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Comprehensive Review of Application of Solvothermal technique in Organic synthesis

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Abstract: The hydrophobic effect can result in different selectivities and rate accelerations, making water a helpful solvent in chemical and biochemical reactions that are also benign to the environment. In light of these compelling advantages, which include those associated with green chemistry, water ought to replace more conventional solvents in the synthesis of chemicals. Because of this, the purpose of this article is to make an effort toward presenting a thorough profile of the synthetic value of water in organic synthesis.

Keywords: Solvothermal, Autoclaves, Heterocycles

1. Introduction:

The majority of chemical reactions used to create compounds, such as medicines, are often carried out in the solution phase. This is also true for any type of study to create new compounds. Earlier days the solution phase was solvents, generally Volatile Organic Solvents (VOCs) which were posing environmental issues. Researchers even worked on Microwave assisted reactions for carrying out the reactions [1].

Researchers also started working on supercritical carbon dioxide which becomes liquid under pressure, however

that also posed problems as it will release green-house gas if it's not completely reused and contained. As a result, a lot of attention was turned to water to be used as solvent for chemical reactions where biochemical reactions are performed in nature.

Water is a greener solvent as it is environmentally benign, hence it as solvent for most of the reactions. Further, taking into consideration of the temperature and pressure conditions present in the earth layer, water can form a significant role in the crystal growth and synthesis of minerals. The invention of advanced equipment's particularly

reactor vessels toward the start of thirties led to the research activities involving aqueous solutions and water under medium temperatures and high pressures. Hydrothermal processes were dynamically carried out by different research groups. [2-4]. “Hydrothermal” for many years to explain the reactions which has taken place at increased pressure and temperature in water.

A few specific reactions have recently been induced using a variety of non-aqueous solvents. G. Demazeau et al. [5] proposed the term “Solvothetical reactions” to describe these non-aqueous reactions in a way that is universal and independent of the type of solvent used. “Reaction or a transformation of reactive in a closed system, in presence of a solvent at a temperature higher than its boiling point” is how solvothetical reactions are defined. Solvothetical reactions can also be conducted in subcritical or supercritical environments. Materials sciences have improvised these processes, using aqueous or non-aqueous solutions in a variety of media.

2. Materials Methods Apparatus

The materials employed under aqueous conditions requests a pressure vessel equipped for holding the extremely corroding solvent at increased pressure and temperature which facilitates the synthesis, able to control, and for recording the pressure and temperature. The most difficult task in hydrothermal associated reactions relies on the construction of hydrothermal apparatus popularly known as autoclaves [6].

A perfect hydrothermal autoclave ought to have the accompanying features [7].

- a) Inactive toward oxidizing agents, bases, and acids.
- b) Simple to assemble and disassemble
- c) To get the appropriate pressure and temperature, it should be long enough.
- d) In order to prevent fabrication or treatment after each experimental run, the material should be strong enough to support high temperature and high pressure studies for an extended period of time.

Morey autoclaves

The most prevalent equipment used for hydrothermal growth is the Morey autoclaves. The typical Morey autoclaves used have internal diameters of 2.5 cm and lengths of 10 to 20 cm. The initial difficulties experienced by Morey and his coworkers were eventually eased by Morey [8] in which the closure was prepared by Bridgman, unsupported region seal gasket composed of silver or copper.

Compression is used to achieve the sealing when the prime nut or fixing nut is tightened. Giving an axial hole along the closure nut can allow the pressure to be measured and controlled during a trial.

A thermocouple is placed inside the wall closure and brought into contact with the sample furnace such that the entire Morey autoclave and closure are contained within the furnace’s element. Following the trial, the entire apparatus is immersed in water, splashed with air, and the closure seal is broken. The Morey autoclaves in the current work, shown in Fig. 1 and 2, were made of SS316 steel.



