Chemistry & Biology Interface, 2018, 8, 3, 177-183

RESEARCH PAPER ISSN: 2249 –4820

CHEMISTRY & BIOLOGY INTERFACE

An official Journal of ISCB, Journal homepage; www.cbijournal.com

"Facile and efficient one-pot three-component synthesis of some new pyridine substituted pyrazole derivatives through greener phase transfer catalyst"

Mitesh B. Vekariya and Hitendra S. Joshi*

Department of Chemistry, Saurashtra University-Rajkot
E-mail: drhsjoshi49@gmail.com, miteshvekariya15@gmail.com
Received 21 March 2018; Accepted 21 May 2018

Abstract: An efficient, rapid and greener catalytic synthesis of 2-amino-4-(1,3-diphenyl-1*H*-pyrazole-4-yl)-6-(substituted phenylthio)pyridine-3,5-dicarbonitrile derivatives was developed by one pot three component condensation of 1,3-diphenyl-1*H*-pyrazole-4-carbaldehyde, malononitrile and substituted thiophenol in methanol using tetra-n butyl ammonium bromide(TBAB) as a green phase transfer catalyst. The leading parameters of the work are high yield output, low catalyst loading, short time product formation, easy workup procedure and synthesis ofa new class of pyrazole and pyridine hybrid heterocyclic compounds. All the synthesized compounds were characterized by IR, ^{1}H-NMR, ^{13}C-NMR and mass spectroscopic techniques.

Keywords: Pyrazolopyridine derivatives, green phase transfer catalyst, high yield, short time, easy work-up.

1. Introduction:

There are great and depth research behind pyrazole and pyridine containing organic compounds have been reported in past few decades by chemist over the globe. A large number of medicinally important drug molecules have these heterocycles. The pyrazole and pyridine both are nitrogen-containing heterocyclic compounds and so that they are highly potent as far as biological activity is a concern. In present work, we have combined such a two heterocycle to synthesize more potent and broad range of biological activity containing organic compounds.

Pyrazoles are five-memberedheterocycles having a nitrogen as a heteroatom at the 1st and 2nd position. From the survey of literature, it has been found that they are showna broad range of biological activities such as anti-microbial, anti-fungal, antitubercular, anti-inflammatory, anticonvulsant, anticancer, anti-viral, angiotensin-converting enzyme (ACE) inhibitory, neuroprotective and estrogen receptor (ER) ligand activity etc.[1,2]

On another hand single nitrogen-containing,the six-membered aromatic ringisknown as pyridine and its derivatives contain a wide range of naturally occurring and synthetic medicinally important compounds.[3] The pyridine cycle containing derivatives with aryl thio substituent at 6thposition provides a new broad class of medicinally important compounds. They possessimportant biological activities such as anti-hepatitis, antibacterial, an anticancer agent, antipirone, non- nucleoside agents of human adenosine A1, an inhibitor of HIV-1 integrase, anti-inflammatory agents, analgesics and muscle relaxants.[4-12]

Vora*et al.*[13] have reported the synthesis of schiff base of -{(1E)-[3-(mono or di-substituted aryl)-1-phenyl-1*H*-pyrazol-4-yl]-methylene}-4-methylpyridine-2-amine **(1)** as potent anti-microbial activity. Another same type of potent antimicrobial derivative as 5-aryl-1-isonicotinoyl-3-(pyridine-2-yl)-4,5-dihydro-1*H*-pyrazole **(2)** was reported by Mamolo*et al.*[14] (see structure in **fig.1**).

