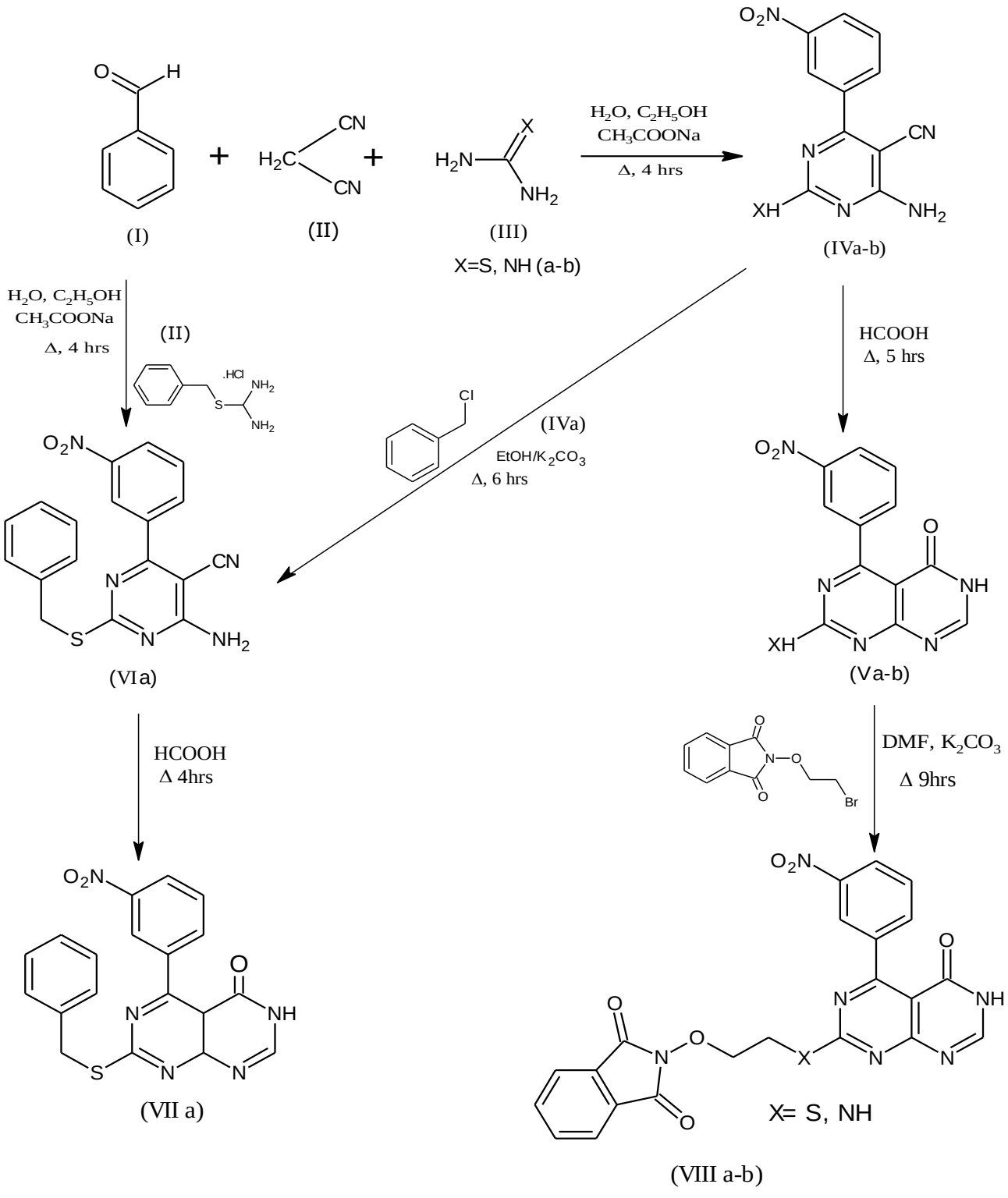
Synthesis of 4-amino-6-(3-nitrophenyl)-2-sulfanylpyrimidine-5-carbonitrile (IV a): An equimolar mixture of aromatic aldehyde (0.01 mole), malononitrile (0.01 mole), Sodium acetate (0.01 mole) & Thiourea (0.01 mole) was refluxed in EtOH:Water (2:8) (20 ml) for 3 hrs. After completion of reaction (TLC) the reaction mixture was removed from the heating source and kept at room temperature for at least 2 hrs. A crystalline product was obtained which was collected by filtration, washed with chilled EtOH, dried & recrystallization from Ethanol to give desired pure product.

