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Short Communication

Use of Green Chemical Techniques for High Throughput Generation of NCE-Libraries

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New Drug Discovery Research (N.D.D.R.) remains a continuously ongoing process in developed and developing countries. Besides, discovering new potential drug molecules, their successful development into a real drug to be effectively useful in therapy, is rather the most challenging and costly process. New Drug Discovery thus, is a very costly, complex, intellectual, time consuming and challenging process. Speeding up the process of discovery is very important to achieve the success in the markets and to remain competitive. Thus, the word "High throughput" has assumed great importance in both the contexts, namely: Synthesis and Screening of the NCE's.

One-pot Multicomponent Organic Reactions (MCORs) have emerged as an efficient tool for the high throughput synthesis of NCE libraries by virtue of their convergence, productivity, facile execution, and generation of highly diverse and complex products from easily available starting materials in a single operation or step! MCORs are now being tuned for synthesizing various heterocyclic compounds as NCE's due to their diverse biological activities. The environmental acceptability of the process is improved if the multicomponent strategy is applied under environmentally safe green chemical techniques, such as:

1. Use of microwave for energy efficiency,
2. Employing catalytic solvents like, ionic liquids,
3. Sonochemistry,
4. Solvent free reactions,
5. Photo catalysis,
6. Use of water as a solvent,
7. Use of catalysts like PTCs etc.

Subtle variations and manipulations of reactions conditions, stoichiometry of reactants, as well as, judicious selection of solvents and catalysts can help converting multistep synthetic protocols to single step ones amenable to parallel synthesis, as well as causing drastic reduction of overall time required for the conversion of starting materials to the desired product, i.e., NCE, with improvements in overall yields and purity. Sometimes the dual use of a reactant as solvent also helps substantially to achieve speed, yields and purity. Single pot protocols avoid multistep workups and thus save time and loss of overall yields. Microwave Assisted Organic Synthesis (MAOS) has proved to be a suitable tool for above purpose since past 2 decades. It remarkably reduces the reaction time from hours to minutes and yet offers better yields and purity. Since, microwave offers very uniform heating throughout the reaction medium, the selection of a proper solvent with appropriate dielectric constant and loss tangent, makes the reaction to go to completion and avoids side reactions, thus offering crystalline products with high purity. Every Solvent interacts with microwave energy differently depending upon its polarity.

Water becomes a more interesting solvent at higher temperatures and pressures. Under normal conditions it maintains a high dielectric constant and persistent hydrogen bonding. As its temperature and pressure increase, it begins to act more like an organic solvent. It changes from very polar to an almost nonpolar solvent, solubilizing many organic compounds otherwise insoluble in it. With these enhanced conditions its acidity increases, density decreases, and dielectric constant lowers. With MWI the supercritical levels of water (Tc = 374, Pc = 218 atm, psi = 221 bar), where gaseous and liquid water co-exist are never quite reached. Nevertheless, the increased temperature and pressures can be advantageous for organic synthesis in aqueous media. Moreover, it is a benign solvent with zero pollution.

There are specifically designed multimode microwave systems for high throughput parallel syntheses of NCE libraries for N.D.D.R. e.g. Initiator 60 by Biotage AB, Voyager by CEM Corporation, CombiCHEM system by Milestone Inc., Synthos 3000 by Anton Paar GmbH, etc.

Sonochemistry involves the use of ultrasound to speedup chemical reactions in solutions by providing specific activation based on a physical phenomenon: acoustic cavitation. Cavitation is a process in which mechanical activation destroys the attractive forces of molecules in the liquid phase. Applying ultrasound, compression of the liquid is followed by rarefaction (expansion), in which a sudden pressure drop forms small, oscillating bubbles of gaseous substances. These bubbles expand with each cycle of the applied ultrasonic energy until they reach an unstable size; they can then collide and/or violently collapse.

Ionic liquids (IL) double up as reaction media, as well as promoters replacing volatile organic compounds (VOC's) in conventional organic synthesis and in many instances obviate the need for the use of an additional acid catalyst. The inherent Bronsted/Lewis acidity of the ILs allows them to forge hydrogen bonded interactions with suitable functionalities thereby enhancing the reactivity of the later. This enables the reaction to be carried out in a short time in the MCR mode, allowing for the generation of a combinatorial library of such molecules as part of the drug discovery process.

Phase Transfer Catalysis (PTC) technique is used for conducting reactions between two or more phases and is basically concerned with conversions between chemicals species situated in different (heterogeneous) phases. Under Neutral Conditions PTC permits or accelerates reaction between a water-soluble ionic compound with an organic, water insoluble substrate in solvents of low polarity. Under Basic Conditions a PTC transfers the anion generated *in situ* from the interface to the organic layer.

Thus, intelligent design of reaction protocols suitable for parallel syntheses, by suitable combinations of above techniques can achieve high throughput library syntheses of N.C.E.'s. This field of research is very much fertile for further exploration [1-11].

Bibliography

1. D Scharn., *et al.,* "Spatially Addressed Synthesis of Amino- and Amino-Oxy-Substituted 1,3,5-Triazine Arrays on Polymeric Membranes". *Journal of Combinatorial Chemistry* 2.4 (2000): 361-369.

2. KS Jain., *et al.,* "Impact of Microwave Assisted Heating on the Combinatorial and Parallel Syntheses of Compound Libraries for New Drug Discovery Research". *Indian Drugs* 46.10 (2009): 747-774.

3. KS Jain., *et al.,* "Novel Dual use of Formamide-POCl3 mixture for the efficient, one-pot synthesis of Condensed 2H-pyrimidin-4-amine libraries under microwave irradiation". *Synthetic Communications* 43.5 (2013): 719-727.

4. RJ Nevagi., *et al.,* "Use of Ionic Liquids as Neoteric Solvents in the Synthesis of Fused Heterocycles". *Archiv der Pharmazie - Chemistry in Life Sciences* 347 (2014): 1-12.

5. KV Srinivasan., *et al.* "Microwave Assisted Synthesis of Fused Heterocyclic Compounds". *Heterocycles* 83.11 (2011): 2451-2488.

6. KS Jain., *et al.,* "Green Synthesis of 2-Amino-4-Arylthiazoles Employing MWI and Water, Efficient and Rapid Synthesis (ISBN 978-3-8465-9512-1), Lap-Lambert Publications, Saarbrücken, Germany (2013).

7. SN Dighe., *et al.,* "A remarkably high speed solution phase combinatorial synthesis of 2-substitutedamino-4-arylthiazoles in polar solvents in the absence of a catalyst under ambient conditions and study of their antimicrobial activities". *ISRN Organic Chemistry* (2011): 1-6.

8. KS Jain., *et al.,* "An efficient and rapid synthesis of 2-amino-4-arylthiazoles employing microwave irradia- tion in water". *Green and Sustainable Chemistry* 1 (2011): 36.

9. MS Phoujdar., *et al.,* "Microwave Based Synthesis of Novel Thienopyrimidine Analogs of Gefitinib". *Tetrahedron Letters* 49 (2008): 1269.

10. MK Kathiravan., *et al.,* "Efficient and rapid one-pot synthesis of substituted 2-amino-3-carbethoxythiophenes under Microwave Irradiation". *Synthetic Communications* 37 (2007): 4273.

11. KS Jain., *et al.,* "A facile synthesis of 2-amino-5-cyano-4,6-disubstitutedpyrimidines under MWI". *The Journal of Organic Chemistry* 1 (2011): 51.

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