

Review

General Characteristics and Applications of Microwaves in Organic Synthesis

Monika Gupta,* Satya Paul and Rajive Gupta

Department of Chemistry, University of Jammu, Jammu 180006

* Corresponding author: E-mail: monika.gupta77@indiatimes.com;

Received: 02-12-2008

Abstract

This review focusses upon the key achievements made in organic synthesis using microwave-assisted reactions in the solid phase, with neat reactants and under solvent-free conditions. It also highlights the general characteristics of microwave applications in organic synthesis. It shows that reactions under microwaves are fast, with often increased reaction rates and lead to better selectivity. Some of the microwave-assisted reactions can even be carried out under neat conditions therefore leading to the area of green chemistry.

Keywords: Microwaves, green chemistry, activation, solid phase, neat, solvent-free, alkylation, heterocycles

1. Introduction

In the context of green chemistry, among the non-conventional methods of reaction activation in organic synthesis, microwave irradiation for reaction activation provides an alternative to the conventional heating for introducing energy into chemical reactions by using the ability of some liquids and solids to transform electromagnetic energy into heat. This *in situ* mode of heat generation has attracted many chemists because its magnitude depends on the dielectric properties of the molecules. The microwave-assisted reactions are fast, clean, economic and eco-friendly and this technique has been proposed as the “technology of tomorrow”.

2. Advent of Microwaves

The magnetron,¹ a remarkable device for generating fixed-frequency microwaves, was designed by Randall and Booth at the University of Birmingham. A magnetron is a vacuum device which converts DC electrical energy into microwaves.

In early days, it was recognized that microwaves could heat water in a dramatic fashion. Domestic and commercial appliances for heating and cooking of foods began to appear in the 1950s. In 1947, the appliance called “Radarange” appeared on the market; it was intended for

food processing. The first microwave oven was introduced by Tappan in 1955 but the widespread use of domestic microwave ovens occurred during the 1970s and 1980s. The first application of microwave irradiation in chemical synthesis was published in 1986.²

3. Microwaves in Organic Synthesis

Microwaves have been used to speed up chemical reactions in the laboratory,³ which led scientists to investigate the mechanism of microwave dielectric heating and to identify the advantages of the technique for chemical synthesis.⁴

During recent years, microwaves have been extensively used for carrying out chemical reactions and have become a useful non-conventional energy source for performing organic synthesis.⁵ This is supported by a great number of publications in recent years, particularly in 2003, related to the application of microwaves as a consequence of a great availability of dedicated and reliable microwave instrumentation.^{6–9}

The first recorded application of microwave (MW) energy in organic synthesis is the aqueous emulsion polymerization of butyl acrylate, acrylic acid and methacrylic acid using pulsed electromagnetic radiation.¹⁰ The start of the rapid growth of microwave-assisted procedures in organic synthesis was ignited in 1986 by pioneering papers

by Gedye and co-workers⁹ and Giguere and co-workers.¹⁰ During the last two decades, the activity in this new technique has experienced exponential growth and has been extensively reviewed.^{13–17} Kappe and Dallinger have reported the impact of microwaves on drug discovery.¹⁴ Even microwave-assisted reactions under solvent-free conditions promoted the synthesis of Zincke's salt and its conversion to chiral pyridinium salts in water¹⁵ and microwave-assisted organic transformations using benign reaction media have also been reported.^{16,18} Moreover, Varma and co-workers have reported the drug discovery by using aqueous microwave chemistry.^{15,16}

4. Principles of Microwave Activation

In the electromagnetic spectrum the microwave radiation region is located between infrared radiation and radio-waves.¹⁷ Telecommunication and microwave radar equipment occupy many of the band frequencies in this region. In order to avoid interference with these systems, the household and industrial microwave ovens operate at a fixed frequency of 2.45 GHz.^{19–21} The energy of the quantum involved can be calculated by the Planck's law $E = h \nu$ and is found to be 0.3 cal mol^{-1} .

Presently, organic transformations take place by either of the two ways:

Conventional heating: In this method of heating, reactants are slowly activated by a conventional external heat source. Heat is driven into the substance, passing first through the walls of the vessel in order to reach the solvent and the reactants. This is a slow and inefficient method for transferring energy into the reacting system.

Microwave heating: Here, microwaves couple directly with the molecules of the entire reaction mixture, leading to a rapid rise in the temperature. Since the process is not limited by the thermal conductivity of the vessel, the result is an instantaneous localized superheating of any substance that will respond to either dipole rotation or ionic conductivity.

Only the reaction vessel contents are heated and not the vessel itself; better homogeneity and selective heating of polar molecules might be achieved.

The acceleration of chemical reactions by microwave exposure results from the interactions between the material and electromagnetic field leading to the thermal and specific (non-thermal) effects. For microwave heating, the substance must possess a dipole moment. A dipole is sensitive to external electric field and tries to align itself with the field by rotation. If submitted to an alternating current, the electric field is inversed at each alteration and therefore dipoles tend to move together to follow the inversed electric field.

Such a characteristic induces rotation and friction of the molecules, which dissipates as internal homogeneous heating. The electric field of commonly used irradiation

frequency (2450 MHz) oscillates 4.9×10^9 times per second. Thus, microwave heating is directly dependent on dielectric properties of a substance, dielectric constant (ϵ') and dielectric loss (ϵ'').^{17,22} The ability of a material to convert electromagnetic energy into heat energy at a given frequency and temperature, is calculated using

$$\epsilon'' / \epsilon' = \tan \delta \quad (1)$$

where δ is the dissipation factor of the sample, ϵ'' is the dielectric loss, which measures the efficiency with which heat is generated from the electromagnetic radiation and ϵ' is the dielectric constant which gives the ability of a molecule to be polarized by an electric field. The high value of dissipation factor δ indicates large susceptibility to microwave energy.²²

The conduction mechanism leads, due to the much stronger interaction of ions with electric field, to the generation of heat. The ions will move under the influence of an electric field, resulting in expenditure of energy due to an increased collision rate, converting kinetic energy into heat. The heat generated by both mechanisms adds up resulting in a higher final temperature.

Main benefits of microwave heating are:^{23,24}

- very fast heating;
- absence of inertia;
- ease of use, i.e. power regulation is easy with an instantaneous, “on and off” control;
- better homogeneity in temperature with quick transfer of energy into the whole mass without superficial heating;
- the selective heating of the polar molecules.

Since the ability of a molecule to couple with the microwave radiation is a function of its molecular polarizability (i.e. a function of its dipole moment), only polar molecules interact with microwave energy. As a guide, compounds with high dielectric constants such as water, ethanol, acetonitrile, *N,N*-dimethylformamide (DMF), acetic acid, chloroform, dichloromethane, acetone, ethylene glycol etc., tend to heat rapidly under microwave irradiation, while less polar substances, such as aromatic and aliphatic hydrocarbons or compounds with no net dipole moment, such as carbon dioxide, carbon tetrachloride, diethyl ether etc. as well as highly ordered crystalline substances, are poorly absorbing. Thus, polar molecules in a non-polar solvent would absorb energy, but not the solvent or the reaction vessel, if it is made of teflon ($\mu = 2.1$ at 22°C) or ceramic or even pyrex ($\mu = 4.5\text{--}6.0$). Sometimes it is possible to use mixtures comprising microwave active reactants and microwave inactive solvents. It has also been suggested that if microwave energy is absorbed by the solvent and not by the substrate, only modest rate increase will result relative to those observed with conventional energy. If, on the other hand, the microwave energy is absorbed selectively by a reactant, by a complex or by an intermediate during the rate determining step, then large rate increase will result.

A microwave heating technique should be a promising candidate, replacing conventional heaters because microwave-assisted organic syntheses can lead to a large decrease in reaction time and to an enhancement of conversion and selectivity, compared to conventional heating.^{25–27} These microwave effects could be attributed to the characteristic heating modes of the microwaves, caused by the interaction of oscillating electromagnetic fields with the assemblies of the polar molecules, expressed as dielectric loss, leading to the unusual phenomenon called superheating²⁸ or hot spots.^{25,29} Instantaneous heat release at the molecular level should favourably induce certain thermal reactions taking place through a polar charge-transfer or polar transition state as is often observed in photo-induced chemical reactions.

5. Equipment

Two types of microwave reactors can be used in the laboratory: multimode microwave reactors and monomode microwave reactors

5.1. Multimode Microwave Reactors

Even though the microwave reactors have been introduced on the market as household devices for cooking, heating and thawing of food, they have found use in organic laboratory for carrying out organic synthesis on the laboratory scale. Most of the publications in the area of microwave chemistry from Asian countries involve use of domestic microwave ovens. These ovens (with limited power 800–1000 W) are characterized by a non-homogeneous distribution of electric field due to several reflections off the metallic walls of the oven. Since the field is heterogeneous, so their use in synthetic purposes requires mapping of the field, involving determination of hot spots of high energy using a filter paper sheet impregnated with a solution of cobalt chloride.³⁰

Some modifications of domestic microwave ovens have been suggested by various workers³¹ such as introduction of condensers³² by boring through the top of the oven or reaction flasks being fitted with condensers³³ and charged with pre-cooled, microwave-inactive coolants, like xylene, carbon tetrachloride etc.

In addition to these, there are many dedicated large multimode versions with rotors (8 or more reactions simultaneous), but claimed to have (quasi) in-phase microwave irradiation achieved by special design of their equipment.

The use of multimode reactors has however, following limitations:

- a) the distribution of electric field inside the cavity results from multiple reflections off the walls and reaction vessel and is consequently heterogeneous;
- b) the temperature cannot be simply and accurately measured;
- c) the power is not tuneable.

There are a few examples in the literature which indicate that microwave heating was used in stirred tank reactors, for example for the esterification of benzoic acid with ethanol by conventional and microwave heating,³⁴ for the hydrolysis of sucrose by conventional and microwave heating³⁵ and for the esterification of benzoic acid with 2-ethylhexanol.³⁶

In addition to it, microwave heating of the continuous-flow catalytic reactor in a non-uniform electric field³⁷ was also well presented in the literature.

5.2. Monomode Microwave Reactors

In the monomode microwave oven the dimensions of wave belt (wave guide) and excitations are specially calculated so to allow only one mode of propagation or resonance. They are able to obtain a homogeneous distribution of the electric field in the wave belt (focalised fasciculus) and hence in the heated reaction mixtures. They are used with less power emitted with a high return of energy, and thus, the utilization of monomode reactor is energy-efficient and leads to better yields in organic synthesis, while preserving the thermally unstable products.

Microwave-assisted organic chemistry is reviewed³⁸ in the context of the methods employed. A range of technical difficulties indicated that specifically designed microwave reactors are required. Hence, the CSIRO continuous microwave reactor (CMR) and microwave batch reactor (MBR) were developed for organic synthesis. On the laboratory scale, they operate at temperatures (pressures) up to 200 °C (1400 kPa) and 260 °C (10 MPa), respectively.

