Print ISSN: 0976-2876 Online ISSN: 2250-0138

Available online at: http://www.ijsr.in

INDIAN JOURNAL OF SCIENTIFIC RESEARCH

DOI:10.32606/IJSR.V11.I2.00014

Received: 12-07-2020 Accepted: 05-12-2020 Publication: 31-01-2021

Indian J.Sci.Res. 11 (2): 77-83, 2021 Original Review Article

A BRIEF REVIEW ON RECENT DEVELOPMENTS IN ULTRASOUND ASSISTED SYNTHESIS OF HETEROCYCLES

RAJANI SINGH[1]

Chemistry Department, T.D.P.G. College, Jaunpur, Uttar Pradesh, India

ABSTRACT

Ultrasonication is one of the ecofriendly implement for the synthesis of heterocyclic compounds. This technique is of increased efficiency and selectivity besides the conventional methods. The US irradiations shorten the reaction time and result an excellent yield of product. Heterocyclic compounds have important role in most fields of sciences like medicinal chemistry and biochemistry. In this article our aim is to review the recently reported US-assisted syntheses of some important heterocyclic compounds.

KEYWORDS: Ultrasound, Heterogeneous

The ultrasonication technique is an rapid and ecofriendly protocol for the synthesis of heterocyclic compounds. The ultrasound waves of frequency (about 20-100 KHz) are of much interest for accelerating chemical reactions (Cella *et al*., 2009).

The ultrasound waves in solution of reactants furnish a specific activation based on acoustic cavitations. The reactant molecules run towards cavities and thus they undergo collisions. As a result of collision, they have sufficient energy to react rapidly resulting product (Morey *et al.*, 2015). It is also suggested that the sound waves propagation pass through liquid medium and bubbles are formed. These cavitations bubbles collapse and very high temperature (5000ºC) and high pressure (1000 bar) may be created. The reagent vapours suffer fragmentation to generate reactive species (Free radicals and Carbenes). These high energy species lead to intermolecular reactions to result product in high yield with decreasing the percentage of by-products. There is enhanced reaction rate. Thus US-assisted protocol for synthesizing heterocyclic compounds as reported in literature is based on following important points:

1. New green US assisted method for synthesis of heterocyclic compounds to be more advantageous than conventional methods.
2. This technique is simple, economical and ecofriendly.
3. The time of chemical reaction is reduced from hours to few minutes.
4. The products are obtained in increased percentage of yield as compared to conventional methods.

The heterocyclic compounds played a vital role in biological process and have proved to be broadly and economically useful as therapeutic agents. The high therapeutic properties of Imidazoles (Bhandari *et al*., 2010), Pyrazoles (Selvan *et al*., 2014), Pyridines (Ghattas *et al*., 2016), Sym-triazoles (Singala *et al*., 2018), Benzodiazepines (Ishwar Bhat *et al*., 2014), Pyrimidines (Abbas *et al*., 2016), Quinazolines (Nofal *et al*., 2011), quinolines (Thigulla *et al.*, 2016) derivatives have encouraged the researchers to design ecofriendly benign protocol to synthesise these heterocyclic compounds. It is a challenge to medicinal chemists to follow US-assisted synthesis of compounds and also by using green solvents or developed solvent free US-assisted synthesis. The use of some green reusable heterogeneous catalyst in US-assisted synthesis also resulted the products in high yield and in lesser time as compared to conventional methods. Thus ultrasound assisted protocol is a boon in the synthesis of heterocyclic compounds.

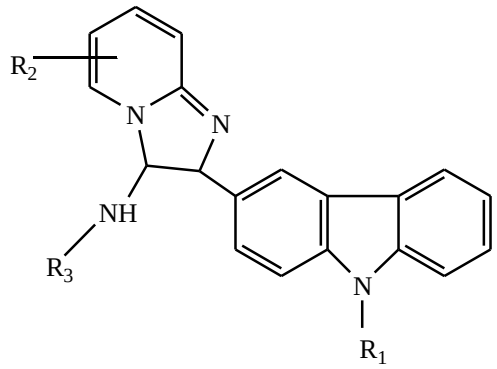
ULTRASOUND-ASSISTED SYNTHESIS OF HETEROCYCLIC COMPOUNDS

A large number of heterocycles have been synthesised as reported in literature by sonication technique. In this review we have mentioned the ultrasound promoted recently reported synthesis of some heterocyclic compounds on the basis of various literature surveys.

