Chapter 1
The Spread of the Application of the Microwave Technique in Organic Synthesis

Erika Bálint and György Keglevich

Abstract The first chapter summarizes the birth and spread of the application of the microwave (MW) technique in organic syntheses placing the stress on the development of the MW equipment. These days professional batch and continuous flow reactors are available, and the application is knocking at the door of industry.

Keywords Microwave · Batch reactors · Continuous reactors

These days, the protection of our environment and our health is becoming increasingly important due to the worldwide spread of green chemistry. According to the 12 principles of green chemistry [1], preparation and development of environmentally-friendly and harmless products and technologies are the main tasks. In this context, the application of the microwave (MW) technique in organic, inorganic, medicinal, analytical and polymer chemistry has spread fast [2–8].

The first domestic microwave oven was introduced by at the end of 1955, but the widespread use of these ovens in households occurred during the 1970s and 1980s. From the middle of 1970s, engineers and researchers started to apply the MW technique in food processing, in the drying industry, in waste remediation and in analytical chemistry. In the latter case, this technique has been used for sample preparation (e.g. digestion, extraction, dissolution, etc.) [9–12]. The first application of microwave irradiation in chemical synthesis was published in 1986 by the groups of Gedye and Giguere [13, 14]. Since then, the number of publications in this field has sharply increased (Fig. 1.1). Most of these publications describe important acceleration of a wide range of organic chemical reactions, excellent repro-

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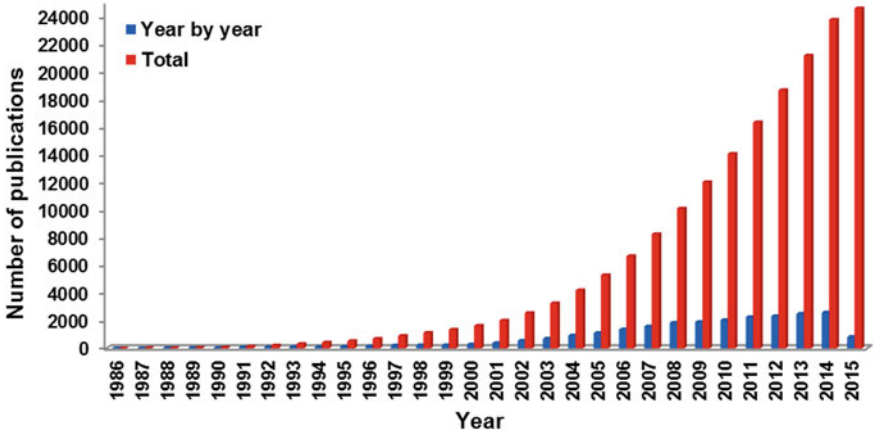


Fig. 1.1 The number of publication on MW-assisted synthesis (1986–2015). Web of Science keyword search on "microwave synthesis"

ducibility, improved yields and less side reactions compared to conventional heating.

Early pioneering experiments were performed in domestic MW ovens, where the irradiation power was controlled generally by on-off cycles of the magnetron, and it was not possible to monitor the inner temperature in a reliable way, thus the reactions were not reproducible. The other problems were on the safety issues of such experiments [15–17]. From the early 2000s, dedicated MW instruments started appearing in market, which are indeed suitable for performing chemical reactions under controlled conditions [2, 3, 18]. All commercially available dedicated MW reactors consist of a MW cavity, magnetic stirrer, sensor probe (IR sensor or fiber optic probe), and software that enables on-line temperature/pressure control by regulating the MW power output.

The MW instruments are classified in two types, monomode (single mode) and multimode MW reactors. The main difference between the two systems is that while in monomode reactors only one reaction vessel can be irradiated, multimode reactors may accommodate several vessels simultaneously.

A monomode instrument has a small compact cavity, where the microwave energy is generated by a single magnetron, and directed through a rectangular waveguide to the reaction mixture, which is positioned at a maximized energy point (Fig. 1.2). A highly homogenous energy field of high power intensity is provided, resulting in exceedingly fast heating rates.

