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ORIGINAL ARTICLE

“Greener” chemical syntheses using mechanochemical mixing or microwave and ultrasound irradiation

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Various emerging “greener” strategic pathways, researched primarily in the author’s own laboratory, are summarized. They include solvent-free mechanochemical methods that involve the use of hypervalent iodine reagents at room temperature for the synthesis of heterocyclic entities, and useful conversion of ketones into β -keto sulfones and their α -tosyloxy derivatives in high yields. A solvent-free approach that involves microwave (MW) exposure of neat reactants (undiluted) catalyzed by the surfaces of less-expensive and recyclable mineral supports, such as alumina, silica, clay, or “doped” surfaces, is described; it is applicable to a wide range of cleavage, condensation, cyclization, rearrangement, oxidation, and reduction reactions, including rapid one-pot assembly of heterocyclic compounds from in situ generated reactive intermediates. The strategy is adaptable to multi-component reactions, e.g. Ugi and Biginelli reactions, for rapid assembly of a library of compounds. Synthesis of a wide variety of significant precursors and intermediates, namely enones, imines, enamines, nitroalkenes, and oxidized sulfur species, is possible and their value in concise MW synthesis of 2-arylbenzofurans and thiazole derivatives is illustrated. Ultrasound- and MW-assisted solventless preparation of ionic liquids and their application in alkylation and metal-catalyzed multi-component reactions are described. With a view to consume greenhouse gas, carbon dioxide (CO₂), efficient reaction of epoxides with CO₂ provides ready access to cyclic carbonates using only a catalytic amount of recyclable indium-based ionic liquid. MW heating in aqueous reaction media enables expeditious *N*-alkylation reactions of amines and hydrazines to afford a series of heterocyclic ring systems, such as *N*-azacycloalkanes, 4,5-dihydropyrazoles, and pyrazolidines. A general and expeditious MW-enhanced nucleophilic substitution approach uses easily accessible starting materials such as halides or tosylates in reaction with alkali azides, thiocyanates, or sulfinates in the absence of any phase transfer catalyst to produce azides, thiocyanates, and sulfones, respectively, wherein a variety of reactive functional groups are tolerated. A three-component condensation (MCC) approach for the synthesis of useful 2-amino-2-chromenes is described using a recyclable nanosized magnesium oxide catalyst in aqueous poly (ethylene glycol) (PEG) medium at room temperature. A general greener approach to shape-selective generation of nanomaterials is summarized including their potential application as nanocomposites.

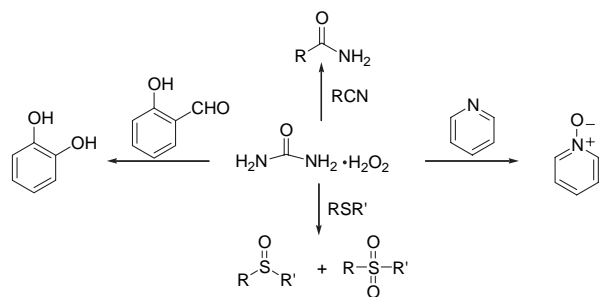
Keywords: microwave irradiation; mechanochemical mixing; ultrasound irradiation; Green chemical synthesis; ionic liquids; heterocycles; nano-materials; solid-supported reactions; aqueous media

Introduction

The varied nature of the chemical world requires various greener pathways in our quest towards attaining sustainability. The emerging area of green chemistry envisages minimum hazard as the performance criteria while designing new chemical processes (1). Rather than end-of-the-pipe remediation approach, which involves cleaning up of waste after it has been produced, the main objective is to avoid waste generation in the first place. There are different shades of greener processes being developed as we continue exploring alternatives to conventional che-

mical synthesis and transformations. The desired approach will require new environmentally benign syntheses, catalytic methods, and chemical products that are ‘benign by design’ and that utilize renewable resources wherever possible (1). One of the thrust areas for achieving this target is to explore alternative efficient reaction conditions and eco-friendly reaction media to accomplish the desired chemical transformations with minimized by-products or waste, as well as eliminating the use of conventional organic solvents wherever possible. Consequently, several newer strategies have appeared, such as solvent-free

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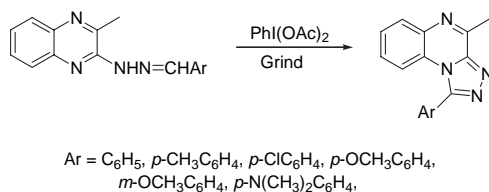


Scheme 1. Solventless oxidations using urea hydrogen peroxide complex.

