December 2008 *Volume 3 Issue 3*

Trade Science Inc.

Environmental Science

An Indian Journal

Current Research Papers

ESAIJ, 3(3), 2008 [277-284]

Environmentally eco-friendly alternate : Dry media reactions

Ashu Chaudhary[1]*, D.Kumar[1], R.V.Singh[2]

[1]Department of Chemistry, Banasthali University, Rajasthan-304022, (INDIA)

[2]Department of Chemistry,University of Rajasthan, Jaipur-302 004, (INDIA)

E-mail : ashuchaudhary21@gmail.com, achaudhary21@hotmail.com

Received: 31st August, 2008 ; Accepted: 5th September, 2008

ABSTRACT

Green Chemistry is placed in the frontier areas of research and has been focused for considerable recent research. Green Chemistry, the design of chemical products and processes that reduce or eliminate the use and generation of hazardous substances is an overarching approach that is applicable to all aspects of chemistry. From feedstocks to solvents, to synthesis and processing green chemistry actively seeks ways to produce materials in a way that is more begin to human health and the environment. The current emphasis on green chemistry reflects a shift away from the historic "command-and-control" approach to environmental problems that mandated waste treatment, control and clean up through regulation and towards preventing pollution at its source rather than accepting pollution at its source. Rather than accepting waste generation and disposal as unavoidable, green chemistry seeks new technologies that are cleaner and economically competitive. Utilizing green chemistry for pollution prevention demonstrates that power and beauty of chemistry : through careful design, society can enjoy the products on which we depend while benefiting the environment. The economic benefits of green chemistry are central drivers in its advancement. Industry is adopting green chemistry methodologies because they improve the corporate bottom line. A wide array of operating costs are decreased through the use of green chemistry. When less waste is generated, environmental compliance casts go down. Treatment and disposal become unnecessary when waste is eliminated. Decreased solvent usage and fewer processing steps lessen the material and energy costs of manufacturing and increase material efficiency. The environmental, human health, and the economic advantages realized through green chemistry are serving as a strong incentive to industry of adopt greener technologies. Solvents represent the single largest challenge to green chemistry. They are widely and intensively used in chemical and pharmaceutical processes, in formulation, cleaning and other sectors that the part of the modern industrial consumer society. Unfortunately many of the solvents are used in industry and retail are volatile organic compounds which inevitably lead to environmental damage, through pollution, risks to human health and to resource depletion, we need to develop and apply more environmentally friendly approaches. The fundamentally attractive concept of green chemistry is solvent free reactions. Solvent free reactions can be accelerated by microwave activation and this combined clean technology approach to "greening" chemical reactions. A solvent-free approach has been describes for organic synthesis which involves microwave (MW) exposure of neat reactants (undiluted) either in the presence of a catalyst or catalyzed by the surfaces of inexpensive and recyclable mineral supports such as alumina, silica, clay, or "doped" surfaces, namely, Fe(NO3)3-clay (clayfen), Cu(NO3)2-clay (claycop), NH2OH-clay, PhI(OAc)2-alumina, NaIO4-silica, MnO2-silica, and NaBH4-clay. A variety of deprotection, condensation, cyclization, oxidation, and reduction reactions are presented including the efficient one-pot assembly of heterocyclic molecules from *in situ* generated intermediates such as enamines and ⟨-tosyloxyketones. The application of this solvent-free MW approach to multicomponent reactions is highlighted that can be adapted for high-speed parallel synthesis of the library of dihydropyrimidine-2(1*H*)-ones and imidazo 1,2-a]annulated pyridines, pyrazines, and pyrimidines.

Current Research Paper

INTRODUCTION

The present day industrialization has led to immense environmental deterioration. The increasing environmental consciousness throughout the world has put a pressing need to develop an alternate synthetic approach for biologically and synthetically important compounds. This requires a new approach, which will reduce the material and energy intensity of chemical processes and products, minimize or eliminate the dispersion of harmful chemicals in the environment in a way that enhances the industrially benign approach and meets the challenges of green chemisty[1].

