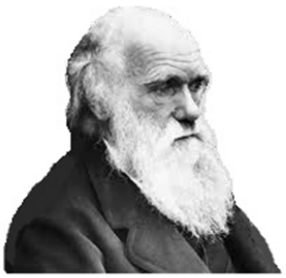
Available online at www.worldnewsnaturalsciences.com



World News of Natural Sciences

An International Scientific Journal

WNOFNS 37 (2021) 92-101 EISSN 2543-5426

Synthesis and characterization of novel pyrimidine derivatives of N-pentyl-2,7-diphenyl-3,8a-dihydroimidazo[1,2-a]pyrimidin-3-amine via 4-phenylpyrimidin-2-amine

Kadachha Raju Ramade[1], Atul J. Rojivadiya[1], Yogesh T. Naliapara[2], Jayesh S. Babariya[3,*]

[1]Department of Chemistry, Maharshi Dayanand Science College, Porbandar, Gujarat, India

[2]Department of Chemistry, Saurashtra University, Rajkot, Gujarat, India

[3]Department of Chemistry, Shree H.N. Shukla Group of Colleges, Rajkot, Gujarat, India

*E-mail address:jayeshbabariya50@gmail.com

ABSTRACT

The target compound N-pentyl-2,7-diphenyl-3,8a-dihydroimidazo[1,2-a]pyrimidin-3-amine have been synthesized by4-phenylpyrimidin-2-amine with Triflouro acetic acid and benzyldehyde. The obtained products were characterized by ^{1}H NMR, Mass and IR Spectra. Purity of all the compounds has been checked on thin layer chromatographic plate and NMR analysis technique.

***Keywords*:** imidazole, pyrimidine, N-pentyl-2.7-diphenyl-3.8a-dihydroimidazo[1.2-a]pyrimidin-3-amine, 4-phenylpyrimidin-2-amine, triflouro acetic acid, benzyldehyde

1. INTRODUCTION

A massive number of Heterocyclic compounds are known and are increasing rapidly. The literature on the subject is very wide. Heterocyclic systems are found in variety of naturally occurring and synthetic compounds and are essential to life. They are important components of alkaloids, antibiotics, hormones and large number of synthetic drugs and dyes. The Nitrogen

(Received 02 May 2021; Accepted 22 May 2021; Date of Publication 23 May 2021)

Heterocyclics are of great importance as they are present in nucleic acids, vitamins, proteins and other biologically important molecular systems.

During last few years, interest in this area was focused on the evaluation of biological activities of various heterocyclic compounds with chemical moieties such as Pyridine, Pyrimidines, Pyrazoline, Thiazolidine, Azetidines, Imidazole, Thiazole, etc. Pyrimidine and their derivatives play a vital role in the field of drugs and agricultural chemicals. Pyrimidine could be a basic nucleus in DNA & RNA.

Pyrimidine derivatives are well-known for their pharmacological properties. These compounds, structurally related to nucleic acids, have been reported to be anticancer, interferon inducer, antiviral, antihypertensive, antitubercular, hypoglycemic, analgesic and anti-inflammatory drugs.

Several methodologies are available for synthesizing this pharmacologically interesting class of heterocycles. Most of them make use of a condensation reaction between a Michael intermediate (arylidine) and amidines, guanidine, urea, thiourea, methylisourea and methylisothiourea in the presence of organic bases as catalysts. The most common path for the synthesis of pyrimidine is a reagent containing C-C-C and N-C-N skeleton.

The C-C-C skeleton was obtained from the reaction of reagents with active methelene group and aryl aldehyde whereas N-C-N skeleton can be obtained from urea, thiourea or guanidine.

Synthetic approaches to the construction of bicyclic systems containing the imidazole nucleus have been considered. Methods for obtaining derivatives of imidazo[1,2-*a*]pyrazine and imidazo[1,2-*a*]pyrimidine have been studied, and methods have been developed for catalytic hydrogenation of these compounds. Partial reduction of the imidazole ring on imidazo[1,2-*a*]pyrimidine hydrogenation has been discovered for the first time [1-42].