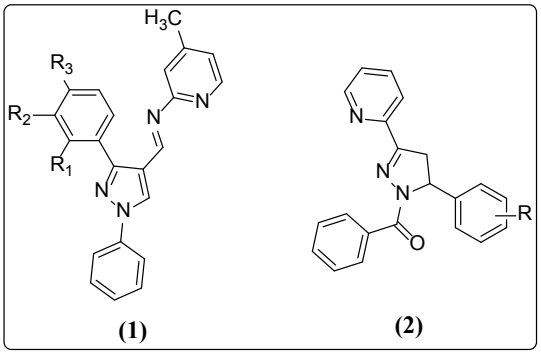

Figure 1: some reported antimicrobial pyrazole and pyridine contains derivatives

Besides the biological importance, the main focus of our work is to use shorter way of synthesis, avoid the use of hazardous solvents and reagents, use of greener phase transfer catalyst. In present work, we have touse tetra-n butyl ammonium bromide (TBAB) as a catalyst. The condensation between aryl aldehyde, malononitrile and thiophenol are reported earlier by several chemists by use of so many metal complexes catalyst and some green solvents. In reported synthesis, there are use heterogeneous Cu(II)/L-His@ Fe_3O_4nanocatalyst, borax powder, an ionic liquid such as 2-hydroxyethanaminium acetate, ethanaminium, 2-hydroxy-*N,N,N*-trimethylmethoxide, potassium carbonate and solvents like ethanol, ethylene glycol,and water were used.[15-20] Some other catalyst used are triethyl amine[14], DABCO, piperidine, tetrabutylammonium hydroxide[12], $ZnCl_2$[21] silica nanoparticle[22], $KFAl_2O_3$[23], TBAF[24], [bmim]BF_4[25], $ZrOCl_2.8H_2O$/ $NaNH_2$[26] and DMSO containing ammonium hydroxide.[27]

The present work describedthe synthesis of such type of penta-substituted pyridine derivatives using TBAB as a catalyst. The reported synthesis incorporated withsome problems like low yield formation, more time required to complete reaction, difficult purified compounds and removal of excess reactant and other reagents, in present work we try to minimize those problems by changing reaction condition and catalyst. The use of TBAB gives good yield and shorten the reaction time as well.

2. Material and Methods:

2.1 Chemistry:

All chemicals were purchased and used without any further purification. Reactions were monitored by thin layer chromatography (TLC) on silica gel-G plates (G60 F254 (Merck)) of 0.5 mm thickness, visualizing was made with ultraviolet light (254 and 365 nm), or with iodine vapor chamber and aq. $KMnO_4$ reagent. Melting point was determined using a Buchi B-540 open capillary apparatus and are uncorrected. IR spectra were recorded on an FTIR-8400 S, CE Shimadzu instrument and are expressed in cm^{-1}. Mass spectra were recorded on Shimadzu

GC-MS-QP-2010 model using direct inlet probe technique. ^{1}H-NMR and ^{13}C-NMR spectra were recorded on a BrukerAvance 400 MHz and Bruker DRX 101 MHz spectrometer respectively in deuterated solvents like $CDCl_3$ or DMSO-d_6 solvent. Chemical shift values (δ) are expressed in ppm (parts per million) relative to TMS. Solvents were evaporated with a BUCHI rotary evaporator. The purification of all synthesized compound was performed by borosil glass column having a length about 1000mm.

2.2 General procedure for the synthesis of 2-amino-6-((substitutedphenyl)thio)-4-(1,3-diphenyl-1*H*-pyrazole-4-yl)pyridine-3,5-dicarbonitrile (MTS 801-810):

A mixture of 1,3-diphenyl-1*H*-pyrazole-4-carbaldehyde (**Int.2**) (200 mg, 0.8 mmol), malononitrile (132 mg, 2 mmol), substituted thiophenol (0.96 mmol), tetra-n butyl ammonium bromide(TBAB) (13 mg, 5 %) as phase transfer catalyst and cesium carbonate(13 mg, 5 %) refluxed in 10 ml of methanol for 2 hours. Filter the solid was precipitated out after the completion of reaction. Wash the solid with cooled methanol and dry it to furnished final compounds as **MTS 801-810**.