The synthesis of seventeen novel 1,3-imidazo[1,2-a] pyridine carbazoles bound type bis-heterocycles (in one pot) by ultrasound irradiation assisted GBB reaction by using ammonium chloride

[1]Corresponding author

catalyst and green solvent (Ethanol) at room temperature in high yield has been reported (Kurva *et al*., 2018).

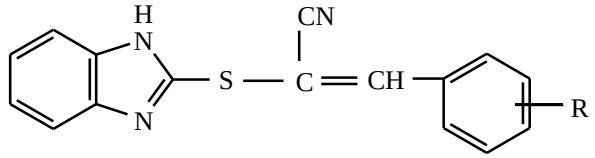


$R_1 = C_3H_7, C_5H_{17}$

R_2 = H, 4-Me, 5-Cl, 5-CN, 4-COOMe, 6-Br, 3-OBr

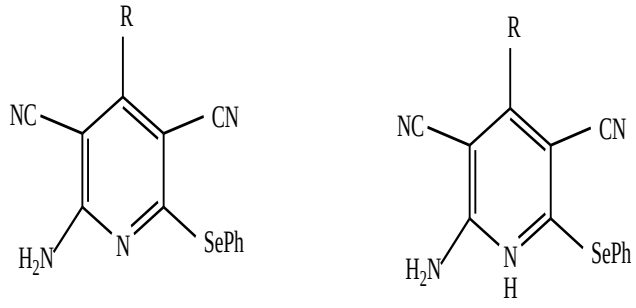
R_3 = O-Hex, 4-OMePh, t-Bu, 2,6-dimethlphenyl.

The US-assisted synthesis of light benzimidozolyl thiounsaturated nitriles using water as green solvent in short reaction time has been reported (Rao *et al*., 2014).



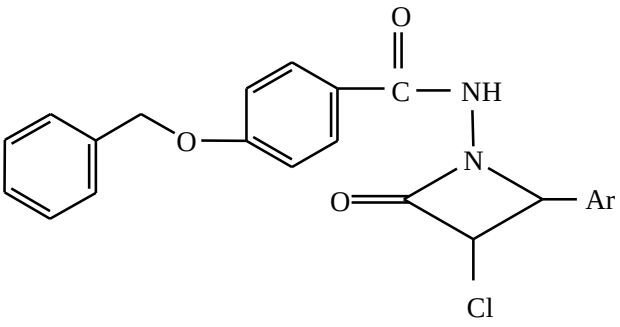
R = o-nitro, m-nitro, p-nitro, o-tolyl, p-tolyl, p-hydroxy, o-hydroxy, 3,4-dimethoxy.

A simple and benign one-pot synthesis of highly functionalized seleno dihydropyridines and seleno pyridines has been reported (Khan *et al*., 2015) using ultrasound assisted multi-component reactions of malonitrile, aldehydes and benzeneselenol in reusable PEG-400 as reaction medium.



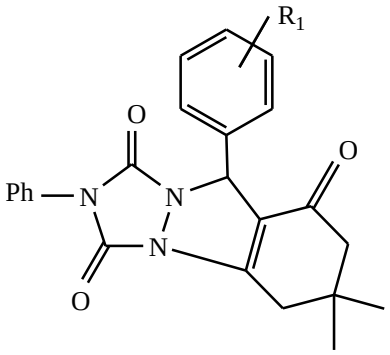
R = o, o´-disubstituted Aryl

Some novel derivatives of 4-(benzyloxy)-N-(3-chloro-2-(substituted phenyl)-4-oxoazetidin-1-yl)benzamid were synthesiszed in high yield by ultrasound irradiation using triethylamine as catalyst involving staudinger Ketene-imine cyclo addition (Nimbalket *et al*., 2018).