2. MATERIALS METHODS

All research chemicals were purchased from Sigma–Aldrich and used as it is for the reactions. Reactions were monitored by thin-layer chromatography (TLC) on precoated silica gel GF254 plates from E-Merck Co and compounds visualized either by exposure to UV. Melting points were determined in open capillaries and are uncorrected.

The IR spectra were recorded on SHIMADZU- FTIR-8400 spectrophotometer using KBr pellet method. ^{1}H NMR spectra were recorded on Bruker 300-MHz NMR spectrometer in $CDCl_3$ with TMS as internal standard. Mass spectrum was recorded on JOEL SX 102/DA-600-Mass spectrometer.

3. EXPERIMENTAL

General synthesis method for INT-01

Take 5 gm p-bromoacetophenone and 20 ml DMF-DMA (Dimethyl formamide, Dimethylacetal) and 1 ml glacial acetic acid stir reaction mixture for 12 hour at 100 °C. After completion of reaction add reaction mixture in ice cold water dropwise, wash product with water and yellow colour product obtained.

General synthesis method for 4-phenylpyrimidin-2-amine (INT-02)

Take 5 gm of 1-(4-bromophenyl)-3-(dimethylamino)prop-2-en-1-one (1 equivalent) and 20 gm guanidine hydrochloride (4 equivalent) and 10 gm of sodium methoxide (2 equivalent) in 20 ml of methanol, put reaction for 12 hour at 70 °C. After the completion of reaction pour it into ice cold water filters it, white colour product obtained.

General synthesis of N-pentyl-2,7-diphenyl-3,8a-dihydroimidazo[1,2-a]pyrimidin-3-amine

To a well stirred reaction mixture of methanol 20ml and catalytic amount of Trifluoro acetic acid, different substituted 4-phenylpyrimidin-2-amine (0.1 mol) and benzaldehyde (0.1 mol) and 1-isocynopentane (0.1 mol) was added. Resultant reaction mixturewas stirred at room temperature for 3 to 4hr. after completion of the reaction, reaction mixture was poured in to the crushed ice. Filter the separated product and was with water. Finally purification was done by column chromatography using methanol and MDC as a solvent system to get pure title compound.