In addition, monomode instruments with a self-tuning circular waveguide are also available (Fig. 1.3). This cavity features multiple entry points for introducing the microwave energy into the vessel.

Multimode reactors have larger cavities, in which the microwaves are reflected from the cavity walls, and distributed in a rather chaotic manner (Fig. 1.4). The reaction vessels are continuously rotated within the cavity, to provide a steady

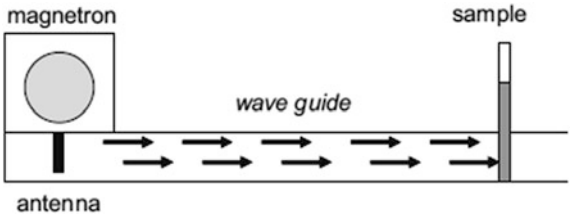


Fig. 1.2 The microwave field distribution in a monomode reactor [3]

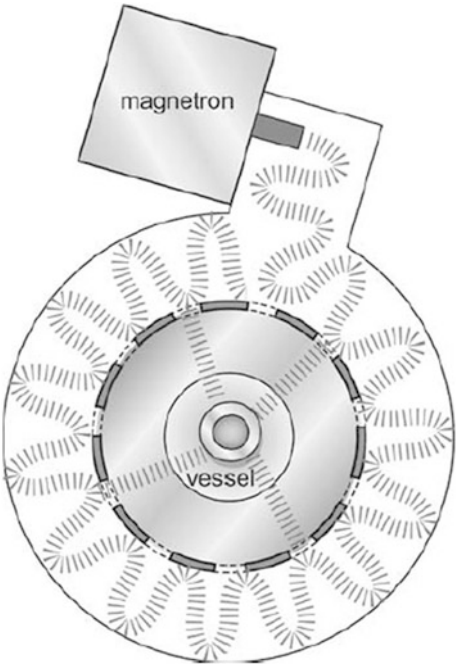


Fig. 1.3 Circular single-mode cavity [2]

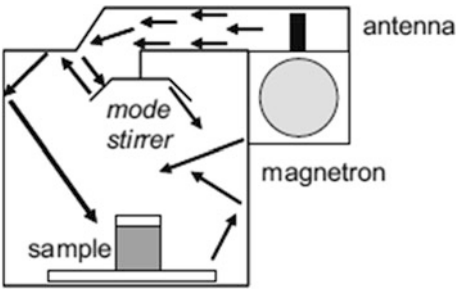


Fig. 1.4 The microwave field distribution in a multimode parallel synthesis reactor [3]

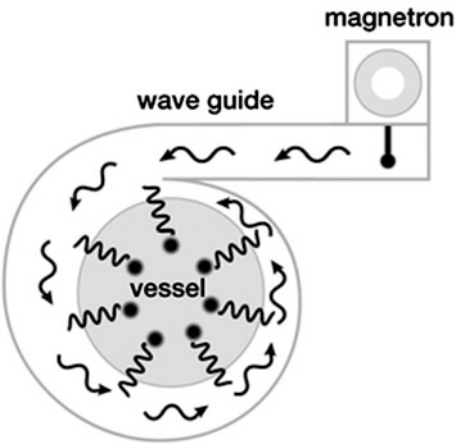


Fig. 1.5 The microwave field distribution in a multimode single-batch reactor (top view)

energy distribution. Multimode instruments allow conveniently for parallel syntheses or scale-up. These reactors can host different rotors which are used for parallel reactions in a scale range from several µl up to multi g synthesis in 100 mL reaction vessels.

There is another type of multimode reactor containing a circular waveguide, where various modes of the electromagnetic waves interact with the vessel content at different spots for efficient heating of larger scales (Fig. 1.5). A single few liter vessel is positioned in the cavity, which provides optimal heating rates for large volumes due to the relatively high field density (compared to common multimode microwave oven shown in Fig. 1.4). This kind of multimode reactor is applied for single-batch scale-up procedure, if up to 2 kg of product is required.