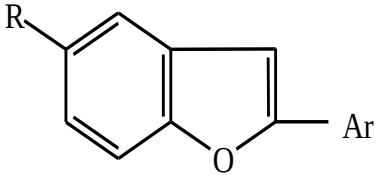
Ar = p-Hydroxyphenyl, p-methoxyphenyl, p-fluorophenyl, p-chlorophenyl

Ultrasound assisted high-yield multicomponent synthesis of triazolo [1,2-a] indazole-triones using silica-coated ZnO nanoparticles as a heterogeneous catalyst in deionized water at about 60ºC, has been reported by the condensation of reaction of dimidone, 4-phenylurazole and aryl aldehydes (Verma *et al*., 2017).



The synthesis of 2,2,4-trisubstituted-2,3-dihydro-1H-1,5-benzodiazapine derivatives was carried out (Chikhale et al., 2013) through a reaction using silica gel as green catalyst and ultrasound as green reaction medium.

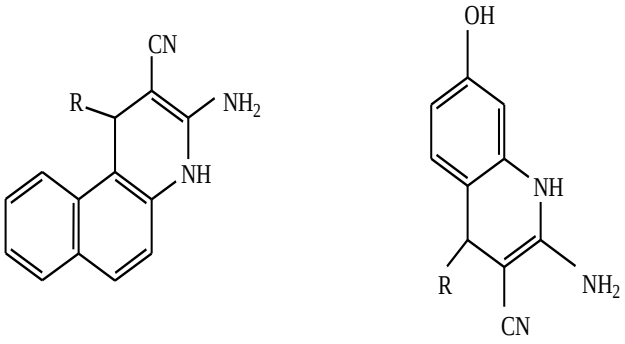
The ultrasound assisted synthesis (Singh *et al*., 2018) of 2-arylbenzofurons in good yield is reported by iodine (III) catalyzed oxidative cyclisation of 2-hydroxy stilbene using $PhI(OAc)_2$ as catalyst in presence of m-chloroperbenzoic acid)



R = H, Me,

Ar = Ph, 3-FC_6H_4, 2-ClC_6H_4, 4-ClC_6H_4, 4-BrC_6H_4, 3-MeC_6H_4, 4Me-C_6H_4, 4-$MeOC_6H_4$, 3,4-$(MeO)_2$ C_6H_3, 1-naphthy

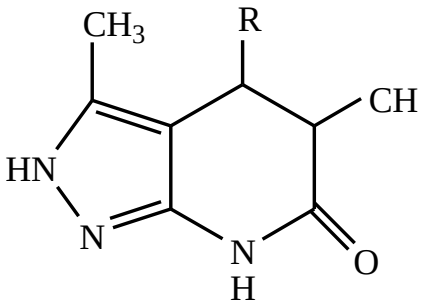
Biologically promising dihydroquinoline derivatives were synthesized (Pagadala *et al*., 2014) via US-assisted one pot four component catalyst free reaction, in higher yield than conventional methods.



R = Ph, 4-BrPh, 4-ClPh, 2-ClPh, 4-OHPh;

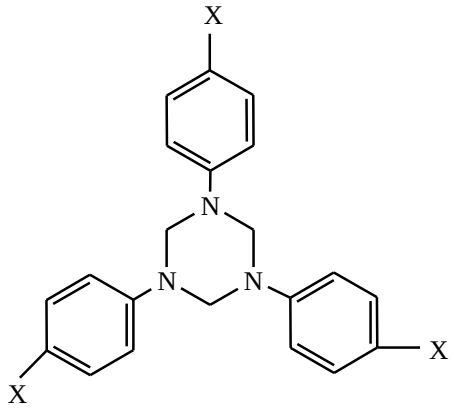
R = Ph, 4-BrPh, 4-OHPh, 4-ClPh

An ultrasound assisted chemo selective synthesis of pyrazolo [3,4-b] pyridine-5-carbonitriles in aqueous medium using NaCl as catalyst has been reported (Dandia *et al*., 2014). Here twelve derivatives were synthesized in 84-95% yield.