4. REACTION SCHEME

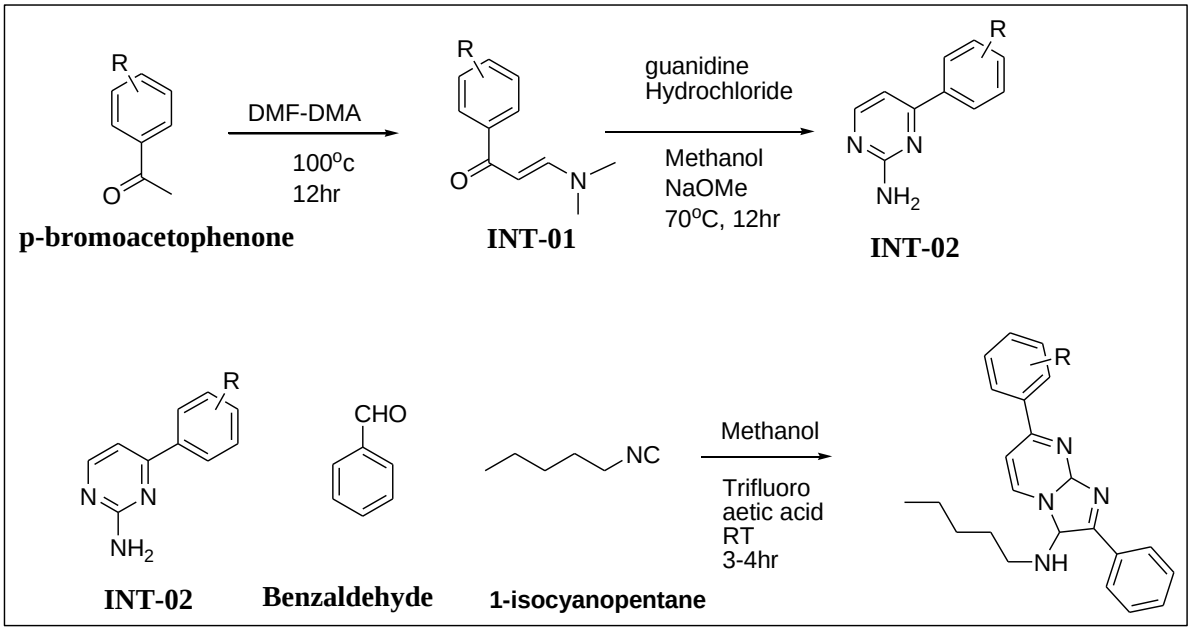


Table 1. Physical constant of synthesized library.

Code	M.F.	R	M.W.	M.P. °C	% Yield
RRK-101	$C_{23}H_{26}N_4$	H	358	413	71

RRK-102	$C_{23}H_{25}BrN_4$	4-Br	437	485	86
RRK-103	$C_{23}H_{25}ClN_4$	4-Cl	392	455	61
RRK-104	$C_{24}H_{28}N_4O$	4-OCH_3	388	459	84
RRK-105	$C_{24}H_{28}N_4$	4-CH_3	372	436	65
RRK-106	$C_{25}H_{29}N_5O$	4-$NHCOCH_3$	415	614	61
RRK-107	$C_{23}H_{26}N_4O$	4-OH	374	524	76
RRK-108	$C_{23}H_{25}FN_4$	4-F	376	426	70
RRK-109	$C_{23}H_{25}BrN_4$	2-Br	437	485	64
RRK-110	$C_{23}H_{25}ClN_4$	2-Cl	392	455	82
RRK-111	$C_{23}H_{25}FN_4$	2-F	376	426	68
RRK-112	$C_{24}H_{28}N_4O$	2-OCH_3	388	458	63
RRK-113	$C_{24}H_{28}N_4$	2-CH_3	372	436	71
RRK-114	$C_{23}H_{25}ClN_4$	3-Cl	392	455	80
RRK-115	$C_{24}H_{28}N_4$	3-CH_3	372	436	88
RRK-116	$C_{25}H_{30}N_4$	2,4-dimethyl	386	460	70
RRK-117	$C_{23}H_{24}Cl_2N_4$	2,4-dichloro	427	497	61

5. SPECTRAL DATA OF SYNTHESIZES COMPOUND

N-pentyl-2,7-diphenyl-3,8a-dihydroimidazo[1,2-a]pyrimidin-3-amine (RRK-101)

White solid, Rf Value 0.50 (Ethyl acetate 2:Hexane 3), IR (KBr pallet) in CM^{-},3832, 3508,3301, 3202, 3070, 2952, 2682, 2014, 1685, 1519, 1406, 1257, 1188,1032, 824, 696. ^1H NMR ($CDCl_3$) in δ PPM: 7.26-7.61 (Multiplet, 15H aromatic), 3.03-3.05 (Triplet, 2H $–CH_2$), 1.60 (Singlet, 1H of -NH), 7.03 (Singlet, 1H –CH), 1.34-1.35 (Triplet, 3H of $–CH_2$), 0.89 (Singlet, 1H – CH_3) 1.25-1.35 (Multiplet, 8H-CH_2), Analytical calculated for Molecular formula $C_{23}H_{26}N_4$is C; 77.06%, H; 7.31%, N; 15.63%, found C; 70.30%, H; 6.22%, N; 14.01%.