Yield: 65%; M.P.: 260-262ºC; IR (KBr) cm-1: 3426, 3393 (NH2 str.), 3032 (C-H str., Ar-H), 2222 (CN str.), 1650 (C=N str.). 1H NMR (DMSO) δ: 3.32 (s, 1H, SH), 4.14 (s, 2H, NH2), 7.61-7.96 (m, 4H, Ar-H). MS: m/z; 273, Anal. calcd for $C_{11}H_7N_5O_2S$: C 48.35; H 2.58; N 25.63; O 11.71; S 11.73%. Found: C 48.31; H 2.52; N 25.60; O 11.73; S 11.69%.

Synthesis of 3, 5-diamino-3'-nitrobiphenyl-2-carbonitrile (IV b): An equimolar mixture of aromatic aldehyde (0.01 mole), malononitrile (0.01 mole), Sodium acetate (0.01 mole) & Guanidine nitrate (0.01 mole) was refluxed in EtOH:Water (2:8) (20 ml) for 3 hrs. After completion of reaction (TLC) the reaction mixture was removed from the heating source and kept at room temperature for at least 2 hrs.Yellow coloured crystals were obtained which was collected by filtration, washed with chilled EtOH, dried & recrystallization from Ethanol to give desired pure product.

Yield: 60%; M.P.: 146-148ºC IR (KBr) cm-1: 3412, 3397 (NH2 str.), 3032 (C-H str., Ar-H), 2222 (CN str.), 1643 (C=N str.). 1H NMR (DMSO) δ: 4.48 (s, 4H, NH2) 7.63-7.96 (m, 4H, Ar-H). MS: m/z; 256,. Anal. calcd for $C_{11}H_8N_6O_2$: C 51.56; H 3.15; N 32.80; O 12.49%., Found: C 51.49; H 3.11; N 32.76; O 12.52%.

Synthesis of 7-Substituted-5-(3-nitrophenyl) pyrimido [4, 5-*d*] pyrimidin-4(3*H*)-one (V a-b): Compound (IV a-b) (0.01 mole) was taken in 250 ml RB flask and formic acid (40 ml) was added to it. The reaction flask is attached to reflux condenser and the reaction mixture is heated to reflux for 5 hrs. After completion of reaction (TLC) reaction mixture was cooled and poured in crushed ice. A yellow brown colour precipitate obtained which was separated by filtration, washed with water, dried & recrystallized by ethanol to give pure product.



Reaction Scheme

5-(3-nitrophenyl)-7-sulfanylpyrimido [4,5-*d*]pyrimidin-4(3*H*)-one (Va): Yield: 59%; M.P.: 244-248ºC IR (KBr) cm-1: 3391 (NH str.), 3200 (SH), 3031 (C-H str., Ar-H), 2936 (C-H Aliphatic) 1692 (CO str.), 1645 (C=N str.). 1H NMR (DMSO) δ: 1.56 (s, 1H, CH) 3.32 (s, 1H, SH) 8.56 (s, 1H, NH), 7.63-7.96 (m, 4H, Ar-H), Anal. calcd for $C_{12}H_7N_5O_3S$: C 47.84; H 2.34; N 23.25; O 15.93; S 10.64%. Found: C 47.72; H 2.34; N 23.28; O 15.87; S 10.54%.