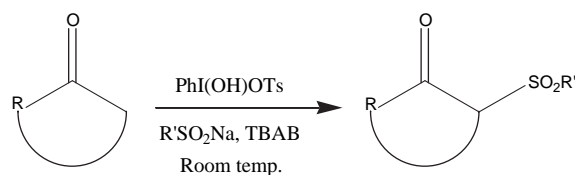
(dry media), solid-supported with and without microwave (MW) irradiation (2–6), and mechanochemical mixing (grinding) (7–9); and the use of room temperature ionic liquids (10,11), supercritical carbon dioxide, and water (12) as reaction media that can be combined with MW or ultrasonic irradiation for rapid synthesis. Indeed, the best solvent is “no solvent,” but in such cases the problems of handling of materials and heat and mass transfer aspects persist and need to be addressed in close co-operation with chemical engineers.

The newer challenges that face the chemical industry are the safety, security, and changing regulatory requirements that dictate the improvements in the manufacturing efficiency via introduction of newer and efficient eco-friendly “greener” technologies. These technologies may help improve the “triple bottom line” performance of a company, by containing the cost of the new chemical entities by speeding up the innovation and waste reduction while complying with the regulations. Presidential Green Chemistry Challenge Awards, instituted in 1995, have promoted this activity by identifying manufacturing processes that prevent pollution and are economically competitive, and several such cases have been summarized (13). Among several examples, a concise synthesis of Ibuprofen, a commonly used analgesic, summarizes this green chemistry theme by eliminating large quantities of waste via a three-step atom-economical route which replaced a six-step process using aluminium chloride (13).

Oxidative transformations are important in organic synthesis and several reagents are available to



Scheme 2. Synthesis of 1-aryl-4-methyl-1,2,4-triazolo[4,3-a]quinoxalines.



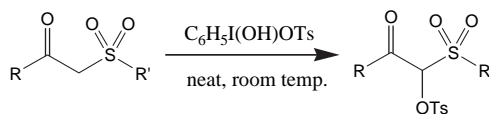
Scheme 3. One-pot solvent-free synthesis of β -keto sulfones from ketones.

accomplish this task. Most of these processes, however, suffer from drawbacks, such as the use of corrosive acids, hazardous peracids, and metallic compounds that are inherently toxic and generate noxious waste streams. A solvent-free oxidation of a variety of organic groups using an inexpensive, safe, and easily handled reagent, urea-hydrogen peroxide (UHP), is now possible (Scheme 1); oxidations include hydroxylated aldehydes and ketones (to phenols), sulfides (to sulfoxides and sulfones), nitriles (to amides), and *N*-heterocycles (to *N*-oxides) (14). Ideally, the use of molecular oxygen in conjunction with a heterogeneous catalyst would be the most preferred alternative (15).

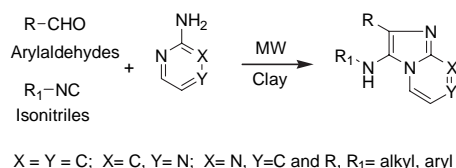
Mechanochemical reactions

Solid-state chemistry is a rapidly developing frontier, and several technological applications are appearing wherein mechanochemical forces are successfully utilized in accomplishing the chemical reactions (7–9). Such reactions between two macroscopic solid particles have now been well studied and are believed to proceed via liquefaction where eutectic mixture exists (7b).

We have studied some oxidative transformations by mechanochemical mixing of substrates with non-metallic hypervalent iodine reagents which enables the syntheses of relatively complex molecules, such as quinoxaline derivatives (16), β -ketosulfones (17), and α -tosyloxy β -ketosulfones (18). The oxidative transformation of arenecarbaldehyde 3-methylquinoxalin-2-yl-hydrazones to 1-aryl-4-methyl-1,2,4-triazolo[4,3-a]quinoxalines (Scheme 2) occurs readily by a simple grinding process using a friendlier non-metallic oxidant, iodobenzene diacetate, PhI(OAc)₂ (16). This protocol simply involves grinding of the two solid substrates using a pestle and mortar; a mildly



Scheme 4. Solvent-free synthesis of α -tosyloxy β -keto sulfones.