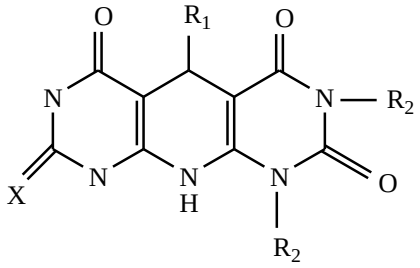
R = Ph, 2F-6ClC_6H_3, 4-ClC_6H_4, 4-BrC_6H_4, 4-OHC_6H_4, 4-$OCH_3C_6H_4$, 4-$CH_3C_6H_4$, 4F-C_6H_4, 3,4,5-$(OH)_3C_6H_2$, 3-$OC_6H_5C_6H_4$

Ultrasound-assisted synthesis of symmetrical hexahydrotriazines (Singh *et al*., 2011) has been reported using ethanol and water as solvent in good yield in short time.



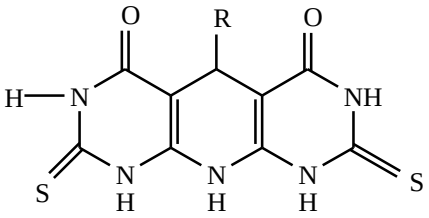
X = H, CH_3, OCH_3, NH_2, Cl, $–NO_2$

A series of pyrimidine annulated fused heterocycles were synthesiszed (Mosslenin *et al*., 2010) in high yields via an ultrasound-assisted method using piperidine as catalyst in water at 60ºC.



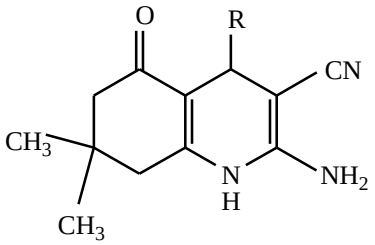
X = O, S; R = H, CH_3, R_1 = C_6H_5, 4-ClC_6H_4, 4-$CH_3C_6H_4$, 4-$NO_2C_6H_4$, 2-furyl, 2-thiophenyl, R_2 = H, CH_3

The US-assisted synthesis of pyrido[2,3-d; 6,5-d] dipyrimidines was developed (Naeimi *et al*., 2017) using nanocopper ferrite as heterogenius catalyst in water in high yields.



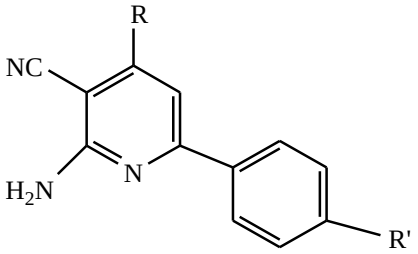
R = C_6H_5, 4-ClC_6H_5, 4-$CH_3C_6H_4$, 2-$NO_2C_6H_4$, 4-$NO_2C_6H_4$, 3-$OCH_3C_6H_4$, 2-FC_6H_4, 2-OH naphthyl, 2-pyridyl, p-phenylene.

A series of biologically active and highly substituted 2-amino 1,4,5,6,7,8- hexahydroquinoline-3-carbonitriles were synthesised (Siddekha *et al*., 2014) is a ultrasound-assisted reactions using K_2CO_3 as a catalyst in aqueous medium at 26ºC.



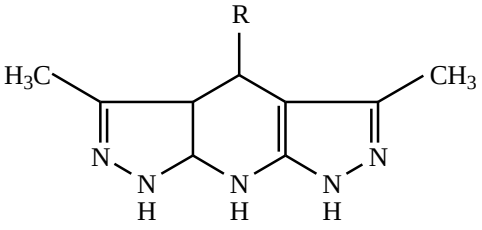
R = 4-$OCH_3C_6H_4$, 4-ClC_6H_4, 3-$NO_2C_6H_4$, 4-OHC_6H_4, 4-$NO_2C_6H_4$, 3,4,5-$(OCH_3)_3C_6H_2$, 3-OCH_3-4-OHC_6H_3.

The ultrasound assisted (Safari *et al.*, 2012) catalyst free high yielding synthesis of 2-amino-4,6-diphenylnicotino nitriles in water at 50ºC in shorter time has been reported.