7-(4-bromophenyl)-N-butyl-3,8a-dihydro-2-phenylimidazo[1,2-a]pyrimidin-3-amine (RRK-102)

White solid, Rf Value 0.49 (Ethyl acetate 2:Hexane 3), IR (KBr pallet) in CM^{-}, 3868, 3645, 3397, 3336, 3190, 2854, 2808, 2364, 2003, 1748,1609, 1550, 1428, 1402, 1346,878 752. ^1H NMR ($CDCl_3$) in δ PPM: 7.31-7.49 (Multiplet, 15H aromatic), 3.06-3.09 (Triplet, 2H $–CH_2$), 8.37-8.39 (Triplet, 2H $–CH_2$), 8.07-8.09 (Triplet, 2H $–CH_2$), 1.41 (Singlet of -NH) 7.62-7.64

(Singlet, 1H –CH), 1.38-1.40 (Triplet, 3H of $–CH_2$), 0.89 (Singlet, 1H – CH_3), 1.25-1.36 (Multiplet, 8H-CH_2). Analytical calculated for Molecular formula $C_{23}H_{25}BrN_4$ is C; 63.16%, H; 5.76%, Br; 18.27% N; 12.81%, found C; 60.31%, H; 5.62%, Br; 17.87% N; 11.71%.

7-(4-chlorophenyl)-3,8a-dihydro-N-pentyl-2-phenylimidazo[1,2-a]pyrimidin-3-amine (RRK-103)

White solid, Rf Value 0.51 (Ethyl acetate 2:Hexane 3), Analytical calculated for Molecular formula $C_{23}H_{25}ClN_4$ is C; 70.31%, H; 6.41%, Cl; 9.02% N; 14.26%, found C; 69.01%, H; 5.99%, Cl; 8.41% N; 13.51%.

3,8a-dihydro-7-(4-methoxyphenyl)-N-pentyl-2-phenylimidazo[1,2-a]pyrimidin-3-amine (RRK-104)

White solid, Rf Value 0.50 (Ethyl acetate 2:Hexane 3), Analytical calculated for Molecular formula $C_{24}H_{28}N_4O$is C; 74.20%, H; 7.24%,N; 14.42%, found C; 73.63%, H; 6.19%, N; 13.87%.

3,8a-dihydro-N-pentyl-2-phenyl-7-p-tolylimidazo[1,2-a]pyrimidin-3-amine(RRK-105)

White solid, Rf Value 0.48 (Ethyl acetate 2:Hexane 3), Analytical calculated for Molecular formula $C_{24}H_{28}N_4$ is C; 77.38%, H; 7.58%, N; 15.04%, found C; 76.77%, H; 6.99%, N; 14.17%.

N-(4-(3,8a-dihydro-(pentylamino)-2-phenylimidazo[1,2-a]pyrimidin-7-yl)phenyl) acetamide (RRK-106)

White solid, Rf Value 0.49 (Ethyl acetate 2:Hexane 3), Analytical calculated for Molecular formula $C_{25}H_{29}N_5O$ is C; 72.26%, H; 7.03%, N; 16.85%, found C; 71.18%, H; 6.34%, N; 15.54%.

4-(3,8a-dihydro-3-(pentylamino)-2-phenylimidazo[1,2-a]pyrimidin-7-yl)phenol (RRK-107)

White solid, Rf Value 0.51 (Ethyl acetate 2:Hexane 3), Analytical calculated for Molecular formula $C_{23}H_{26}N_4O$ is C; 73.77%, H; 7.00%, N; 14.96%, found C; 72.99%, H; 6.65%, N; 13.84%.

6. RESULTS AND DISCUSSION

The advantages of this current developed method over other prevailing methods are reduced milder conditions, higher yields, low costs and environmental safety. A series of substituted N-pentyl-2,7-diphenyl-3,8a-dihydroimidazo[1,2-a]pyrimidin-3-amine have designed andsynthesized in good to excellent yield. Suitable reaction condition for the synthesis of targeted compounds was studied. All the compounds are well characterized by various analytical techniques. Thus, to synthesized target molecules, the various 1-(4-bromophenyl)-3-(dimethylamino)prop-2-en-1-one react with 20 gm guanidine hydrochloride (4 equivalent) and 10 gm of sodium methoxide (2 equivalent) in 20 ml of methanol, put reaction for 12 hour

at 70 °C. After the completion of reaction pour it into ice cold water filters it, white colour product obtained. To a well stirred reaction mixture of methanol 20ml and catalytic amount of Trifluoro acetic acid, different substituted 4-phenylpyrimidin-2-amine (0.1 mol) and benzaldehyde (0.1 mol) was added. Resultant reaction mixturewas stirred at room temperature for 3 to 4hr. Aftercompletion of the reaction, reaction mixture was poured in to the crushed ice. Filter the separated product and was with water.