Scheme 5. MW-assisted three-component Ugi reaction.

exothermic reaction results in the formation of a yellowish eutectic melt and the reaction is completed in a few minutes.

The work has now been extended to the synthesis of β -ketosulfones in high yields (17) from ketones employing another hypervalent iodine reagent, hydroxytosyloxy iodobenzene (PhI(OH)OTs), which involves in situ generation of α -tosyloxyketones followed by nucleophilic substitution with sodium arene sulfinate in the presence of tetra-butylammonium bromide at room temperature (Scheme 3).

Similarly, novel α -tosyloxy β -ketosulfones, valuable precursors for heterocyclic compounds of therapeutic interests, have been prepared under solvent-free conditions by a simple mechanochemical mixing of β -ketosulfones with [hydroxyl(tosyloxy)iodo]benzene (Scheme 4) (18). The research activity in this fruitful area continues, as recently exemplified by a facile and environmentally benign solvent-free protocol described for the preparation of boronic esters from the corresponding boronic acids by simply grinding the two components together (19).

Solvent-free microwave-assisted reactions

Solvent-free approaches that involve MW exposure of neat reactants catalyzed by the surfaces of less expensive and recyclable mineral supports, such as alumina, silica, clay, or "doped" surfaces, are applicable (2–6) to a wide range of cleavage, condensation, cyclization, rearrangement, oxidation, and reduction reactions, including rapid one-pot assembly of het-

erocyclic compounds from in situ generated reactive intermediates (20–23). Heterocyclic chemistry (21) has been a major beneficiary of MW-expedited solvent-free chemistry utilizing mineral-supported reagents which have been exploited for parallel synthesis, a strategy that is adaptable for multi-component reactions, such as Ugi (23) and Biginelli reactions (22), for rapid assembly of a library of compounds (24). A representative multi-component condensation reaction to create a small-molecule library of imidazo[1,2-a]pyridines, imidazo[1,2-a]pyrazines and imidazo[1,2-a]pyrimidines is depicted in Scheme 5 (23).

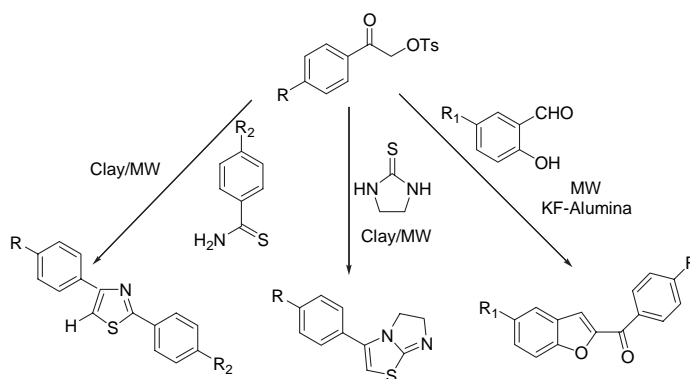
In a process that eliminates the use of lachrymatory α -haloketones, Varma et al. have synthesized a variety of heterocyclic compounds (25) via simple solvent-free reactions of thioamides, ethylenethioureas, and salicylaldehydes with α -tosyloxyketones, which are generated in situ from arylmethyl ketones and [hydroxy(tosyloxy)iodo]benzene (HTIB) under MW irradiation conditions (Scheme 6).

Solvent- and catalyst-free MW-reactions

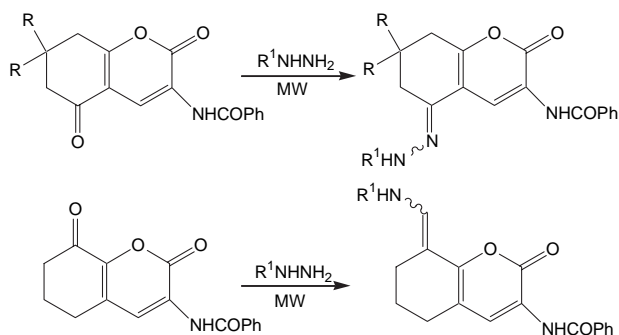
The MW-facilitated reaction between two solids, in a solvent- and catalyst-free environment, has been shown to provide rapid access to useful heterocyclic hydrazones via the formation of a eutectic melt below the melting point of either reactant (26); neat 5- or 8-oxobenzopyran-2(1H)-ones react with a variety of aromatic and heteroaromatic hydrazines generating several synthetically useful heterocyclic hydrazones (Scheme 7) (26).