7-amino-5-(3-nitrophenyl) pyrimido [4,5-*d*]pyrimidin-4(3*H*)-one (Vb): Yield: 62%; M.P.: 220-225ºC IR (KBr) cm-1: 3411, 3389 (NH2 & NH str.), 3032 (C-H str., Ar-H), 2931 (C-H Aliphatic) 1696 (CO str.), 1647 (C=N str.). 1H NMR (DMSO) δ: 1.48 (s, 1H, CH) 4.56 (s, 2H, NH2) 8.41 (s, 1H, NH), 7.26-7.91 (m, 4H, Ar-H), Anal. calcd for $C_{12}H_8N_6O_3$: C 50.71; H 2.84; N 29.57; O 16.89%. Found: C 50.55; H 2.76; N 29.51; O 16.91%.

Synthesis of 4-amino-2-(benzylsulfanyl)-6-(3-nitrophenyl) pyrimidine-5-carbonitrile (VIa): Method A (from IVa): Compound (IV a) (0.01 mole) was taken in 250 ml RB flask and benzyl chloride (0.01 mole) and K2CO3 (0.01 mole) was taken in 20 ml DMF and the reaction mixture was refluxed for 6 hrs. After completion of the reaction (TLC) the reaction mixture was cooled and poured in crushed ice. A precipitated product separated which was collected by filtertation, washed with water dried and recrystallized from ethanol.

Method B (Direct method): An equimolar mixture of aromatic aldehyde (0.01 mole), malononitrile (0.01 mole), Sodium acetate (0.01 mole) & phenylisothiouranium chloride (0.01 mole) was refluxed in EtOH:Water (2:8) (20 ml) for 3 hrs. After completion of reaction (TLC) the reaction mixture was removed from the heating source and kept at room temperature for at least 2 hrs. A crystalline product was obtained which was collected by filtration, washed with water, dried & recrystallization from Ethanol to give desired pure product.

Yield: 65%; M.P.: 146-148ºC IR (KBr) cm-1: 3426, 3393 (NH2 str.), 3032 (C-H str., Ar-H), 2950 (C-H str. Aliphatic), 2222 (CN str.), 1650 (C=N str.). 1H NMR (CDCl3) δ: 2.42 (s, 2H, CH2), 4.14 (s, 2H, NH2), 7.61-7.96 (m, 9H, Ar-H). MS: m/z; 273, Anal. calcd for $C_{18}H_{13}N_5O_2S$: C 59.49; H 3.61; N 19.27; O 8.81; S 8.82%. Found: C 59.41; H 3.55; N 19.14; O 8.71; S 8.74%.

Synthesis of 7-(benzylsulfanyl)-5-(3-nitrophenyl)-4a, 8a-dihydropyrimido [4,5-*d*]pyrimidin-4(3*H*)-one (VIIa): Compound (VI a) (0.01 mole) was taken in 250 ml RB flask and formic acid (40 ml) was added to it. The reaction flask is attached to reflux condenser and the reaction mixture is heated to reflux for 4 hrs. After completion of reaction (TLC) reaction mixture was cooled and poured in crushed ice. A yellow brown colour precipitate obtained which was separated by filtration, washed with water, dried & recrystallized by ethanol to give pure product.

Yield: 55%; M.P.: 162-164ºC IR (KBr) cm-1: 3326 (NH str.), 3072 (C-H str., Ar-H), 2910 (C-H str. Aliphatic), 1692 (C=O Str.), 1650 (C=N str.). 1H NMR (CDCl3) δ: 4.12 (s, 2H, CH2), 1.31 (1H, CH) 9.14 (s, 1H, NH), 7.14-7.96 (m, 9H, Ar-H). MS: m/z; 393, Anal. calcd for $C_{19}H_{15}N_5O_3S$: C 58.01; H 3.84; N 17.80; O 12.20; S 8.15%. Found: C 58.07; H 3.81; N 17.86; O 12.17; S 8.11%.