Finally purification was done by column chromatography using methanol and methylene dichloride (MDC) as a solvent system to get pure title compound.

7. CONCLUSION

In summary, we have described the synthesis of substituted imidazo(1,2a)pyrimidine derivatives in moderate yield andlowcosts and environmental safety. The simple, economical and potentially viable reaction method makes it useful and captivating process for commercial application. The reaction of various 1-(4-bromophenyl)-3-(dimethylamino)prop-2-en-1-one withguanidine hydrochloridewas afforded the N-pentyl-2,7-diphenyl-3,8a-dihydroimidazo [1,2-a]pyrimidin-3-amine derivatives in moderate to good yield in the presence of base. Sodium methoxide was found as an efficient base. All the compounds were synthesized in good to excellent yield.

ACKNOWLEDGEMENTS:

We are very much thankful to Department of Chemistry of Maharshi Dayanand Science College, Porbandar in Saurashtra University Rajkot for providing lab facilities.

References

[1] A. Aly (2006) Synthesis and Pharmacological Activity of Annelated Pyrimidine Derivatives. *Phosphorus, Sulfur, and Silicon and the Related Elements,* 181:6, 1285-1298, DOI: 10.1080/10426500500326792

[2] Sobhi M. Gomha, Mohamed G. Badry, Mohamed M. Abdalla. (2016) Isoxazolopyrimidinethione and Isoxazolopyridopyrimidinethione Derivatives: Key Intermediates for Synthesis of Novel Fused Triazoles as Potent 5α-Reductase Inhibitors and Anti-Prostate Cancer. *Journal of Heterocyclic Chemistry* 53: 2, pages 558-565

[3] Wafaa S. Hamama, Mohamed A. Ismail, Hanaa A. Al-Saman, Hanafi H. Zoorob. (2013) Facile construction of substituted pyrimido[4,5-d]pyrimidones by transformation of enaminouracil. *Journal of Advanced Research* 4: 2, pages 115-121

[4] Xi-Cun Wang, Ying Wei, Yu-Xia Da, Zhang Zhang, Zheng-Jun Quan. (2011) One-Step Synthesis of Tetrazolo[1,5-a]pyrimidines by Cyclization Reaction of Dihydropyrimidine-2-thiones with Sodium Azide. *Heterocycles* 83: 12, pages 281

[5] Esvet Akbas, Abdulkadir Levent, Selcuk Gumus, Mehmet Rauf Sumer, Inci Akyazi. (2010) Synthesis of Some Novel Pyrimidine Derivatives and Investigation of their

Electrochemical Behavior. *Bulletin of the Korean Chemical Society* 31: 12, pages 3632-3638

[6] Changsheng Yao, Song Lei, Cuihua Wang, Chenxia Yu, Shujiang Tu. (2008) Solvent-free synthesis of 5-methyl-7-aryl-4,7-dihydrotetrazolo[1,5- *a*]pyrimidine-6-carboxylic esters catalyzed by sulfamic acid. *Journal of Heterocyclic Chemistry* 45: 6, pages 1609-1613

[7] Esvet Akbał, Furgan Aslanoğlu, Ahmet Şener, Bariş Anil. (2008) A simple one-pot synthesis of 1,2,3,4-tetrahydro-2-thioxopyrimidine derivatives. *Journal of Heterocyclic Chemistry* 45: 5, pages 1457-1460

[8] Esvet Akbaş, Furgan Aslanoğlu. (2007) Studies on Reactions of Pyrimidine Compounds. 2[1]. Microwave-Assisted Synthesis of 1,2,3,4-Tetrahydro-2-Thioxopyrimidine Derivatives. *Phosphorus, Sulfur, and Silicon and the Related Elements* 183:1, pages 82-89