Solvent-free synthesis of ionic liquids

Ionic liquids, being polar and ionic in character, couple to MW irradiation very efficiently, and, therefore, have been considered MW absorbing candidates for expediting chemical reactions. Unfortunately, most of the initial preparative pro-

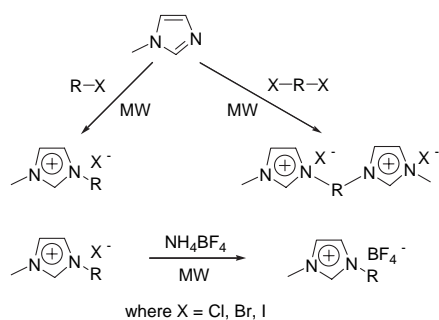


Scheme 6. Synthesis of heterocycles from in situ generated α -tosyloxyketones.

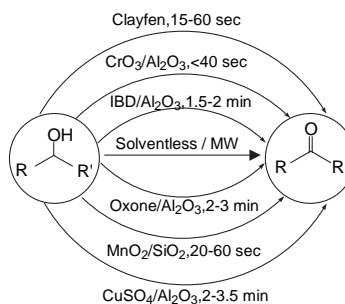


Scheme 7. Solvent-free preparation of hydrazones using microwaves.

cesses for the preparation of ionic liquids involve several hours of heating in refluxing solvents, and use a large excess of alkyl halides/organic solvents that diminish their true potential as “greener” solvents. The first solventless preparation of the 1,3-dialkylimidazolium halides via MW heating has been described by Varma et al. (Scheme 8); the reaction time was reduced from hours to minutes and the use of a large excess of alkyl halides/organic solvents as the reaction medium was avoided (10,27,28). The approach has been extended to other ionic salts bearing tetrafluoroborate anions, and involves exposing *N, N'*-dialkylimidazolium chloride and ammonium tetrafluoroborate salt to MW irradiation (Scheme 8) (28), using dedicated MW equipment (29). Similarly, gallium and indium containing ionic liquids (30,31) have been prepared and used in catalytic amounts for the reaction of epoxides with carbon dioxide, affording a greener route to useful cyclic carbonates (32); this strategy focuses on the utilization of greenhouse gas, carbon dioxide, to generate valuable materials. The surge of interest continues in this area for the use of ultrasonic pathways to prepare these solvents (11) and their use as catalysts for alkylation of isobutane with 2-butene (33), for ruthenium-catalyzed tandem migration (34a), and silver-catalyzed coupling reactions (34b).



Scheme 8. Solventless MW ionic liquid preparation.



Scheme 9. MW-assisted solvent-free oxidation of alcohols to carbonyls.

The intrinsic reactivity of these low temperature molten salts, especially from the viewpoint of altered reactivity of dissolved substrate, has recently been reviewed (35).

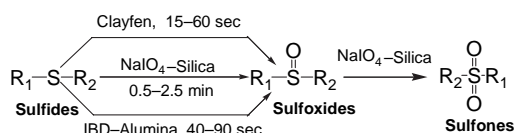
Microwave-assisted reactions on solid supports

MW protocols using immobilized reagents on solid supports have been extensively explored as inexpensive kitchen MW ovens provided the usual heating medium (2).

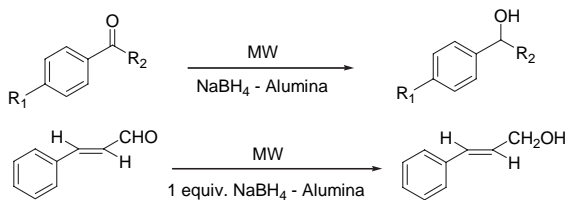
Oxidation reactions

The simple oxidation reactions involve solvent-free mixing of neat substrates with, for example, clay-supported iron (III) nitrate (clayfen) (36) or iodobenzene diacetate (IBD) as an oxidant (37), and brief MW irradiation for 15–60 sec (Scheme 9) (2–6). The solid state utility of clayfen-iron(III) nitrate on clay as an oxidant has afforded higher yields and is more efficiently supported on clay since the amounts used in these protocols are half those used earlier in solution phase reactions.