Synthesis of 2-(2-{[4-(3-nitrophenyl)-5-oxo-5,6-dihydropyrimido[4,5-*d*]pyrimidin-2-yl] sulfanyl} ethoxy)-1*H*-isoindole-1,3(2*H*)-dione (VIIIa): Bromoethoxy phthallimde (0.01 mole) and compound **(Va**) (0.01 mole) was dissolved in DMF (20 ml) and Na metal (0.01 mole) is added. Then the reaction

mixture is stirred on a magnetic stirrer for 3 hrs at room temperature. After that the reaction mixture was refluxed for 4 hrs. After completion of reaction (TLC) the reaction mixture is cooled and poured in crushed ice and precipitate of compound (**VIIIa**) was formed which was filtered, washed with cold water, dried and recrystallized from ethanol.

Yield: 65%; M.P.:-224-226ºC; IR (KBr) cm-1: 3329 (NH Str.)3026 (C-H str., Ar-H), 2921 (C-H, str. Aliphatic) 1661 (C=N str.), 1682 (CO-NH str.), 1724, 1694 (CO-N-CO). 1H NMR (CDCl3) δ: 1.25 (s, 1H, CH), 4.45 (t, 2H, OCH2), 3.33 (t, 2H, NCH2), 7.26-7.81 (m, 18H, Ar-H), 8.91 (s, 1H, NH). MS: m/z; 490. Anal. calcd for $C_{22}H_{14}N_6O_6S$: C 53.88; H 2.88; N 17.14; O 19.57; S 6.54%. Found: C 53.83; H 2.84; N 17.16; O 19.52; S 6.51%.

Synthesis of 2-(2-{[4-(3-nitrophenyl)-5-oxo-5,6-dihydropyrimido[4,5-*d*]pyrimidin-2-yl] amino} ethoxy) -1*H*-isoindole-1,3(2*H*)-dione (VIIIb):Bromoethoxy phthallimde (0.01 mole) and compound **(Vb**) (0.01 mole) was dissolved in DMF (20 ml) and Na metal (0.01 mole) is added. Then the reaction mixture is stirred on a magnetic stirrer for 3 hrs at room temperature. After that the reaction mixture was refluxed for 4 hrs. After completion of reaction (TLC) the reaction mixture is cooled and poured in crushed ice and precipitate of compound (**VIIIb**) was formed which was filtered, washed with cold water, dried and recrystallized from ethanol.

Yield: 61%; M.P.:-183-186ºC; IR (KBr) cm-1: 3310 (NH Str.)3015 (C-H str., Ar-H), 2931 (C-H, str. Aliphatic) 1645 (C=N str.), 1691 (CO-NH str.), 1730, 1699 (CO-N-CO). 1H NMR (CDCl3/DMSO) δ: 4.14 (t, 2H, OCH2), 2.93 (t, 2H, NCH2), 7.14-8.12 (m, 18H, Ar-H), 8.91 (s, 1H, NH), 6.11 (s, 1H, NH). MS: m/z; 473. Anal. calcd for $C_{22}H_{15}N_7O_6$: C 55.82; H 3.19; N 20.71; O 20.28%. Found: C 55.80; H 3.15; N 20.73; O 20.26%.

ANTIMICROBIAL ACTIVITY

All the synthesized compounds of present work were *in vitro* screened for the antibacterial and antifungal activity using 500 ppm concentration in DMF by cup and well method. The micro-organisms *Bacillus subtilis, Proteus mirabilis, Klebsiella pneumoniae, Escherichia coli* were used as antibacterial strains and *Candida albicans* and *Aspergillus fumigatus* were used as fungal strains. The activity is presented as zone of inhibition in mm and compared with activity of controls C1 and C2 (for antibacterial activity CI= ciprofloxacin for antifungal activity C2=flucanazole) to give activity index value **(Table 1).**

All the compounds showed poor activity against *K pneumonia* and *E. coli* whereas moderate to strong activity was shown against *P. mirabilis* and *B. subtilis.* Activity index value against *P. mirabilis* and *B. subtilis* was more than one for majority of compounds. It was interesting to note that all the compounds showed stronger activity than the standard used against *Candida albicans* and *Aspergillus fumigatus.* It was concluded from the activity study that compound VIIIa & VIIIb was found to be the strongest amongst all synthesized compounds. Compounds under study showed more comprehensive fungus-inhibiting properties than that of the bacterial. Even two folds antifungal activity was observed for these compared to standard.

