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Green Chemistry: A Boon to Pharmaceutical Synthesis

Chemistry

KEYWORDS : Microwave synthesis, Sonochemistry, Combinatorial chemistry, Solvent free reaction, Photo catalysis.

Dr. Savita J. Tauro — Department of Pharmaceutical Chemistry, St. John Institute of Pharmacy & Research, Palghar (E) Dist: Thane (M.S) India

Jineetkumar B. Gawad — Department of Pharmaceutical Chemistry, St. John Institute of Pharmacy & Research, Palghar (E) Dist: Thane (M.S) India

ABSTRACT

Green chemistry is an extension of synthetic chemistry comprising of an attempt to reduce the generation of hazardous substances. The vital role of green chemistry is in controlling harm to the environment in the way of chemical waste. Thus it prevents wastes, stochiometric reagents, design less hazardous chemical synthesis, use catalyst, maximize atom economy and minimize the potential for accidents. This includes lesser consumption of resources and develop alternative and more sustainable synthetic pathway. This includes methods like microwave synthesis, catalytic reactions, sonochemistry, combinatorial chemistry, solvent free reaction, photo catalysis, multicomponent reactions, water as a solvent, etc. Green chemistry is rapidly developing new field that provides us a proactive avenue for the sustainable development of future science and technologies.

Introduction

Green chemistry involves set of approaches that reduces or eliminates the use of hazardous substances in the design, manufacture and application of chemical products. green chemistry is often an elegant procedure used in synthesis of pharmaceuticals. This includes development of new methods of synthesis of pharmaceuticals to synthesize entity with less consumption of resources and less production of waste and development of alternative and more sustainable starting materials. Green chemistry approach plays a vital role in controlling environmental hazards via use renewable feed stocks, catalysts, non stochiometric reagents, maximize the atomic economy, use of safer solvents and reaction conditions, increase of energy efficiency and minimizing potential for accidents. But it has certain limitations such as boiling points of solvents are reached rapidly, often inducing safety problems like explosions. To solve such problems, the operation has to be carried out in closed vessels, generally made of Teflon, a material transparent to microwave and resistant up to 250°C and 80 psi and using only small amounts of products i.e. roughly 1/10 of the total volume. This of course constitutes a serious limitation i.e. reduction in microwave efficiency as the penetration dept is far below λ, scaling up, etc. Another significant demerit is the absence of measurement and control of temperature. However, these limitations can be overcome by the following approaches,

1. The use of solvent free techniques.
2. Operation with an adequate reactor allowing homogeneity of electric field and temperature provided by a wave guide or wave diffuser.

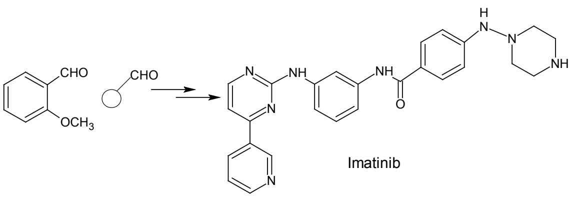
IMPORTANT APPROACHES REGARDING GREEN CHEMISTRY SYNTHESIS

1. Use of microwave for energy efficiency.
2. Catalytic reaction.
3. Sonochemistry.
4. Combinatorial chemistry.
5. Solvent free reactions.
6. Photo catalysis.
7. Multicomponent reactions.
8. Water as a solvent.

MICROWAVE SYNTHESIS

Microwave chemistry is the science of applying microwave irradiation reactions. Microwave acts as high frequency electric fields which generally heat anything with mobile electric charge. Polar solvents are heated as their components molecules are forced to rotate with the field and loose energy in collisions. Semiconducting and conducting samples heat when ions or electrons within them form an electric current current and energy is lost due to the electrical resistance of material. An extension of microwave assisted synthesis is microwave assisted solid phase synthesis.

Examples: Microwave assisted using solid phase synthesis of Imatinib, a blockbuster anticancer drug. An expeditious, high yield and convenient synthesis of Imatinib was carried out on an aldehydic, super acid-sensitive resin, through an efficient, microwave-assisted synthetic protocol. The high versatility of the reaction scheme may enable the straightforward preparation of libraries of potential protein kinase inhibitors endowed with large molecular diversity.