2.3 Spectral data of synthesized compounds:

2-Amino-4-(1,3-diphenyl-1*H*-pyrazol-4-yl)-6-(phenylthio)pyridine-3,5-dicarbonitrile (MTS-801): Yield: 68%, Light yellow solid, M.P.: 285-287°C; **IR :(Vmax/ cm^{-1}):** 3462-3340(-NH str. –NH_2, aromatic), 3051-2845(C-H str. alkene), 2222(-CN str.), 1533(-C=C-, str. aromatic), 1259(C-H bending), 775-684(mono subs. ring); **^{1}H-NMR(400 MHz, $CDCl_3$):δ(ppm):** 5.40(s, 2H, -NH_2), 7.36-7.42(m, 4H, Ar-H), 7.43-7.53(m, 7H, Ar-H), 7.56-7.58(m, 2H, Ar-H), 7.79-7.81(d, 2H, Ar-H, *J*=7.6 Hz), 8.26(s, 1H, Ar-H); **MS:** 471(M+1)$^+$,469(M-1)$^+$; Anal. Calcd. for $C_{28}H_{18}N_6S$; C,71.47; H, 3.86; N,17.86; Found: C, 71.42; H, 3.82; N, 17.83%.

2-Amino-6-((3-chlorophenyl)thio)-4-(1,3-diphenyl-1*H*-pyrazol-4-yl)pyridine-3,5-dicarbonitrile (MTS-802): Yield: 74%, white solid, M.P.: 290-292°C; **IR :(Vmax/ cm^{-1}):** 3522-3500(-NH str. –NH_2, aromatic), 3182-2897(C-H str. alkene), 2220(-CN str.), 1625, 1533, 1504 (-C=C-, str. aromatic), 987, 956, 765(meta disubs. ring);**^{1}H-NMR(400 MHz, DMSO-d_6): δ(ppm):** 7.41(s, 2H, -NH_2), 7.43(m, 2H, Ar-H), 7.52-7.55(m, 3H, Ar-H), 7.59-7.62(m, 4H, Ar-H), 7.72(s, 1H, Ar-H), 7.97-7.99(d, 4H, Ar-H, *J*= 8 Hz), 9.09(s, 1H, Ar-H); **^{13}C-NMR(100 MHz, DMSO-d_6):δ(ppm):** 88.20, 94.25, 114.14, 118.49, 127.23, 128.63, 129.10, 129.81, 130.27, 131.02, 131.68, 133.57, 133.61, 134.09, 138.73, 149.98, 150.96, 159.65, 165.64; **MS:** 505(M+1)$^+$, 503(M-1)$^+$; Anal. Calcd. for $C_{28}H_{17}ClN_6S$; C, 66.60; H, 3.39; N, 16.64; Found: C, 66.53; H, 3.37; N, 16.61%.

2-Amino-6-((4-bromophenyl)thio)-4-(1,3-diphenyl-1*H*-pyrazol-4-yl)pyridine-3,5-dicarbonitrile(MTS-803): Yield: 65%, white solid, M.P.: 275-277°C; **IR :(Vmax/ cm^{-1}):** 3458-3296(-NH str. –NH_2, aromatic), 3039-2806(C-H str. alkene), 2229-2214(-CN str.), 1643, 1533(-C=C-, str. aromatic), 1381-1224(C-H bending), 1060-954(peradisubs. ring); **^{1}H-NMR(400 MHz, DMSO-d_6):δ(ppm):** 7.41-7.47(m, 4H, Ar-H), 7.51-7.54(m, 3H, Ar-H), 7.58-7.72(m, 4H, Ar-H), 7.72-7.724(d, 1H, Ar-H, *J*=1.6 Hz), 7.96-7.98(d, 2H, Ar-H), 7.96-7.98(s, 2H, -NH_2), 9.09(s, 1H, Ar-H); **^{13}C-NMR(100 MHz, DMSO-d_6):δ(ppm):** 88.18, 94.22, 114.13, 114.68, 118.48, 126.88, 127.24, 128.63, 128.86, 129.08, 130.27, 131, 131.67, 133.58, 134.10, 138.72, 149.98, 150.95, 159.64, 165.65; Anal. Calcd. for $C_{28}H_{17}BrN_6S$; C, 61.21; H, 3.12; N, 15.30; Found: C, 61.18; H, 3.06; N, 15.27%.

