Journal of Chemistry
Vol. 45B, October 2006, pp. 2305-2312

Greener organic syntheses under non-traditional conditions

Rajender S Varma

Sustainable Technology Division, National Risk Management Research Laboratory
U.S. Environmental Protection Agency, 26 West Martin Luther King Drive, MS 443, Cincinnati, Ohio 45268, USA
E-mail: Varma.Rajender@epa.gov

Received 12 June 2006

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 presented which 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-aroylbenzofurans, 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 is described. Efficient reaction of epoxides with carbon dioxide 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, pyrazolidines etc.

Keywords: Green chemistry, organic synthesis, solvent-free reactions, microwave irradiation, ultrasonic irradiation, ionic liquids, aqueous media

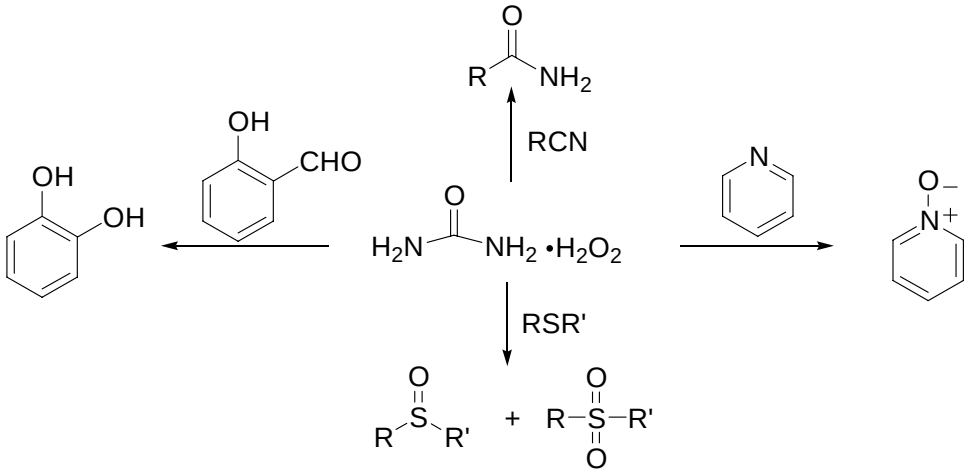
IPC Code: Int. Cl.[8] CO7D

The diverse nature of chemical universe requires various green strategic 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. One of the thrust areas for achieving this target is to explore alternative reaction conditions and 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 (dry media), solid supported[1-4] and solid/solid reactions (grinding), the use of room temperature ionic liquids[5], supercritical carbon dioxide, and water[6] as reaction media that can be combined with microwave or ultrasonic irradiation. Indeed, the best solvent is 'no solvent', but in such cases the problem of handling of materials and heat- and mass-transfer aspects need to be addressed in close cooperation with chemical engineers.

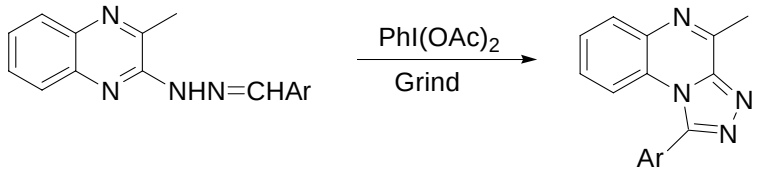
Results and Discussion

There are different shades of greener processes as we continue exploring several alternatives to conventional chemical transformations. Rather than remediation, which involves cleaning up of waste after it has been produced, the main objective is to avoid waste generation in the first place. That approach will require new environmentally benign syntheses, catalytic methods and chemical products that are "benign by design" and that utilize renewable resources wherever possible.

As an example, conventional oxidation processes involve danger in handling of metal complexes, inherent toxicity, and waste disposal problems. A solvent-free oxidation of a variety of organic groups using an inexpensive, safe and easily handled reagent, urea-hydrogen peroxide (UHP), has been discovered by Varma and Naicker (**Scheme I**) and this general solid-state oxidative protocol is applicable in oxidizing hydroxylated aldedydes and ketones



Scheme I — Solventless oxidations using UHP



Ar = C_6H_5, *p*-$CH_3C_6H_4$, *p*-ClC_6H_4, *p*-$OCH_3C_6H_4$,
m-$OCH_3C_6H_4$, *p*-$N(CH_3)_2C_6H_4$,

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

(to phenols), sulfide (to sulfoxides and sulfones), nitriles (to amides), and *N*-heterocycles (to *N*-oxides)[7].