Fig 1: Morey Autoclave

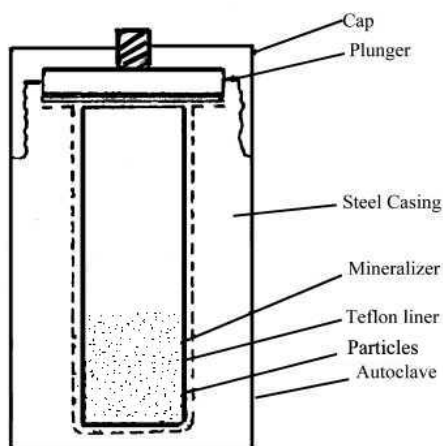


Fig 2: Schematic diagram of Morey autoclave

Liners

As early as 1851 AD, De Senarmont used the glass tube as a liner for the production of sulphides, sulfates, and carbonates, sulfates, and sulfides. [9]

Noble metals or other appropriate metal coating is outfitted for autoclaves like Bridgman and Morey (flat plate). The main problem associated in designing the lining that it should be free of ridges or in-holes, cracks, and it should be sharpened to approach reflect finish. Noble metals are used for the Tuttle cold-cone-seal autoclaves capsules. The liners are filled to the necessary percentage and sealed. Since the autoclave's inner wall and the space between the liners are both filled

to a similar percentage or slightly above that level, a pressure balance is made possible and the liner produces almost no pressure. The liner may burst as a result of the strain irregularity. Teflon beakers or liners are the most cost-effective and commonly used because they facilitate the growth of high virtue crystals in solutions of extremely corrosive media at lower temperatures and pressure. The liner may burst as a result of the strain irregularity. Teflon beakers or liners are the most cost-effective and commonly used because they facilitate the growth of high virtue crystals in solutions of extremely corrosive media at lower temperatures and pressure.

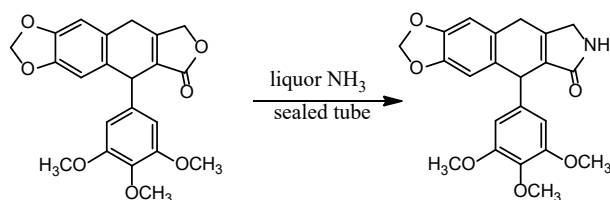
Teflon liners or containers must fit precisely within the autoclave without leaving any room, or else a technique for controlling the pressure will probably need to be used. Since the Teflon liner and cap cannot be soldered, slightly greater pressures of close to 1 to 2 percent fill outside the Teflon liners are preferred.

3. Synthetic utility of Solvothermal reactions

By raising the pressure, certain reactions that would otherwise go more slowly under normal conditions might speed up. You can achieve this by heating the reactants in a sealed environment.

Solvothermal reactions are interesting because they have the potential to produce environmentally friendly reaction conditions by reducing the weight of organic solvent discharge. Heterogeneous chemical reactions that take place at solid-liquid or solid-liquid-gas interfaces at higher temperatures and pressures are included in the solvothermal process.

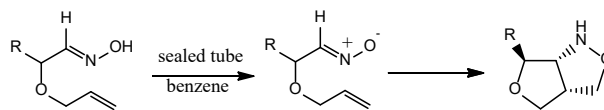
We have so far carried out a few reactions under solvothermal conditions. By heating the amide with liquid ammonia in a sealed glass tube at water bath temperature for 10 to 12 hours (Scheme 1), Rai et al. successfully converted the lactone to amide for the first time in 1986 [10]. In recent years, lactones have been converted to amides via nickel-catalyzed processes. [11]



Scheme 1

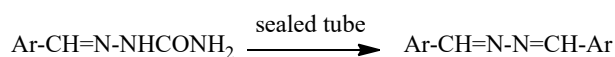
This prompted our group to carry out intramolecular 1,3-dipolar cycloaddition of oxime with olefins to tetrahydrofuranoisoxazolidines by means of nitron intermediate successfully in a sealed tube at 100°C employing benzene as the solvent (Scheme 2) [12].