Green Chemistry is the utilization of a set of principles that reduces or eliminates the use or generation of hazardous substances in the design, manufacture and application of chemical products. Our environment, which is endowed by nature, needs to be protected from ever increasing chemical pollution associated with contemporary lifestyles and emerging technologies. Developments in water treatment, waste disposal methods, agricultural pesticides and fungicides, polymers, materials science, detergents and so forth have all contributed to the improvement in our quality of life, but all these advances come with price tag-of pollution[2]. In recent times, with the environmental degradation beginning to take alarming proportions, the chemical industries worldwide is facing the challenges of stringent environmental regulation and unprecedented economic, environmental and societal pressure for innovation of new efficient protocols that circumvent the hazards due to waste effluents and by products arising from manufacturing processes, With the preservation of environment being a major concern, the chemical industries has to now seek to wean users away from the conventional methodologies by driving towards more efficient and Eco-friendly processes which can harmoniously connect synthesis and environment.

Hence, the need of new millennium to develop such procedures which can increase synthetic efficiencies as well as minimize environmentally hostile wastes, led to the concept of a new, cleaner, enviro-economic branch of chemistry i.e. 'Green Chemistry' to crystallize in 1990's. By definition, 'Green Chemistry[3], is the design, development and implantation of chemical, products and processes to reduce or eliminate the use of

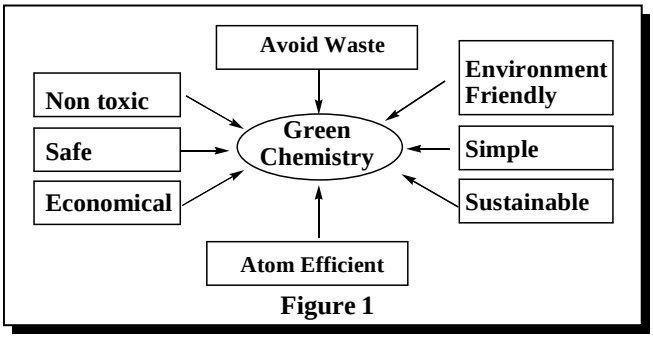
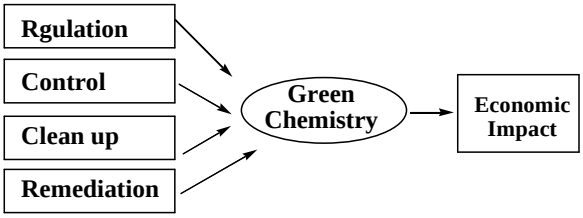


Figure 1



Figuer 2 : Environmental protection activities that require the intervention of green chemistry to minimize their impact

substances hazardous to human health and environment[4,5]. It includes modification of engineering practices, bioremediation and promotes Eco-friendly reaction media as well as the concept of atom economy leading to almost zero waste.The fundamental issues of "Green Chemistry" are:

- Reduction or replacement of volatile organic solvents.
- Pollution and waste prevention
- Atom economization
- Toxicity reduction

Green chemistry by the design[6] of environmentally compatible chemical reactions, offers tools to approach pollution and sustainability concerns at the source. Environmentally benign synthesis, also known as "Green Chemistry", seeks to incorporate environmental and toxicological awareness at the design phase of a synthesis process. The basic concept is that it is far better to develop a synthetic strategy that avoids the use of hazardous material in the first phase than to face cleaning-up, containment and waste disposal.

The combination of solvent free procedures and microwave irradiation can be used to carry out a wide range of reactions with in short reaction times and with high conversions and selectivity. Yields and purity of the products as proved by GC analysis are generally improved when compared to those obtained by conventional heating. This approach is efficient, easy-to-perform, economic and less polluting as avoiding sol-

vents. Some specific, non-purely thermal, effects of the radiation are often evidenced depending on the reaction mechanism and enhancement in polarity during the reaction progress.

Among the most promising ways in procedures for Green Chemistry, solvent free techniques hold a strategic position as solvents are very often toxic, expensive, and problematic to use and to remove. It is the main reason for the development of such modern technologies. These approaches can also enable experiments avoiding the use of strong mineral acids (i.e. HCl, H_2SO_4 for instance) that can in turn cause corrosion safety, mainpulation and pollution problems as wastes. These acids can be replaced advantageously by solid, recyclable acids such as clays (montmorillonites).