2-Amino-4-(1,3-diphenyl-1*H*-pyrazol-4-

yl)-6-((3-methoxyphenyl)thio)pyridine-3,5-dicarbonitrile(MTS-804): Yield: 72%, pale yellow solid, M.P.: 285-286°C; **IR :(Vmax/ cm^{-1}):** 3614-3518(-NH str. –NH_2, aromatic), 3332-3280(C-H str. alkene), 3037(C-H str. alkane), 2212-2073(-CN str.), 1625, 1544, 1529(-C=C-, str. aromatic), 1226(C-H bending), 783, 761, 692(meta disubs. ring); **^{1}H-NMR(400 MHz, DMSO-d_6):δ(ppm):** 3.81(s, 3H, -CH_3), 7.06-7.09(m, 1H, Ar-H), 7.18-7.20(d, 2H, Ar-H, *J*= 8 Hz), 7.39-7.48(m, 5H, Ar-H), 7.52-7.53(d, 2H, Ar-H), 7.58-7.62(t, 3H, Ar-H, *J*= 8.4 Hz), 7.93(s, 2H, -NH_2), 7.97-7.99(d, 2H, Ar-H, *J*= 8Hz), 9.09(s, 1H, Ar-H);**^{13}C-NMR(100 MHz, DMSO-d_6):δ(ppm):** 55.36, 88.01, 94.26, 114.22, 114.75, 115.03, 115.97, 118.48, 119.70, 126.72, 126.88, 127.22, 127.92, 128.62, 128.85, 129.81, 130.25, 131.72, 138.74, 149.98, 150.92, 159.57, 166.19; Anal. Calcd. for $C_{29}H_{20}N_6OS$; C, 69.58; H, 4.03; N, 16.79; Found: C, 69.52; H, 4.01; N, 16.75%.

2-Amino-4-(1,3-diphenyl-1*H*-pyrazol-4-yl)-6-((2-fluorophenyl)thio)pyridine-3,5-dicarbonitrile (MTS-805): Yield: 70%, light yellow solid, M.P.: 293-295°C; **IR :(Vmax/ cm^{-1}):** 3460(-NH str. –NH_2, aromatic), 3182(C-H str. alkene), 2212(-CN str.), 1625, 1546, 1502, 1462(-C=C-, str. aromatic), 1228(C-H bending), 1068, 987(orthodisubs. ring); Anal. Calcd. for $C_{28}H_{17}FN_6S$; C, 68.84; H, 3.51; N, 17.20; Found: C, 68.80; H, 3.47; N, 17.14%.

2.4 Synthesis:

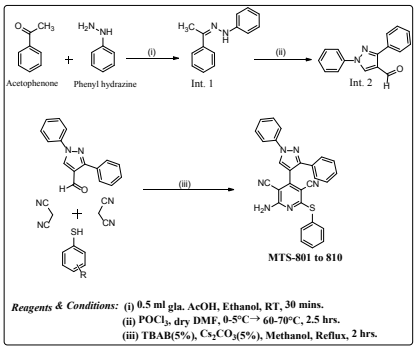

Figure 2: Reaction scheme

All over the route of synthesis are shown in **fig.2**, first step is acid catalysed formation of phenyl hydrazone (**Int.1**) by the condensation between acetophenone and phenyl hydrazine in ethanol at room temperature.[13,28,29]The next step was followed by cyclization through double vilsmeier-haack reaction to formed*N*-phenyl substituted pyrazolo aldehyde (**Int.2**).[30-32] In lastone pot three component condensation between **Int.2**, two equivalent of malononitrile and aryl thiophenol in methanol and catalytic amount of TBAB(5%) and Cs_2CO_3(5%) to obtained title compounds as **MTS-801-810**. [24,33,34]

2.5 Mechanistic study:

The entire plausible reaction mechanism of reaction scheme is shown in fig. 3, in which the acid catalyzed phenyl hydrazone formation from acetophenone and phenylhydrazine. Followed by double vilsmeier-haack to form a pyrazole aldehyde. Which on base catalyzed condensation with malononitrile and thiophenol to gave title compounds.