This ring closure proceeded stereo specifically to generate three adjacent stereochemical centres. The iridium-catalyzed intramolecular chemo- and enantioselective *N*-allylation of oximes has been reported recently. [13]

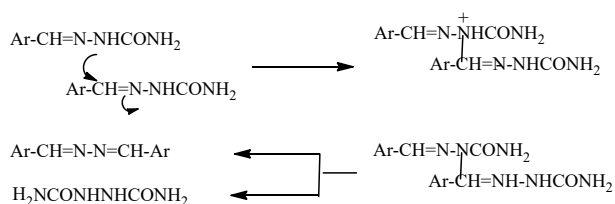


Scheme 2

Transformation of aldehyde semicarbazones to bishydrazones by thermolysis under high pressure was accomplished using ethanol as solvent with 90-95% yield (Scheme 3)[14]. This transformation of semicarbazones to bishydrazones (azine) presumably occurs via the elimination of bisurea from two molecules of semicarbazones (Scheme 4). Earlier bishydrazones synthesis was reported by other methods. [15]



Scheme 3



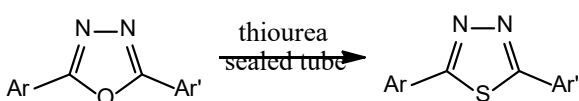
Scheme 4

Thiocarbonyl-containing compounds are adaptable synthetic intermediates with numerous uses in the production of complicated natural products. [16]

Despite the fact that there are numerous reagents for thionation of esters or amides, they have significant drawbacks. Lawesson's reagent, hydrogen sulfide, phosphorous pentasulfide, hexamethyldisilathiane, $R_3OBF_4/NaSH$, R_2PSX , $(Et_2Al)_2S$, bis(tricyclohexylstannyl)sulfide/boron trichloride, thiourea etc. are some of the different thionating reagents. For example,

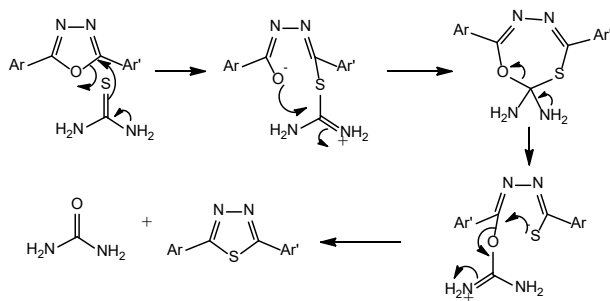
many of these reagents require prolonged reaction durations, high temperatures, or harsh reaction conditions to be successful. Additionally, they frequently require painful chromatograms to separate used reagents from desired products.

Because of this, Rai decided to employ thiourea as a thionating agent to convert 1, 3, 4-oxadiazole into 1, 3, 4-thiadiazole under solvothermal reaction conditions (Scheme 5) [17].



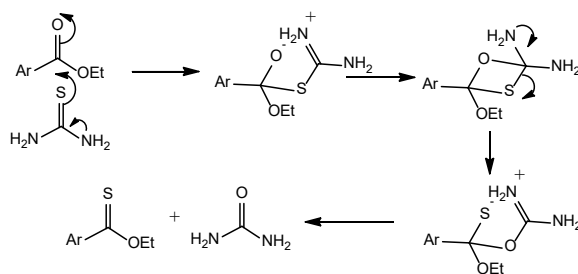
Scheme 5

The predicted process for the synthesis of 2,5 diaryl 1,3,4-thiadiazole entails the initial attack of thiourea's sulfur atom on the nitrogen at positions 2 or 5 of the compound, assisted by a lone pair of electrons, followed by a ring opening reaction to produce the thiuronium salt. By forming an oxathiadiazepine derivative, this thiuronium salt undergoes rearrangement to generate mesomeric oxouronium salt. With the elimination of the urea molecule, further ring closure of the oxouronium salt will result in the synthesis of thiadiazole (Scheme 6).



