Chemistry by microwaves*

Adamo Fini and Alberto Breccia

Istituto di Scienze Chimiche, Universita di Bologna, Italy

INTRODUCTION

The purpose of this paper is to provide useful details concerning the application of microwaves to chemical reactions. Many researchers have had probably some previous home experience of the microwave action in domestic chemical and physical processes, such as cooking and defrosting food: they surely realized the notable rate of the heating.

The pioneers of the application of microwaves into more canonic systems thought that it could produce similar effects in assisting the reactions carried out in research laboratories. In most cases it was soon evident that reactions were more rapid, cleaner and with an easier workup of the final material, saving a great deal of time [1]. These findings stimulated the diffusion of microwave ovens in many laboratories to take advantage of this instrument for their reactions.

The action of the microwave radiation on chemical systems is still under debate. Many researchers think that the observed acceleration of the reaction rates (compared to normal reflux conditions) could be due to the different mode of transferring heat to the reagents and solvent. Others, on the contrary, suggest that absorption of microwave radiation has some specific activating (nonthermal) effect on the reagent molecules.

Regardless of the mechanism of action of microwaves on the chemical systems, this paper will deal with a few points that seem in a peculiar way to characterize the use of microwaves in carrying out chemical reactions.

MICROWAVE RADIATION

Microwaves are electromagnetic radiations. Microwave energy is therefore similar to that transported by infrared or visible or ultraviolet waves and all follow the same laws. The frequencies of microwaves range from 300 MHz to 30 GHz (1–0.01 m wavelength). 2.45 GHz (12.3 cm wavelength) is a frequency allotted by an international Commission for domestic or industrial ovens [2]. Microwaves represent a nonionizing radiation, that influences molecular motions such as ion migration or dipole rotations, but not altering the molecular structure. In 2.45 GHz microwaves the oscillation of the electric field of the radiation occurs 4.9×10^9 times per second; the timescales in which the field changes is about the same as the response time (relaxation time) of permanent dipoles present in most organic and inorganic molecules are [3]. This fact represents a fundamental characteristic for an efficient interaction between the electromagnetic field of microwaves and a chemical system. The absorption of microwaves causes a very rapid increase of the temperature of reagents, solvents and products. Moreover in the case of solutions containing salts or strong acids and bases the energy can also be dissipated through ionic conduction, causing heating or overheating of the solvent (together with a possible increase of the pressure, when the reaction is carried out in closed vessels).

DIELECTRIC HEATING

Microwave heating arises from the ability of some liquids and solids to transform the absorbed electromagnetic energy into heat: the heating effect originates from the microwave electric field which

forces dipoles to rotate and ions to migrate and from a slower response of dipoles and ions to follow the rapid reversal of the electric field. The ability of a material to increase its temperature under microwave at a given frequency and temperature is referred to the dissipation factor, defined as $\tan \Delta = \epsilon''/\epsilon'$, where ϵ'' is the dielectric loss factor, related to the efficiency of a medium to convert microwave energy into heat, while ϵ' is the dielectric constant and measures the ability of a molecule to be polarised by an electric field. In the case of water, ϵ' is relatively high at low frequency but rapidly drops to zero above 30 GHz, while ϵ'' shows a parabolic profile reaching a maximum at around 20 GHz. The frequency of 2.45 GHz, chosen for practical purposes, represents a compromise both to minimize the drop of the dielectric constant with the increasing frequency and to maximize the penetration depth of the radiation: in short, to maximize the heating rate of an absorbing mass of water [2,4]. This choice has also a historical valency, since it is related to the previous domestic application of microwaves toward water either in defrosting or cooking food. This frequency can be successfully applied also to heat short-chain aliphatic alcohols [2].

THE MICROWAVE OVEN

The heart of the oven is the magnetron, an oscillator that converts high voltage pulse into a pulse of microwave power. The microwave enters a waveguide, whose reflective walls allows the transmission of the radiation from the magnetron into the cavity. The cavity is a sort of box and is the part of the oven where microwaves interact with the chemical system. A microwave oven is constructed to deliver a preset frequency (2.45 GHz in most cases) and power: a control unit regulates the power value introduced into the cavity in each run through an automatic on/off cycle of the magnetron. A typical energy output in a microwave system is 6–700 Watts: in 5 min irradiation, approximately 43 000 cal are delivered into the cavity.