The oxidation of sulfides is achieved in a similar manner using MW irradiation with desired selectivity to either sulfoxides or sulfones over sodium periodate (NaIO_4) on silica (20%) (Scheme 10) (38). A noteworthy feature of the protocol is its applicability to long chain fatty sulfides, which are insoluble in most solvents, and are consequently difficult to oxidize. Further, it circumvents the use of oxidants, such as nitric acid, hydrogen peroxide, chromic acid, and peracids, conventionally used for the oxidation



Scheme 10. MW-assisted oxidation of sulfides to sulfoxides and/or sulfones.



Scheme 11. Solvent-free reduction of carbonyls on alumina.

of sulfides to the corresponding sulfoxides and sulfones.

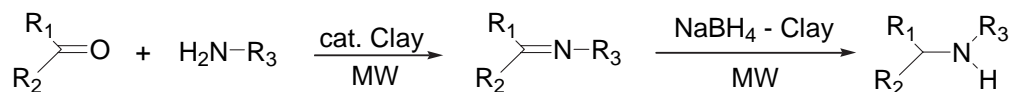
Reduction reactions

The relatively inexpensive and safe sodium borohydride (NaBH_4) has been extensively used as a reducing agent because of its compatibility with protic solvents. Varma et al. have reported a simple method for the expeditious reduction of aldehydes and ketones that uses alumina-supported NaBH_4 and proceeds in the solid state accelerated by MW irradiation (Scheme 11) (39a). The useful chemoselective feature of the reaction is apparent from the reduction of *trans*-cinnamaldehyde.

The reaction rate improves in the presence of moisture and the reaction does not proceed in the absence of alumina. The alumina support can be recycled and reused for subsequent reduction, repeatedly, by mixing with fresh borohydride without any loss in activity. In terms of safety, the air used for cooling the magnetron ventilates the MW cavity, thus preventing any ensuing hydrogen from reaching explosive concentrations.

Solvent-free reductive amination protocol for carbonyl compounds using sodium borohydride supported on moist montmorillonite K10 clay is facilitated by MW irradiation (Scheme 12) (39b). Clay serves the dual purpose of a Lewis acid and also provides water from its interlayers that enhance the reducing ability of NaBH_4 .

This approach has been elegantly utilized for the MW-enhanced solid-state deuteration reactions using sodium borodeuteride impregnated alumina (40a). Subsequent extension of these studies to specific labeling has been explored (40b) including deuterium exchange reactions for the preparation of reactive intermediates (40c).



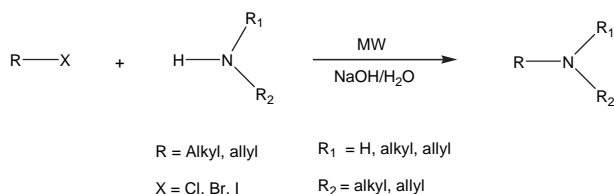
Scheme 12. Reductive amination of carbonyls using clay-supported borohydride.

Microwave-assisted reactions in aqueous medium

Organic synthesis in aqueous media (12,41,42) is rapidly gaining ground in view of the fact that the use of many toxic and volatile organic solvents, particularly chlorinated hydrocarbons, contributes to pollution. Utilization of water as a reaction medium in conjunction with MW irradiation is one of the emerging non-conventional methods being recognized as viable environmentally benign alternatives (43–45). The nucleophilic substitution reaction of alkyl halides with amines is accelerated by MWs because of the polar nature of the reactants; such *N*-alkylations proceed in basic water without any phase transfer reagent (Scheme 13) (46).