CATALYTIC REACTIONS

In chemistry and biological system catalysis refers to the acceleration of the rate of a chemical reaction by a substance, called a catalyst, which remains unaffected by the overall reaction. Zeolite effects in the sustainable and green synthesis of intermediates and fine chemicals – A non-exhaustive review with personal emphasis on the selected examples was made, illustrating how zeolite-based catalysts can be effective for improved green and sustainable catalysis in the areas of fine chemicals and their intermediates.

Laccases: blue enzymes for green chemistry- Laccases are oxidoreductases belonging to the multinuclear copper containing oxidases; they catalyse the monoelectronic oxidation of substrates at the expense of molecular oxygen. Interest in essential 'eco-friendly' enzymes – they work with air and produce water as the only by-product – has grown significantly in the recent years.

SONOCHEMISTRY

Ultrasonic irradiation leads to the acceleration of numerous catalytic reactions as well as in the homogeneous and heterogeneous systems. The sonochemical phenomena originate from the interaction between suitable fields of acoustic waves and a potentially reacting chemical system; the reaction takes place through the intermediate phenomena of acoustic cavitations.

For example: in chemical kinetics, it has been observed that ultrasound can greatly enhance chemical reactivity in a number of systems; effectively acting as a catalyst by exciting the electronic and molecular modes of the system (such as vibrational, rotational and transitional modes). In addition, in reactions that uses solids, ultrasound breaks up those solid pieces from the released energy from the bubbles created by cavitations collapsing through them. This gives the solid reactant a larger surface area for the reaction to proceed over, increasing the observed rate of reaction. Ultrasound produces radicals in liquids due to the high temperatures and pressures experienced locally when a bubble collapses.

COBINATORIAL CHEMISTRY

Synthesis of molecules in a combinatorial fashion can quickly lead to large numbers of molecules. For examples, a molecule with three points of diversity (R1, R2 and R3) can generate possible structures. In its modern form, combinatorial chemistry has probably had its biggest impact in the pharmaceutical industry. Researchers attempting to optimize the activity profile of a compound create a 'library' of many different but related compounds. Advances in robotics have lead to an industrial approach to combinatorial synthesis. Combinatorial synthesis is the one of the important new methodologies developed by the academics and researchers in the pharmaceutical, agrochemical and biotechnology industries to reduce the tome costs associated with producing effective, marketable and competitive new drugs. Scientists use combinatorial chemistry to create large populations of molecules.

Example: Transition state analogue HIV protease inhibitors extensive efforts towards the rational design of aspartyl protease inhibitors such as rennin and HIV have led to the discovery of several transition-states analogue mimics. These templates can serve as central unit around which molecular diversity can be generated by application of appropriate chemistries. Recently solid phase is applied for synthesis of hydroxyethylamine and 1, 2-diol transition-state pharmacophore units and their utility for synthesis for synthesis of HIV protease inhibitors.

SOLVENT FREE REACTIONS

A dry media reaction or solid-state reaction is a chemical reaction system in the absence of a solvent. The drive for the development of dry media reactions in chemistry is-

1. Economics (save money on solvents).
2. Ease of purification (not required to remove a solvent post synthesis)
3. Solvent is not required.
4. High reaction rate (due to high concentration of reactants).

A reaction which is closer to a true solventless reaction is a Knoevenagel condensation of ketones with (malononitrile) where a 1:1 mixture of the two reactants (and ammonium acetate) is irradiated in a microwave oven. Collin Raston's research group have been responsible for a number of new solvent free reactions. In some of these reactions all the starting materials are solids, they are ground together with some sodium hydroxide to form a liquid, which turns into a paste which then hardens to a solid.