Special MW reactors are also known, where the microwave is combined with other techniques, such as UV, ultrasound or high pressure systems (e.g. supercritical reactor) [2].

The scale-up of MW-assisted reactions is of specific interest in many industrial laboratories. The safety limitations of using large batch reactors have promoted the development of continuous flow or stopped-flow MW reactors [19, 20]. These reactors usually comprise three parts, such as the dispensing units for the starting reagents, the MW cavity and the product collector (Fig. 1.6). The reagents are pumped using a HPLC pump or even two pumps. The pressure is controlled by a back-pressure regulator, and the temperature is monitored using a fiber optic sensor or a built-in IR sensor. Usually, the reactors are made from Pyrex or Teflon. The efficiency of the continuous flow MW systems can be increased by using parallel reactors.

Nowadays, there are many types of continuous flow MW reactors, which include a normal flask or tube [21], a fixed bed turbular coil [22–24], an Ω- or U-shaped tube [25–28], a filled column [22, 24, 29] (Fig. 1.7), a spiral glass tube [21, 30–32] (e.g. Emry-type reactor [33] (Fig. 1.8)), a mixed tube [34] (Fig. 1.9) or a capillary reactor [27, 28, 35–37].

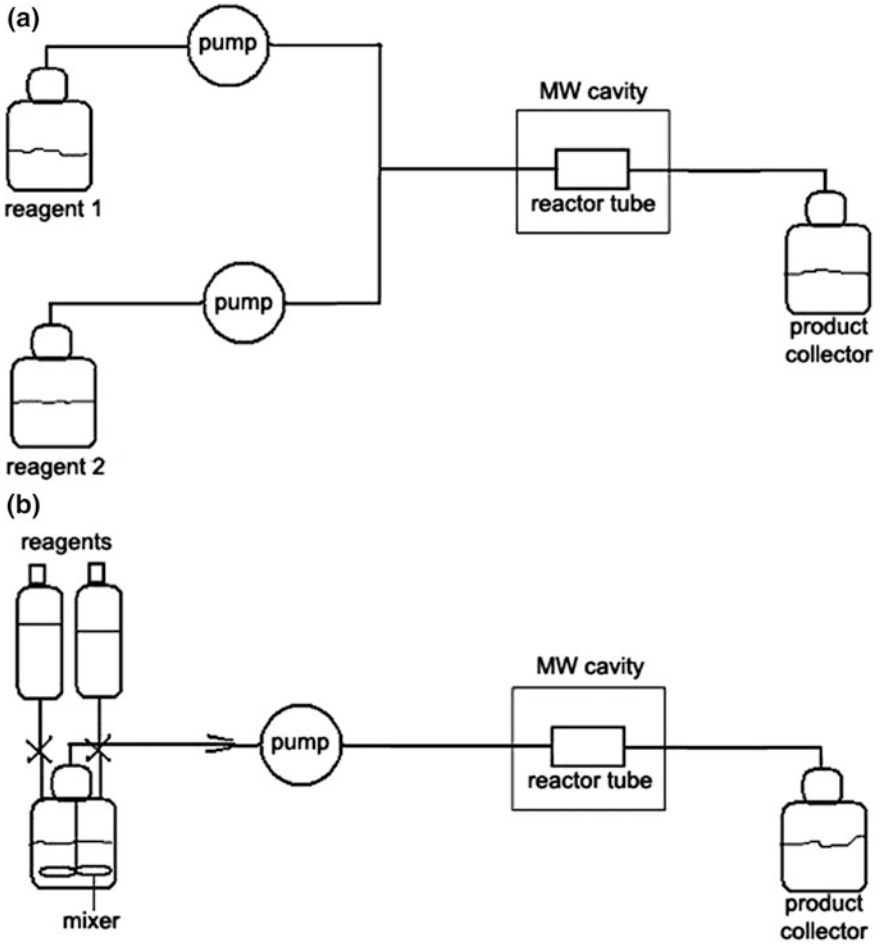
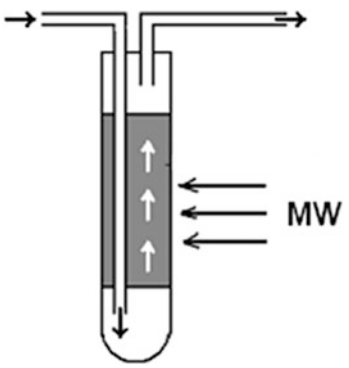