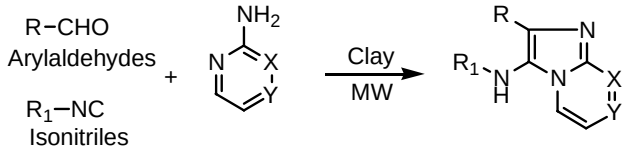
We have found an oxidative transformation of arenecarbaldehyde 3-methylquinoxalin-2-yl-hydrazones to 1-aryl-4-methyl-1,2,4-triazolo[4,3-*a*]quinoxalines (**Scheme II**) by simple grinding using a friendlier non-metallic oxidant iodobenzene diacetate, $PhI(OAc)_2$ (ref. 8a), and now the work has been extended to the synthesis of β-ketosulfones[8b] employing another hypervalent iodine reagent, hydroxytosyloxy iodobenzene.

The oxidative protocol simply involves grinding of the two solid substrates using a pestle and mortar; mildly exothermic reaction results in the formation of a yellowish eutectic melt and the reaction gets completed in a few minutes.

Solvent-free approach that involves microwave (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 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[9-11].

Synthesis of heterocycles — applications in combinatorial chemistry. Heterocyclic chemistry has been a major beneficiary of MW-expedited solvent-free chemistry utilizing mineral supported reagents which has been exploited for parallel synthesis, a strategy that is adaptable for multi-component reactions such as Ugi[11a] and Biginelli reactions[11b] for rapid assembly of a library of compounds[11c]. A representative multi-component condensation reaction to create small-molecule library of imidazo[1,2-*a*]pyridines, imidazo[1,2-*a*] pyrazines and imidazo[1,2-*a*]pyrimidines is depicted in **Scheme III**.

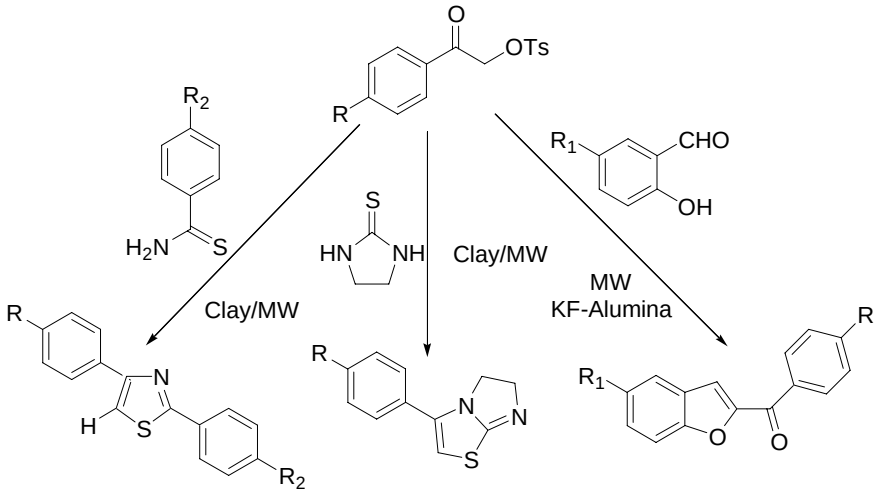
The conventional preparations of thiazoles and 2-aroylbenzo[*b*]-furans require the use of lachrymatory α-haloketones and thioureas (or thioamides). In a process which eliminates this problem, Varma *et al.* have now synthesized various heterocyles via simple solvent-free reaction of thioamides, ethylenethioureas and salicylaldehydes with α-tosyloxyketones that is generated *in situ* from arylmethyl ketones and [hydroxy(tosyloxy)iodo]benzene (HTIB) under MW irradiation conditions (**Scheme IV,** ref.12).