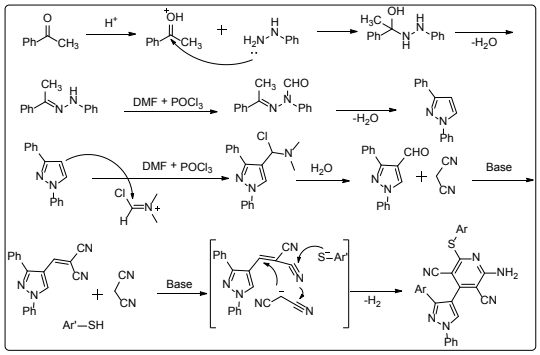

Figure 3: Plausible reaction mechanism

3. Result and discussion:

From the literature, it has been found that there is a wide scope of research behind nitrogen-containing heterocyclic compounds are still exist. In nitrogen-containingheterocycle, the pyridine is most important as far as biological

activity is a concern. Addition of another two nitrogen-containingfive-membered ring pyrazolesignificantlyincreased the potentiality of the compounds.

Starting reaction of acetophenone with phenyl hydrazine, Schiff base like reaction to formed phenyl hydrazone. The resulting phenyl hydrazone on single vilsmeier-haack reaction to gave*N*-formyl intermediate, which on instant cyclization with neighbouring methyl group afforded pyrazole derivatives. This pyrazole derivativesundergoes nucleophilic reaction with formyl ion generated through vilsmeier-haack adduct to form a pyrazole aldehyde, which undergoes one pot-three component condensation to obtained title compounds.

The physical constant of all the synthesized compounds is shown in **Table 1**.

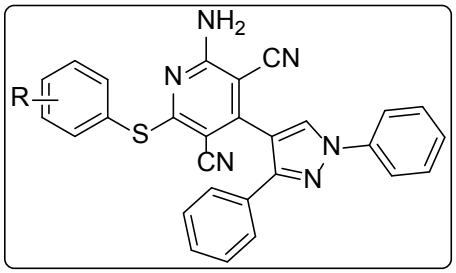

Table 1: Physical constant of synthesized compounds

Comp. code	Substituent R	M.F.	M.W. gm/mole	Yield %	M.P. °C
MTS-801	-H	$C_{28}H_{18}N_6S$	470.55	72	285-287
MTS-802	3-Cl	$C_{28}H_{17}ClN_6S$	504.09	65	290-292
MTS-803	4-Br	$C_{28}H_{17}BrN_6S$	548.04	69	275-277
MTS-804	3-OCH_3	$C_{29}H_{20}N_6OS$	500.14	73	285-286
MTS-805	2-F	$C_{28}H_{17}FN_6S$	488.12	61	293-295
MTS-806	3,5-bis-CF_3	$C_{30}H_{16}F_6N_6S$	606.11	58	260-262
MTS-807	4-CF_3	$C_{29}H_{17}F_3N_6S$	538.12	60	265-267
MTS-808	4-Cl	$C_{28}H_{17}ClN_6S$	504.09	67	288-290
MTS-809	4-F	$C_{28}H_{17}FN_6S$	488.12	69	287-289
MTS-810	3-CH_3	$C_{29}H_{20}N_6S$	484.15	70	291-293

3.1 Optimization of reaction conditions for one pot three-component reaction:

Table 2: Screening of PTC used in the reaction

Entry No.	PTC	Proportion	Time (h)	Yield %
1	TBAF	5%	5	38
2	TBAF	10%	5	40
3	**TBAB**	**5%**	**2**	**72**
4	TBAB	10%	2	70
5	TBAH	5%	3	51
6	TBAH	10%	3	53
7	18-crown-6	5%	3.5	25
8	18-crown-6	10%	3.5	26
9	No PTC	-	6	36

The screening of PTC used in the reaction are shown in **Table 2**, it shows that there is the minimum effect of the amount of PTC rather than the type of PTC on time and yield of the reaction.The 3rd experiment shows the maximum conversion of reactant into the product in minimum time by use of TBAB as PTC in 5% proportion. After the screening of PTC, we have optimized the temperature, base and solvent used in the reaction.