Reactivity

Accelerations of reactions can result from increasing concentrations in reactants when a diluting agent such as a solvent is avoided. As concentrations in reactive species are optimal, reactivity is notifceably increased and only mild conditions can be required. In several cases difficult reactions using solvents can be easily achieved under solvent free conditions. Another important advantage lied in the fact that higher temperatures, when compared to classical conditions, can be used in open vessels without the limitation imposed by solvent boiling points.

Selectivity

The layout of reacting systems can be increased when high concentrations/aggregation of charged species are involved. It can lead to some modifications in mechanisms resulting in a decrease in molecular dynamics and induce subsequent special selectivities (stereo - regio - or enantioselectivity). Weak interactions can appear (such as T-stacking) which are usually masked by solvents, inducing further benefic consequences on selectivity.

Reactions on solid mineral supports[7]

Reactants are previously impregnated onto solid mineral supports such as aluminas, silicas and clays as neat liquids or via their solutions in an adequate organic solvent and further solvent removal. Reaction in "Dry media" is then performed between individually impregnated reactants, possibly under heating. At the end of reaction, organic products are easily removed by elution with diethyl ether or dichloro-methane and a simple filtration to eliminate the solids.

Solid-liquid phase transfer catalysis (PTC)[8]

Reactions occur between neat reactant sin quasi-equivalent amounts in the presence of a catalytic quantity of tetraalkylammonium salts or cation complexing agents. When the reaction is performed in the absence of solvent, the liquid organic phase consists of the electrophilic reagent then possibly the reaction product (Figure 1). Nucleophilic anionic species can be generated in situ by reacting their conjugated acids with solid bases of increased strength due to ion-pair exchange with $R_4N^+X^-$.

Reactions without any solvent support, or catalyst[9,10]

The heterogeneous reactions are carried between neat reactants in quasi equivalent amounts without any adduct. In the case of solid-liquid mixtures, the reaction implies either solubilization of the solid in the liquid phase or adsorption of the liquid on the solid surface as an interfacial reaction.

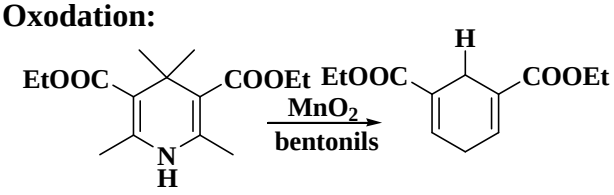
Striking examples of solvent-free synthesis under microwaves[11-15]

Alkylation :

$$CH_3COO^-K^+ + nC_8H_{17}X \xrightarrow[Al_2O_3]{} CH_3COOnH_{17}$$

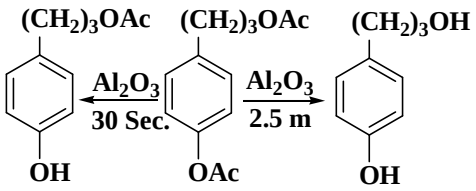
98% 2 min. (186°C), b < % 2 min. (186°C)

Oxodation:



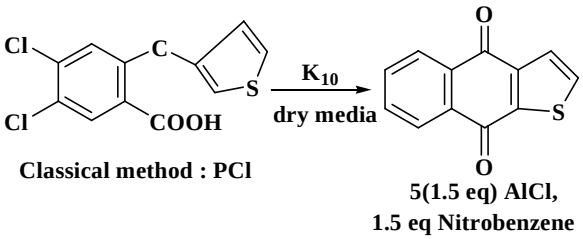
HANTZSCH D.H.P. **100% 6 min.**

Deacetylation:



Synthesis of fused anthraquinones using clay under microwaves

Current Research Paper



Classical method

PCl (1.5eq)AlCl,	1.5 eq	Nitrobenege
4 Hrs.	140°C	70%

Dry media condition

3 min.	320°C	MW	92%
1 hr.	320°C	Δ	4.1%

Solvent-free esters saponification[14,15]

R	R^1	Time (min.)	Final temp. °C	Yield %	Time (min.)	Final temp °C	Yield (%)
Ph	Me	1	205	96	1	205	90
	nOct	2	210	94	2	210	72
Ph	Me	2	240	87	2	240	38
	nOct	4	223	82	4	223	0