[9] Furgan Aslanoğlu, Esvet Akbaş, Mehmet Sönmez, Barış Anıl. (2007) Studies on Reactions of Pyrimidine Compounds: Synthesis and Reactions of 5-Benzoyl-4,6-Diphenyl-1,2,3,4-Tetrahydro-2-Thioxopyrimidine. *Phosphorus, Sulfur, and Silicon and the Related Elements* 182:7, pages 1589-1597

[10] Shipra Baluja, Kajal Nandha, Paras Ramavat, Solubility of pyrimidine derivatives in different organic solvents at different temperatures. *World Scientific News* 44 (2016) 13-34

[11] Hardik K. Senjani, H. D. Joshi, Synthesis and characterization of diversely substituted pyrimidine-3-carboxamide and their antimicrobial evaluation. *World Scientific News* 150 (2020) 39-77

[12] Yogesh M. Ajudiya, Jayesh S. Babariya, J. J. Upadhyay, Synthesis and characterization of 2-(methylthio)-6-oxo-6H-chromeno[3,4-e]pyrazolo[1,5-a]pyrimidine-3-carbonitrile derivatives. *World Scientific News* 123 (2019) 258-264

[13] Gautamkumar Dhuda, Paresh Ladwa, Jayesh J. Modha, Gewald reaction for the synthesis of benzo[4,5]-thieno[2,3-d]pyrimidin-4(3H)-one derivatives and it's antimicrobial study. *World Scientific News* 151 (2021) 110-122

[14] Shantaram Gajanan Khanage, S. Appala Raju, Popat Baban Mohite, Ramdas Bhanudas Pandhare. Synthesis and Pharmacological Evaluation of Some New Pyrimidine Derivatives Containing 1,2,4-Triazole. *Adv Pharm Bull.* 2012 Dec; 2(2): 213–222. doi: 10.5681/apb.2012.033

[15] Cieplik, J., Stolarczyk, M., Pluta, J., Gubrynowicz, O., Bryndal, I., Lis, T., & Mikulewicz, M. (2011). Synthesis and antibacterial properties of pyrimidine derivatives. *Acta Poloniae Pharmaceutica*, 68(1), 57–65

[16] Kidwai, M.; Saxena, S.; Rastogi, S.; Venkataramanan, R. Pyrimidines as Anti-Infective Agents. *Current Medicinal Chemistry - Anti-Infective Agents*, Volume 2, Number 4, 2003, pp. 269-286. DOI: https://doi.org/10.2174/1568012033483015

[17] Olga Bruno, Silvia Schenone, Angelo Ranise, Francesco Bondavalli, Elisabetta Barocelli, Vigilio Ballabeni, Milena Chiavarini, Simona Bertoni, Massimiliano

Tognolini, Mariannina Impicciatore. New polycyclic pyrimidine derivatives with antiplatelet in vitro activity: synthesis and pharmacological screening. *Bioorganic & Medicinal Chemistry*, Volume 9, Issue 3, 2001, Pages 629-636, https://doi.org/10.1016/S0968-0896(00)00272-8

[18] Burnstock, G. Purine and pyrimidine receptors. *Cell. Mol. Life Sci.* 64, 1471 (2007). https://doi.org/10.1007/s00018-007-6497-0

[19] Zia Ul Haq Khan, Arif Ullah Khan, Pingyu Wan, Yongmei Chen, Dandan Kong, Shafiullah Khan & Kamran Tahir (2015) *In vitro* pharmacological screening of three newly synthesised pyrimidine derivatives. *Natural Product Research*, 29:10, 933-938, DOI: 10.1080/14786419.2014.964707

[20] Zia Ul Haq Khan, Amjad Khan, Pingyu Wan, Arif Ullah Khan, Kamran Tahir, Nawshad Muhammad, Faheem Ullah Khan, Hidayat Ullah Shah, Zia Ullah Khan. (2018) New natural product -an efficient antimicrobial applications of new newly synthesized pyrimidine derivatives by the electrochemical oxidation of hydroxyl phenol in the presence of 2-mercapto-6-(trifluoromethyl) pyrimidine-4-ol as nucleophile. *Natural Product Research* 32: 10, pages 1161-1169