Under microwave irradiation two main problems arise: the uniformity of the absorption and the reflection of the waves. The microwave energy travels on a beam: escaping from the guide the wave is deviated by the circulator (that works similar to a roundabout) into the cavity. The cavity walls reflect the beam, until it hits the sample and is absorbed. To increase the probability of interaction between the sample and the wave, to maximize absorption, the sample is put on a rotating glass disk. To absorb the excess microwaves a beaker of water is placed inside the cavity, which acts as a dummy load. This way the magnetron (and also the operator) is protected from the reflected power.

To carry out chemical reactions the cavity of domestic microwave ovens can easily be modified: a hole in the top often accomodates a reflux condenser for working at room pressure. Otherwise it is common to work in beakers with high walls, topped only by a watch glass or in flasks with a funnel placed in the neck. Since glass practically does not absorb microwaves, the upper part of the glass container, not in contact with solvents, remains cool during irradiation and acts as condenser for the vapours [1].

THE BEHAVIOR OF THE SOLVENT

Together with the ability to dissolve reagents and products, a solvent under microwaves can play a more active role. The acceleration of a chemical reaction under microwaves depends on the dielectric properties of the solvent. Solvents able to directly absorb microwaves increase the reaction rate of the dissolved reagents. Solvents, such as hydrocarbons, that cannot absorb microwaves themselves, can be indirectly heated under microwaves, only when in the presence of materials able to interact with the radiation. Polar solvents of low molecular weight and high dielectric constant irradiated by microwaves increase their temperature very rapidly, reaching boiling point in a short time: in this class of solvents the rate of a given reaction is more enhanced. Typical solvents widely employed in microwave chemistry are water, methanol, ethanol, acetone. Dimethyl formamide is also a useful solvent for operating under microwaves: it is completely miscible with water, is a good solvent for polar and less polar solutes, has a high boiling point, allowing the use of open vessels in carrying out chemical reactions.

There are some additional problems related to solvents and solutions.

Ions interact very strongly with the electrical field of microwaves: reacting systems containing ionized reagents and products undergo unforeseen increase of temperature, that further accelerate the reaction. As a consequence, reactions involving strong acids or bases or carded out in solutions of high ionic strengths can be potentially risky, even under experimental conditions that are normally considered mild.

A phenomenon frequently observed when microwaves are applied to chemical processes is the overheating of the solvent. In the presence of microwaves, common solvents are found to boil at higher temperatures: for water the difference is about $5\,°C$; $19\,°C$ for methanol, up to $36\,°C$ was the difference measured for tetrahydrofuran and acetonitrile. These differences were explained with the different mode of energy supply. The transfer of heat from an electrical bath to the solution inside the vessel ('traditional heating'), is affected by the imperfections of the glass surface, which activate the boiling. Driven by this activation the solvent boils at a lower temperature and, according to this view, the boiling temperatures, as they are reported for most solvents, could be underestimated. This activation is absent in the presence of microwaves: the radiation reaches the bulk of the solvent directly and the transfer of energy is no longer mediated by the vessel surface. Many authors suggested that the boiling temperature measured in this way should be 'true', reflecting real intermolecular interactions existing inside the liquid phase [1].

This phenomenon was suggested as responsible of the higher reaction rates observed under microwaves in most cases. In fact, since each $10\,°C$ temperature increase causes the reaction rate to double, it can easily be understood how chemical reactions can be speeded up in the presence of microwaves.

If overheating may be observed in open vessels, in closed vessels this phenomenon can lead an increase of the pressure of the system. Especially with low boding solvents and in the presence of large volumes in low-capacity vessels, there is a risk of explosion. The rapid increase of temperature under microwaves can cause a quick increase of the internal pressure, which can be potentially dangerous in the absence of a safety apparatus. The development of high pressures and the necessity to use specialized Teflon vessels represent major limitations of microwaves in chemical systems [5].

An obvious solution to these problems is to operate in open vessels at room pressure, avoiding closed reactors. An additional suggestion could be the use of limited amounts of solvent, just enough to prepare a slurry reacting mixture: the dissolution of the solid and the achievement of a homogeneous system occurs at the reaction temperature.

MATERIALS AND MICROWAVES

An important problem in microwave application to chemical reactions is related to the nature of the solid materials present in different modes inside the system crossed by the radiation. These can be part of the chemical system: solvent, reagents, products and catalysts; or be part of the apparatus and oven.

Materials can be divided into three broad categories: materials which reflect microwaves; materials which are crossed by the microwaves, without being absorbed; materials which absorb the radiation and are therefore, able to start the heating or to activate a chemical reaction. Many materials are practically transparent (quartz) and can be penetrated by the radiation; some others materials, such as metals, reflect the radiation: other materials, such as dielectrics, interact with microwaves to different extents [6]. Chemical reactors must be transparent to microwaves and are made of Teflon or poly(ethylene); glass is also a suitable material, especially for high temperature reactions, but it is not completely transparent to microwaves.