- Easy Saponification of Hindered Esters due to solvent free PTC^+ MW coupling
- M.W. specific effect is clearly substrate dependent

Difficult reaction (late TS) with Polar TS

Classical method	200-240°C	100mgHq	20Hrs	20-30%
Microwaves				
R = R'=Ph	(A)120W	20 min.	187°C	80%(Δ - 2%)
	(B) 60 W	30 min.	202°C	99%(Δ - 3%)
R=Ph, R'=CH_2Ph =	(B) 60W	30 min.	210°C	95%(Δ -12%)

Leuckart reduction amination of ketons[15]

In the electromagnetic radiation spectrum, microwaves (0.3 GHz–300 GHz) lie between radiowave (Rf) and infrared (IR) frequencies with relatively large wavelength. Microwaves, a nonionizing radiation incapable of breaking bonds, are a form of energy and not heat and are manifested as heat through their interaction with the medium or materials wherein they can be reflected (metals), transmitted (good insulators that will not heat) or absorbed (decreasing the available microwave energy and rapidly heating the sample).

Microwave (MW) irradiation, an unconventional energy source, has been used for a variety of applications including organic synthesis[16], wherein chemical

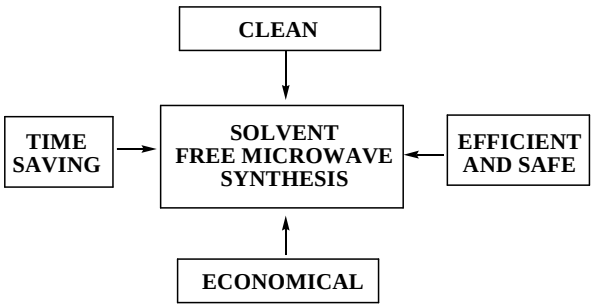


Figure 3

reactions are accelerated because of selective absorption of MW energy by polar molecules, nonpolar molecules being inert to the MW dielectric loss. Heterogeneous reactions facilitated by supported reagents on inorganic oxide surfaces have received attention in recent years. The application of microwave irradiation in conjunction with the use of catalysts or mineral-supported reagents, under solvent-free conditions, enables organic reactions to occur expeditiously at ambient pressure[16,21-23], thus providing unique chemical processes with special attributes such as enhanced reaction rates, higher yields, and the associated ease of manipulation. The results from our laboratory on this MW-expedited approach are described for the synthesis of a variety of industrially significant compounds and intermediates, namely, imines, enamines, enones, nitroalkenes, oxidized sulfur species, and heterocycles. This methodology is exemplified by a concise synthesis of flavones, tetrahydroquinolones, 2-aroylbenzofurans, and thiazole derivatives and demonstrates the exploitation of in situ generated reactive intermediates in one-pot synthesis of heterocyclic compounds. The adaptability of the protocols to rapid and parallel synthesis in solvent-free multicomponent reactions is demonstrated in the assembly of imidazo[1,2-a]annulated pyridines, pyrazines, and pyrimidines (Ugi reaction) and dihydroprimidine-2(1H)-ones (Biginelli reaction).

Functional group transformations

Synthesis of thioketones, thiolactones, thioamides, thionoesters, and thioflavonoids

Cleavage reactions are expedited by MW exposure of protected molecules on mineral oxides or benign "doped" reagents, as has been shown in the regeneration of alcohols, acids, and carbonyl compounds[24-27]. Among several expeditious chemical