[21] Nadieh Dorostkar-Ahmadi, Abolghasem Davoodnia, Niloofar Tavakoli-Hoseini, Hossein Behmadi, Mahboobeh Nakhaei-Moghaddam. (2019) Facile synthesis of new pyrazolo[4′,3′:5,6]pyrano[2,3-d]pyrimidin-5(1H)-ones via the tandem intramolecular Pinner–Dimroth rearrangement and their antibacterial evaluation. *Zeitschrift für Naturforschung B* 74: 2, pages 175-181

[22] Nasrinsadat Hosseininasab, Abolghasem Davoodnia, Faramarz Rostami-Charati, Niloofar Tavakoli-Hoseini, Amir Khojastehnezhad. (2018) Synthesis of New Pyrimido[4′,5′:3,4]pyrazolo[1,2- *b*]phthalazine-4,7,12-triones: Derivatives of a New Heterocyclic Ring System. *Journal of Heterocyclic Chemistry* 55: 1, pages 161-165

[23] Salwa F. Mohamed, Alhusain A. Ibrahiem, Abd El-Galil E. Amr and Mohamed M. Abdalla, 2015. SARS-CoV 3C-Like Protease Inhibitors of some Newly Synthesized Substituted Pyrazoles and Substituted Pyrimidines Based on 1-(3-Aminophenyl)-3-(1*H*-indol-3-yl)prop-2-en-1-one. *International Journal of Pharmacology*, 11: 749-756. DOI: 10.3923/ijp.2015.749.756

[24] Abdel Mohsen HT, Ragab FAF, Ramla MM, El Diwani HI. 2010. Novel benzimidazole–pyrimidine conjugates as potent antitumor agents. *Eur J Med Chem.* 45(6): 2336–2344

[25] Abu-Hashem AA, Youssef MM, Hussein HAR. 2011. Synthesis, antioxidant, antitumor activities of some new thi-azolopyrimidines, pyrrolothiazolo pyrimidines and tri azolopyrrolothiazolo pyrimidines derivatives. *J Chin Chem Soc.* 58: 41–48

[26] Amin KM, Awadalla FM, Eissa AAM, Abou-Seri SM, Hassan GS. 2011. Design synthesis and vasorelaxant evaluation of novel coumarin–pyrimidine hybrids. *Bioorg Med Chem.* 19: 6087–6097

[27] Chandrashekaran S, Nagarajan S. 2005. Microwave-assisted synthesis and anti-bacterial activity of some 2-amino-6-aryl-4-(2-thienyl) pyrimidines. *IL Farmaco.* 60: 2, 79–282

[28] Falcao EPDaS, de Melo SJ, Srivastava RM, Catanho MT, Do Nascimento SC. 2006. Synthesis and anti-inflammatory activity of 4-amino-2-aryl-5-cyano-6-{3- and 4-(*N*-phthalimidophenyl)} pyrimidines. *Eur J Med Chem.* 41: 276–282

[29] Ingaral N, Saravanan G, Amutha P, Nagarajan S. 2007. Synthesis, *in vitro* antibacterial and antifungal evaluations of 2-amino-4-(1-naphthyl)-6-arylpyrimidines. *Eur J Med Chem.* 42: 517–520

[30] Khan ZUH, Chen Y, Khan SU, Kong D, Liang MH, Wan P, Jin X. 2014. Electrochemical initiation of nucleophilic substitution of hydroquinone with 4,6-dimethylpyrimidine-2-thiol. *Int J Electrochem Sci.* 9: 4665–4674

[31] Sirisoma N, Kasibthala S, Nguyen B, Pervin A, Wang Y, Claassen G, Tseng B, Drewe J, CaiSX. 2006. Discovery of substituted 4-anilino-2-(2-pyridyl) pyrimidine as a new series of apoptosis inducers using a cell- and caspase-based high throughput screening assay. Part 1: structure-activity relationships of the 4-aniline group. *Bioorg Med Chem.* 14: 7761–7773