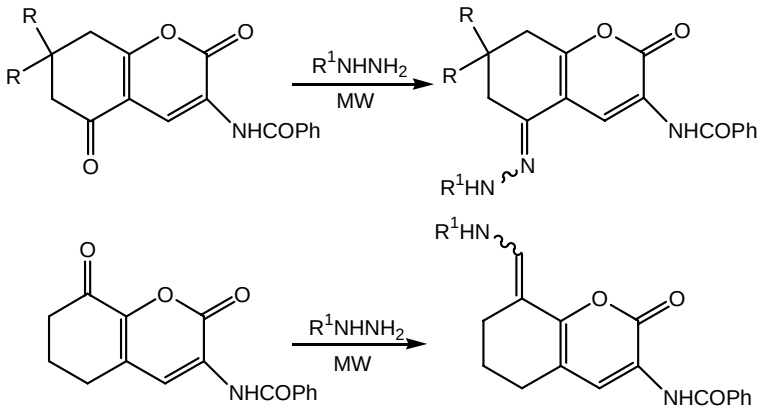
Scheme III — MW three-component Ugi reaction

The only example of a reaction between two solids, under solvent-free and catalyst-free environment, was demonstrated by Varma *et al.* when the reaction of neat 5- or 8-oxobenzopyran-2(1*H*)-ones, with a variety of aromatic and heteroaromatic hydrazines, could provide rapid access to several synthetically useful heterocyclic hydrazones **(Scheme V,** ref. 13**)**.

Solvent-free synthesis of ionic liquids. Ionic liquids, being polar and ionic in character, respond to MW irradiation very efficiently and therefore have been considered microwave absorbing candidates for



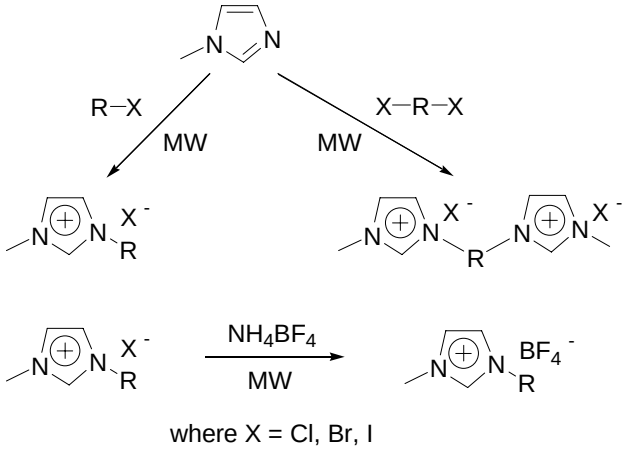
Scheme IV — Synthesis of heterocycles from *in situ* generated α-tosyloxyketones



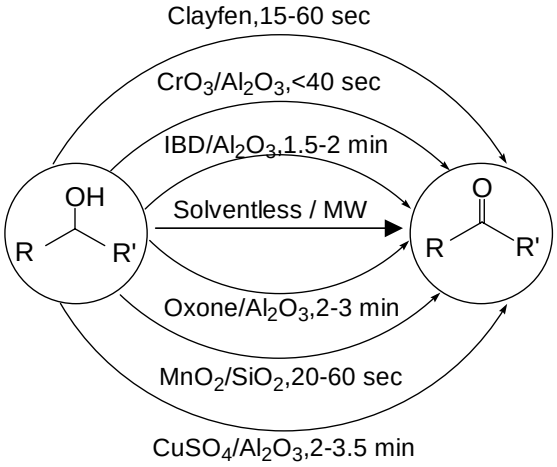
Scheme V — Solvent-free preparation of hydrazones using microwaves