CEM Discover Focused Microwave Equipment

Bridging the gap between functionality and economy, the Discover System by CEM is the smallest instrument on the market today. This reactor is a stand-alone equipment with a small footprint, and allows the use of the standard glassware reaction vessels (1 mL up to 125 mL) for the reactions executed at the atmospheric pressure and the use of septum sealed 10 mL vials for high-pressure reaction conditions (up to 30 bar). The Discover System also controls reaction temperature, pressure and stirring speed.

Over 30 international patents in the field of microwave technology, together with over 6,000 units installed worldwide are the testimony of its importance. The aim is to provide organic chemists with the safest, most effective tools for microwave-enhanced chemistry.

6. Working of the Microwave Oven

In a microwave oven, microwaves are generated by a magnetron. A magnetron is a thermo-ionic diode having an anode and a directly heated cathode. As the cathode is heated, electrons are released and are attracted towards

the anode. The anode is made up of an even number of small cavities, each of which acts as a tuned circuit. The anode is, therefore, a series of circuits, which are tuned to oscillate at a specific frequency or at its overtones.

A very strong magnetic field is induced axially through the anode assembly and has the effect of bending the path of electrons as they travel from the cathode to the anode. As the deflected electrons pass through the cavity gaps, they induce a small charge into the tuned circuit, resulting in the oscillation of the cavity. Alternate cavities are linked by two small wire straps, which ensure the correct phase relationship. This process of oscillation continues until the oscillation has achieved a sufficiently high amplitude. It is then taken off by the anode via an antenna. The variable power available in domestic ovens is produced by switching the magnetron on and off according to the duty cycle.

Microwave dielectric heating is effective when the matrix has a sufficiently large dielectric loss tangent (i.e. contains molecules possessing a dipole moment). The use of a solvent is not always mandatory for the transport of heat.³⁹ Therefore, reactions performed under solvent-free conditions present an alternative in the microwave chemistry and constitute an environmentally benign technique, which avoids the generation of toxic residues, like organic solvents and mineral acids, and thus allows the attainment of high yields of products at reduced environmental costs. This emerging environmentally benign technique belongs to the upcoming area of green chemistry.

7. Various Types of Microwave-Assisted Organic Reactions

The microwave-assisted organic reactions have been broadly classified into two categories: microwave-assisted reactions using solvents; microwave-assisted reactions using solvent-free conditions.

7.1. Microwave-Assisted Reactions Using Solvents

In the case of the microwave-assisted reactions using (organic) solvents, the reactants are usually dissolved in the solvent, which often couples effectively with microwaves and thus acts as the energy transfer medium.

The use of aqueous media for organic reactions^{40–44} is also under active investigation and temperatures of up to 100 °C and above have been employed for the syntheses^{45,46,48} often intended to exploit the hydrophobic effect.⁴⁷ Water has a dielectric constant 78 at 25 °C which decreases to 20 at 300 °C; the latter value being comparable with that of the solvents, such as acetone, at ambient temperature.⁴⁸ Thus, water at elevated temperature can behave as a pseudo-organic solvent⁵³ and is a possible environmentally benign replacement for organic sol-

vents. In addition to the environmental advantages^{49,50} of using water instead of the organic solvents, isolation of the products is often facilitated by the decrease of the solubility of the organic material upon post-reaction cooling.⁵²

An alternative method for performing microwave-assisted organic reactions, termed enhanced microwave synthesis (EMS),⁵¹ has also been examined. By externally cooling the reaction vessel with compressed air, while simultaneously administering microwave irradiation, more energy can be directly applied to the reaction mixture. In the conventional microwave synthesis (CMS), the initial microwave power is high, increasing the bulk temperature (T_B) to the desired value very quickly. However, upon reaching this temperature, microwave power decreases or shuts off completely in order to maintain the desired bulk temperature without exceeding it. When microwave irradiation is off, classical thermal chemistry takes over, losing the full advantage of microwave irradiation, which is used to reach T_B faster. Microwave enhancement of chemical reactions will only take place during the application of the microwave energy. This source of energy will directly activate the molecules in a chemical reaction, and therefore it is not desirable to suppress its application. EMS ensures that a high, constant level of microwave energy is applied, resulting in the significantly greater yields and cleaner chemistries.

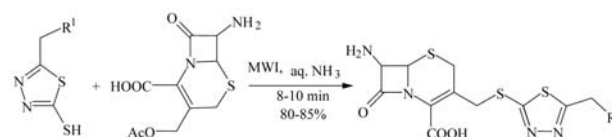
Recently, the combination of two prominent green chemistry principles, namely microwaves and water has become very popular and received substantial interest.

A plethora of very recent synthetic applications describes a variety of new chemistries that can be performed with microwave irradiation but a wide range of microwave-assisted applications is still waiting.⁵⁴ Many organic transformations proceed via radical chemistry. As chemists wonder if microwave irradiation can promote radical transformations, microwave-assisted free-radical chemistry is increasingly being explored.⁵⁵ Microwave irradiation is applicable not only to the solvent phase chemistry, but also to the solid-phase organic synthesis.

7.1.1. Examples of Microwave-Assisted Reactions Using Solvents

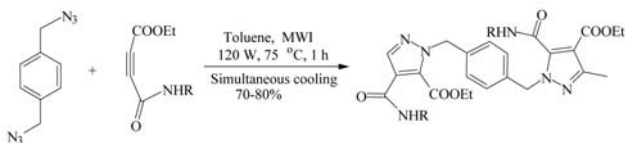
Nucleophilic substitution^{53,56}

Kidwai and co-workers examined the nucleophilic substitution reaction of an acetyl group with the SH group of a substituted thiadiazoles in aqueous ammonia for 8–10 min under microwave irradiation. The product was isolated in 80–85% yield.



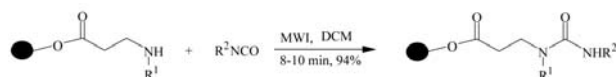
Cycloaddition reactions

1,3-Dipolar cycloadditions⁵⁷ are important reactions in organic synthesis. Cycloadducts were prepared by carrying out the reaction between an azide and a substituted amide in toluene. This reaction was carried out under microwave irradiation at 120 W at 75 °C for 1 h. The product was isolated in 70–80 % yield.



N-Acylations⁵⁸

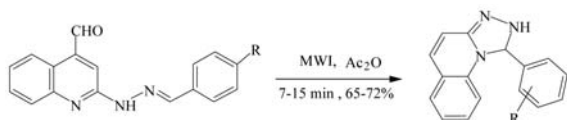
N-Acylations were carried out using secondary amines and isocyanate in dichloromethane under microwave irradiation (8–10 min), yielding the product in 94% yield.



Synthesis of Heterocycles

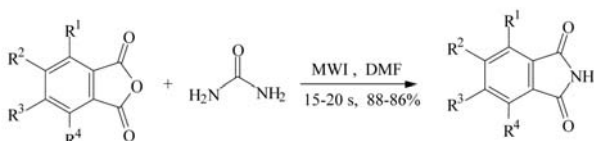
Synthesis of Triazoles^{59,60}

Synthesis of triazoles occupies a unique position in the organic synthesis. Substituted triazoles can be prepared in good yields (65–72%) by the cyclization of substituted hydrazines, carried out in acetic anhydride under microwave irradiation for 7–15 min.



Synthesis of Phthalimides⁶¹

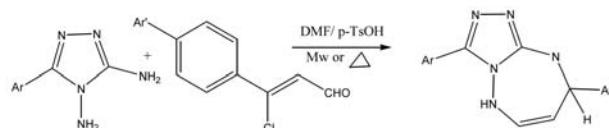
The synthesis of phthalimides was carried out by the reaction between benzophthalanhydrides and urea in DMF under microwave irradiation (15–20 s) with 86–88% yields.



Synthesis of Triazolo-Triazepines⁶²

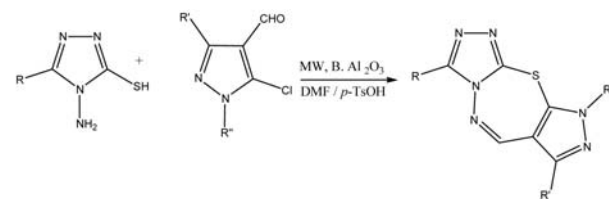
Synthesis of triazolo-triazepines is an important procedure in heterocyclic chemistry. These compounds possess a broad spectrum of biological activities. Gupta synthesized triazolo-triazepines by the condensation reaction between 5-aryl-3,4-diamino-1,2,4-triazole and β-chlorocinnamaldehyde in the presence of a catalytic amount of *p*-TsOH under microwave as well as conventio-

nal heating. The products were isolated in good yields.



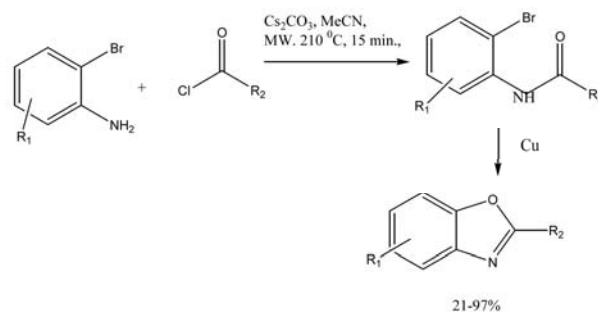
Synthesis of Triazolo-Thiadiazepines⁶³

Gupta and co-workers have reported an efficient synthesis of triazolo-thiadiazepines under microwave irradiation. These reactions have been carried out by irradiating a mixture of triazole, 5-chloro-1*H*-2-pyrazole-4-carbaldehyde, basic alumina and DMF at 640 W.



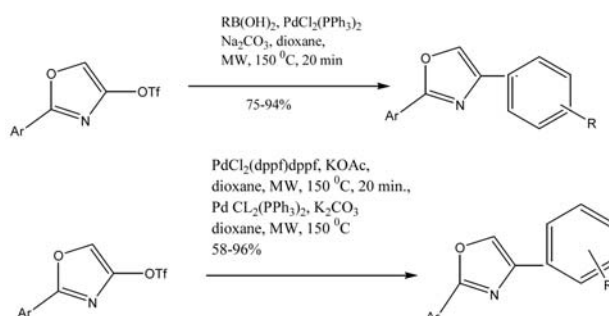
Synthesis of Benzoxazole⁶⁴

Batey carried out a copper catalyzed one-pot synthesis of benzoxazoles using bromoanilines and acyl halides in the presence of a base and a solvent giving intermediates which finally gave pure benzoxazoles (21–97% isolated yields), exhibiting a broad range of biological activities. They can also be used as precursors in the synthesis of drugs. Similarly, syntheses of benzoxazoles have also been carried out.^{65,66}



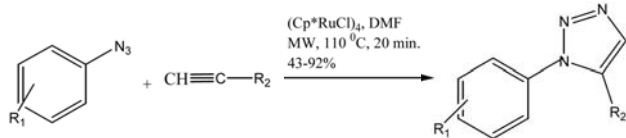
Synthesis of Oxazoles⁶⁷

There is also a report on Suzuki coupling giving oxazoles in 75–94% isolated yields.