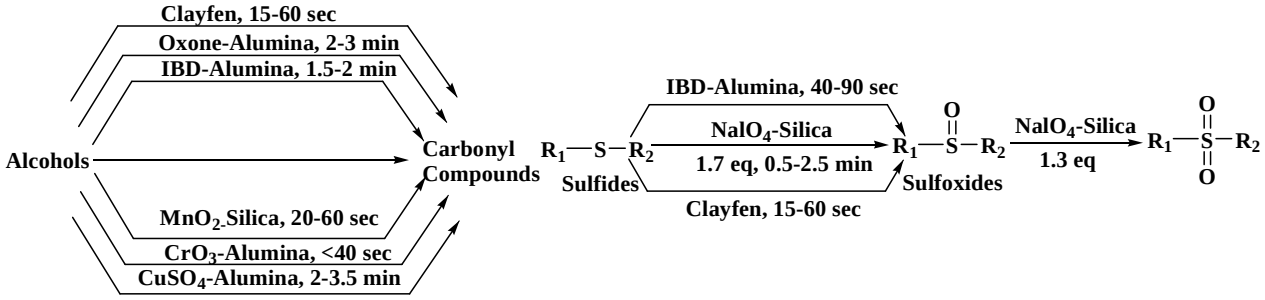


Figure 4: Oxidation of alcohols to carbonyl compounds and oxidation of sulfides to sulfoxides and sulfones

transformations that can be accomplished under these solvent-free conditions, the conversion of carbonyl compounds to the corresponding thio analogs is especially useful. The usual synthesis of thioketones involves the reaction of substrates with hydrogen sulfide in the presence of acid, phosphorous pentasulfide under basic conditions, or Lawesson's reagent.Using our approach, the carbonyl compounds are simply admixed with neat Lawesson's reagent (0.5 equiv.) and irradiated under solvent-free conditions that do not require any acidic or basic media.This benign approach is general and is applicable to the high-yield conversion of ketones, flavones, isoflavones, lactones, amides, and esters to the corresponding thio analogs. This eco-friendly, solvent-free protocol uses comparatively much smaller amount of Lawesson's reagent and avoids the use of large excess of dry hydrocarbon solvents such as benzene, xylene, triethylamine, or pyridine that are conventionally used[28].

Oxidation reactions

The introduction of metallic reagents on solid supports have solved some of the associated toxicity problems and provides an attractive alternative to the conventional oxidation reactions in view of the selectivity and ease of manipulation. We have developed several MW-assisted oxidative protocols[29–32] using an array of supported reagents applicable to both alcohols and sulfides (Figure 4).

Reduction reactions

The solid-state selective reduction of carbonyl compounds occurs readily with alumina-supported sodium borohydride (NaBH4) in a reaction that is accelerated by moisture[33]. The alumina support can be reused repeatedly by simply washing off the product a process

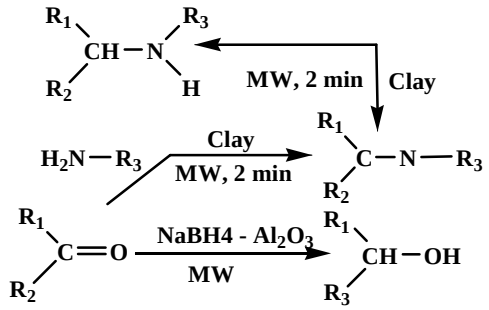


Figure 5: Borohydride reduction of carbonyl compounds and reductive amination reactions

that hydrates the alumina surface to facilitate subsequent reduction reactions. Our earlier optimized imine-forming (Schiff bases) reaction using catalytic amount of clay[34] can be adapted for the borohydride reduction in the same pot, thus providing a simple route to secondary and tertiary amines[35]. Clay serves the dual purpose of a Lewis acid and also provides water from its interlayers, which enhances the reducing ability of NaBH4(Figure 5).

Synthesis of heterocyclic compounds

A variety of heterocyclic compounds can be rapidly assembled employing this solvent-free approach as demonstrated by the synthesis of flavonoids using Baker–Venkataraman rearrangement and related cyclization of 2′-aminochalcones to 2-aryl-1,2,3,4-tetrahydro-4-quinolones on clay[36]. A concise onepot method can be used to synthesize isoflav-3-enes bearing basic amino substituents at 2 position via the intermediacy of *in situ* generated enamine derivatives followed by reaction with o-hydroxyaldehydes[37]. This convergent strategy has been extended to the synthesis of naturally occurring and pharmacologically active 2-aroylbenzo[b]furans that proceeds rapidly via the condensation of *in situ* generated α-tosyloxyketones with