The same nucleophilic substitution chemistry can be manipulated by means of MWs to afford a variety of cyclic amines as building blocks in natural product syntheses via double *N*-alkylation (47,48) of primary amines (Scheme 14). The protocol circumvents the difficulty associated with running multi-step reactions to assemble *N*-aryl azacycloalkanes and avoids the use of expensive metal catalysts in building aryl C–N bonds. Further, reactive functional groups, such as carbonyl, ester, and hydroxyl, remain unaffected under these mild reaction conditions. The *N*-alkylation reaction is now also extended to hydrazines to deliver dihydropyrazoles, pyrazolidines, and dihydropthalazines (Scheme 14) (47,48).

It is noteworthy that this reaction is not a homogeneous single-phase system as neither reactant is soluble in the aqueous alkaline reaction medium. The selective absorption of MWs by polar molecules and intermediates in a multiphase system could substitute as a phase transfer catalyst without using any phase transfer reagent, thereby providing the observed acceleration, as has been observed for ultrasonic irradiation (49,50). The experimental observation is consistent with the mechanistic postulation wherein the polar transition state of the reaction is favored by MW irradiation with respect to the dielectric polarization nature of MW energy transfer (47,48,51). In large scale experiments, the phase separation of the desired product in either solid or liquid form from the aqueous medium can facilitate product purification by simple filtration or decantation instead of tedious column chromatography, distillation, or extraction processes, which eventually reduces the usage of volatile organic solvent required for extraction or column chromatography.

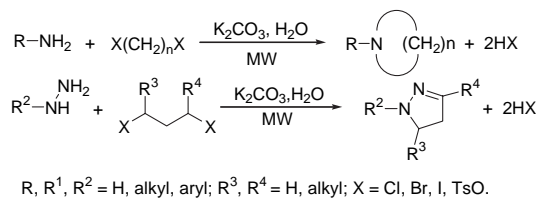
Scheme 13. MW-assisted *N*-alkylation of amines by alkyl halides in basic water.

MW-assisted synthesis of azides, thiocyanates, and sulfones (52) has also been developed, starting from readily available halides or tosylates (Scheme 15), and has proved a useful alternative which avoids the use of environmentally detrimental volatile chlorinated hydrocarbons (52). Various functional groups, such as ester, carboxylic acid, carbonyl, and hydroxyl, were unaffected under the mild reaction conditions employed. This method involves simple experimental method, benign product isolation protocol, and avoids the use of phase-transfer catalysts, and is expected to contribute to the development of a greener strategy for the preparation of various azides, thiocyanates, sulfones, and other useful compounds.

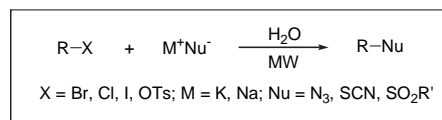
Dioxane rings are common structural motifs in numerous bioactive molecules, such as (+)-dactyloide (a cytotoxic agent), derivatives of 2-substituted-1,3-dioxanes (antimuscarinic agents), and (+)-SCH 351448 (a novel activator of low density lipoprotein receptor promoters). Varma et al. have developed a one-pot protocol for their synthesis via a tandem *bis*-aldol reaction of ketone with paraformaldehyde, catalyzed by polystyrenesulfonic acid (PSSA) in aqueous medium (Scheme 16) (53).

This reaction may find a useful place in drug discovery for the synthesis of bio-active molecules bearing 1,3-dioxane moiety. It is noteworthy that these reactions proceed well in an aqueous medium without using any phase transfer catalyst (PTC). This may be due to selective absorption of MWs by reactants, intermediates, and polar aqueous medium, which accelerate the reaction even in the absence of PTC.

Dihydropyrimidinones are an important class of organic compounds that show prominent biological activity and we have used the aforementioned cata-



Scheme 14. MW-assisted formation of cyclic amines.



Scheme 15. Microwave-enhanced nucleophilic substitution reactions.

lyst, PSSA, for their synthesis using the Biginelli reaction (Scheme 17) (54).

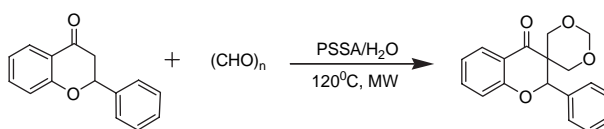
Again, this efficient protocol for the synthesis of substituted 3,4-dihydropyrimidin-2(1H)-ones proceeds efficiently in water in the absence of organic solvent, under MW irradiation conditions. Also, the use of polymer-supported, low toxic, and inexpensive PSSA as a catalyst renders this method eco-friendly, with a very simple isolation procedure that simply entails the filtration of the precipitated products.