expediting chemical reactions. Unfortunately, most of the initial preparative processes for the preparation of ionic liquids involve several hrs 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* microwave heating has been described by Varma *et al*. (**Scheme VI,** ref. 5,14**)** that reduces the reaction time from hours to minutes and avoids the use of a large excess of alkyl halides/organic solvents as the reaction medium; the S_N2 alkylations using neutral nucleophiles as amines has been further exploited in the synthesis (*vide supra*). The approach has been extended to other ionic salts bearing tetrafluoroborate anions[15a], that involves exposing *N, N'*-dialkylimidazolium chloride and ammonium tetrafluoroborate salt to MW irradiation (**Scheme VI**). Similarly, gallium and indium containing ionic liquids[15b,c] have been prepared; catalytic amount of tetrachloroindate-based ionic liquid efficiently catalyzes the reaction of epoxides with carbon dioxide affording a greener route to useful cyclic carbonates[15d]. The surge of interest continues in this area and we have explored the use of ultrasonic pathway to prepare these solvents[5b] and their use as catalysts for alkylation of isobutane with 2-butene[16], for ruthenium-catalyzed tandem migration[17], and silver-catalyzed coupling reactions[18].



Scheme VI — Solventless MW ionic liquid preparation



Scheme VII — MW-assisted solvent-free oxidation of alcohols to carbonyls

Oxidation reactions on solid supports. The utility of oxidants in oxidation processes is compromised for several reasons including potential danger in handling of metal complexes, inherent toxicity, cumbersome product isolation and waste disposal problems. Immobilization of metallic reagents on solid supports has addressed some of these limitations **(Scheme VII)** as the containment of metals on the support surface that precludes them from leaching into the environment. There are several examples:

(i) Silica supported manganese dioxide (MnO_2) (ref.19). (ii) Chromium trioxide (CrO_3) immobilized on pre-moistened alumina affords efficient oxidation of benzyl alcohols to carbonyl compounds by simple mixing (**Scheme VII**). Remarkably, neither the overoxidation to carboxylic acids nor the usual formation of tar, a typical occurrence in many CrO_3 oxidations, is observed[20].

A rapid MW oxidation protocol for the oxidation of alcohols to carbonyl compounds has been reported by Varma *et al.* using montmorillonite K10 clay-supported iron(III) nitrate (clayfen). The simple solvent-free experimental procedure involves mixing of neat substrates with clayfen and a brief MW irradiation for 15-60 seconds[21]. The solid state utility of clayfen - iron(III) nitrate on clay as an oxidant has afforded higher yields (**Scheme VII**) and is more efficient supported on clay since the amounts used in these protocols are half of that used in solution phase reactions by Laszlo *et al.*[22a,b].

Varma *et al.* have reported for the first time the use of supported iodobenzene diacetate (IBD) as an oxidant; the use of alumina as a support improved the yields markedly as compared to neat IBD (**Scheme VII,** ref. 23). The solid IBD-alumina

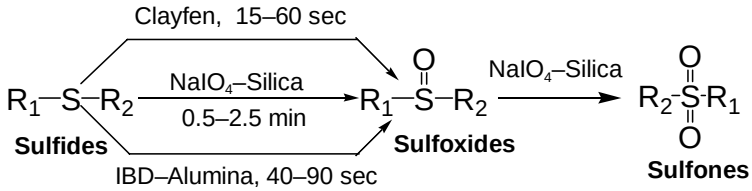
system has also been used for the rapid, high yielding and selective oxidation of alkyl, aryl and cyclic sulfides to the corresponding sulfoxides upon MW irradiation[24].

The oxidation of sulfides to sulfoxides and sulfones is achieved in a selective manner using MW irradiation under solvent-free conditions with desired selectivity to either sulfoxides or sulfones over sodium periodate ($NaIO_4$) on silica (20%) (**Scheme VIII,** ref. 25). A noteworthy feature of the protocol is its applicability to long chain fatty sulfides that 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 of sulfides to the corresponding sulfoxides and sulfones.