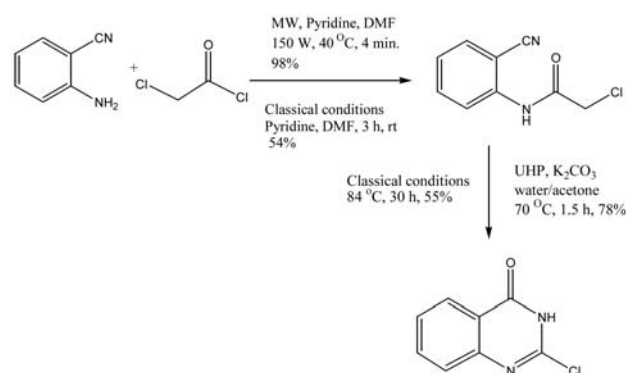
Synthesis of Substituted Triazoles⁶⁸

Fokin et al. reported the formation of substituted triazoles using aryl azides and alkynes using a solvent affording the products in 43–92% isolated yields.



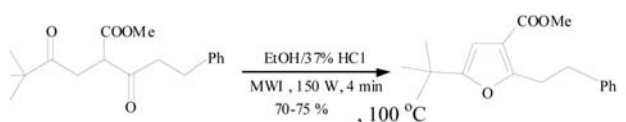
Synthesis of Quinazolines⁶⁹

Vanelle and co-workers have reported a microwave-assisted green synthesis of quinazoline derivatives possessing anticancer activity. The products were obtained via an S_NR1 reaction.



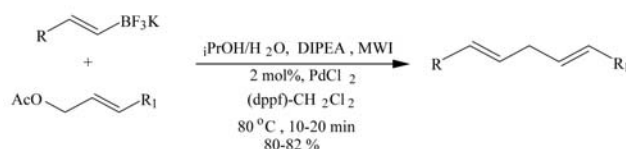
Paal–Knorr Condensation⁷⁰

Paal–Knorr synthesis is an important way towards substituted furans, starting from dicarbonyl compounds. Under microwave irradiation (solvent-free, 100 °C, 4 min at 150 W) using EtOH and 37% HCl, products were obtained in 70–75% isolated yields.



Synthesis of 1,4-Pentadiene⁷¹

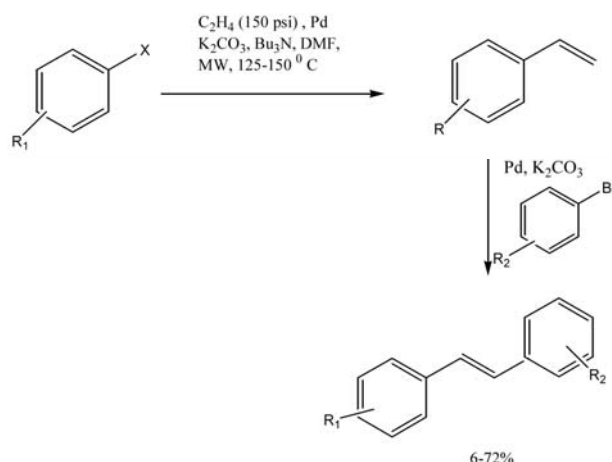
Synthesis of 1,4-pentadiene can start from two unsymmetrical alkenes in the presence of isopropanol, 2 mol % palladium chloride under microwave irradiation under solvent-free conditions at 80 °C for 10–20 min yielding 1,4-pentadienes in 80–82% yields.



Synthesis of Non-Symmetrically Substituted Stilbenes⁷²

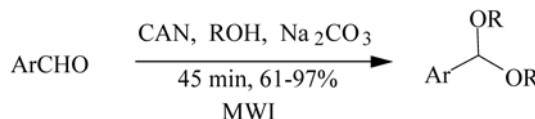
Leadbeater and co-workers prepared non-symmetrically substituted stilbenes using a base and a solvent un-

der irradiation with microwaves, products were isolated in 6–72% yields.



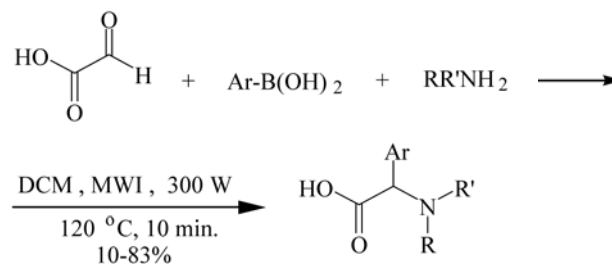
Protection of Aldehydes^{73,74}

Protection and deprotection plays a pivotal role in organic synthesis. Protection reactions of aldehydes with alcohols are performed using ceric ammonium nitrate (CAN) and sodium carbonate under microwave irradiation (45 min). Protected products are obtained in 61–97% yields.



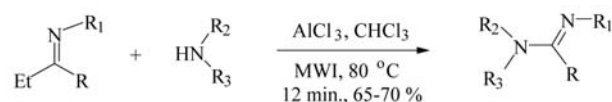
Three-Component Petasis Boronic-Mannich Reaction⁷⁵

Three-component Petasis boronic-Mannich reaction is carried out between glyoxal, aryl boronic acids and substituted primary amines. It was observed that substituted amines are formed under microwave irradiation (300 W, 120 °C, 10 min) in 10–83% yields.



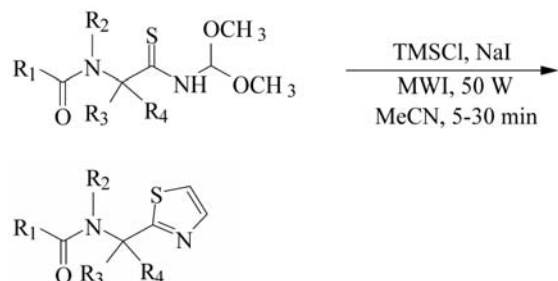
Synthesis of Polysubstituted Amidines⁷⁶

Polysubstituted amidines are synthesized from secondary amines and substituted nitriles using aluminum chloride in chloroform under microwave irradiation (80 °C, 12 min) in 65–70% yields.



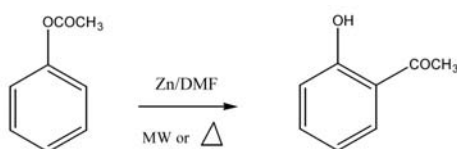
Synthesis of Endothiopeptides⁷⁷

Syntheses of endothiopeptides are carried out by the cyclization of a substituted thiourea in trimethyl silylchloride with sodium iodide under microwave irradiation (50 W, 5–30 min). The products were isolated in quantitative yields.



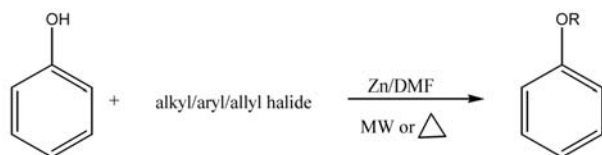
Fries Rearrangement⁷⁸

Fries rearrangement occupies a unique place in both industry as well as in academia. Paul and Gupta studied this rearrangement of substituted aryl acetates using Zn and DMF under both microwave and conventional heating. The products were formed in excellent yields.



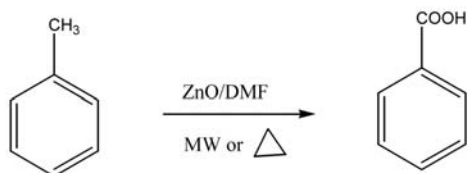
Williamson Ether Synthesis⁷⁹

Williamson ether synthesis, an important organic reaction for their preparation, can be carried out between alkyl, aryl or allyl halides and phenols using Zn in DMF under microwave irradiation (800 W, 2–15 min) yielding ethers in excellent yields.



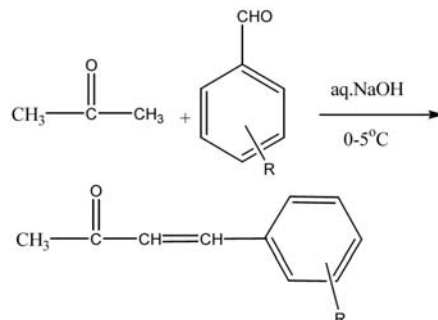
Oxidation of Alkyl Benzene⁸⁰

Oxidation of toluene was studied using ZnO/DMF reagent under microwave irradiation (800 W, 3–15 min). This method was also found to be effective under conventional heating. Moreover, benzoic acid was obtained in a good yield.



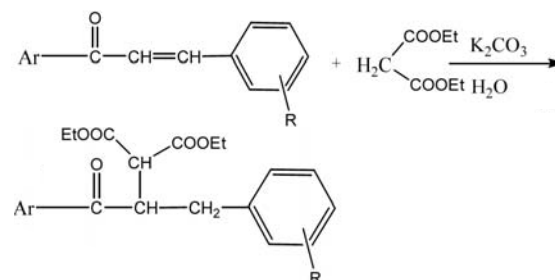
Synthesis of Monosubstituted Chalcones⁸¹

Selective reactions occupy an important place in organic synthesis. Chalcones were found to be useful precursors for flavonoids, perfumes and in the synthesis of heterocycles. Syntheses of monosubstituted chalcones are carried out by the reaction between acetone and aryl aldehydes using aqueous sodium hydroxide at 0–5 °C. This was found to be a simple, efficient and selective procedure for the synthesis of monosubstituted chalcones.



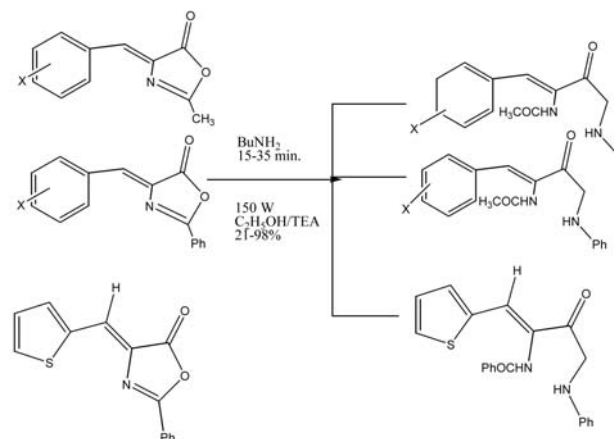
Michael Addition⁸²

Michael addition is an important reaction for C–C bond formation; it can be carried out using chalcones and compounds with active methylene groups in the presence of K₂CO₃ and H₂O under microwave irradiation (480 W, 1–3 min) yielding the products in good yields.