Miscellaneous reactions

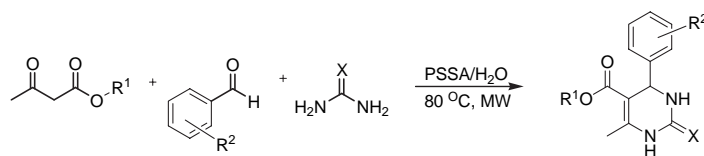
Metal-catalyzed reactions

The application of MW heating in the transition metal-catalyzed homogeneous reactions has been very well explored resulting in robust and selective methods (55a); a variety of coupling as well as asymmetric catalysis reactions have been developed.

Suzuki reaction. Polyethylene glycol (PEG) is an inexpensive and non-toxic reaction medium for the MW-assisted Suzuki cross-coupling of arylboronic acids with aryl halides (Scheme 18) (55b). This environmentally friendly MW protocol offers the ease of operation and enables the recyclability of catalyst and the synthesis of a variety of substituted biaryls employing palladium chloride as catalyst and potassium fluoride as the base. PEG offers a convenient, non-toxic, thermally stable, inexpensive and recyclable reaction medium for Suzuki coupling by substituting for volatile organic solvents. The MW heating offers a rapid and clean alternative at high solid concentration and reduces the reaction time from hours to minutes. Further, the deployment of inexpensive forms of palladium (palladium chloride) as the catalyst and tolerance of a variety of functional groups bodes well for the general utility of the reaction. The recyclability of the catalyst makes the reaction economically and potentially viable for commercial applications.



Scheme 16. Bis-aldol reaction of flavanone in water.



Scheme 17. Biginelli reaction in aqueous medium.

Multi-component one-pot condensation reaction

A nanosized magnesium oxide catalyzed three-component condensation reaction of aldehyde, malononitrile, and α -naphthol proceeds rapidly in water/PEG to afford corresponding 2-amino-2-chromenes in high yields at room temperature (Scheme 19) (56).

The greener protocol is found to be fairly general and the catalyst is reused in subsequent reactions with consistent activity. The attractive features of this protocol are the simple experimental procedure, use of benign reaction solvents, cost effectiveness, the recyclability of catalysts, and its adaptability for the synthesis of a diverse set of substituted 2-amino-2-chromenes (56).

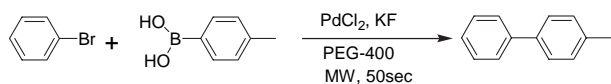
Green synthesis of nanomaterials

Nanometals. In the synthesis of metal nanoparticles via the reduction of the corresponding metal ion salt solutions, there are three areas of opportunity to engage the green chemistry principles: (i) choice of solvent, (ii) the reducing agent employed, and (iii) the capping agent (or dispersing agent). In this context, it would of great interest to identify environmentally friendly materials that are multifunctional. The synthesis and self-assembly of noble nanometals are carried out by reacting respective metal salts with vitamin B₂ dissolved in solvents of varying densities, such as ethylene glycol ($\rho = 1.113$), acetic acid ($\rho = 1.049$), *N*-methyl pyrrolidinone (NMP; $\rho = 1.03$), water ($\rho = 0.998$), isopropanol ($\rho = 0.790$), acetone ($\rho = 0.790$), and acetonitrile ($\rho = 0.782$) at room temperature (57). The vitamin B₂ used in this study functions both as a reducing as well as a capping agent for Au and Pt metals. In addition to its high water solubility, biodegradability, and low toxicity compared to other reducing agents, such as sodium borohydride (NaBH₄) and hydroxylamine hydrochloride, it appears to be an ideal multifunctional agent for the production of nanomaterials. The rationale

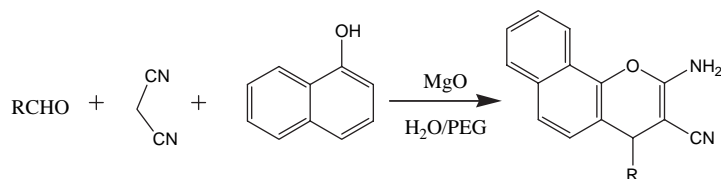
for using vitamin B₂ is that it is the most frequently encountered organic cofactor in nature and it can assume three different redox states: fully oxidized, one-electron reduced, and fully reduced. Each of these redox states exists in a cationic, neutral, and anionic form, depending on the pH of the solution, and can transfer electrons. This environmentally benign approach provides facile entry in producing multiple shaped noble nanostructures that could find widespread technological and medicinal applications (57).