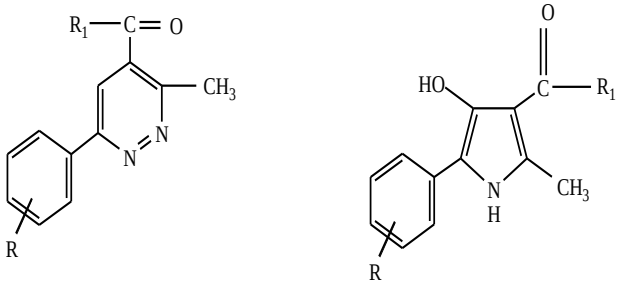
R = H, OH, R^1 = H, 4-CH_3, 4-OCH_3, 4-Cl, 3-NO_2, 4-Br, 4-pyridyl, 2-OCH_3, 2-F, 2-Cl, 3-F, 3-Cl, 3-OH, 2-Furyl, 2-Thienyl

The ultrasound promoted synthesis of tetrahydro dipyrazolo pyridines in aqueous medium without catalyst was reported (Shabalala *et al.*, 2015) as advantageous method with respect to reaction time and yields when compared to conventional method.



R = Ph, 4-$OCH_3C_6H_4$, 4-BrC_6H_4, 4-$N(CH_3)_2$-C_6H_4, 4-OHC_6H_4, 2-BrC_6H_4, 2-$OCH_3C_6H_4$, 2-ClC_6H_4, 2-$NO_2C_6H_4$.

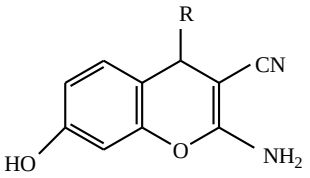
The catalyst free ultrasound-promoted synthesis (Eftekhari-sis, 2013) of 6-aryl-3-methylpyridazine-4-carboxylic acid esters and 5-aryl-4-hydroxy-2-methyl-1H-pyrrole-3-carboxylic acid esters in aqueous media at room temperature.



R = H, 4-Br, 4-Cl, 4-NO_2

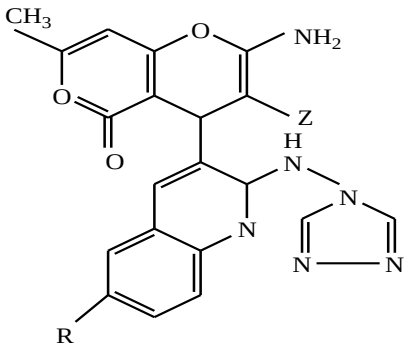
R_1 = OCH_3, OC_2H_5, $OC(CH)_3$, CH_3

An environmentally benign ultrasound promoted aqueous mediated synthesis (Safari *et al.*, 2015) of 2-amino-4H-chromenes in presence of Fe_3O_4-Chitoson nano-particles as catalyst has been reported.



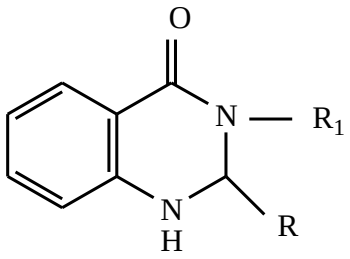
R = 4-FC_6H_4, 2-FC_6H_4, 4-ClC_6H_4, 3-ClC_6H_4, 2-ClC_6H_4, 4-$CH_3C_6H_4$, 3-OCH_3-4-OHC_6H_3, 4-BrC_6H_4, 2,4$(Cl)_2C_6H_3$, 3,5$(OCH)_2C_6H_3$, 3-$NO_2C_6H_4$, 2-$NO_2C_6H_4$, 1,4-phenylene, 3-pyridyl, 2-naphthyl

The ultrasound-assisted synthesis (Gohil, J.D., *et al.*, 2016) of a series of biologically active 2-amino-3-cyano-pyrano [4,3-b] pyrans has been reported.



R = H, CH_3; Z = CN

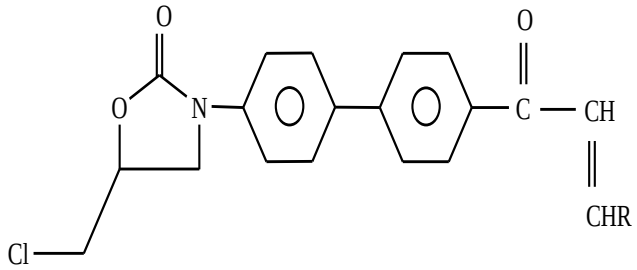
The ultrasound-assisted synthesis (Chen *et al.*, 2015) of 2,3-dihydroquinazolium-4(1H)-one derivatives in presence of catalyst p-dodecylbenzene sulphonic acid in water has been reported.