Table 1: Antimicrobial activity of the synthesized compounds (**IVa-b), (Va-b), (VIa), (VIIa), (VIIIa-b)**

Antibacterial activity					**Antifungal activity**	
S.No.	**Bacillus Subtilis**	**Protius Mirabilis**	**Klebsilla Pneumonia**	**Escherichia Coli**	**Candida Albicans**	**Aspergillus Fumigatus**
IVa	17 (0.98)	18 (1.11)	19 (0.97)	17 (1.94)	18 (0.90)	20 (1.01)
IVb	21(1.18)	20 (0.45)	20 (0.41)	21(1.03)	19 (1.08)	18 (1.02)
Va	20 (0.57)	21 (1.13)	21 (1.08)	20 (1.25)	17 (1.05)	18 (1.09)
Vb	24(1.34)	23 (1.29)	20 (1.37)	21(1.03)	18 (1.08)	19 (1.12)
VIa	16 (1.38)	18 (1.11)	19 (0.97)	17 (0.94)	18 (0.90)	20 (1.11)
VIIa	24(1.34)	23 (1.29)	20 (0.41)	21(1.03)	16 (1.08)	19 (1.02)
VIIIa	24 (1.37)	24 (1.29)	23 (1.18)	24 (1.25)	23 (1.05)	24 (1.13)
VIIIb	24(1.34)	23 (1.29)	20 (1.37)	21(1.03)	22 (1.08)	22 (1.02)
C1	18	17	18	18	-	-
C2	-	-	-	-	20	20

(Activity index) = Inhibition zone of compound/Inhibition zone of the standard drug
For antibacterial activity: C1 = Ciprofloxacin
For antifungal activity: C2 = flucanazole

CONCLUSION

In the synthesized compounds **IVb, Va, Vb, VIIa, VIIIa, VIIIb** give good activity and others show moderate activity against all four bacterial and **VIIIa** & **VIIIb** give good activity against two fungal.

ACKNOWLEDGEMENT

Authors are thankful to the Head, Department of Chemistry, Mewar University, Gangrar, Chittorgarh for providing Laboratory facilities and to the Director, MRC, MNIT, Jaipur, India for providing spectral and analytical data.

REFERENCE

1. C. Sharma, S. Sharma, N. Hussain and G. L. Talesara, Synthesis and Antimicrobial Activity of Some New Phthalimidoxy Derivatives of Triazine Containing Pyrimidine and Isoxazole, *J. Ind. Council Chem*.; 2009, Vol. 26, No. 1, pp. 31-36.
2. R. R. Dangi; N. Hussain, A. Joshi, G. Pemawat and G. L Talesara, Design, facile synthesis and biological evaluation of quinazoline containing pyrazolothiazolyl, triazinone and their ethoxyphthalimide derivatives, *Indian Journal of Chemistry*, 2011, 50 B, 1165-1172.
3. N. Hussain, R. R. Dangi, D.K. Sain and G. L. Talesara, Synthesis and biological evaluation of some N-ethoxyphthalimido-4-phenyl-6-subsitutedphenyl-2,3,4,5-

tetrahydro-3H-indazol-3-one via Robinson annulations reaction, *Iranian Journal of Organic Chemistry;* 2010, Vol. 2, No1, 328-337.

4. N. Hussain, R.R. Dangi, C. Sharma and G. L. Talesara, ChemInform Abstract: Synthesis of Some N,N-Diethoxyphthalimido-5- (substitutedphenyl)-3-methyl-1,3a,4,5-tetrahydropyrazolo [3,4-c]pyrazole-4-spiro-5-substituted-1H-indole-2-one, *Indian Journal Of Chemistry*, 2011, Vol. 50B, pp. 885-889.