Table 3 Screening of base, solvent,and temperature used in the reaction

Entry No.	Base	Solvent	Time (h)	Yield %
1	K_2CO_3	Methanol	6 h, reflux	52
2	Na_2CO_3	Methanol	6 h, reflux	45
3	Na_2CO_3	Ethanol	6.5 h, reflux	48
4	Cs_2CO_3	Methanol	5 h, RT	30
5	**Cs_2CO_3**	**Methanol**	**2 h, reflux**	**70**
6	Cs_2CO_3	Ethanol	5 h, reflux	56

Table 3 shows the screening of base and solvent used in the reaction, total three type of base and two solvents are used for screening. Out of six entries, the 5th experiment shows maximum

practical yield by use of cesium carbonate as base and methanol as a solvent in reflux condition for 2 hours to givethe maximum product.

From above optimization, we found that use of TBAB as phase transfer catalyst in 5% proportion, Cs_2CO_3as base and methanol as a solvent in reflux condition to the afforded maximum product.

All the synthesized compounds are well purified through column chromatography and characterized by various spectroscopic techniques like IR, ^{1}H-NMR, ^{13}C-NMR and mass spectroscopy. The infrared spectra of compounds show characteristic peaks bands around 3500 to 3300 cm^{-1}, shows $–NH_2$group, the band around 2200 cm^{-1} is confirmation band for cyano group. Other IR bands are in the aromatic region also confirmed the structure of compounds. In ^{1}H-NMR spectra there are all peaks are comes into an aromatic region, the sharp singlet with two protons around 5 δppm for $CDCl_3$ and around 7δppm for DMSO-d6 shows an amino group signal. All another signal between 5 to 7 δppm are of aromatic proton signal. The ^{13}C-NMR also showed all carbon signal according toitschemical environment. The mass spectra of the compounds are shows at its molecular weight either plus one or minus one.

4. Conclusion:

The present work indicatesa facile and efficient synthesis of some new 2-amino-6-((substitutedphenyl)thio)-4-(1,3-diphenyl-1*H*-pyrazole-4-yl)pyridine-3,5-dicarbonitrile as contains pyridine and pyrazole both active heterocycles. The synthetic route is well designed in such a way that reaction required a minimum time for completion with the less catalytic ratio, and easy work up and purification process. The range of yield is moderate to good with maximum purity.

Acknowledgments:

Authors are thankful to UGC-Special Assistance Program (SAP), Department of Science and Technology, Fund for Improvement of Science and Technology (FIST) and UGC-BSR for financial supports and Department of Chemistry, Saurashtra University-Rajkot for providing research facilities also NFDD, Rajkot for providing the spectra of compounds.

References:

1. Katz, A. M.; Pearson, C. M.; Kennedy, J. M. *Clin. Pharmacol. Ther.***1965**, *6* (1), 25.
2. Naim, M. J.; Alam, O.; Farah Nawaz, M.; Alam, J.; Alam, P. *J. Pharm. Bioallied Sci.***2016**, *8* (1), 2.
3. Patil, P.; Sethy, S. P.; Sameena, T.; Shailaja, K. *Asian J. Chem***2013**, *10*, 888.
4. Weber, L. *Curr. Med. Chem.***2002**, *9* (23), 2085.
5. Hulme, C.; Gore, V. *Curr. Med. Chem.***2003**, *10* (1), 51.
6. Cocco, M. T.; Congiu, C.; Lilliu, V.; Onnis, V. *Eur. J. Med. Chem.***2005**, *40* (12), 1365.
7. May, B. C. H.; Zorn, J. A.; Witkop, J.; Sherrill, J.; Wallace, A. C.; Legname, G.; Prusiner, S. B.; Cohen, F. E. *J. Med. Chem.***2007**, *50* (1), 65.
8. Heitman, L. H.; Mulder□Krieger, T.; Spanjersberg, R. F.; Von Frijtag Drabbe Künzel, J. K.; Dalpiaz, A.; IJzerman, A. P. *Br. J. Pharmacol.***2006**, *147* (5), 533.
9. Deng, J.; Sanchez, T.; Al-Mawsawi, L. Q.; Dayam, R.; Yunes, R. A.; Garofalo, A.; Bolger, M. B.; Neamati, N. *Bioorg. Med. Chem.***2007**, *15* (14), 4985.
10. Evdokimov, N. M.; Kireev, A. S.; Yakovenko, A. A.; Antipin, M. Y.; Magedov, I. V; Kornienko, A. *J. Org. Chem.***2007**, *72* (9), 3443.
11. Mamgain, R.; Singh, R.; Rawat, D. S. *J. Heterocycl. Chem.***2009**, *46* (1), 69.
12. Reddy, T. R. K.; Mutter, R.; Heal, W.; Guo, K.; Gillet, V. J.; Pratt, S.; Chen, B. *J. Med. Chem.***2006**, *49* (2), 607.
13. Vora, J. J.; Vasava, S. B.; Parmar, K. C.; Chauhan, S. K.; Sharma, S. S. *J. Chem.***2009**, *6* (4), 1205.
14. Mamolo, M. G.; Zampieri, D.; Falagiani, V.; Vio, L.; Banfi, E. *Farm.***2001**, *56* (8), 593.
15. Norouzi, M.; Ghorbani-Choghamarani, A.; Nikoorazm, M. *RSC Adv.***2016**, *6* (95), 92387.
16. Sobhani, S.; Honarmand, M. *Comptes Rendus Chim.***2013**, *16* (3), 279.
17. Kidwai, M.; Chauhan, R. *J. Iran. Chem. Soc.***2014**, *11* (4), 1005.
18. Chaudhari, M. A.; Gujar, J. B.; Kawade, D. S.; Jogdand, N. R.; Shingare, M. S. *Cogent Chem.***2015**, *1* (1), 1063830.