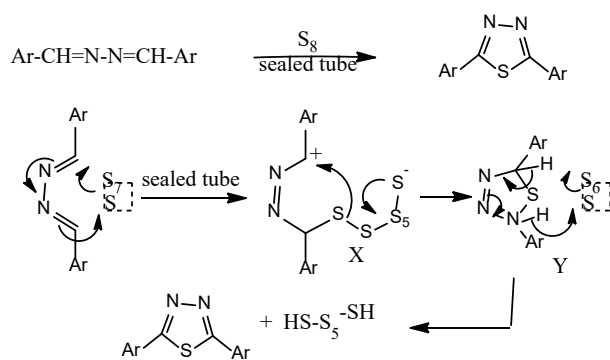
Scheme 6

Thiourea's effectiveness as a reagent for the solvothermal conversion of esters or amides into thioesters or thioamide, respectively, was further demonstrated by Rai et al (Scheme 7). In a typical synthesis, equimolar amounts of thiourea and ester were added to a stainless steel autoclave of the SS316 Morey type that had a 30 ml capacity teflon liner. It produces 85 to 90% of ethylthiobenzoate during routine workup [18].



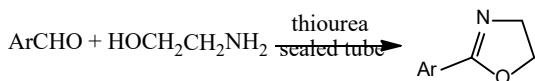
Scheme 7

Further, the azine derivatives were reacted with elemental sulphur under solvothermal condition leading to the formation of 2,5-diaryl-1,3,4-thiadiazole derivatives (Scheme 8)[19].



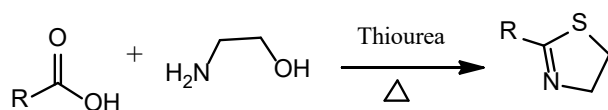
Scheme 8

Rai et al synthesized 2-aryl oxazolines by the heterocyclization of ethanolamine and aryl aldehyde under solvothermal condition (Scheme 9) [20].

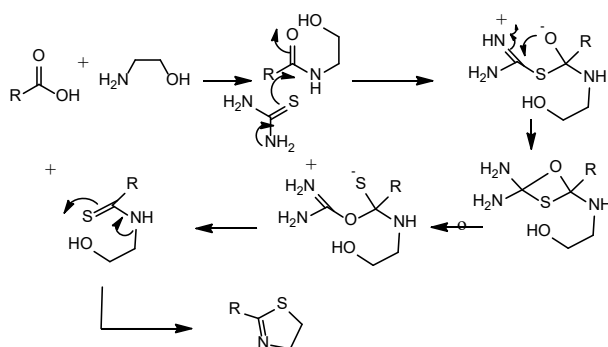


Scheme 9

It is highlighted in Scheme 10 that a novel strategy for the synthesis of 2-alkyl thiazolines that avoids any environmental pollution involves thionation of the amide produced by the heterocyclization of ethanolamine in the presence of a long chain saturated/unsaturated fatty acid. The potential method for thiazoline synthesis is depicted in Scheme 11.



Scheme 10



Scheme 11

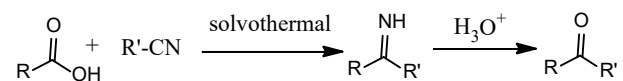
Hugo et al [18] 's effective Meerwin-Pondroff reduction-type procedure involved reducing carbonyl compounds utilising secondary alcohols without the need of a catalyst under super critical condition.

The decarboxylation of aromatic carboxylic acid with the hydrocarbons via direct acylation of aromatic hydrocarbons is a topic covered in a large body of literature. Acyl halides are typically used to acylate aromatic rings in the presence

of Friedel-Crafts catalysts like AlCl_3 [19] as well as other catalysts like CuCl_2 and FeCl_3 . Aromatic carboxylic acids are frequently decarboxylated by heating with copper and quinolone [22], and there are a good amount of reports for this kind of reaction as well.

Under solvothermal conditions, Rai et al. [23] attempted to carry out the esterification of carboxylic acid with alcohols. As a result, it didn't happen, but when acetonitrile was used as the solvent, they produced acetophenone in a good yield rather than esters.