A particular problem in this context is the measurement of the temperature, which cannot be obtained using conventional instruments, such as mercury thermometers or metal thermocouples. The temperatures can be measured by thermal indicators or indirectly by the melting of suitable probes: glass fiber thermocouples are suggested.

Mechanical stirrers, made of Teflon and glass, are preferred to a magnetic bar. In most cases, however, stirring is not necessary to homogenize the distribution of heat, since microwaves can reach the bulk of even a slurry mass directly [7].

Materials that absorb microwaves can display different rates of heating, according to their composition and the dimension of their particles, when solids [6]. The inclusion of such materials in the form of powder or fibers within the mass of polymer can improve microwave absorption and locally raise the temperature, thus increasing the hardening or improving the compaction of polymeric materials, indirectly acting as an adhesive.

THE TYPE OF CHEMICAL REACTIONS

The effect of microwaves on chemical reactions is generally evaluated by comparing the time needed to obtain a given yield of the final products with respect to traditional heating. In most examples reported in the literature [8–10] the amount of reagents employed in these tests ranges from a few milligrams to a few grams. The reaction vessel is simply kept in the oven for a preset time, following most of the details described above.

One of the most interesting problems that modem technology should solve is the possibility of scaling-up the processes under microwaves. For this purpose flux reactors have been suggested. The reagents pass into the oven continuously through a serpentine at such a rate that each portion of the mass absorbs a fixed amount of microwave energy. Power levels can be modulated through the microwave output: at a fixed power of the oven for varying times; or for a fixed time by varying patterns of on-off cycles [11].

Reactions which benefit more from the presence of microwaves are obviously those which have low rates under traditional conditions [12–14]. The reactions examined represent a large variety, ranging from hydrolysis of nitriles, amides and esters, to the formation of esters and ethers- oxydation and hydrogenations; rearrangements and polymerizations, etc. [9,15].

The Diels–Alder reaction represents a good model to study the effect of microwaves [9]: the carbonyl group, besides being important in driving the reaction, acts as a sort of antenna towards the radiation. The reaction is rapid when the starting diene is electron-rich and the dienophile is electron-poor; when dienophiles lack of activating groups the reactions require a high temperature ($>300\,°C$). The reaction between antracene and maleic anhydride is a classical example of this. This reaction has recently been proposed for undergraduate microwave experiments, because it is simple to carry out and its rate is strongly accelerated in the presence of microwaves [16].

Esters, amides and nitriles are hydrolysed very slowly either in basic or acidic medium under traditional conditions. Hydrolysis of these compounds offers a typical example of application of microwaves. A positive role is played in this case by the presence of strong acids or bases, that increase the heating rate under microwave irradiation.

Esterification is a reaction largely studied under microwaves. The rate of esterification of benzoic acid was found to be increased under microwaves and the increase is a function of the length the hydrocarbon chain of the alcohol. It must be pointed out that the boiling point of the alcohol also increases: higher temperatures of the reaction can therefore also be used in the traditional method: as a consequence in this case the comparison between the two techniques is no longer homogeneous [9].

In the case of the Williamson reaction to form ethers between alkoxydes and alkyl chlorides the ratio between substitution and elimination did not change [9].

On the contrary in the case of the sulphonation of naphtalene, the substitution in position 2 preferentially occurs under microwaves at temperature higher than $130\,°C$; while under traditional heating the final product contains almost equimolar of 1 and 2 naphtalene-sulfonic acids at temperature lower than $130\,°C$ [17].

Polymer chemistry will probably benefit greatly from the application of microwaves: in fact the presence of polar groups in the starting materials particularly favours the absorption of microwaves, allowing rapid and controlled synthesis, hardening and curing of the final products [18]. In these systems different modes of energy supply can drive a reaction differently: e.g. in the case of epoxy resins, short impulses favour self-polymerization, whereas longer impulses of microwaves allow the reaction with amines.

The use of solid materials for the so-called *dry-chemistry,* or without solvent, appears very interesting and represents a new frontier for chemistry under microwaves [19,20].

Moreover the experimental conditions adopted in these cases simplify the chemical system, due to the absence of solvent and the problems related to it, such as loss for evaporation or pressure increase in closed vessels. According to this methodology the reagents are dispersed on the surface of an inorganic and insoluble support, such as silica gel, alumina, commercial bentonite and other oxides or silicates. Kept thus in close proximity on a large surface, the reagents are irradiated by microwaves in the absence

of solvents and the reaction is very efficiently driven. At the end of the reaction the final products can simply be washed by a solvent and processed as usual. An acetylenic alcohol adsorbed on montmorillonite undergoes 92% rearrangement under microwaves, while, under conventional heating at the same temperature and for the same time, gives only a trace of the final product [21,22].