Bulk and shape-controlled synthesis of gold (Au) nanostructures with various shapes, such as prisms, cubes, and hexagons, can also be accomplished via MW-assisted spontaneous reduction of noble metal salts using an aqueous solution of α -D-glucose, sucrose, and maltose (58). The expeditious reaction is completed under MW irradiation in 30–60 sec and can be applied to the generation of nanospheres of silver (Ag), palladium (Pd), and platinum (Pt). The noble nanocrystals undergo catalytic oxidation with monomers, such as pyrrole, to generate noble nanocomposites that have potential functions in catalysis, biosensors, energy storage systems, nanodevices, and ever expanding other technological applications (58). The MW strategy has also been extended to combustion synthesis of porous nanocrystalline titania and carbon-coated titania using dextrose as template (59); such "doped" titania may be utilized for photodegradation of pollutants in the visible light. This general method and eco-friendly protocol utilizes benign natural polymer dextrose and can be extended to other transition metal oxides, e.g. ZrO₂, Al₂O₃ and SiO₂, and may find widespread applications, such as fuel cell, membrane, dielectrics, and catalysis (59).

Nanocomposites. The environmental impact of handling nanomaterials is being debated at this time both by industry and the government. To avoid such handling, one can envision the generation of these materials in the medium of choice, for example coating or membrane materials. We have developed a facile method utilizing MW irradiation that accomplishes cross-linking reaction of poly (vinyl alcohol) (PVA) with metallic and bimetallic systems. Nanocomposites of PVA cross-linked metallic systems, such as Pt, Cu, and In and bimetallic systems, such as Pt-In, Ag-Pt, Pt-Fe, Cu-Pd, Pt-Pd, and Pd-Fe, are



Scheme 18. Suzuki cross-coupling of arylboronic acids with aryl halides.



Scheme 19. MgO catalyzed three-component condensation reaction.

prepared expeditiously by reacting respective metal salts with 3 wt% PVA under MW irradiation maintaining a temperature at 100°C, a radical improvement over the literature methods to prepare cross-linked PVA (60). The general preparative procedure is versatile and provides a simple route to manufacturing useful metallic and bimetallic nanocomposites with varying shapes, such as spheres, dendrites, and cubes (60). This general approach has also been adopted for cross-linking reaction of PVA with single-wall carbon nanotubes (SWNT), multi-wall carbon nanotubes (MWNT), and Buckminsterfullerene (C-60) using MWs (61). Nanocomposites of PVA cross-linked with SWNT, MWNT and C-60 are prepared expeditiously by reacting respective carbon nanotubes with 3 wt% PVA under MW irradiation maintaining a temperature of 100°C. This preparative and versatile MW procedure provides a simple route to manufacture useful SWNT, MWNT, and C-60 nanocomposites (61). The use of abundant biodegradable materials, such as carboxymethyl cellulose (CMC), in generating thin films with embedded nanometals is being pursued (62) under similar conditions.

Conclusions

The eco-friendly advantages of the synthetic alternatives based on unconventional activation via MW or ultrasound irradiation or the use of friendly reaction media, such as water and PEG (55b), are becoming increasingly apparent and may be adopted by the chemical and pharmaceutical industry to reduce or eliminate volatile organic solvents, thus preventing pollution “at source.” The acceleration of synthesis processes by MW/ultrasonic irradiation to shorten the reaction time and elimination or minimization of side product formation is already finding acceptance in the pharmaceutical industry (combinatorial chemistry) and polymer syntheses and may pave the way towards a greener and more sustainable approach to chemical syntheses (63). The newer strategies to generate nanomaterials in a variety of media for their safer use may benefit from the practice of green chemistry principles (64).

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