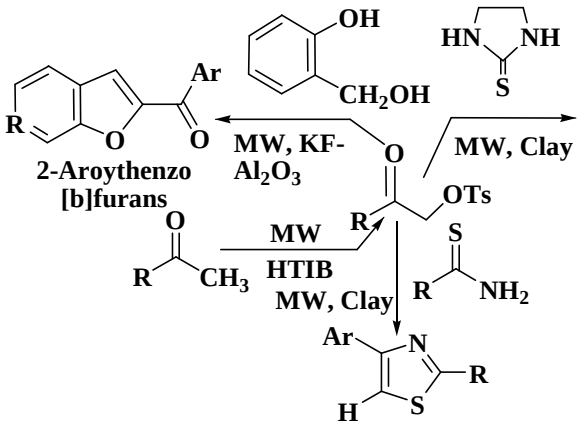


Figure 6: Synthesis of thiazoles and aroylbenzofurans via α-tosyloxyketones, *Microwave-accelerated multicomponent reactions*

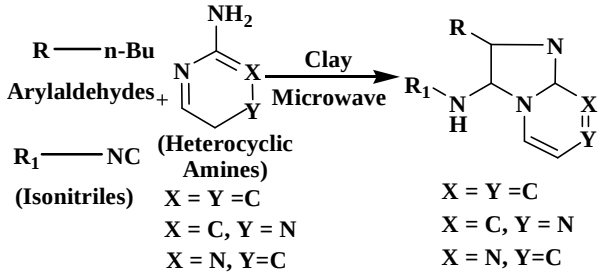


Figure 7: Three-component condensation reaction using microwaves

a variety of salicylaldehydes on potassium fluoride "doped" alumina (Figure 4), the process avoids the use of lachrymatory starting materials[38]. Similarly, thiazoles can be readily obtained by the reaction of thioamides with α-tosyloxyketones in a clay-catalyzed reaction (Figure 5). A typical experimental procedure entails mixing thioamides in an open glass container with *in situ* generated α-tosyloxyketones and montmorillonite K 10 clay. The reaction mixture is irradiated in a microwave oven for 3-6 min with intermittent irradiation to afford substituted thiazoles in 88-96% yields. The versatility of the MW approach becomes apparent in the synthesis of bridgehead heterocycles when reactants are cyclic thioureas (Figure 6).

Combinatorial chemistry has gained significant importance as a tool for the synthesis of a wide variety of useful compounds, including pharmaceuticals. In this context, the multiple component condensation (MCC) approach is especially appealing in view of the fact that products are formed in a single step, and the diversity can be readily achieved simply by varying the reacting components. The generation of small-molecule libraries requires the development of efficient methodologies with special emphasis on manipulative ease of the reaction. Such a facile protocol is developed which is amenable to the generation of a library of imidazo[1,2-a]pyridines, imidazo[1,2-a]pyrazines and imidazo[1,2-a]pyrimidines[39] under solvent-free conditions using MW irradiation (Figure 5). The conventional two-component synthesis requiring lachrymatory α-haloketones and 2-amino-heterocycles restricts the generation of a diverse library of these molecules. This solvent-free one-pot method involves MW irradiation of mixture of aldehydes and corresponding 2-amino-pyridine, pyrazine, or pyrimidine in presence of a catalytic amount of clay (50 mg) to generate iminium intermediate. Subsequently, isocyanide is added to the same container, and the reactants are further exposed to MW at a reduced power level (50%) to afford the corresponding imidazo[1,2-a]pyridines, imidazo[1,2-a]pyrazines, and imidazo[1,2-a]pyrimidines (Figure 7). Further, the protocol is general for all the three components involved, e.g., aldehydes (aliphatic, aromatic, and vinylic), isocyanides (aliphatic, aromatic, and cyclic) and amines (2-amino pyridine, 2-aminopyrazine, and 2-aminopyrimidine). Thus, a library of imidazo[1,2-a]pyridines, imidazo[1,2-a]pyrazines, and imidazo[1,2-a]pyrimidines can be readily obtained by simply varying the three components[40].

