



Practical Microwave Synthesis for Organic Chemists

Since its dawn in 1986 with the seminal publications from the groups of Gedye and Giguere/Majetich, the application of microwave irradiation in organic synthesis has gained popularity in organic synthetic laboratories. Starting out as a curiosity, this way of transferring energy to a reaction mixture is steadily becoming the Bunsen burner of the present day. However, although successfully introduced as a standard technique in an increasingly growing number of research labs, there is still a long way to go before microwave irradiation will be generally accepted as the method of choice, instead of the last resort when a reaction fails under conventional heating conditions. Conservatism amongst chemists is undoubtedly hampering a fast introduction, but so is the relatively high prices of the commercially available dedicated microwave instruments.

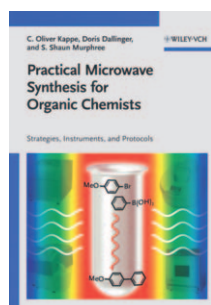
The main author of this book, C. O. Kappe, started to teach short courses about microwave-assisted organic synthesis in 2003, one of which I had the pleasure to attend. I believe that this book is the long expected necessary addition to this short course, appropriately addressing the different items taught and thus providing an introductory treatise for beginners. Moreover, the book gives a succinct literature overview, appropriately divided in several chapters and subchapters, which enables the microwave novice to find his way in the nowadays overwhelming amount of literature.

After a general introduction in chapter 1, the authors outline in chapter 2 the basics of the application of microwave irradiation to organic synthesis. Of particular interest is the discussion of the various microwave effects, which comprise thermal effects, specific microwave effects, and non-thermal (athermal) microwave effects. It is certainly one of the merits of the authors that they have clearly defined the more popular term “special microwave effect” as a “non-thermal (athermal) microwave effect” as there is a lot of confusion about this in the scientific community. The authors also clearly stress the importance of correct temperature monitoring in microwave chemistry as, according to them, especially in the early days, inappropriate temperature measurement has led to false conclusions about non-thermal microwave effects. When measuring the temperature with an external infrared (IR) sensor, care must be taken since the reactor wall is typically the coldest part of the reaction system, because of the inverted temperature gradient compared to conventional heating. The issue of simultaneous

cooling during microwave irradiation has also been addressed at the end of this chapter.

In chapter 3 the authors give a very detailed description of the multimode and monomode instruments available since 2008, including various accessories and special application tools. The apparatus from the different microwave instrument companies, Biotage AB, CEM Corporation, Milestone s.r.l., and Anton Paar GmbH, are described and well illustrated with several photographs and schematic drawings. Also, sufficient attention has been paid to the available instruments, addressing the scale-up issue of microwave-assisted reactions from gram to kilogram quantities, as this is of specific interest for industrial laboratories. However, although I understand this is maybe not the most appropriate forum, it would have been instructive if the authors had commented on the pros and cons of the different instruments on the basis of their undoubtedly rich experience with several of them. A clear argumentation is formulated against the use of domestic microwave ovens for research purposes, so that even the microwave novice, seduced by the relatively low prices, should be convinced not to use these unsuitable kitchen ovens. Besides the production of an inhomogeneous field by the low-cost multimode design, there is also the lack of safety controls, so the use of such equipment cannot be recommended for scientific purposes.

Chapter 4 is undoubtedly the most instructive, as it gives a comprehensive overview of the presently existing variety of microwave processing techniques by referring to appropriate examples taken from the literature. Although the application of sealed vessels is the preferred technique today, in the early days of microwave-assisted organic synthesis, because of the unavailability of dedicated instruments, most reactions were run in open vessels and under solvent-free conditions. It is good to see that even the relatively scarce work that was performed with pre-pressurized reaction vessels has been cited by the authors. Of interest is also the description of the use of passive heating elements, such as for example, Carboflon (CEM) and Weflon (Milestone) as well as silicon carbide (SiC), which offer a solution for poorly microwave-absorbing reaction mixtures. Alternatively, the problem can be solved by doping the mixture with an ionic liquid, although care must be taken for incompatibilities with certain reagents. The authors also address problems and cite the different solutions which were proposed, as for example, for the appearance of temperature gradients across a microtiter plate during parallel processing in a multimode microwave instrument. The chapters dedicated to the scale-up of microwave-assisted processes clearly indicate that, although a lot of effort has been spent so far, there is still a long way



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to go to make microwave-assisted synthesis a fully accepted technology that can routinely provide products on a multi-kilogram scale.

Chapter 5 represents a well-written guide for the microwave chemistry novice and contains valuable information for getting started with microwave-assisted organic synthesis. For those who are not familiar with the technique it will be very helpful for the selection of appropriate conditions to run the first experiments in a dedicated microwave instrument. Certainly very helpful might be the list of “Frequently Asked Questions” (FAQs) at the end of the chapter.

Finally, chapter 6 provides a number of well-chosen experimental protocols, mostly originating from the author’s laboratory, which illustrate the numerous experimental applications of microwave irradiation discussed in the previous chapters. The experiments are described in full detail, also giving the power/pressure/temperature profiles. Although

the reagents and hazard information is, in my opinion, not suited to this kind of book, it renders the elaborated experiments directly suitable for use in a practical course.

Sufficient attention has been paid to the table of contents and to the index, thus making it easy to retrieve different subjects.

I read this book with pleasure during the free hours of the Zing conference on Microwave and Flow Chemistry 2009, chaired by the main author, C. O. Kappe. I am sure that this excellent guide will become the standard reference work in the field and clearly is a “must have” for anybody getting started with microwave-assisted organic chemistry.

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