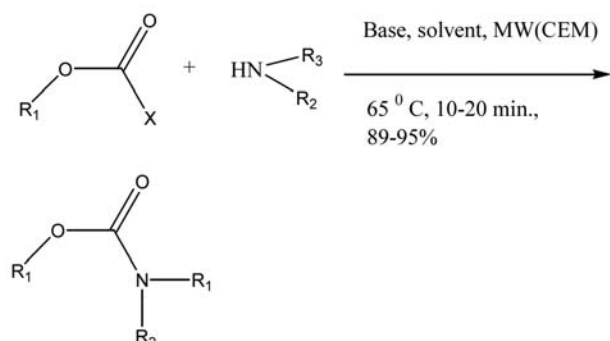
Ring Opening of Azalactones⁸³

Valdes and co-workers have reported the microwave-assisted ring opening of azalactones. Reaction was carried out in a solvent under microwave irradiation (150 W) yielding the products in a pure state with 1–98% isolated yields.



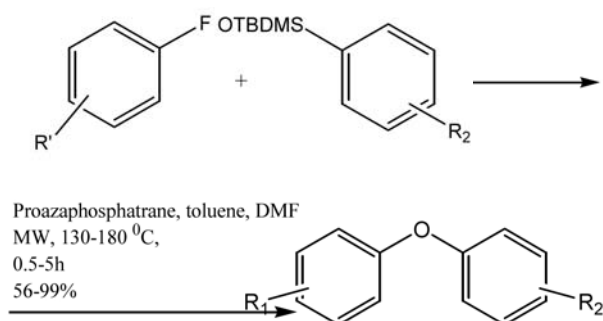
Carbamoylation of Amines⁸⁴

Dettori and co-workers reported the microwave-assisted carbamoylation of amines using a base and a solvent giving the products in 89–95% isolated yields.



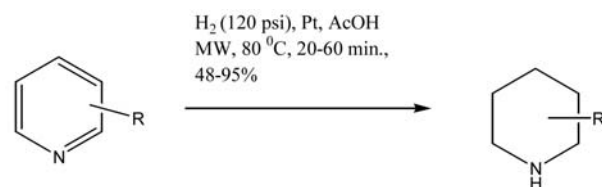
Synthesis of Diaryl Ethers⁸⁵

Verkade and Raders synthesized diaryl ethers in 56–99% isolated yield using prophosphatane under microwaves (0.5–5 h). These products are of great importance in the synthesis of flavonoids, also gaining attraction in academia.



Hydrogenation of Pyridines⁸⁶

Taddei hydrogenated pyridines affording cyclic amines in 48–95% isolated yield.



7. 1. 2. Microwave-Assisted Reactions Under Solvent-Free Conditions

Due to the environmental concerns, there has currently been an increasing demand for efficient synthetic processes and solvent-free reactions. Some old and new methodologies are being used to diminish and prevent pollution caused by chemical activities. In this context, the microwaves have become an important source of energy in many laboratory procedures.⁸⁷

Furthermore, microwave-assisted solvent-free organic synthesis (MASFOS) has been developed as an environmentally friendly process as it combines the selectivity associated with most reactions carried out under microwaves with solvent and waste-free procedures in which organic solvents are avoided throughout all stages.⁸⁸

In these environmentally conscious days, the research and development are directed towards devising cleaner processes. Environmental hazards and the subsequent degradations are instrumental for the rapid evolution of green chemistry concept involving benign reagents and conditions. The MASFOS reactions are of three types:

- reactions using neat reactants;
- reactions using solid-liquid phase transfer catalysis (PTC);
- reactions using solid mineral supports.

7. 1. 2. 1. Reactions Using Neat Reactants

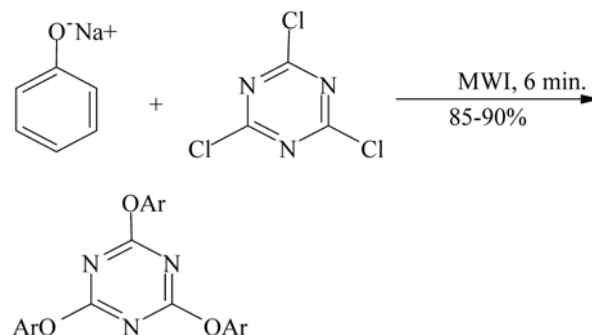
For carrying out reactions with neat reactants i.e. without the use of a solvent or a support (heterogeneous reactions), at least one of the reactants at the reaction temperature should normally be liquid. In such a set-up, either the solid is partially soluble in the liquid phase or the liquid is adsorbed onto the surface of solid with the reaction occurring at the interface. There is also another possibility, namely that both the reactants are solid. Usually, they melt during the reaction course and then undergo reaction as described above.⁸⁹

7. 1. 2. 1. 1. Examples of the Reactions with Neat Reactants

Aromatic Nucleophilic Substitutions

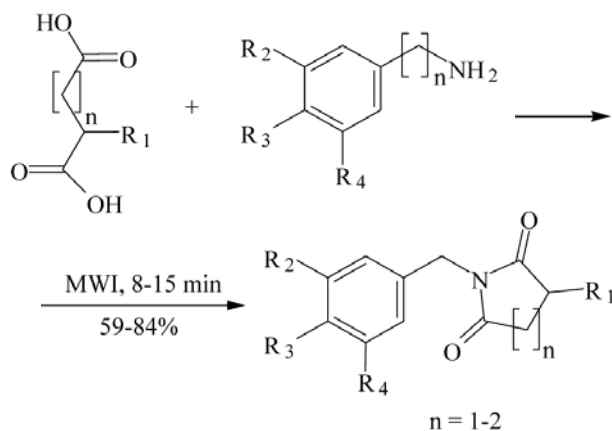
Formation of Substituted Triazines^{90,91}

Aromatic nucleophilic substitutions are carried out using sodium phenoxide and 1,3,5-trichlorotriazine under microwave irradiation (6 min). The products, 1,3,5-triarylloxytriazines are obtained in 85–90% yields.



N-Acylation⁹²

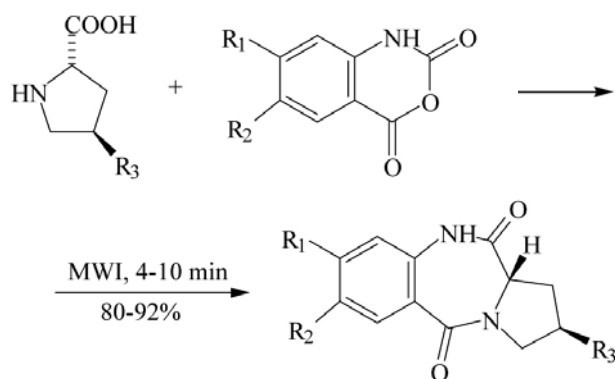
N-Acylation can be carried out between amines and poly acids under microwave irradiation (8–15 min) under solvent-free conditions giving the products in 59–84% yields.



Synthesis of Heterocycles

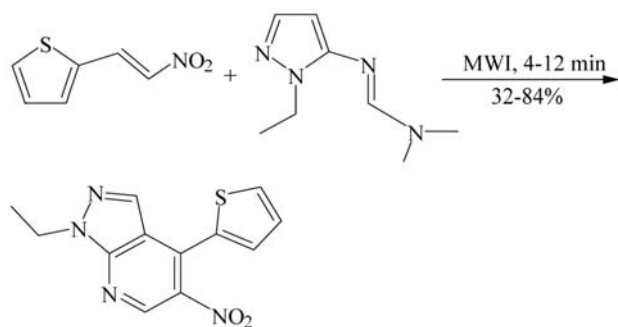
Synthesis of Benzodiazepine^{93,94}

Seven membered ring systems possess a broad spectrum of biological activities, such as antifungal, antiviral and anti-inflammatory activities. Syntheses of benzodiazepines can be carried out under microwave irradiation (4–10 min) in solvent-free conditions giving the products in 80–92% yields. Due to the solvent-free conditions, without support and because of the increased yields, the synthesis is a part of green chemistry.



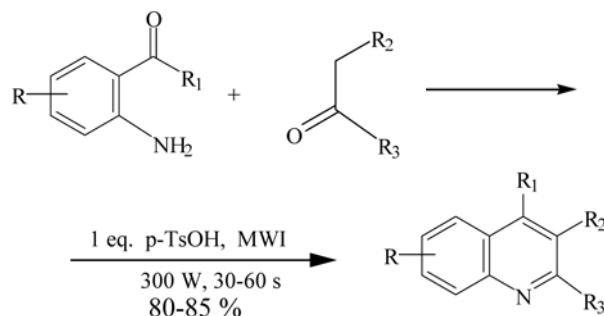
Synthesis of Pyridines⁹⁵

Díaz-Ortiz and co-workers studied the synthesis of substituted pyridines under solvent-free conditions starting from thiophenes and pyrazoles under microwave irradiation (4–12 min), leading in 32–84% isolated yields to the required pyridines.



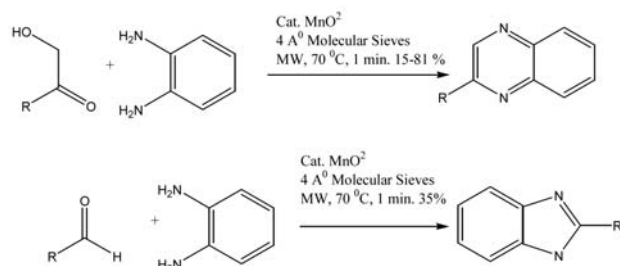
Synthesis of Poly-Substituted Quinolines⁹⁶

Substituted quinolines possess a broad spectrum of biological activities. Their synthesis can be carried out between anthranilic acids and unsymmetrical ketones in the presence of *p*-TsOH under microwave irradiation (300 W, 30–60 s), with isolated yields of 80–85%.



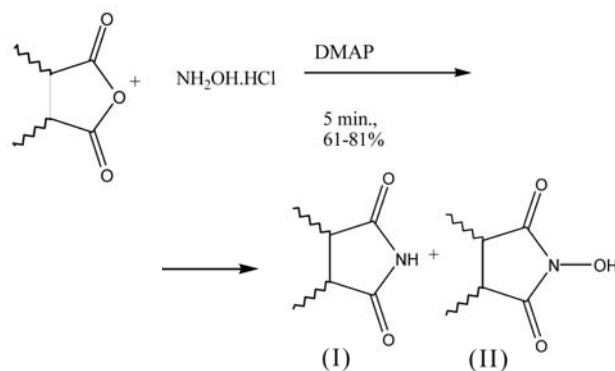
Synthesis of Quinoxaline⁹⁷

A synthesis of quinoxalines using manganese oxide as the catalyst and molecular sieves under microwave irradiation affording the products in 15–81% isolated yields was reported.