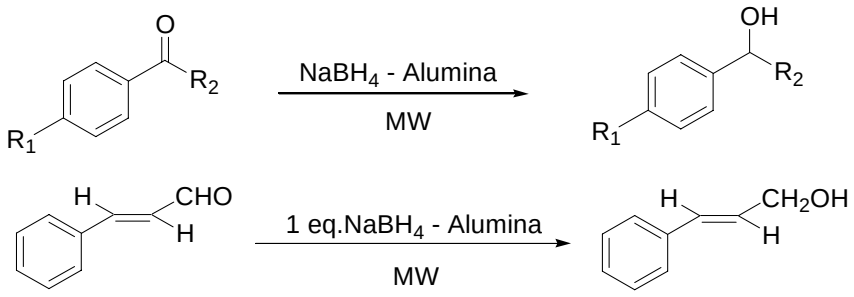
Reduction reactions. The relatively inexpensive and safe sodium borohydride has been extensively used as a reducing agent because of its compatibility with protic solvents. A simple method for the expeditious reduction of aldehydes and ketones that uses alumina-supported $NaBH_4$ and proceeds in the solid state accelerated by MW irradiation[26] (**Scheme IX**). 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 microwave cavity, thus preventing any ensuing hydrogen from reaching explosive concentrations. The process has been nicely utilized for the MW-enhanced solid-state deuteriation reactions using sodium borodeuteride impregnated alumina[27]. Subsequent extension of these studies to specific labeling has been explored[28] including deuterium exchange reactions for the preparation of reactive intermediates[29].

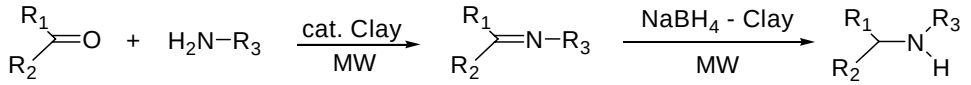
Solvent-free reductive amination protocol for carbonyl compounds using sodium borohydride supported on moist montmorillonite K10 clay is facilitated by MW irradiation (**Scheme X**, ref. 30). Clay serves the dual purpose of a Lewis acid and also provides water from its interlayers that enhance the reducing ability of $NaBH_4$.



Scheme VIII — MW-assisted oxidation of sulfides to sulfoxides and/or sulfones



Scheme IX — Solventless reduction of carbonyls on alumina



Scheme X — Reductive amination of carbonyl compounds

Reactions in aqueous media. Organic synthesis in aqueous media is rapidly gaining importance in organic synthesis in view of the fact that the use of many toxic and volatile organic solvents, particularly chlorinated hydrocarbons, contribute to pollution. Consequently, it is highly desirable to develop environmentally benign processes that can be conducted in aqueous media. Furthermore, using water as a solvent offers many advantages such as simple operation and high efficiency in many organic reactions that involve water soluble substrates and reagents. Utilization of water as reaction media[31] in conjunction with microwave irradiation is one of the emerging non-conventional methods being recognized as viable environmentally benign alternatives[1,9,10,32].

We envisioned that the nucleophilic substitution reaction of alkyl halides with amines will be accelerated by microwave energy because of their polar nature. Indeed, a friendlier synthesis of tertiary amines *via* direct *N*-alkylation of primary and secondary amines by alkyl halides under microwave irradiation is possible that proceeds in basic water without any phase transfer reagent [33].

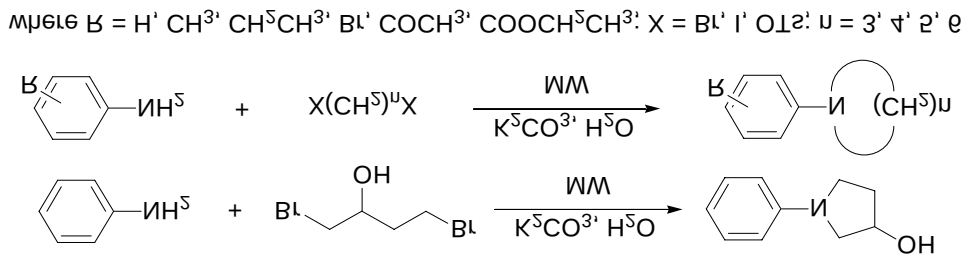
The same nucleophilic substitution chemistry can be manipulated by means of microwaves to afford a variety of cyclic amines as building blocks in natural product syntheses *via* double *N*-alkylation of primary amines (**Scheme XI,** ref. 34). The protocol circumvents the difficulty associated with running 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, hydroxyl etc., remain unaffected under these mild reaction conditions. The *N*-alkylation reaction is now extended to hydrazines as well[34b,c].