19. Sobhani, S.; Honarmand, M. *Appl. Catal. A Gen.***2013**, *467*, 456.
20. Safaei-Ghomi, J.; Eshteghal, F.; Ghasemzadeh, M. A. *Acta Chim. Slov.***2014**, *61* (4), 703.
21. Sridhar, M.; Ramanaiah, B. C.; Narsaiah, C.; Mahesh, B.; Kumaraswamy, M.; Mallu, K. K. R.; Ankathi, V. M.; Rao, P. S. *Tetrahedron Lett.***2009**, *50* (27), 3897.
22. Banerjee, S.; Sereda, G. *Tetrahedron Lett.***2009**, *50* (50), 6959.
23. Das, B.; Ravikanth, B.; Kumar, A. S.; Kanth, B. S. *J. Heterocycl. Chem.***2009**, *46* (6), 1208.
24. Shinde, P.; Shingate, B. B.; Shingare, M. S. *Chinese J. Chem.***2011**, *29* (5), 1049.
25. Ranu, B. C.; Jana, R.; Sowmiah, S. *J. Org. Chem.***2007**, *72* (8), 3152.
26. Heravi, M. R. P.; Fakhr, F. *Tetrahedron Lett.***2011**, *52* (50), 6779.
27. Nazeruddin, G. M.; Shaikh, Y. I.; Shaikh, A. A. RJPBCS 2014,.
28. Li, D. F.; Wang, Y.; Yang, G. C.; Ma, X. R.; Han, S.; Song, R. G.; Xie, Z. Y. In *Advanced Materials Research*; Trans Tech Publ, 2012; Vol. 455, pp 565–574.
29. Parmar, K.; Sutariya, S.; Shukla, M.; Goswami, K. *J. Chem. Pharm. Res.***2012**, *4*, 3478.
30. Rathelot, P.; Azas, N.; El-Kashef, H.; Delmas, F.; Di Giorgio, C.; Timon-David, P.; Maldonado, J.; Vanelle, P. *Eur. J. Med. Chem.***2002**, *37* (8), 671.
31. Vora, J. J.; Patel, D. R.; Patel, A. R.; Patel, Y. S. *Der Pharma Chem.***2010**, *2* (3), 257.
32. Padilha, G.; Kaufman, T. S.; Silveira, C. C. *Tetrahedron Lett.***2016**, *57* (30), 3349.
33. Panchani, N. M.; Joshi, H. S. *Chem. Biol. Interface***2016**, *6* (2).
34. Kamble, V.; Atkore, S.; Pisal, P.; Sadaf, M.; Thakre, R. V. *Q. Iran. Chem. Commun.***2016**, *4*, 186.