R = C_6H_5, 4-ClC_6H_4, 4-$NO_2C_6H_4$, 4-$OCH_3C_6H_4$, 2-ClC_6H_4,

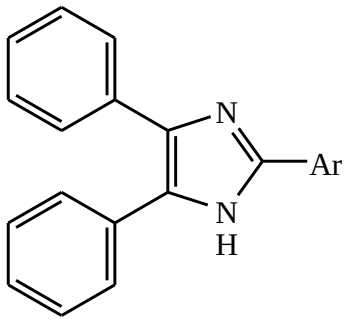
R_1 = C_6H_5, CH_3, 4-$CH_3C_6H_4$, C_2H_5,

The US-assisted synthesis (Panigrahi *et al*., 2019) of novel oxaizolidinone biphenyl chalcone hybrid derivatives in presence of Cu I has been reported.

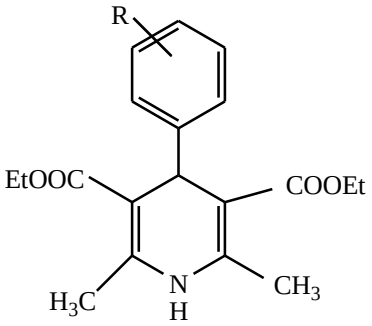


R = C_6H_5, 4-$OCH_3C_6H_4$, 2-ClC_6H_4, 3,4-$(OCH_3)_2C_6H_3$, 2-thiophenyl

The ultrasound-assisted synthesis of poly substituted imidazoles (Sansi *et al*., 2016) using recyclable spinel nano copper ferrite as heterogenius catalyst has been reported.

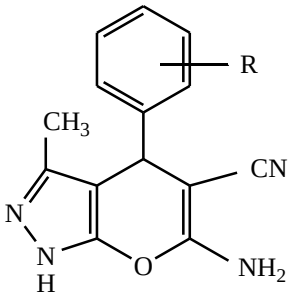


The ultrasonicated synthesis of 1,4-dihydropyridines using robust laterite catalyst has been reported recently (Chine *et al*., 2019).



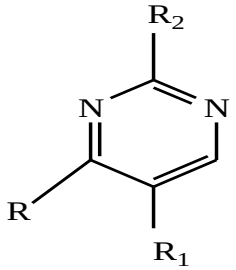
R = 4-ClC_6H_4, 4-$OMeC_6H_4$, 4-OHC_6H_4, 4-$NO_2C_6H_4$, Ph, 4-BrC_6H_4,

The synthesis of pyranopyrazoles using laterite catalyst in presence of ethanol by ultrasonication has been recently reported (Chine *et al*., 2018).



R = 4-ClC_6H_4, 2-ClC_6H_4, 4-$OCH_3C_6H_4$, 4-OHC_6H_4, 2-Furyl, 4- $CH_3C_6H_4$,

The cyclocondensation of □–ketoesters and amidines was promoted by UV irradiation in presence of K_2CO_3 (Vidal M., *et al*., 2016) to result 2,4,5-subsituted pyrimidines inexcellent yields.

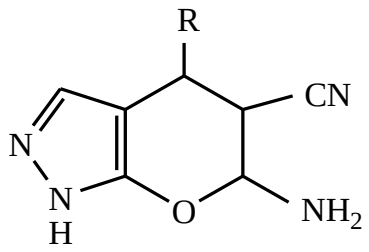


R = Alkyl, CF_3;

R_1 = H, Me;

R_2 = Ar, alkyl

Ultrasound irradiated catalyst free synthesis of dihydropyrano [2,3-c] pyrazoles at 50ºC was reported (Zou *et al*., 2011) at enhanced rate.