It is noteworthy to mention that this reaction is not a homogeneous single phase system as neither reactant is soluble in aqueous alkaline reaction medium. We believe that the selective absorption of microwaves 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[35].

The experimental observation is consistent with the mechanistic postulation wherein the polar transition state of the reaction is favored by microwave irradiation with respect to the dielectric polarization nature of microwave energy transfer[34,36]. In large scale experiments, the phase separation of the desired product in either solid or liquid form from the aqueous media can facilitate product purification by simple filtration or decantation instead of tedious column chromatography, distillation or extraction processes which eventually reduce the usage of volatile organic solvent required for extraction or column chromatography.

Experimental Section

Solvent-free MW reactions. Most of the neat reactions (undiluted) without solvents or using supported reagents were performed in open glass vessels using a Panasonic household microwave oven (1000 W) equipped with a turntable and operating at 2450 MHz. This MW oven uses inverter technology for realistic modulation of power level operations which was especially useful for preparation of polar and ionic compounds such as ionic liquids that required intermittent heating. An alumina-bath (neutral alumina: 125 g, mesh ~150, Aldrich; bath: 5.7 cm diameter) was used as a heat sink inside the MW oven to irradiate the reaction mixtures. The average bulk temperature at the end of the reaction was measured by inserting a thermometer in the alumina-bath housing the reaction vessel or using an IR sensor.



SchemeXI — MW-assisted formation of cyclic amines

Preparation of ionic liquids using ultrasound irradiation — Representative procedure for bromides and iodides. 1-Bromobutane (11 mmoles) and MIM (10 mmoles) were placed in a screw-cap test tube and subjected to ultrasound irradiation on a Fisher Scientific ultrasonicator (Model FS 220) for 2 hr until a clear single phase of ionic liquid is obtained; temperatures of the bath before and after sonication were 23 and 40°C, respectively. The residual 1-butyl bromide was removed under vacuum at 80°C (94%). A similar experiment on the same scale, but using conventional heating (oil-bath, 50°C, 6hr) did not afford any product. An experiment on a relatively large scale (55 mmoles of 1-bromobutane and 50 mmoles of MIM) afforded 98% yield.

General MW procedure for the synthesis of α-tosyloxyketones. A mixture of arylmethylketone (1 mmole) and [hydroxy(tosyloxy)iodo] benzene (1.2 mmole) was mixed in a glass tube and was placed in an alumina-bath inside the MW oven and irradiated for 30 sec at 50% power level. After completion of the reaction, determined by TLC examination, the crude products were washed with hexane to afford α -tosyloxyarylmethylketones that were used in subsequent reactions.

Synthesis of 2-aroylbenzo[*b*]furans (Scheme IV). Salicylaldehyde (0.122 mg, 1 mmole), potassium fluoride (KF)-alumina (0.620 g, 0.2 mmole of KF) and α-tosyloxyketone (1 mmole) were mixed in a glass tube and then placed in an alumina-bath inside the MW oven and irradiated (intermittently with 1.5 min interval; 130°C). On completion of the reaction, followed by TLC examination (hexane:ethyl acetate, 9:1), the product was extracted into methylene chloride, solvent removed and the residue was crystallized from ethanol to afford high yield of 2-aroylbenzo[*b*]furans.

Synthesis of 2,4-disubstituted thiazoles (Scheme IV). α-Tosyloxyketone (1 mmole), appropriate thioamide (1 mmole) and montmorillonite K 10 clay (125 mg) were mixed thoroughly using a pestle and mortar. The reaction mixture was placed into a glass tube and exposed to MW irradiation in an alumina-bath for 2-5 min (intermittently with 1.5 min interval; 130°C). The product was extracted into methylene chloride and purified by crystallization from ethanol-hexane to afford corresponding thiazoles.