Synthesis of Unsubstituted Cyclic Imides⁹⁸

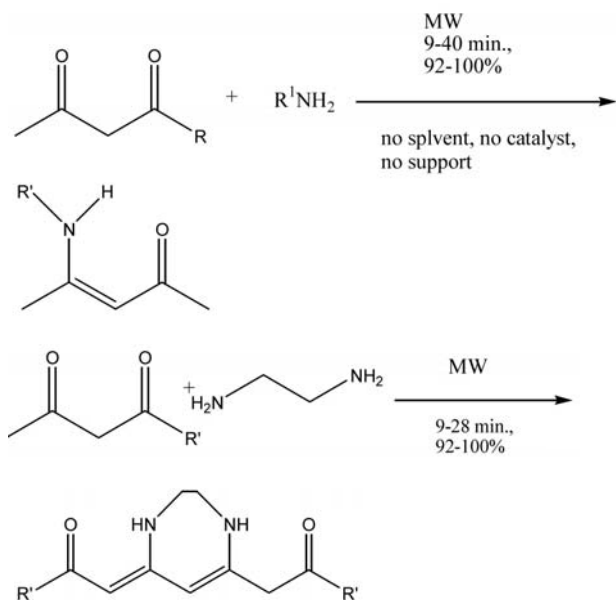
A synthesis of polysubstituted cyclic imides using microwave irradiation affording the product (I) in 61–81% yields was reported.



Synthesis of Enamines⁹⁹

Ranu and co-workers have performed the synthesis of enamines under MW irradiation (9–40 min) without any solvent, catalyst and support. The enamines, including cyclic, were synthesized in 92–100% yields.

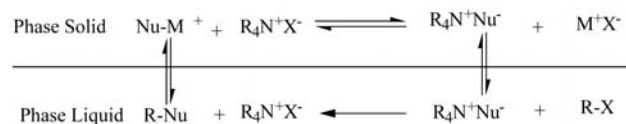
7. 1. 2. 2. Reactions Using Solid-Liquid Phase



Transfer Catalysis (PTC)

Solid-liquid phase transfer catalysis (PTC) has been described as an effective method in organic synthesis and is under active investigation.⁹⁵⁻⁹⁷ This method is specific for anionic reactions as it involves “anionic activation”. A catalytic amount of a tetralkylammonium salt or a cation complexing agent is added to the mixture (in equimolar amounts) of both pure reactants. Reactions occur in the liquid organic phase, which consists here only of the electrophile R–X (then possibly to the product R–Nu). The presence of an additional liquid component (solvent) is disadvantageous as it induces a dilution of reactants and consequently a decrease in reactivity. The electrophile R–X is therefore both the reactant and the organic phase for the reaction. (See Scheme 2)

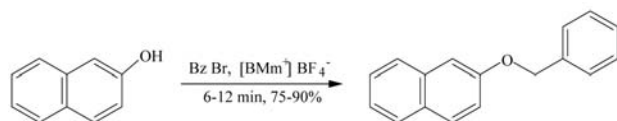
7. 1. 2. 2. 1. Examples of the Reactions Using PTC



Alkylations

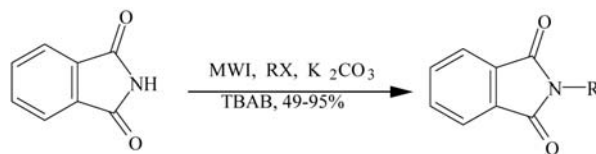
O-Alkylation¹⁰⁰

Preparations of ethers were carried out from β -naphthol using benzyl bromide and 1-butyl-3-methylimidazolium tetrafluoroborate under microwave irradiation (6–12 min), the products were isolated in 75–90% yields.



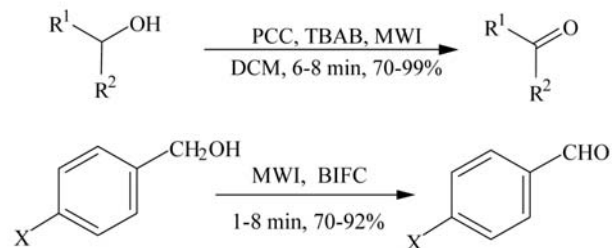
N-Alkylations¹⁰¹

N-Alkylations under microwave irradiation using phase transfer catalysts occupy a unique place in organic chemistry. Bogdał and co-workers reported the synthesis of N-alkyl phthalimides using phthalimide, alkyl halides, potassium carbonate and TBAB; giving products in 45–98% yields.



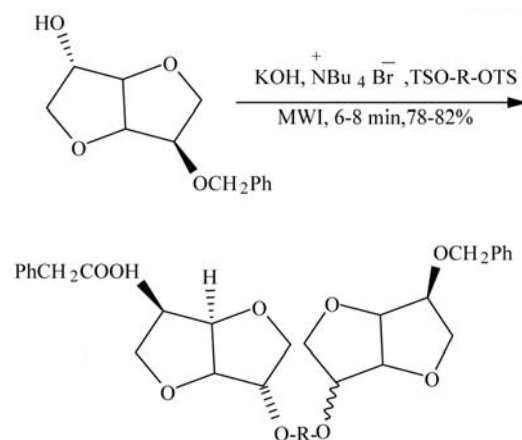
Oxidations¹⁰²

Chakraborty reported the oxidation of secondary alcohol and benzyl alcohols using phase transfer catalysts. Oxidation of secondary alcohols to acetone derivatives was carried out using PCC, tetrabutylammonium bromide and dichloromethane under microwave irradiation (6–8 min), products were isolated in 70–99% yields. Oxidation of benzyl alcohols was conducted using BIFC under microwave irradiation (1–8 min) yielding benzaldehyde derivatives in 70–92% yields.



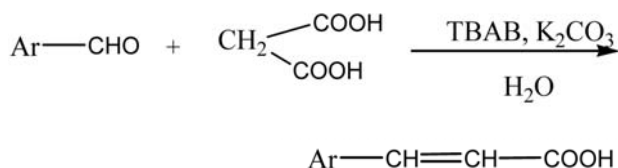
Alkylation of Dianhydrohexitols¹⁰³

Alkylation of dianhydrohexitols was carried out using potassium hydroxide, tetrabutylammonium bromide and alkyl tosylates under microwave irradiation (6–8 min), products were isolated in 78–82% isolated yields.

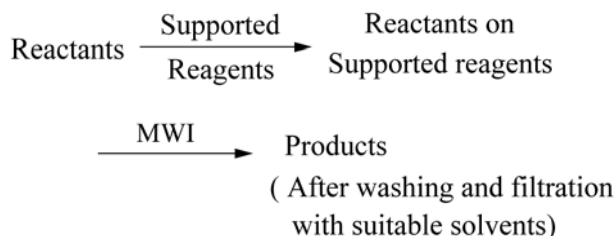


Knoevenagel Condensation¹⁰⁴

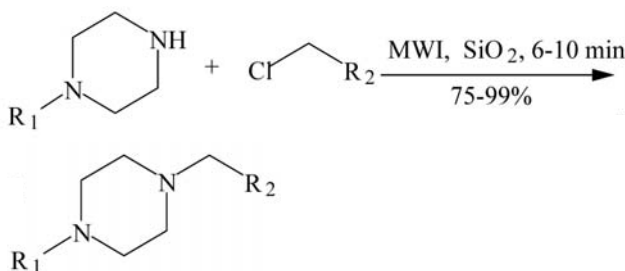
Knoevenagel condensation is a well known organic reaction, often applied in the synthesis of unsaturated acids, which are used as precursors for perfumes, flavonoids and as building blocks of many heterocycles. Gupta and Wakhloo studied Knoevenagel condensation between carbonyl compounds and active methylene compound, such as malonic acid, using tetrabutylammonium bromide, potassium carbonate in water forming unsaturated acids in excellent yields and purity under microwave irradiation.

**7. 1. 2. 3. Reactions on Solid Mineral Supports in Dry Media**

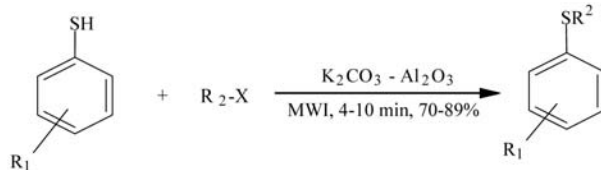
Solid supports are often very poor conductors of heat but behave as very efficient microwave absorbers. This, in turn results in very rapid and homogeneous heating. Consequently, they display very strong specific microwave effect with significant improvement in temperature homogeneity and heating rates enabling faster reactions and less degradation of final products as compared to the classical heating.

**7. 1. 2. 3. 1. Examples of Microwave Activation With Supported Reagents****Alkylations*****N*-Alkylations**¹⁰⁵

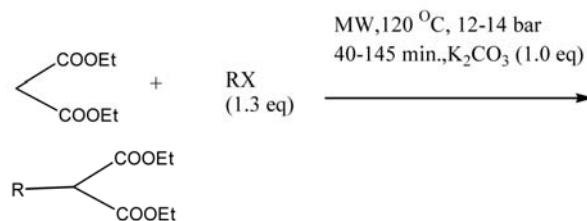
N-Alkylations were carried out between piperidines and chloroalkanes in the presence of silica as the solid support under microwave irradiation (6–10 min). *N*-Alkyl products were isolated in 75–99% yields.

***S*-Alkylations**¹⁰⁶

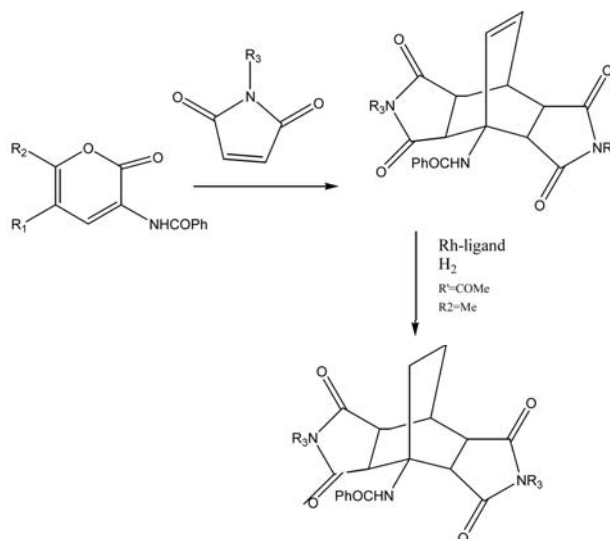
S-Alkylation was studied and accomplished by carrying out the reaction between mercaptobenzenes and alkyl halides using potassium carbonate and alumina under microwave irradiation (4–10 min). Products were isolated in 70–89% yields.