R = 4- $CH_3C_6H_4$, 4-ClC_6H_4, 3-ClC_6H_4, 4-FC_6H_4, 4-BrC_6H_4, 4-OHC_6H_4, 4-$NO_2C_6H_4$, 2-thienyl, 2-pyridyl

CONCLUSION

On the basis of recent literature survey the ultrasonication protocol to synthesise heterocyclic compound is an ecofriendly benign method. This method shortens the reaction time with high yield of product. Heterocyclic compounds are considered one of the most important classes of compounds representing important place in medicinal chemistry. It is advisable to researchers and chemists to develop such green economical lesser time taking protocol to synthesise medicinal heterocycles in very high yields without the use of hazardous solvents. Hence ultrasonication technique must be widely accepted for the synthesis of heterocyclic compounds.

REFERENCES

Bhandari K., Srinivas N., Marapu V.K., Verma A., Srivastava S. and Gupta S., 2010. Biorganic and Medicinal Chemistry. Letters, **20**: 291-293.

Cella R. and Stefani H.A., 2009. Ultrasound in heterocycles chemistry. Tetrahedron, **65**: 2619-41.

Chen B.H., Li J.T. and Chen G.F., 2015. Efficient synthesis of 2,3-disubstituted-2,3-dihydroquinazolin-4(1*H*)-ones catalyzed by odecylbenzenesulfonic acid in aqueous media under ultrasound irradiation. Ultrasn Sonochem, **23**: 59-65.

Chikale R. and Khedekar Pramod B., 2013. Ultrasound asisted one-pot synthesis of some 1,5-benzodiezapine derivatives. Current Science, **2**(2): 111-115.

Chine S.S. and Patil C.S., 2018. Laterite catalyzed ultrasound assisted greener protocol for synthesis of pyranopyarazoles. International Journal of Research and Analytical Review, **5**(2): 1786-1789.

Chine S.S. and Patil C.S., 2019. A novel method for synthesis 1,4-dihydropyridines using robust laterite catalyst under ultrasonic irradiation. Asian Journal of Chemistry, **31**(1): 128-134.

Dandia A., Gupta S.L. and Parewa V., 2014. An efficient ultrasound assisted one pot chemo selective synthesis of pyrazole [3,4-b] pyridine-5-carbonitriles in aqueous medium using NaCl as a Catalyst. RSC Advances, **4**: 6908.

Eftekhari-sis B. and Khajeb-Vahdti S., 2013. Curr. Chem. Lett., **2**: 85.

Ghattas A.F.A.G., Khodairy A., Moustafa H.M. and Hassein B.R.M., 2016. J. Heterocycl. Chem. Abbas AF, Zimam EH, 2016, Int. J. Chem Tech. Res., **9**(11): 206-217.

Gohil J.D., Patil H.B. and Patel M.P., 2016. Heterocyclic Lett., **6**: 123-132.

https:11doi.org/10.1002/Jhet.1722.

Ishwar Bhat K., Chauhan Manoj Kumar S.S.H., Kumar A. and Kumar P., 2014. Journal of Heterocyclic Chemistry, **51**(4).

Khan M.N., Karantullah S., Chaudhary Lokman H. and Faizi M.S.H., 2015. Ultrasound assisted multicomponent reactions: a green method for the synthesis of highly functionalized selonopyridines using reusable polethylene glycol as reaction medium. RSC Advances 28, https://doi.org/10.1034/C5RA02403J.

Kurva M., Pharande S.G., Quezada-Soto A. and Rocio G.M., 2018. Ultrasound assisted green synthesis of bond type bis-heterocyclic carbazolyl imidazo [1,2-a] pyridines via GBB reaction. Tetrahedron Letters, **59**(16): 1596-1599.

Mamkrao A.M., Shinde P.N., Khatale P.N., Dhawale S.C., Panasenko O.I., Knysh E.G. and Morey P.B., 2015. Ultrasonic Insight into Substituted Thiazoles and its Biological Activity. Res J. Chem. Sci., **5**(3): 69-76.

Mosslenin M.H. and Nateghi M.R., 2010. Rapid and efficient synthesis of fused heterocyclic pyrimidine under ultrasonic irradiation. Ultrasonics Sonochemistry, **17**(1): 162-167.