Synthesis of 3-aryl-5,6-dihydroimidazo[2,1-*b*] thiazole (Scheme IV). α-Tosyloxyketone (1 mmole), ethylenethiourea (1 mmole) and montmorillonite K 10 clay (100 mg) were mixed thoroughly in a pestle and mortar. The contents were transferred into a glass tube followed by intermittent microwave irradiation in an alumina-bath for 3 min. The ensuing thiazole salt was neutralized by the addition of a dilute aqueous sodium hydroxide. The product was extracted into methylene chloride and purified by crystallization from benzene-hexane to afford corresponding 3-aryl-5,6-dihydroimidazo[2,1-*b*] thiazole (**Scheme IV**).

Reactions in aqueous media-synthesis of *N*-aryl azacycloalkanes. In a representative reaction, 1.0 mmole aniline derivatives, 1.1 mmole dihalides and 1.1 mmole potassium carbonate in 2 mL of distilled water were placed in a 10 mL crimp-sealed thick-wall reaction tube equipped with a pressure sensor and a magnetic stirrer. The reaction tube was placed in the microwave cavity (CEM Discover Focused Microwave Synthesis System with a built-in infrared temperature sensor), operated at 120 $\pm$ 5°C, power 80-100 Watt and pressure 65-70 psi for 20 min. After completion of the reaction, the organic portion was extracted into ethyl acetate. Removal of the solvent under reduced pressure and flash column chromatography furnished the desired product.

Conclusion

The eco-friendly advantages of these reactions may be found in instances where catalytic amounts of reagents or supported agents are used since they provide reduction or elimination of solvents or utilize water as reaction media thus preventing pollution 'at source'. Although not delineated completely, the reaction rate enhancements achieved in these methods may be ascribable to non-thermal effects. The rationalization of microwave effects and mechanistic considerations possibly involving the intermediacy of polar transition states have been discussed[34,36]. The acceleration of synthesis processes by microwave/ultrasonic irradiation to shorten the reaction time and elimination or minimization of side product formation is already finding acceptance in pharmaceutical industry (combinatorial chemistry) and polymer syntheses may pave the way towards the greener and more sustainable approach to chemical syntheses.

References

1 Varma R S, in "*Microwaves in Organic Synthesis*" edited by A. Loupy, Chapter 6, **2002**, (Wiley-VCH, Weinheim) pp 181-218.

2 (a) Varma R S, *Pure Appl Chem*, 73, **2001**, 193.
(b) Varma R S, *Green Chem,* 1, **1999**, 43.

3 Pillai U, Sahle-Demessie E & Varma R S, *J Mat Chem,* 12, **2002**, 3199.

4 Varma R S, *Tetrahedron,* 58, **2002**, 1235.

5 (a) Varma R S in *Ionic Liquids as Green Solvents. Progress and Prospects,* edited by R Rogers & K R Seddon, ACS Symposium Series 856 (American Chemical Society, Washington, DC) Chap. 7, **2003**, pp 82-92.
(b) Namboodiri V V & Varma R S, *Org Lett,* 4, **2002**, 3161.

6 Wei W, Keh C C K, Li, C J & Varma R S, *Clean Tech & Environ Policy,* 7, **2005**, 62.

7 Varma R S & Naicker K P, *Org Lett*, 1, **1999**, 189.

8 (a) Kumar D, Chandra Sekhar K V G, Dhillon H, Rao V S & Varma R S, *Green Chem*, 6, **2004**, 156.
(b) Kumar D, Sundaree S, Rao V S & Varma R S, *Tetrahedron Lett*, 47, **2006**, in press.

9 Varma R S, *Microwave Technology — Chemical Applications,* Kirk-Othmer Encyclopedia of Chemical Technology, 5th Edn (**2004**).

10 Varma R S, *Advances in Green Chemistry: Chemical Syntheses Using Microwave Irradiation,* AstraZeneca Research Foundation India, Bangalore, India **2002**.

11 (a) Kappe C O, Kumar D & Varma R S, *Synthesis,***1999**, 1799.
(b) Kumar D & Varma R S, *Tetrahedron Lett*, 40, **1999**, 7665.
(c) Varma R S, *J Heterocyclic Chem,* 35, **1999**, 1565.