***C*-Alkylations**¹⁰⁷

Keglevich and co-workers have reported the *C*-alkylation by subjecting a mixture of diethyl malonate and alkyl halides to microwave irradiation in the presence of potassium carbonate. The products were obtained in good to excellent yields and were characterized by spectroscopic methods.

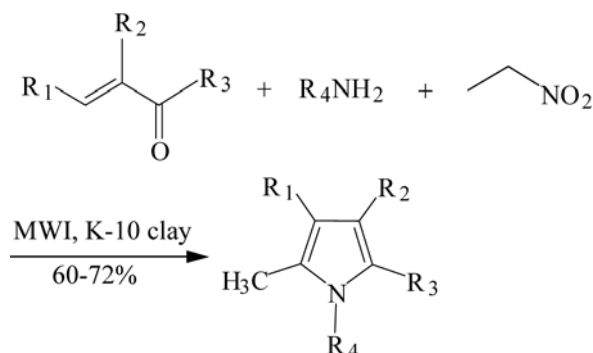
**Cycloaddition Reactions**¹⁰⁸

Kočevar and co-workers have reported the microwave-assisted Diels–Alder cycloaddition reaction and heterogeneous hydrogenation sequence in water and under solvent-free conditions (without solid support). Products were obtained in good to excellent yields.

**Synthesis of Heterocycles****Synthesis of Pyrroles**¹⁰⁹

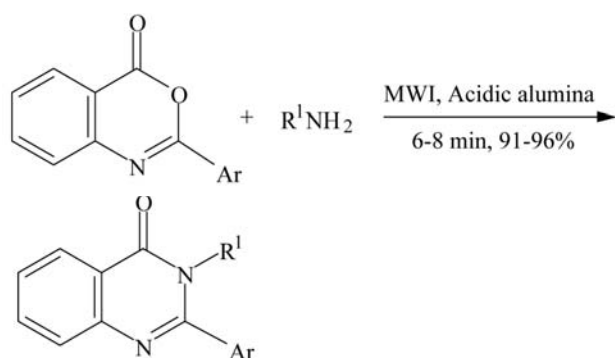
Pyrroles are associated with a vast range of biological activities. Synthesis of pyrroles was studied by carr-

ying out the reaction between α,β -unsaturated ketones, alkylamines and nitroalkanes using K-10 clay under microwave irradiation, forming the substituted pyrroles in 60–72% yields.



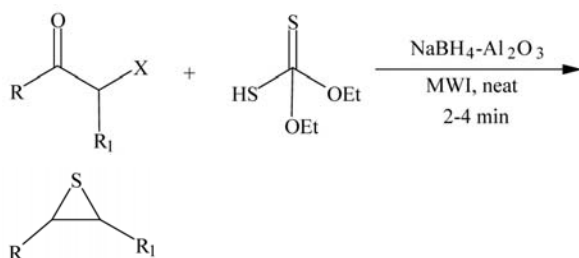
Synthesis of Quinazolin-4(3H)-ones¹¹⁰

Synthesis of substituted quinazolines was carried out using a substitution reaction between lactones and alkylamines using acidic alumina under microwave irradiation (6–8 min), giving the products in 91–96% yields.



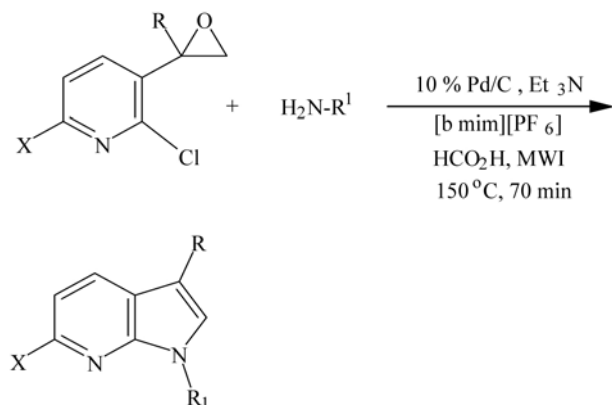
Synthesis of Thiiranes¹¹¹

A synthesis of thiiranes was reported that applied sodium borohydride and alumina under microwave irradiation, forming the products in excellent yields.



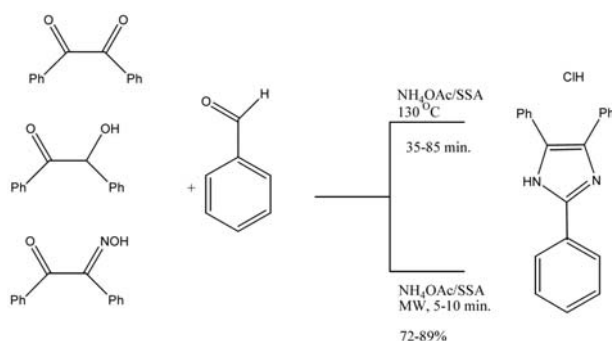
Synthesis of 1,3- and 1,3,6-Trisubstituted-7-Azaindoles¹¹²

Many syntheses of azaindoles were reported in the literature. They were prepared by the reaction of a substituted pyridine and primary amine in the presence of a palladium species, triethylamine, formic acid in an ionic liquid under microwave irradiation (150 °C, 70 min). Products were obtained in excellent yields.



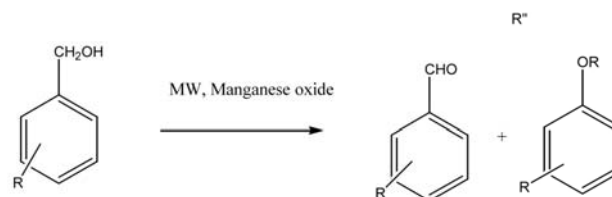
Synthesis of Trisubstituted Imidazoles¹¹³

Shaabani and co-workers have reported a silica-supported sulphuric acid-promoted one-pot synthesis of trisubstituted imidazoles. Comparative studies between conventional and microwave irradiation indicate that products were obtained in excellent yields under microwave irradiation.



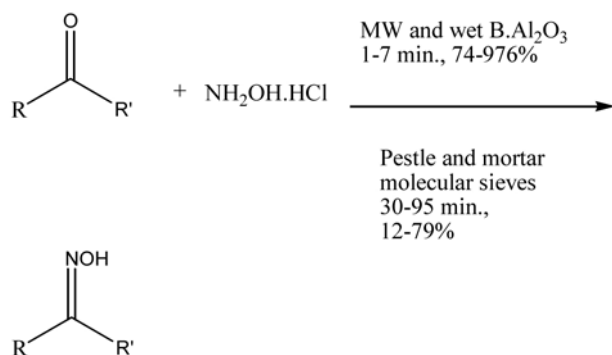
Oxidation of Benzyl Alcohols¹¹⁴

Su and co-workers have reported an oxidation of benzyl alcohols to aldehydes and ethers. Both were formed in a selective fashion under microwave irradiation using manganese oxide as the catalyst.



Protection of Carbonyl Compounds¹¹⁵

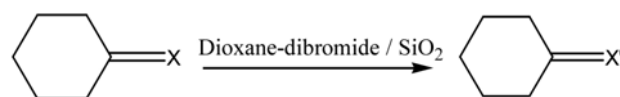
Kad and co-workers have executed the protection of carbonyl compounds under solvent-free conditions (green chemistry). Comparative studies were carried out for the protection of carbonyl compounds using microwave irradiation and by grinding at room temperature. Products were isolated after a short time and in excellent yields under microwave irradiation.



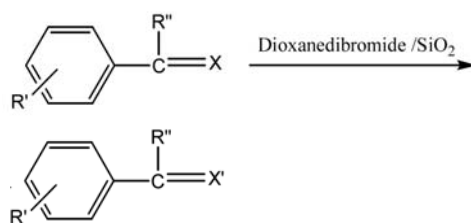
Deprotection

Regeneration of Carbonyl Compounds From Nitrogenous Derivatives¹¹⁶

This was carried out by irradiating (320 W) a mixture of phenylhydrazone or semicarbazone and dioxane-dibromide and silica gel. Highly pure products were obtained in good to excellent yields.

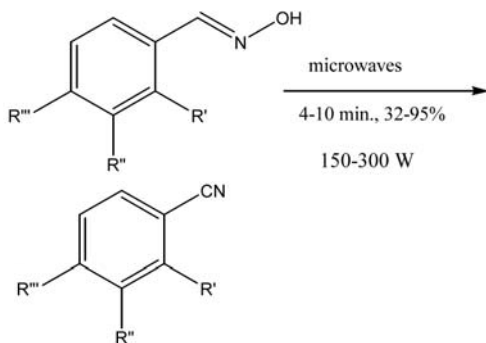


X = NOH, X' = O



Deprotection of Oximes to Nitriles¹¹⁷

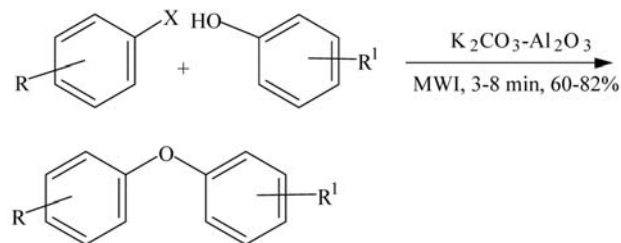
Hegedüs and co-workers have done a deprotection of oximes in the presence of zeolites under microwave irradiation. The regenerated products were obtained in excellent yields.



Synthesis of Diaryl Ethers¹¹⁸

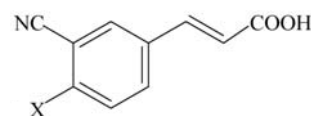
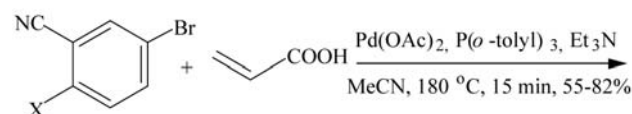
Syntheses of diaryl ethers find a unique place in both industry and academia. This synthesis was carried out between aryl halides and phenols using potassium carbonate and alumina under microwave irradiation (3–8

min), diaryl ethers were formed in 60–82% isolated yields.

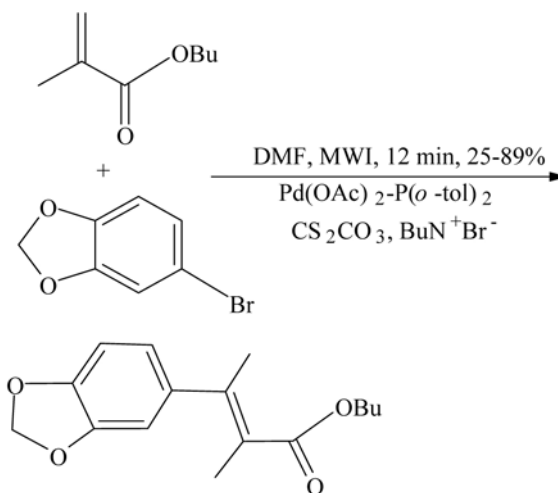


Heck Reaction¹¹⁹

Heck reaction is an important organic transformation used for the formation of C–C bond. It was carried out between acrylic acid and aryl bromides using a palladium complex, acetonitrile and triethylamine under microwave irradiation (180 °C, 15 min). Unsaturated acids were obtained in 55–82% yield.