Naeimi H. and Didar A., 2017. Recent development or ultrasound-assisted organic synthesis in aqueous medium ultrason. Sonochem, **34**: 889.

Nimbalkar Urja D., Seijas Julio A., Berkute R., Damale M.G., Sangshetti Jaiprahash N., Sarkar D. and Nikalje A.P.G., 2018. Ultrasound assisted synthesis of 4-(Benzyloxy)-N-(3-Chloro-2-(substitutedphenyl)-4-oxazetidin-1-yl) benzamide as challenging anti-tubercular scaffold, Molecules, **23**(8): 1945.

Nofal Z.M., Fahmy H.H., Zarie E.S. and El-Erahy W., 2011. Acta Pol Pharm, **68**(4): 507.

Pagadala R., Maddilas S. and Jonnolangadda S.B., 2014. Ultrasonication mediated catalyst free rapid protocol for the multicomponent synthesis of dihydroquinolene derivatives in aqueous media; Green chemistry Letters and Reviews, **7**: 131-136.

Pamigrahi N., Ganguli S. and Panda J., 2019. Ultrasound assisted synthesis of characterization and antimicrobial evaluation of novel oxazolidinone-biphenyl chalcone hybrid derivatives. Indian Journal of Pharmaceutical Education and Research, **53**(2): 286-300.

Rao S.S., Reddy R.C.V. and Dubey P.K., 2014. An ultrasound mediated green synthesis of benzimidazolyl thioun satruated nitriles using water as a green solvent. Research Article/open Access. https://doi.org/10.1155/ 2014/ 403803.

Sabalala N.G., Pagadala R. and Johnalagadda S.B., 2015. Ultrason. Sonochem, **27**: 423.

Safari J., Banibata S.H. and Khalili S.D., 2012. Ultrason Sonochem, **19**: 1061.

Safari J. and Javadian L., 2015. Ultrason Sonochem, **22**: 341.

Sansi P.D., Majji R.K., Bandaru S., Bass S., Pinnints S., Vasamsetty S. and Korupolu R.B., 2016. Nano copper ferrite catalyzed one pot three and four component synthesis of polysubstituted imidazoles. Modern Research Catal., **5**: 31-44.

Selvan T.P., Kumar P.V., Saravanan G. and Prakash C.R., 2014. Microwave-assisted synthesis of characterization and biological activity of novel pyrazole derivatives. J. Saudi Chem. Soc., **18**: 1051-1021.

Siddekha A., Azzam S.H.S. and Passa M.A., 2014. Synthesis of 2-amino-1,4,5,6,7,8-hexaclroquinole-3-carbanitriles, Synth. Commun., **44**: 424.

Singala P.M., Talpar P.K. and Shah V.H., 2018. Synthesis and Biological assessment of New 1,2,4-triazole derivatives, Research and Review Journal of Chemistry, **7**(1): 14-17.

Singh A., Shukla S.K. and Quraishi M.A., 2011. US-mediated synthesis of hexydro triczines. J. Mater. Environ. Sci., **2**(4): 403-404.

Singh F.V. and Mangaonkar S.R., 2018. Hypervalent iondine (III)-catalyzed synthesis of 2-Arylbenzofurans. Synthesis, **50**: 4940-4948.

Thigulla Y., Kumar T., Trivedi P. and Ghosh P., 2017. Chem. Sel., **7**: 2721-2724.

Verma D., Sharma V., Singh O.G. and Jain S., 2017. Ultrasound assisted high yield multicomponent synthesis of triazolo [1,2-a]indazole-triones using silica-coated ZnO nanoparticles as a heterogenices catalyst. Green Chemistry, **24**. https://pubs.rsc.org>article landing.

Vidal M., Arriagada-Garcia M., Renzende M.C. and Dominguez M., 2016. Ultrasound-promoted synthesis of 4-pyrimidinols and their tosyl derivatives. Synthesis, **48**: 4246-4252.

Zou Y., Wu H., Liu H., Zhao X., Ji H., Shid (2011). A novel and environment-friendly method for preparing dihydropyrano[2,3-*c*]pyrazoles in water under ultrasound irradiation. Ultrason. Sonochem., **13**: 708-712.