Fig. 1.6 Schematic sketch of continuous flow MW reactors

Fig. 1.7 Filled column



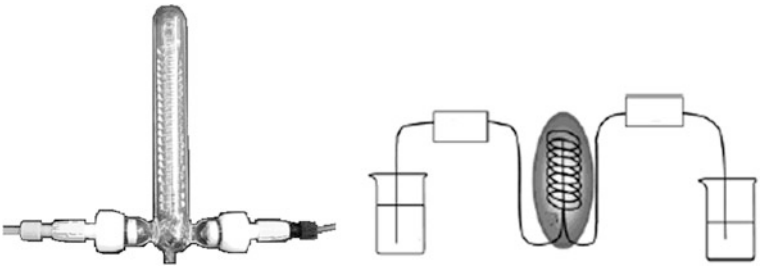


Fig. 1.8 Emry-type reactor

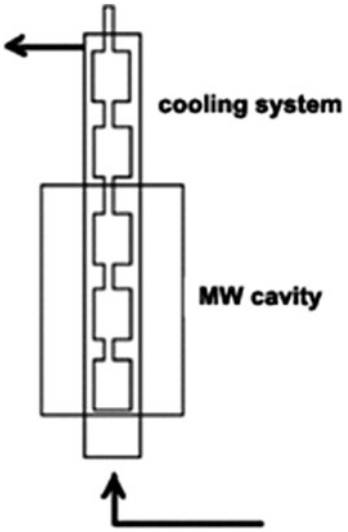


Fig. 1.9 Mixed tube reactor

There is also a continuous equipment to carry out MW-assisted reaction of solid components (Fig. 1.10) [38, 39].

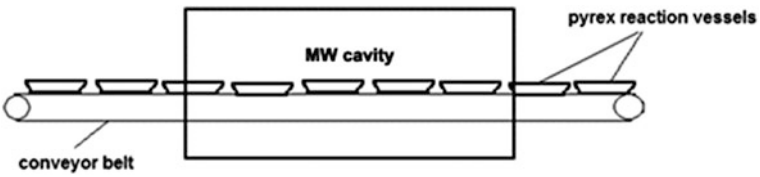


Fig. 1.10 Continuous microwave reactor for solid-phase reaction

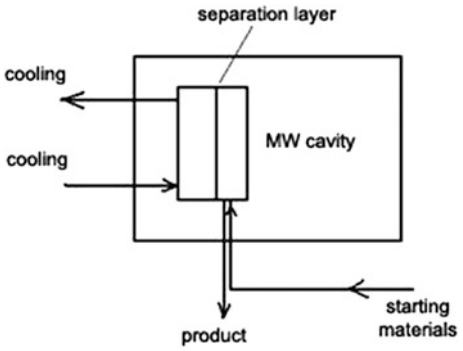


Fig. 1.11 Isothermal MW reactor

Continuous isothermal MW reactor is also known, which is suitable for implementation of isothermal reactions (Fig. 1.11) [40].

Several MW-assisted continuous flow accomplishments on g or kg scale have been reported in the literature [19, 41–54]. Their capacity may reach 500 kg product per day [55].

1.1 Conclusions

In summary, the revolutionary spread of the MW technique resulted in an enormous development in organic chemistry. The appearance of dedicated MW reactors was a "sine qua none" of the new achievements. The mono- and multimode MW batch reactors make possible laboratory scale syntheses, while suitable continuous flow reactors even larger scale production.

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