In some cases the yield of the reaction is affected by the nature of the inorganic support. The influence of microwaves was demonstrated when the pinacol/pinacolone rearrangement takes place in the presence of a charged phyllosilicate: moreover the conversion yield clearly depends on the nature of the interlayer cation of the solid support.

In addition to the benefit of saving solvents, a salient feature of this methodology is the selectivity of some reactions, such as those concerning protection and deprotection of functional groups. A neat selectivity was found in deacetylation of alkyl and aryl esters or among the different positions in the steroid nucleus of a bile acid methyl ester: in this last case, the different options are obtained simply by regulating the time of irradiation of the substrate dispersed on alumina [23].

Using clayfen, i.e. clay-iron (III) nitrate in the solid state, alcohols are readily oxidized in high yields to the corresponding carbonyl compounds. Sulphides can be oxidized to sulphoxides or to sulphones using sodium periodate on silica gel: under microwaves selectivity can be obtained by simply changing the ratio between reagent to oxidant. Another example of reaction carded on a solid support is the condensation between 1-bromooctane and potassium acetate. These reactants do not display any property to absorb microwaves. On the contrary potassium acetate dispersed on alumina reaches 300 °C in 3 min under microwaves: this specific activation makes the reaction rapid; in this respect silica was found less efficient.

A very interesting field for the application of microwaves is the synthesis of radiopharmaceuticals or labelled drugs, especially when very short half-life positron emitters are employed. With isotopes such as ^{122}I (3.6 min), ^{11}C (20 min), ^{18}F (110 min) the gain of even a few minutes in the reaction time could be of extreme importance for the final activity. The reactions of common radioisotopes are also improved in the presence of microwaves: reaction times are reduced as well as exposure to the radioactive emissions and the risks of possible contaminations [24,25].

STILL UNSOLVED PROBLEMS

From the examination of a large number of reactions it appears that microwaves exert a kinetic rather a thermodynamic control on the reaction: it is still doubtful whether there are reactions occurring under microwaves which would not take place under traditional conditions.

Microwave energy is lower than ionisation energy, hydrogen bonds or van der Waals intermolecular interactions: most results concerning rate enhancement can be explained only by thermal effects (superheating, mass heating, fast heating, etc.). The absence of nonthermal effects could be a general conclusion, when a careful control of the temperature is carded out, or the rapid increase of the pressure in scaled reactors is taken into account for accurate comparison [26–28].

However microwave heating is totally different from conventional heating. The specificity of microwave heating consists of dipolar polarization; the rotation of molecules in an attempt to align themselves with applied microwave field produces specific effects which cannot be achieved by conventional heating. Non-thermal effects can therefore originate by a lowering of the Gibbs energy of activation of the reactions through either a storage of microwave energy as vibrational energy of a molecule or some of its functional group (enthalpy effect) or by alignment of molecules (entropy effect) [3].

CONCLUSIONS

The advantages of the use of microwaves on chemical systems can be summarised as follows: (a) volumetric heating, without contact; (b) very high heating rate; (c) good interaction with many insulating materials and poor interaction with many nonferrous metals or gaseous products; and (d) convenient and clean heating system. The presence of microwaves greatly improves the rate of many chemical reactions, with a strong reduction of the reaction time, without altering the final yield. Reactions

can also be carried out in dry conditions or in solvents with a high dielectric constant. Other benefits can derive from the presence inside the chemical system of an insoluble dielectric, able to absorb microwaves: the reaction occurs at the contact surface without involving the bulk, thus avoiding many of the possible side-effects.

Non-thermal specific activation of reactions by microwaves is not yet clearly proved. This problem can be of minor importance if microwaves represent only an alternative way of introducing energy into chemical systems; however, the knowledge of what is happening during microwave irradiation of a chemical system can help to get the best results from it. Regardless of the type of activation or kind of microwave e&ct, microwave energy has its own advantages which are still waiting to be fully and beneficially appreciated and applied in carrying chemical reactions [29].

REFERENCES

1   E. D. Neas, M. J. Coolins. In *Introduction to Microwave Sample Preparation* (H.M. Kingston, L.B. Jassic, eds.), chap. 2, pp. 7–32. ACS Professional Reference Book, Washington, DC (1988).