Decarboxylation produces phenyl radicals that attack the nitrile carbon to yield imine radicals. This radical pulls hydrogen from carboxylic acid to make imine. Isolated imine hydrolyzes to equivalent ketone (Scheme 12).



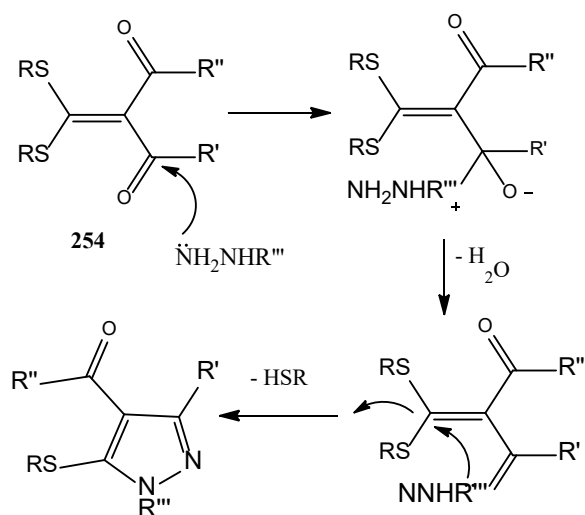
Scheme 12

In a stainless steel SS316 Morey type autoclave with a 30 ml capacity teflon liner, equimolar amounts of benzoic acid and acetonitrile were added and heated to 100–150 oC for 8–10 hours. On the typical workup, the resulting solid product gave an imine of 85–90%. Acetophenone is produced about 85% of the time by acidic hydrolysis of the isolated imine. Rai et al [24] successfully synthesized substituted isoxazoles and pyrazoles from α,α -dioxoketene dithioacetals under solvothermal conditions. α,α -Dioxoketene dithioacetals and (N^1E, N^3E)- N^1, N^3 -bis (3, 4, 5-substitutedbenzlidene) malonohydrazide undergoes heterocyclisation in the presence of

hydrazine derivatives, at relatively low temperature and pressure, under solvothermal conditions, to give the corresponding pyrazole derivatives.

In a typical synthesis, equimolar amounts of phenyl hydrazine and, α,α -dioxoketene dithioacetals were added to a stainless steel SS316 general purpose autoclave that had a Teflon liner with a 30 ml capacity. On the standard workup, it produced 69-96%.

The expected mechanism for the formation of pyrazoles involves the attack of the unsubstituted nitrogen of the hydrazine derivatives to carbonyl carbon of the α,α -dioxoketene dithioacetals to give intermediate adduct. Similarly, in the case of malonohydrazide, the more basic nitrogen $-\text{NH}_2$ attacks carbonyl carbon to give intermediate adduct. In both cases, the intermediate adduct passes intramolecular cyclization to afford product rather than the regiosomeric (3-methylthio-pyrazoles) as illustrated in the Scheme 13.



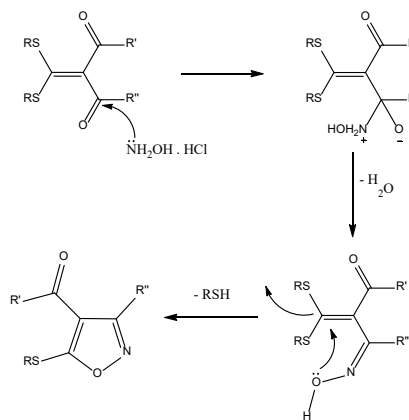
Scheme 13

Raietal[25] reported that 3,4,5-substituted isoxazoles were conveniently prepared

by the reaction of α,α -dioxoketene dithioacetals with hydroxylamine hydrochloride in the presence of pyridine as base while 3,5-disubstituted isoxazoles were prepared from (N^1E, N^3E) - N^1, N^3 -bis (3,4,5-substituted benzlidene) malonohydrazide and hydroxylamine hydrochloride under solvothermal conditions.