5. A. Joshi, D.K. Sain, B. Thadhaney, S. Ojha, N. Hussain, and G.L. Talesara, Synthetic and biological studies on some fused pyrazoles and their ethoxyphthalimide derivatives *Indian Journal of Chemistry*, 2010, 49 B: 965-970.

6. D. K. Sain, B. Thadhaney, A. Joshi, N. Hussain and G. L Talesara, Synthesis, characterization and biological evaluation of some heterocyclic compounds containing ethoxyphthalimide moiety via key intermediate 6-chloro 1, 3 benzothiazole 2-amine, *Indian Journal of Chemistry*, 2010, 49B, 818-825.

7. A. Joshi; N. Hussain, R. Dangi and G. L Talesara, Synthesis and antimicrobial evaluation of some ethoxyphthalimide derivatives of 3-(substitutedphenyl)-4-methyl-3a, 6-dihydropyrazolo [3,4-c]pyrazol-2(3H)-yl(pyridin-3-yl)methanone, *Afinidad*, 2010, 67(548), 306-309.

8. H. Sheibani, A. S. Saljoogi and A. Bazgir, Three-component process for the synthesis of 4-amino-5- pyrimidinecarbonitriles under thermal aqueous conditions or microwave irradiation, ARKIVOC 2008 (ii) 115-123.

9. S. Y. Hassan, Synthesis and Biological Activity of Some New Pyrazoline and Pyrimidine Derivatives, *J. Braz. Chem. Soc.*, 2011, Vol. 22, No. 7, 1286-1298.

10. P. Yogi, M. Ashid, N. Hussain, S. Khan And A. Joshi, One-Pot Synthesis of Thiazoles via Hantzsch Thiazole Reaction and Their Antimicrobial Activity, *Asian Journal of Chemistry*, 2016, Vol. 28, No. 4, 927-932.

11. M. Ashid, P. Yogi, D. Katariya, P. Agarwal and A. Joshi, pyrimidine: medicinal and biological significance a review, *world journal of pharmacy and pharmaceutical sciences*, 2016,Volume 5, Issue 9, 990-1009.

12. M. Ashid, P. Yogi, D. Katariya, P. Agarwal, K. Soni and A. Joshi, a brief study on performance enhancing drugs (ped's), *world journal of pharmaceutical research*, 2016, volume 5, issue 9, 495-533.

13. N. Hussain, S. Khan, M. Ahmed, A. Joshi, M. Ashid and P. Yogi, Synthesis and Antiviral Evaluation against cytomegalovirus (CMV) and Varicella-zoster virus (VZV) in human embryonic lung (HEL) cells of thiadiazol and thioazolidinone derivatives, *Chemistry & Biology Interface*, 2015, 5, 6, 365-377.

14. M. Ashid, P. Yogi, N. Hussain and A. Joshi, Convenient synthesis & Antiviral Evaluation against cytomegalovirus (CMV) and Varicella-zoster virus (VZV) in human embryonic lung (HEL) cells of 7-[Substituted propoxy]-4-methyl-2Hchromen-2-one and 4-methyl-2-

oxo -2Hchromen-7-(Substituted)-yl acetate Via Pechmann Condensation, *International Journal of Pharma Sciences and Research*, 2015, Vol 6 No 10, 1295-1301.

15. N. M. Khalifa, A. H. Adel, A. Rahman, I. Sherein, Abd-Elmoez Omar, A. Fathalla Amina, A. El-Gwaad, A convenient synthesis of some new fused pyridine and pyrimidine derivatives of antimicrobial profiles, *Res Chem Intermed,* 2015, 41, 2295–2305.

Corresponding author: Ajit Joshi*

Synthesis Organic & Medicinal Chemistry lab, Dept of Chemistry, Mewar University, Gangrar, Rajasthan, India (312901)

On line publication Date: 26.12.2016