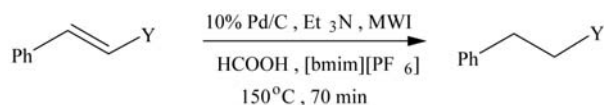


It can also be carried out between an alkene and aryl bromide using DMF, palladium acetate, caesium carbonate and tetrabutylammonium bromide under microwave irradiation (12 min) giving the product in 25–89% yield.



Palladium-Catalyzed Catalytic Transfer Hydrogenation¹²⁰

Palladium catalyzed catalytic hydrogenation of alkenes was carried out using Pd/C, triethylamine, formic acid and an ionic liquid under microwave irradiation (150 °C, 70 min). Products were formed in excellent yields.



8. Conclusion

Microwave-assisted organic synthesis is a technique which can be used to rapidly explore chemistry space and increase the diversity of compounds produced. The examples cited above are impressive and provide a good insight into the field of microwave-assisted organic synthesis.

The benefits of microwave-assisted organic synthesis are increasingly making the technique more established worldwide. In order to achieve further development in this field, novel instruments, which give rise to reproducible performances and that constitute a minimal hazard should be used instead of the domestic microwave ovens.

9. References

1. F. Harvey, *Microwave Engineering*, Academic Press, New York, **1963**.
2. A. G. Horeis, S. Pichler, A. Stadler, W. Gössler, C. O. Kappe, *Microwave-Assisted Organic Synthesis – Back to the Roots* Fifth International Electronic Conference on Synthetic Organic Chemistry (ECSOC-5), <http://www.mdpi.org/ecsoc-5.htm>, 1–30 September 2001.
3. D. M. P. Mingos, *Chem. Ind.* **1994**, 596–599.
4. (a) A. de la Hoz, Á. Díaz-Ortiz, A. Moreno, *Chem. Soc. Rev.* **2005**, *34*, 164–178. (b) A. G. Whittaker, D. M. P. Mingos, *J. Power Electromagn. Energy* **1994**, *29*, 195–199. (c) K. C. Westaway, R. N. Gedye, *J. Microwave Power Electromagn. Energy* **1995**, *30*, 219–223.
5. (a) R. N. Gedye, J. B. Wei, *Can. J. Chem.* **1998**, *76*, 525–527. (b) R. S. Varma, *Green Chem.* **1999**, *1*, 43–55.
6. (a) D. M. P. Mingos, A. G. Whittaker, *Microwave Dielectric Heating Effects in Chemical Synthesis, in Chemistry under Extreme or Non-Classical Conditions*, Ed., R. V. Van Malik, C. D. Hubbard, John Wiley and Sons and Spektrum Akademischer Verlag Co-Publication, New York and Heidelberg, 1997, 479. (b) D. M. P. Mingos, D. R. Baghurst, *Applications of Microwave Dielectric Heating Effects to Synthetic Problems in Chemistry, in Microwave Enhanced Chemistry*, Ed., H. M. Kingston, S. J. Hazel, ACS, Washington D. C., 1997, 455.
7. (a) M. Nüchter, B. Ondruschka, A. Jungnickel, U. Müller, *J. Phys. Org. Chem.* **2000**, *13*, 579–586. (b) M. Nüchter, B. Ondruschka, W. Lautenschlager, *Synth. Commun.* **2001**, *37*, 1277–1283.
8. J. W. Vanderhoff, *U. S. 3*, **1969**, 432, 413; *Chem. Abstr.* **1969**, *70*, 97422v.
9. R. Gedye, F. Smith, K. Westaway, H. Ali, L. Baldisera, L. Laberge, J. Rousell, *Tetrahedron Lett.* **1986**, *27*, 279–282.
10. R. J. Giguere, T. L. Bray, S. M. Duncan, G. Majetich, *Tetrahedron Lett.* **1986**, *27*, 4945–4948.
11. D. M. P. Mingos, D. R. Baghurst, *Chem. Soc. Rev.* **1991**, *20*, 1–47.
12. S. C. Ameta, S. Mehta, A. Sancheti, J. Vardia, *J. Indian Chem. Soc.* **2004**, *81*, 1127–1140.
13. C.-J. Li, *Chem. Rev.* **1993**, *93*, 2023–2035.
14. C. O. Kappe, D. Dallinger, *Nat. Rev. Drug Discovery* **2006**, *5*, 51–63.
15. V. Polshettiwar, R. S. Varma, *Acc. Chem. Res.* **2008**, *41*, 629–639.
16. V. Polshettiwar, R. S. Varma, *Chem. Soc. Rev.* **2008**, *37*, 1546–1557.
17. S. A. Galema, B. S. J. Halstead, D. M. P. Mingos, *Chem. Soc. Rev.* **1998**, *27*, 213–232.
18. R. Trotzki, M. Nüchter, B. Ondruschka, *Green Chem.* **2003**, *5*, 285–290.
19. S. Horikoshi, T. Hamamura, M. Kajitani, M. Yoshizawa-Fujita, N. Serpone, *Org. Process Res. Dev.* **2008**, *12*, 1089–1093.
20. R. S. Varma, *Green Chem.* **1999**, *1*, 43–55.
21. R. N. Gedye, F. E. Smith, K. C. Westaway, *Can. J. Chem.* **1988**, *66*, 17–26.
22. H. M. Kingston, L. B. Jassie, *Introduction to Microwave Sample Preparation*; ACS, Washington D. C., **1988**, ch. 2, pp 110–122.
23. E. D. Neas, M. J. Collins, in *Introduction to Microwave Sample Preparation*; ACS Washington D. C., **1988**, ch. 21, pp 10–18.
24. R. S. Varma, *Advances in Green Chemistry Chemical Syntheses using Microwave Irradiation*, Astra Zeneca Research Foundation India, Bangalore, **2002**.
25. *Microwaves in Organic Syntheses*, ed. A. Loupy, Wiley-VCH, Weinheim, **2002**.
26. A. Loupy, A. Petit, J. Hamelin, F. Texier-Boulett, P. Jacquault, D. Mathé, *Synthesis* **1998**, 1213–1234.
27. D. R. Baghurst, D. M. P. Mingos, *J. Chem. Soc., Chem. Commun.* **1992**, 674–677.
28. S. A. Galema, *Chem. Soc. Rev.* **1997**, *26*, 233–238.
29. A. Loupy, *Spectra Analysis* **1993**, *33*, 175–177.
30. A. Loupy, A. Petit, Pelin-Sud, *Special Researches*, **1997**, Universite Paris-Sud, 84.
31. S. Caddick, *Tetrahedron* **1995**, *51*, 10403–10432.
32. D. Villemin, F. Thibault-Starzyk, *J. Chem. Edu.* **1984**, *68*, 346–346.
33. I. Plazl, *Acta Chim. Slov.* **1994**, *41*, 437–445.
34. I. Plazl, S. Leskovšek, T. Koloini, *Chem. Eng. J.* **1995**, *59*, 253–257.
35. I. Plazl, *Ind. Eng. Chem. Res.* **2002**, *41*, 1129–1134.
36. I. Plazl, G. Pipuš, T. Koloini, *AIChE J.* **1997**, *43*, 754–760.
37. L. D. S. Yadav, R. Kapoor, *Synthesis* **2002**, 2344–2346.
38. Z. Zhang, X. Li, *Shenyang Yaoke Daxue Xuebao*, **1999**, *16*, 304–309.
39. J. Andrews, G. F. Atkinson, *J. Chem. Edu.* **1984**, *61*, 177–178.
40. R. Breslow, *Acc. Chem. Res.* **1991**, *24*, 159–164.