The expected mechanism for the synthesis of isoxazoles depends on the role of the base in these reactions. The limited release of free NH_2OH from its salt does not exert an effect on α,α -dioxoketene dithioacetals under these conditions, which follows the oxime pathway to yield exclusively the corresponding 5-alkylthio isoxazoles instead of 3-alkylthio isoxazoles.

Therefore, as shown in Scheme 14, the mechanism of this reaction is the attack of the nitrogen of the hydroxylamine hydrochloride on the carbonyl carbon, which results in an intermediate adduct that undergoes intramolecular cyclization to afford the desired product rather than the regiosomeric (3-methylthio-pyrazoles).



Scheme 14

By combining anisole and substituted

benzaldehydes with a salen metal catalyst and high temperatures and pressures in a Morey autoclave, Rai et al. [26] suggest a straightforward approach for the synthesis of benzhydrol derivatives.

Conclusions

In this paper, the synthetic value of water in organic synthesis is summarised and highlighted for the reader. When conducting organic synthesis, using water as a solvent lowers the amount of harmful compounds released into the atmosphere, which in turn lowers the amount of pollution produced. This is an effective example of green chemistry in action.

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Conflicts of Interest

“The authors declare no conflict of interest.”

References

1. i) Song, L.; Cai, L.; Van der Eycken, E.V. Microwave-Assisted Post-Ugi Reactions for the Synthesis of Polycycles. *Molecules* **2022**, *27*, 3105. <https://doi.org/10.3390/molecules27103105>. ii) Dhanush, P. C.; Padinjare Veeti saranya.; Gopinath Anilkumar. Microwave assisted C-H activation reaction: An overview, *Tetrahedron.*, **2022**, *105*, 132614. <https://doi.org/10.1016/j.tet.2021.132614>.
2. Morey, G.W.; Naggli, P.; The Hydrothermal Formation of Silicates, A Review. *J. Am. Chem. Soc.*, **1913**, *35*, 1086. <https://doi.org/10.1021/ja02198a600>.
3. Roy, R.; Tuttle, O.F.; Investigations under hydrothermal conditions. *Physics and Chemistry of the Earth*, **1956**, *1*, 138-180. [https://doi.org/10.1016/0079-1946\(56\)90008-8](https://doi.org/10.1016/0079-1946(56)90008-8).
4. i) Yixian Xue; Li Bai; Mingshu Chi; Xiuling Xu; Zhao Chen; Kecheng Yu; Zhi Liu. Co-hydrothermal carbonization of pretreatment lignocellulose biomass and polyvinyl chloride for clean solid fuel production: Hydrochar properties and its formation mechanism, *Journal of Engineering*, **2022**, *10*, 106975, <https://doi.org/10.1016/j.jece.2021.106975>. ii) Simiya, S.; Hydrothermal Processing of Ceramics, 7th CMMTEC meeting, **1990**.
5. Dubious.; Demazeau, G.; Proceedings of 4th International Symposium on Hydrothermal Reactions, Nancy, 39-41, Ed. Cuney, M.; Cathelineau, M.; Institut Lorrain des Geosciences (Nancy France), **1993**.
6. Gooch, D.B.; Autoclaves for Pressure-Temperature Reactions. *Ind. Eng. Chem.*, **1943**, *35*, 9, 927-946. <https://doi.org/10.1021/ic50405a002>.
7. i) Byrappa, K.; Masahiro Yoshimura.; Handbook of Hydrothermal Technology. Second Edition. Elsevier Publications, 75-128, ISBN: 978-0-12-375090-7. ii) Byrappa, K.; Yoshimura, M. Handbook of Hydrothermal Technology a Technology for Crystal Growth and Materials Processing; Noyes Publications/William Andrew Publishing, LLC: Park Ridge, NY, USA, 2001. [Google Scholar]
8. Morey, G.W.; Hydrothermal Synthesis. *Journal of the American Ceramic Society*, **2006**, *36*, 9, 279 – 285. [10.1111/j.1151-2916.1953.tb12883.x](https://doi.org/10.1111/j.1151-2916.1953.tb12883.x).
9. De Senarmont, M. On the formation of minerals by wet process in concretionary ore deposits *Ann. Chim. Phys.* **1851**, *32*, 129-175.
10. Anjanamurthy, C.; Lokanatha Rai, K.M.; *Ind. J. Chem.*, **1987**, *26B*.
11. Guiying Xiao.; Chaochao Xie.; Qianling Guo.; Guofu Zi.; Guohua Hou.; Yuping Huang. Nickel-Catalyzed Asymmetric Hydrogenation of γ -Keto Acids, Esters, and Amides to Chiral γ -Lactones and γ -Hydroxy Acid Derivatives, *Org. Lett.*; **2022**, *24*, 14, 2722-2727. <https://doi.org/10.1021/acs.orglett.2c00826>.
12. Lokanatha Rai, K.M.; Hassner, A.; Wim Dahean, *Synth. Commun.*, **1994**, *24*, 1669
13. Tobias Sandmeier, Erick M. Carreira. Enantioselective Synthesis of Cyclic Nitrones by Chemoselective Intramolecular Allylic Alkylation of Oximes, *Angewandte Chemie.*, **2021**, *60*, 18, 9913-9918. <https://doi.org/10.1002/anie.202100150>.
14. Linganna, N.; Lokanatha Rai K. M.; Shashikanth, S. *Ind. J. Chem.*, **1999**, *38B*, 1126.
15. Sowmya, P. T.; Lokanatha Rai, K. M.; Anitha Sudhir;