[32] Vega S, Alonso J, Diaz JA, Jonquiere F. 1990. Synthesis of 3-substituted-4-phenyl-2-thioxo-1,2,3,4,5,6,7,8-octahydrobenzo [4,5] thieno [2,3-d]pyrimidines. *J Heterocycl Chem*. 27:269–273

[33] Shin Kamijo, Kaori Kamijo, and Toshihiro Murafuji. Synthesis of Alkylated Pyrimidines via Photoinduced Coupling Using Benzophenone as a Mediator. *The Journal of Organic Chemistry* 2017, *82* (5), 2664-2671. https://doi.org/10.1021/acs.joc.6b03058

[34] Sumaiya Tabassum, K.R. Sunaja Devi, Santhosh Govindaraju. Nano ZnO@PEG catalyzed one-pot green synthesis of pyrano[2,3-d]pyrimidines in ethanol via one-pot multicomponent approach. *Materials Today: Proceedings* 2021, 45, 3716-3721. https://doi.org/10.1016/j.matpr.2020.12.677

[35] Thuraka Sekhar, Pinnu Thriveni, Annavarapu Venkateswarlu, Thathapudi Daveedu, Kotha Peddanna, Sri Bhashyam Sainath, One-pot synthesis of thiazolo[3,2-a]pyrimidine derivatives, their cytotoxic evaluation and molecular docking studies. *Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy*, 10.1016/j.saa.2020.118056, (118056), (2020)

[36] Ajmal R. Bhat, Rajendra S. Dongre, Faisal A. Almalki, Malika Berredjem, Mohamed Aissaoui, Rachid Touzani, Taibi Ben Hadda, Mohammad S. Akhter, Synthesis, biological activity and POM/DFT/docking analyses of annulated pyrano[2,3-d]pyrimidine derivatives: Identification of antibacterial and antitumor pharmacophore sites. *Bioorganic Chemistry*, 10.1016/j.bioorg.2020.104480, (104480), (2020).

[37] Alaa R. Sakr, Mohamed G. Assy, Youssra S. ELasaad, Design and chemical behavior of novel pyrimidine derivatives and their evaluation of cytotoxicity. *Synthetic Communications*, 10.1080/00397911.2020.1735444, (1-7), (2020).

[38] S. Gajalakshmi, I. V. Asharani, D. Thirumalai, Synthesis and Antioxidant Activity of Functionalized Pyridinyl-Methylthiosemicarbazide Derivatives. *Polycyclic Aromatic Compounds*, 10.1080/10406638.2020.1866033, (1-10), (2020)

[39] Kiran N. Patil, Rohan A. Mane, Sandip B. Jadhav, Mansing M Mane, Vasant B. Helavi, One pot multicomponent synthesis of highly functionalized tetrahydropyridine using copper (II) triflate as catalyst and their anti-inflammatory activity, *Chemical Data Collections*, 10.1016/j.cdc.2019.100233, (100233), (2019)

[40] Meeta Sahu, Nadeem Siddiqui, Ramsha Iqbal, Vidushi Sharma, Sharad Wakode, Design, synthesis and evaluation of newer 5,6-dihydropyrimidine-2(1 H)-thiones as GABA-AT inhibitors for anticonvulsant potential, *Bioorganic Chemistry*, 10.1016/j.bioorg.2017.07.017, 74, (166-178), (2017)

[41] Meeta Sahu, Nadeem Siddiqui, Mohd. Javed Naim, Ozair Alam, Mohammad Shahar Yar, Vidushi Sharma, Sharad Wakode, Design, Synthesis, and Docking Study of Pyrimidine–Triazine Hybrids for GABA Estimation in Animal Epilepsy Models, *Archiv der Pharmazie*, 10.1002/ardp.201700146, 350, 9, (2017)

[42] Bagher Mohammadi, Microwave assisted one-pot pseudo four-component synthesis of 2,4,6-trisubstituted pyridines using γ-MnO2 nanoparticles. *Monatshefte für Chemie - Chemical Monthly*, 10.1007/s00706-016-1698-6, 147, 11, (1939-1943), (2016)