41. P. A. Grieco, *Aldrichimica Acta* **1991**, *24*, 59–66; *Chem. Abstr.* **1992**, *116*, 99425r.
42. A. K. Bose, M. S. Manhas, B. K. Banik, E. W. Robb, *Res. Chem. Intermed.* **1994**, *20*, 1–11.
43. A. K. Bose, B. K. Banik, N. Lavlinskaia, M. Jayaraman, M. S. Manhas, *Chem. Tech.* **1997**, *27*, 18–24.
44. A. Lubineau, J. Auge, Y. Queneau, *Synthesis* **1994**, 741–760.
45. P. A. Grieco, E. B. Brandes, S. McCann, J. D. Clark, *J. Org. Chem.* **1989**, *54*, 5849–5851.
46. R. Laurent, A. Laporterie, J. Dubac, J. Balam, S. Lefeuvre, M. Audhuy, *J. Org. Chem.* **1992**, *57*, 7099–7102.
47. W. Blokzijl, J. B. F. N. Engberts, *Angew. Chem., Int. Ed.* **1993**, *32*, 1545–1579.
48. M. Martelanc, K. Kranjc, S. Polanc, M. Kočevar, *Green Chem.* **2005**, *7*, 737–741.
49. E. M. Kirschner, *Chem. Eng. News* **1994**, *72*, 13–17.
50. D. L. Illman, *Chem. Eng. News* **1994**, *72*, 22–25.
51. M. A. Herrero, J. M. Kreamsner, C. O. Kappe, *J. Org. Chem.* **2008**, *73*, 36–47.
52. J. Hren, K. Kranjc, S. Polanc, M. Kočevar, *Synthesis* **2008**, 452–458.
53. L. Williams, *Chem. Commun.* **2000**, 435–436.
54. J. D. Forgyson, *Innovations in Pharmaceutical Technology* **2003**, 78.
55. S. Kaur, *Thesis submitted by Texas*, **2003**.
56. M. Kidwai, K. R. Bhushan, P. Misra, *Chem. Lett.* **1999**, 487–488.
57. A. R. Katritzky, Y. Zhang, S. K. Singh, P. J. Steel, *Arkivoc* **2003**, (xv), 47–64.
58. (a) A. Vass, J. Dudás, R. S. Varma, *Tetrahedron Lett.* **1999**, *40*, 4951–4954. (b) L. Perreux, A. Loupy, F. Volatron, *Tetrahedron* **2002**, *58*, 2155–2162. (c) A. Loupy, D. Monteux, A. Petit, J. M. Azipurua, E. Domínguez, C. Palomo, *Tetrahedron Lett.* **1996**, *37*, 8177–8180. (d) A. R. Hajipour, S. E. Mallakpour, A. Afrousheh, *Tetrahedron* **1999**, *55*, 2311–2316. (e) S. Frère, V. Thiéry, T. Besson, *Tetrahedron Lett.* **2001**, *42*, 2791–2794. (f) J. A. Vega, J. J. Vaquero, J. Alvarez-Builla, J. Ezquerro, C. Handouchi, *Tetrahedron* **1999**, *55*, 2317–2326. (g) A. Díaz-Ortiz, P. Prieto, A. Loupy, D. Abenhaim, *Tetrahedron Lett.* **1996**, *37*, 1695–1698. (h) C. Limousin, J. Cléophax, A. Loupy, A. Petit, *Tetrahedron* **1998**, *54*, 13567–13578. (i) K. Bougrin, A. Loupy, A. Petit, B. Daou, M. Soufiaoui, *Tetrahedron* **2001**, *57*, 163–168. (j) S. Paul, M. Gupta, R. Gupta, A. Loupy, *Tetrahedron Lett.* **2001**, *42*, 3827–3829. (k) K. G. Kabza, B. R. Chapados, J. E. Gestwicki, J. L. McGrath, *J. Org. Chem.* **2000**, *65*, 1210–1214.
59. M. Kidwai, Y. Goel, R. Kumar, *Indian J. Chem.* **1998**, *37B*, 174–179.
60. F. Louërat, K. Bougrin, A. Loupy, A. M. Ochoa de Retana, J. Pagalday, F. Palacios, *Heterocycles* **1998**, *48*, 161–170.
61. K. Mogilaiah, G. R. Reddy, *Indian J. Chem.* **2004**, *43B*, 882–884.
62. M. Gupta, *J. Heterocycl. Chem.* **2007**, *44*, 1023–1025.
63. M. Gupta, S. Paul, R. Gupta, *Indian J. Chem.* **2009**, *49B*, 460–466.
64. R. D. Virre, G. Evindar, R. A. Batey, *J. Org. Chem.* **2008**, *73*, 3452–3459.
65. G. Bram, A. Loupy, J. Sansoulet, *Isr. J. Chem.* **1985**, *26*, 291–293.
66. G. Bram, H. Galons, S. Labidalle, A. Loupy, M. Miocque, A. Petit, P. Pigeon, J. Sansoulet, *Bull. Soc. Chim. Fr.* **1989**, 247–250.
67. E. F. Flegeau, M. E. Popkin, M. F. Greaney, *Org. Lett.* **2006**, *8*, 2495–2498.
68. L. K. Rasmussen, B. C. Boren, V. V. Fokin, *Org. Lett.* **2007**, *9*, 5337–5339.
69. Y. Kabri, A. Gellis, P. Vanelle, *Green Chem.* **2009**, *11*, 201–208.
70. G. Minelto, L. F. Raveglia, A. Sega, M. Teddei, *Eur. J. Org. Chem.* **2005**, *70*, 5277–5280.
71. G. W. Kabalka, M. Al-Masum, *Org. Lett.* **2006**, *8*, 11–13.
72. C. M. Kormos, N. E. Leadbeater, *J. Org. Chem.* **2008**, *73*, 3854–3858.
73. V. Nair, R. Rajan, L. Balagopal, L. G. Nair, S. Ros, K. Mohanan, *Indian J. Chem.* **2005**, *44B*, 141–145.
74. H. M. Meshram, Y. S. S. Ganesh, K. R. Babu, B. Eeshwaraiyah, J. S. Yadav, *Indian J. Chem.* **2005**, *44B*, 193–197.
75. N. J. McLean, H. Tye, M. Whittaker, *Tetrahedron Lett.* **2004**, *45*, 993–995.
76. A. R. Katritzky, C. Cai, S. K. Singh, *J. Org. Chem.* **2006**, *71*, 3375–3380.
77. U. Kazmaier, S. Ackermann, *Org. Biomol. Chem.* **2005**, *3*, 3184–3187.
78. S. Paul, M. Gupta, *Synthesis* **2004**, *11*, 1789–1792.
79. S. Paul, M. Gupta, *Tetrahedron Lett.* **2004**, *45*, 8825–8829.
80. M. Gupta, S. Paul, R. Gupta, A. Loupy, *Tetrahedron Lett.* **2005**, *46*, 4957–4960.
81. S. Paul, M. Gupta, *Synth. Commun.* **2005**, *35*, 213–222.
82. S. Paul, M. Gupta, P. Singh, R. Gupta, *Synth. Commun.* **2005**, *35*, 355–367.
83. R. H. Valdes, D. G. Aranda, H. M. Alvarez, O. A. C. Atunes, *Letts. Org. Chem.* **2007**, *4*, 35–38.
84. U. Azzena, G. Dettori, L. Pisano, M. Pittales, *Synth. Commun.* **2007**, *37*, 3623–3634.
85. S. M. Raders, J. G. Verkade, *Tetrahedron Lett.* **2008**, *49*, 3507–3511.
86. L. Piras, E. Genesio, C. Ghiron, M. Taddei, *Synlett* **2008**, 1125–1128.
87. (a) J. P. Tierney, P. Lidström, *Microwave-assisted Organic Synthesis*, Eds., Blackwell, Oxford, **2005**. (b) P. Lidström, J. Tierney, B. Wathey, J. Westman, *Tetrahedron* **2001**, *57*, 9225–9283.
88. (a) C. O. Kappe, *Angew. Chem. Int. Ed.* **2004**, *43*, 6250–6255. (b) B. L. Hayes, *Aldrichimica Acta* **2004**, *37*, 66–69. (c) R. S. Varma, *Pure Appl. Chem.* **2001**, *73*, 193–197. (d) R. S. Varma, *Indian J. Chem. Sec. B.* **2006**, *45B*, 2305–2307.
89. A. Seijas, M. P. Vazquez-Tato, *Chimica Oggi* **2007**, *25*, 20–26.
90. J. A. Seijas, M. P. Vazquez-Tato, M. M. Martinez, G. N. Corredoira, *J. Chem. Res.(S)* **1999**, 420–425.

91. Z. Dahmani, M. Rahmouni, R. Brugidou, J. P. Bazureau, J. Hamelin, *Tetrahedron Lett.* **1998**, *39*, 8453–8456.
92. D. Scharn, H. Wenschuh, U. Reineke, J. Schneider-Mergener, L. Germeroth, *J. Comb. Chem.* **2000**, *2*, 361–369.
93. A. C. S. Reddy, P. S. Rao, R. V. Venkataratnam, *Tetrahedron Lett.* **1996**, *37*, 2845–2848.
94. A. Kamal, B. S. N. Reddy, G. S. K. Reddy, *Synlett* **1999**, 1251–1252.
95. A. Díaz-Ortiz, J. R. Carrillo, F. P. Cossío, M. J. Gómez-Escalonilla, A. de la Hoz, A. Moreno, P. Prieto, *Tetrahedron* **2000**, *56*, 1569–1577.
96. C.-S. Jia, Z. Zhang, S.-J. Tu, G.-W. Wang, *Org. Biomol. Chem.* **2006**, *4*, 104–110.
97. S. S. Bani, A. K. Bose, A. G. Chaudhary, M. S. Manhas, V. S. Raju, E. W. Robb, *J. Chem. Edu.* **1992**, *69*, 938.
98. J. W. Elder, *J. Chem. Edu.* **1994**, *71*, A142, A144.
99. B. C. Ranu, A. Hajra, U. Jana, *Synlett* **2000**, 75–76.
100. B. M. Khadilkar, P. M. Bendale, *Synth. Commun.* **1997**, 2051–2056.
101. D. Bogdał, J. Pielichowski, A. Boroń, *Synlett* **1996**, 873–874.
102. V. Chakraborty, M. Bordoloi, *J. Chem. Res. (S)* **1999**, 118–122.
103. A. Lew, P. O. Krutzik, M. E. Hart, A. R. Chamberlin, *J. Comb. Chem.* **2002**, *4*, 95–105.
104. M. Gupta, B. P. Wakhloo, *Arkivoc* **2007**, (i), 94–98.
105. M. M. Heravi, N. Farhangi, Y. S. Beheshtiha, M. Ghassenizadeh, K. Tabar-Hydar, *Indian J. Chem.* **2004**, *43B*, 430–431.
106. Q. Xu, B. Chao, Y. Wang, D. C. Dittmer, *Tetrahedron* **1997**, *53*, 2131–2134.
107. G. Keglevich, T. Novák, L. Vida, I. Greiner, *Green Chem.* **2006**, *8*, 1073–1075.
108. K. Kranjc, M. Kočevar, F. Iosif, S. M. Coman, V. I. Parvulescu, E. Genin, J.-P. Genêt, V. Michelet, *Synlett* **2006**, 1075–1079.
109. Y. M. Kim, T. W. Kwon, S. K. Chung, M. B. Smith, *Synth. Commun.* **1999**, *35*, 343–347.
110. K. Bougrin, A. Loupy, A. Petit, B. Daou, M. Soufiaoui, *Tetrahedron* **2001**, *57*, 163–168.
111. H. Schirok, *J. Org. Chem.* **2006**, *71*, 5538–5545.
112. S. Chatti, M. Bortolussi, A. Loupy, *Tetrahedron* **2000**, *56*, 5877–5883.
113. A. Shaabani, A. Rahmati, E. Farhangi, Z. Badri, *Catal. Commun.* **2007**, *8*, 1149–1152.
114. Y. Su, L.-C. Wang, Y.-M. Liu, Y. Cao, H.-Y. He, K.-N. Fan, *Catal. Commun.* **2007**, *8*, 2181–2185.
115. G. L. Kad, M. Bhandari, J. Kaur, R. Rathee, J. Singh, *Green Chem.* **2001**, *3*, 275–277.
116. S. Juneja, M. Gupta, S. Paul, R. Gupta, *Bull. Korean Chem. Soc.* **2008**, *29*, 11, 2337–2340.
117. A. Hegedüs, A. Cwik, Z. Hell, Z. Horváth, Á. Esek, M. Uzsocki, *Green Chem.* **2002**, *4*, 618–620.
118. M. Rahimizadeh, Z. Tavallai, M. Bakavoli, *Indian J. Chem.* **2004**, *43B*, 679–681.
119. A. V. Narsaiah, K. Nagaiah, *Indian J. Chem.* **2004**, *43B*, 2478–2481.
120. H. Berthold, T. Schotten, H. Honig, *Synthesis* **2002**, 1607–1610.

Povzetek

Ta pregled se osredotoča na glavne dosežke organske sinteze z uporabo reakcij, olajšanih z mikrovalovi v trdni fazi, s čistimi reaktanti in pod pogoji brez uporabe topil. Izpostavlja tudi splošne značilnosti uporabe mikrovalov v organski sintezi. Nakazuje, da so reakcije pod mikrovalovi hitre, s pogosto povečanimi reakcijskimi hitrostmi in da vodijo do boljših selektivnosti. Nekatere izmed reakcij olajšanih z mikrovalovi je možno celo izvesti pod nerazredčenimi pogoji brez topil, kar vodi k temeljem zelene kemije.