Verma[41] and co-workers have reported the synthesis of 4-aryl-3,4-dihydropyrimid-2(1H)-ones (DHPM), employing a solvent-free Biginelli multicomponent condensation reaction. The method uses neat mixtures of aryl aldehydes, β-ketoesters, and urea derivatives in presence of polyphosphate ester (PPE) as a reaction mediator. In view of the readily available aromatic aldehydes, β-keto esters, and urea derivatives, a large collections of DHPMs can be potentially prepared, applying the recently developed automated, high-throughput robotic technologies for performing microwave-assisted combinatorial synthesis[42].

Miscellaneous reactions

Several other reagents can be used under these solvent-free conditions to expedite organic reactions; for example, hydroxylamine on clay directly converts aldehydes to nitriles[43]. A general protocol that is appli-

cable to the oxidation of dihydropyridine derivatives utilizes elemental sulfur[44]. Several nonmetallic hypervalent iodine oxidants can be used without solvents[44], and the crossed Cannizzaro reaction can be accomplished with paraformaldehyde on barium hydroxide surface[45].

In conclusion, this eco-friendly, solvent-free microwave approach opens up numerous possibilities for conducting rapid organic synthesis and functional group transformations more efficiently. Additionally, there are distinct advantages of these solvent-free protocols since they provide reduction or elimination of solvents thereby preventing pollution in organic synthesis "at source". The chemo-, regio- or stereoselective synthesis[45] of high-value chemical entities and parallel synthesis to generate a library of small molecules[39-41] will add to the growth of microwave-enhanced reactions in the near future.

CONCLUSIONS

When coupling to microwave irradiation, solvent free technique revealed to be of special efficiency as furthermore clean and economic procedures. Serious improvements and simplifications over conventional methods originate from the repidity, the enhancements in yields and purities of products.

Non-purely thermal specific MW effects can be involved essentially when non-polar solvents, or better solvent free conditions, are concerned with polar mechanisms (more polar transition states when compared to their ground states) and for difficult reactions, which necessitate high energy of activation (late transition state according to Hammond postulate). In all cases, accurate controls of temperature and microwave emitted power are necessary to ensure reproducible and safe reactions.

ACKNOWLEDGMENTS

The work of Singh research laboratory in this ares of microwave chemistry during last eight years has been supported by C.S.I.R. New Delhi and U.G.C. Delhi. We wish to thank all members of microwave synthesis lab of Prof. Kidwai, Department of Chemistry, University of Delhi. for their essential contribution to microwave chemistry.

REFERENCES

[1] W.Xie, Y.Jin, P.G.Wang; Chem.Tech., **29**, 23 **(1999)**.
[2] T.J.Goehl; 'Green Chemistry', Env.Health Perspectives, **3**, 105 **(1997)**.
[3] P.T.Anastas, C.A.Farris; benign by Design: Alternative Synthetic Design for Pollution Prevention, ACS Symposium, Ser.N.557, Washington DC, **(1994)**.
[4] P.T.Anastas, J.C.Warner, 'Green Chemistry, Theory and Practice', Oxford Science Publications, Oxford, **(1998)**.
[5] T.J.Collins; 'Green Chemistry, Macmillan, Encyclopedia of Chemistry', New York, **(1997)**.
[6] B.M.Trost; Science, **254**, 1471 **(1991)**.
[7] Y.Sasson, R.Neumann; 'Handbook of Phase Transfer Catalysis, Blackie Academic', Professional, Chapman and Hall, London, **(1997)**.
[8] A.Loupy; Modern Solvents in Organic Synthesis, Wiley-VCH, Weinheim, **(2002)**.
[9] P.Lidstrom, J.Tierney, B.Wathey, J.Westman; Tetrahedron, **57**, 9225 **(2001)**.
[10] R.S.Varma; Green Chem., **1**, 43 **(1999)**.
[11] S.Deshayes, M.Liagre A.Loupy, J.L.Luche, A.Petit; Tetrahedron, **51**, 10851 **(1999)**.
[12] R.S.Varma; 'Microwaves in Organic Synthesis', Wiley-VCH, New York, 181 **(2002)**.
[13] A.Stadler, C.O.Kappe; J.Comb.Chem., **3**, 624 **(2001)**.
[14] R.S.Varma, D.Kumar; Tetrahedron Lett., **40**, 7665 **(1999)**.
[15] R.S.Verma, D.Kumar; J.Chem.Soc., Perkin Trans., **1**, 1755 **(1999)**.
[16] R.S.Varma, P.T.Anastas, L.Heine, T.Williamson; 'Green Chemical Syntheses and Processes', ACS Symposium Series No.767, Ch.23, American Chemical Society,Washington DC, 292-313 **(2000)**.
[17] R.S.Varma, P.Tundo, P.T.Anastas; 'Green Chemistry: Challenging Perspectives', Oxford University Press, Oxford, 221-244 **(2000)**.
[18] R.S.Varma; Green Chemistry, **1**, 43 **(1999)**.
[19] R.S.Varma; Clean Products and Processes, **1**, 132 **(1999)**.
[20] R.S.Varma, D.E.Clark, W.H.Sutton, D.A.Lewis; 'Microwaves: Theory and Application in Material Processing IV', American Ceramic Society, Westerville, Ohio, 357-365 **(1997)**.
[21] S.Caddick.Tetrahedron, **51**, 10403 **(1995)**.
[22] A.Loupy, A.Petit, J.Hamelin, F.Texier-Boullet, P.Jacquault, D.Mathe; Synthesis 1213 **(1998)**.