PHOTOLYTIC REACTIONS

In chemistry, photocatalysis is the acceleration of a photoreaction in the presence in the presence of a catalyst. In catalysed photolysis, light is absorbed by an adsorbed substrate. When a divided semiconductor is illuminated with photons of energy higher than or equal to its band gap energy, photoelectrons, e- and photoholes (or) h+ are created. In a fluid reaction medium, reactants can adsorb and react either with electrons (acceptor molecules such as O2) or with holes (donor molecules). Photocatalysis is based on the double aptitude of the photocatalyst (essentially titania) to simultaneously adsorb reactants, and to adsorb efficient photons. The five main parameters which govern the kinetics are (i) the mass of catalyst (ii)the wavelength (iii)the initial concentration (or pressure) of the reactant, (iv) the radiant flux, and (v)exceptionally the temperature in extreme conditions with respect to room temperature. Photo catalysis is efficient in several fields like in selective mild oxidations oxidation of gas and liquid hydrocarbons into aldehydes and ketones.

1. Photocatalysis reactions involving hydrogen- In photocatalytic reactions involving hydrogen, either as a reactant (deuterium-alkane isotopic exchange) or as a product (alcohol dehydrogenation) , the catalyst (such as Pt./TiO2) requires the presence of a noble metal acting as a co-catalyst necessary (i) to dissociate the reactant (D2) and (ii) to recombine H atoms into dihydrogen. This belongs to the field of bifunctional photocatalysis using TiO2-deposited noble metal catalysts.

Thio-photocatalysis

It consists in replacing oxygen as a reactant by sulphur , its next neighbour in group VI, for redox thio-reactions. However, sulphur cannot be used, since it is solid in room temperature (as S8 crown molecules). We chose H2S as a convenient and reactive source. For instance, the conversion of propene in 1-propanthiol was successfully obtained.

MULTICOMPONENT REACTIONS

Multicomponent reactions (MCRs) are convergent reactions, in which three or more starting materials react to form a product, where basically all or most of the atoms contribute to the newly formed product. In a MCR, a product is assembled according to a cascade of elementary chemical reactions. Thus, there is network of reaction equilibria, which all flow finally into an irreversible step yielding the product. The challenge is to conduct a MCR in such a way that the network of pre-equilibrated reactions channel into the main product and do not yield side products. The result is clearly dependant on the reaction conditions: solvent, temperature, catalyst, concentration, the kind of starting materials and functional groups. Such considerations are of particular importance in connection with the design and discovery of novel MCRs. Applications of MCRs in all areas of applied chemistry are very popular because they offer a wealth of products, while requiring only a minimum effort. As opposed to the classical way to synthesize complex molecules by sequential synthesis, MCRs allow the assembly of complex molecules in one pot. The Ugi reaction is a multi component reaction in organic chemistry involving a ketone or aldehyde, an amine, an isocyanide and a carboxylic acid to form a bis-amide.

WATER AS A SOLVENT

Water is good solvent due to its polarity. The solvent properties of water are vital in biology, because many biochemical reactions take place only within aqueous solutions. High-temperature (200-350°C) liquid water (HTW) is a promising reaction medium for conducting acid and base catalysed organic synthesis reactions in an environmentally responsible manner. This article provides a summary of recent advances made concerning acid and base catalysed organic synthesis in HTW. One advance is demonstrating that rates of acid catalyzed reactions conducted in HTW can be accelerated while maintaining the solvent benignity by using CO2 as an additive. A second advance is showing that additional commercially significant chemical products can be synthesized in HTW without catalyst. A third advance is demonstrating that product selectivity can be controlled by process variables such as temperature, water density, and heat up time. A forth advance is the emergence of mechanistic insight regarding acid and base catalyzed reactions in HTW.

ADVANTAGES

1. Green chemistry is the design of product and processes that reduce or eliminate the use of generation of hazardous substances.
2. Green chemistry design chemical synthesis to prevent waste.
3. Green chemistry design chemical products to be fully effective having little or no toxicity.
4. Catalysts are used in small amounts and can carry out small reaction many times during green synthesis.
5. Design chemicals and their forms to minimize potential for chemical accidents including explosions, fires, etc.

CONCLUSION

Green chemistry is a rapidly developing new approach that provides us a proactive avenue for the sustainable development of future science and technologies. When designed properly, clean chemical technology can be developed in water as a reaction medium. The technology generated from such green chemistry endeavours may often cheaper and profitable. Green chemistry is designed to be a basis for all reaction in near future. In this

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context a convenient and rapid synthetic procedures i.e. energy efficient is highly desirable.

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