- Sumana Kotian. Chloramine-T in Organic Synthesis and Analysis of Organic Functional Groups: A Review, *Australian Journal of Chemistry*, **2022**. <https://doi.org/10.1071/CH21089>.
16. Pham, Em C.; Truong, Tuyen Ngoc; Dong, Nguyen Hanh; Vo, Duy Duc; Hong Do, Tuoi Thi. Synthesis of a Series of Novel 2-Amino-5-substituted 1,3,4-oxadiazole and 1,3,4-thiadiazole Derivatives as Potential Anticancer, Antifungal and Antibacterial Agents, *Medicinal Chemistry*, **2022**, *18*, 558-573. <https://doi.org/10.2174/1573406417666210803170637>.
 17. Linganna. N.; Lokanatha Rai, K. M.; *Synth. Commun.*, **1998**, *28*, 4611
 18. Aparna, E; Lokanatha Rai, K.; Byrappa, K.; Sureshbabu, M.; Jagadish, R.L.; Gaonkar, S.L.; *J. Mater. Sci.*, **2006**, *41*, 1391-93
 19. Doddramappa Shridevi,D.; Srikantamurthy Ningaiah, Narayan Kuduva, U.; Raad Yhya, K.; Lokanatha Rai, K.M.; *Synth. Commun.*, **2015**, 1532-2432
 20. Manjula, M.K.; Lokanatha Rai, K.M.; Sureshbabu M.; Byrappa, K. *Bulg. Chem. Commun.*, **2008**, *40*, 2795
 21. Manjula,M.K., Lokanatha Rai, K,M.; *Org. Chem. An Ind. J.*, **2008**, *4*, 36-39
 22. Lena, S.; Esther, R.; Hugo, G.; Aharon, G.; Hoz, S. *J. Org. Chem*, **2004**, *69*, 1492-96
 23. Olah, "Friedel-Crafts and Related Reactions", *Interscience, New York, 1963-64: Vol. 1*
 24. Cohen; Schambach, *J. Am. Chem. Soc.*, **1970**, *92*, 3189
 25. Lokanatha Rai, K.M.; Sureshbabu, K.; Byrappa, K.; *Asian J of Chem.*, **2012**, *24*, 1395-96
 26. Ebraheem Abdu Musad, Lokanatha Rai, K.M.; *Synth. Commun.*, **2010**, *40*, 3569–3576, K. Jailakshmi, K. M. Lokanatha Rai and K. Byrappa, *J. Mater. Sci.*, **2008**, *43*, 2254-57