12 Varma R S, Kumar D & Liesen P J, *J Chem Soc Perkin Trans 1*, **1998**, 4093.

13 Ješelnik M, Varma R S, Polanc S & Kočevar M, *Chem Commun,* 2001,1716; *Green Chem,* 4, **2002**, 35.

14 (a) Varma R S & Namboodiri V V, *Chem Commun*, **2001**, 643.
(b) Varma R S & Namboodiri V V, *Pure Appl Chem*, 73, **2001**, 1309.

15 (a) Namboodiri V V & Varma R S, *Tetrahedron Lett,* 43, **2002**, 5381.
(b) Kim, Y -J & Varma R S, *Tetrahedron Lett,* 46, **2005**, 1467.
(c) Kim, Y -J & Varma R S, *Tetrahedron Lett,* 46, **2005**, 7447.
(d) Kim, Y -J & Varma R S, *J Org Chem,* 70, **2005**, 7882.

16 Yoo K, Namboodiri, V V, Smirniotis P G & Varma R S, *J Catal,* 222, **2004**, 511.

17 Yang X -F, Wang M,.Varma R S & Li C -J, *J Mol Cat A Chemical,* 214, **2004**, 147.

18 Li Z, Wei C, Chen L, Varma R S & Li C -J, *Tetrahedron Lett*, 45, **2004**, 2443.

19 Varma R S, Saini R K & Dahiya R, *Tetrahedron Lett*, 38, **1997,** 7823.

20 Varma R S, Saini R K & Dahiya R, *Tetrahedron Lett*, 39, **1998,** 1481.

21 Varma R S & Dahiya R, *Tetrahedron Lett*, 38, **1997**, 2043.

22 (a) Laszlo P, *Acc Chem Res,*19, **1986**, 121.
(b) Cornelius A & Laszlo P, *Synlett,* **1994**, 155.

23 Varma R S, Dahiya R & Saini R K, *Tetrahedron Lett*, 38, **1997**, 7029.

24 Varma R S, Saini R K & Dahiya R, *J Chem Res (S),* **1998**, 120.

25 Varma R S, Saini R K & Meshram H M, *Tetrahedron Lett*, 38, **1997**, 6525.

26 Varma R S & Saini R K, *Tetrahedron Lett*, 38, **1997**, 4337.

27 Erb W T, Jones J R & Lu S Y, *J Chem Res (S)*, **1999**, 728.

28 Elander N, Jones J R, Lu S Y & Stone-Elander S, *Chem Soc Rev*, 9, **2000**, 239.

29 Fodor-Csorba K, Galli G, Holly S & Gacs-Baitz E, *Tetrahedron Lett*, 43, **2002**, 4337.

30 Varma R S & Dahiya R, *Tetrahedron,* 54*,* **1998**, 6293.

31 (a) Li C -J, *Chem Rev*, 105, **2005,** 3095.
(b) Narayan S, Muldoon J, Finn M G, Fokin V V, Kolb, H C & Sharpless K B, *Angew Chem, Int Ed*, 44, **2005**, 3275.

32 (a) Kappe C O, *Angew Chem Int Ed*, 43, **2004**, 6250.
(b) Bose A K, Manhas M S, Ganguly S N, Sharma A H & Banik B K, *Synthesis,* **2002**, 1578.
(c) Leadbeater N E, *Chem Commun,* **2005**, 2881.
(d) An J, Bagnell L, Cablewski T, Atrauss C R & Trainor R W, *J Org Chem*, 62, **1997**, 2505.

33 Ju Y & Varma R S, *Green Chem*, 6, **2004**, 219.

34 (a) Ju Y & Varma R S, *Org Lett*, 7, **2005**, 2409.
(b) Ju Y & Varma R S, *J Org Chem,* 71*,* **2006**, 135.
(c) Ju Y & Varma R S, *Tetrahedron Lett,* 46, **2005**, 6011.

35 (a) Varma R S & Naicker K. P. *Tetrahedron Lett,* 39, **1998**, 2915.
(b) Varma R S, Naicker K P, Kannan & Aschberger P, *Synth Commun,* 29*,* **1999**, 2823.
(c) Varma R S, Naicker K P & Kumar D, *J Mol Cat A: Chemical,* 149, **1999**, 153.

36 Perreux L & Loupy A, *Tetrahedron,* 57, **2001**, 9199.