2   D. M. Mingos, D. R. Baghurst. *Chem. Soc. Rev.* **20**, 1–47 (1991).

3   A. L. Buchachenko, E. L. Frankevich. *Chemical Generation and Reception of Radio and Microwaves.* VCH Publisher, New York (1994).

4   S. A. Galema. *Chem. Soc. Rev.* **26**, 233–238 (1997).

5   E. R. Peterson. Quality enhancement using microwaves. In *28th Annual Symposium Proceedings*, Montreal, Canada, pp. 89–101. IMPI, Manassas, VA (1993).

6   A. Breccia, A. Fini, G. Feroci, A. M. Grassi, S. Dellonte, R. Mongiorgi. *J Microwave Power Electromagnetic Energy* **30**, 3–9 (1995).

7   A. Fini. *Microwave and High Frequency Heating Principles and Chemical Application* (A. Breecia, A. C. Metaxas, eds), pp. 69–83. UCISCRM, Bologna, Italy (1997).

8   G. Majetich, R. Fficks. *J. Microwave Power Electromagnetic Energy* **30**, 27–45 (1995).

9   G. Majetich, R. Iteks. *Radiat. Phys. Chem.* **45**, 567–579 (1995).

10 A. Breccia, A. Fini, E. Gattavecchia, G. Fereci, E. Ferd. *Chim. Ind* **79**, 209–216 (1997).

11 A. Breccia, B. Esposito, G. Breccia, Fratadoechi, Y. Mancini, A. Fini. *J. Microwave Power Electromagnetic Energy* (1998), in press.

12 R. J. Giguere, T. L. Bray, S. M. Duncan, G. Majetich. *Tetrahedron Lett.* **27**, 4945–4948 (1986).

13 R. N. Cwdye, F. E. Smith, K. C. Westaway, H. Ali, L. Baidisera, L. Laberge, J. Rousell. *Tetrahedron Lett.* **27**, 279–286 (1986).

14 A. K. Bose, M. S. Manhas, M. Ghosh, M. Shah, V. S. Raju, S. S. Bari, S. N. Newaz, B. K. Banik, A. G. Chaudhary, K. J. Barakat. *J. Org. Chem.* **56**, 6968–6970 (1991).

15 D. M. P. Mingos. *Res. Chem. Intermed.* **20**, 85–91 (1994), and references therein.

16 S. S. Bari, A. K. Bose, A. G. Chaudhary, M. S. Manhas, V. S. Raju, E. W. Robb. *J. Chem. Ed.* **69**, 938–939 (1992).

17 D. Stuerga, K. Gonon, M. LaUemant. *Tetrahedron* **49**, 6229–6234 (1993).

18 B. Silinski, C. Kuzniycz, A. Ciourdeme. *Eur. Po. J.* **23**, 273–277 (1987).

19 R. S. Varma. *Microwave and High Frequency Heating Principles and Chemical Applications* (A. Breccia, A. C. Metaxas, eds), pp. 45–67. UCISCRM, Bologna, Italy (1997), and reference therein.

20 M. Hajek. *Microwave and High Frequency Heating Principles and Chemical Applications* (A. Breccia, A. C. Metaxas, eds), pp. 85–95. UCISCRM, Bologna, Italy (1997), and references therein.

21 A. Ben Alloum, L. Boutcha, D. Villemin. *J. Chem. Commun.* 386–387 (1989).

22 E. Gutierrez, A. Loupy, G. Brani, E. Ruiz-Fhtzky. *Tetrahedron Lett.* **30**, 945–948 (1989).

23 B. Dayal, K. Rao, G. Salen. *Steroids* **60**, 453–457 (1995).

24 E. Gattavecchia, A. Breecia, A. Fini, E. Ferd. *Proceedings International Conference on Microwave and High Frequency Heating*, Cambridge. C3, 1 (1995).

25 S. Zijlstra, T. J. DeGroot, L. P. Kok, G. M. Visser, W. Vaalburg. *J. Org. Chem.* **58**, 1643–1645 (1993).

26 R. Laurent, A. Laporterie, J. Dubac, J. Berlan, S. Lefeuvre, M. Audhuy. *J. Org. Chem.* **57**, 7099–7102 (1992).

27 K. C. Westaway, R. N. Gedye. *J. Microwave Power Electromagnetic Energy* **30**, 219–230 (1995).
28 D. A. C. Stuerga, P. Gaillard. *J. Microwave Power Electromagnetic Energy* **31**, 87–113 (1995).
29 R. Dagani. *C&EN.* **2**, 26–32 (1993).