Current Research Paper

[23] R.S.Varma; J.Heterocyclic Chem., **35**, 1565 **(1999)**.
[24] R.S.Varma, M.Varma, A.K.Chatterjee; J.Chem. Soc., Perkin Trans., **1**, 999 **(1993)**.
[25] R.S.Varma, R.K.Saini; Tetrahedron Lett., **38**, 2623 **(1997)**.
[26] R.S.Varma, H.M.Meshram; Tetrahedron Lett., **38**, 7973 **(1997)**.
[27] R.S.Varma, R.Dahiya, R.K.Saini; Tetrahedron Lett., **38**, 8819 **(1997)**.
[28] R.S.Varma, D.Kumar; Organic Lett., **1**, 697 **(1999)**.
[29] R.S.Varma, R.Dahiya; Tetrahedron Lett., **38**, 2043 **(1997)**.
[30] R.S.Varma, R.K.Saini, H.M.Meshram.Tetrahedron Lett., **38**, 6525 **(1997)**.
[31] R.S.Varma, R.Dahiya, R.K.Saini; Tetrahedron Lett., **38**, 7823 **(1997)**.
[32] R.S.Varma, R.Dahiya; Tetrahedron Lett., **39**, 1307 **(1998)**.
[33] R.S.Varma, R.K.Saini; Tetrahedron Lett., **38**, 4337 **(1997)**.
[34] R.S.Varma, R.Dahiya, S.Kumar; Tetrahedron Lett., **38**, 2039 **(1997)**.
[35] R.S.Varma, R.Dahiya; Tetrahedron, **54**, 6293 **(1998)**.
[36] R.S.Varma, R.K.Saini; Synlett, 857 **(1997)**.
[37] R.S.Varma, R.Dahiya; J.Org.Chem., **54**, 8038 **(1998).**
[38] R.S.Varma, D.Kumar, P.J.Liesen; J.Chem.Soc., Perkin Trans., **1**, 4093 **(1998)**.
[39] R.S.Varma and D.Kumar; Tetrahedron Lett., **40**, 7665 **(1999)**.
[40] C.O.Kappe, D.Kumar, R.S.Varma; Synthesis, **(1799)**.
[41] A.Cottrill, A.Y.Usyatinsky, J.M.Arnold, D.S.Clark, J.S.Dordick, P.C.Michels, Y.L.Khmelnitsky; Tetrahedron Lett., **39**, 1117 **(1998)**.
[42] R.S.Varma, K.P.Naicker, D.Kumar, R.Dahiya, P.J. Liesen; J.Microwave Power and Electromagnetic Energy, **34**, 113 **(1999)**.
[43] R.S.Varma, D.Kumar; J.Chem.Soc., Perkin Trans., **1**, 1755 **(1999)**.
[44] R.S.Varma, K.P.Naicker; Tetrahedron Lett., **39**, 8437 **(1998)**.
[45] T.Patonay, R.S.Varma, A.Vass, A.Levai, J.Dudas; Tetrahedron Lett., **42**, 1403 **(2001)**.