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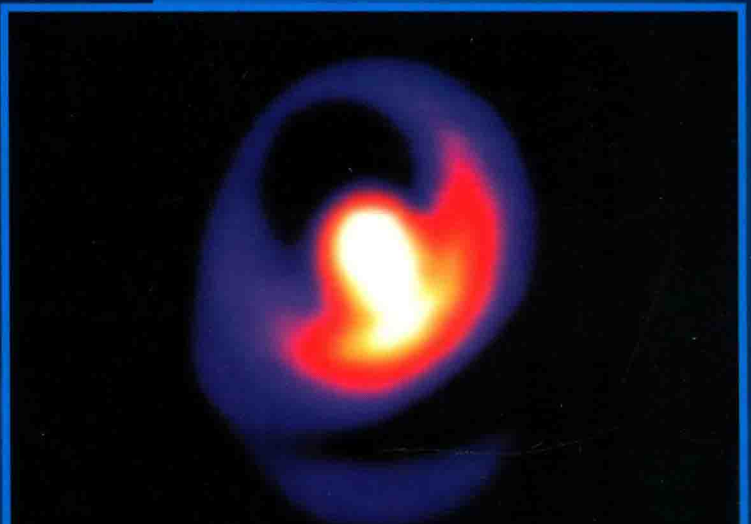
Microwave-assisted Organic Synthesis

One Hundred Reaction Procedures



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VOLUME 25

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In memory of my father ...

Preface

Microwave irradiation is a rapid way of heating materials for domestic, industrial and medical purposes. Microwaves offer a number of advantages over conventional heating such as non-contact heating (reduction of overheating of material surfaces), energy transfer instead of heat transfer (penetrative radiation), material selective and volumetric heating, fast start-up and stopping, and last but not least a reverse thermal effect, in which heat starts to build up from the interior of the material body.

The emergence of microwave-enhanced chemistry as an alternative, more efficient and environmentally friendlier way of performing chemical synthesis promises to be one of the most significant events of the 1990's with tremendous potential for the 21st century. More recently, it has been realized that some features of microwave irradiation i.e., solvent-free reactions, low-waste, energy efficiency, high yield, short reaction time, and usage of alternative solvents, can play an important role in the development of Green Chemistry methods.

This book is written primarily to help students at undergraduate and graduate levels to understand and apply microwave techniques to organic synthesis, using commercially available microwave reactors. It is hoped that the application of different kind of microwave reactors will help to spread ideas of microwave technologies. It should also serve as an introduction to the field for the industrial chemists with no prior training in microwave assisted organic chemistry.

The book will provide an introduction to the theory of microwave chemistry as well as practical laboratory manual by describing the methods of making a large number of compounds. Listing of the chemicals and equipment used in the syntheses and descriptions of the procedures and even the postsynthetic analyses will be very useful for the readers help them to design their own microwave reactions.

In the book, each experiment is introduced with a short discussion of associated hazards, the required equipment and its use, full operating procedure, physical properties of the expected product and extensive references to the source of the preparation and to related published work. Each procedure is checked to help and encourage students to use microwave techniques in the future. A number of methods from the literature which seemed attractive at first sight, are not exemplified in this book, either because they could not be reproduced at all by us or because they appeared to be impractical when performed.

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Kraków, Spring-Summer 2005

Dariusz Bogdał

Contents

Chapter 1

Interaction of microwaves with different materials

Microwaves are electromagnetic radiation placed between infrared radiation and radio frequencies, with wavelengths of 1 mm to 1 m, which corresponds to the frequencies of 300 GHz to 300 MHz, respectively. The extensive application of microwaves in the field of telecommunications means that only specially assigned frequencies are allowed to be allocated for industrial, scientific or medical applications (e.g., most of wavelength of the range between 1 and 25 cm is used for mobile phones, radar and radio-line transmissions). Currently, in order not to cause interference with telecommunication devices, household and industrial microwave ovens (applicators) are operated at either 12.2 cm (2.45 GHz) or 32.7 cm (915 MHz). However, some other frequencies are also available for heating [1]. Most common domestic microwave ovens utilize the frequency of 2.45 GHz, and this may be a reason that all commercially available microwave reactors for chemical use operate at the same frequency.

Heating in microwave cavities is based upon the ability of some liquids and solids to absorb and transform electromagnetic energy into heat. In general, during the interaction of microwaves with materials three different behaviors of a material can be observed depending whether the material is counted among:

- electrical conductors (e.g. metals, graphite - Fig. 1.2a)
- insulators, which are considered as materials with good dielectric properties (extremly poor conductors)(e.g., quartz glass, porcelain, ceramics, Teflon - Fig. 1.2b)
- lossy dielectrics, which are materials that exhibit so called dielectric losses, which in turn results in heat generation in an oscillating electromagnetic field (e.g., water - Fig. 1.2c)

When a strongly conducting material (e.g., a metal) is exposed to microwave radiation, microwaves are largely reflected from its surface (Fig. 1.2a). However, the material is not effectively heated by microwaves, in response to the electric field of microwave radiation, electrons move freely on the surface of the material, and the flow of electrons can heat the material through a resistive (ohmic) heating mechanism. In opposite, in the case of insulators (e.g., porcelain), microwaves can penetrate through the material without any absorption, losses or heat generation. They are transparent to microwaves (Fig. 1.2b).

For some dielectrics, the reorientation of either permanent or induced dipoles during

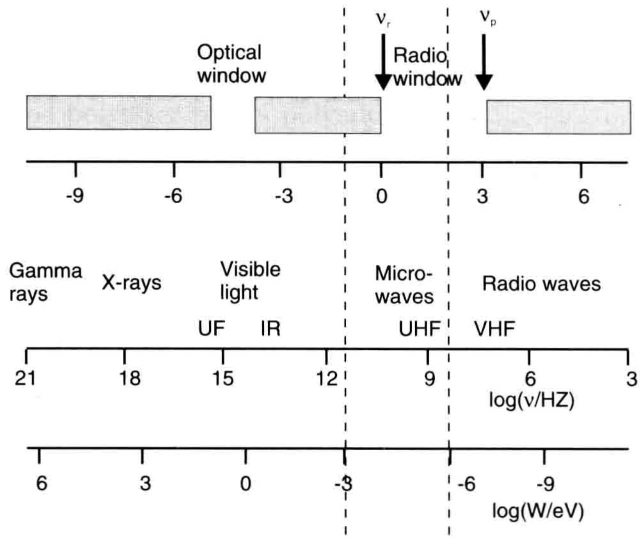

Figure 1.1. Spectrum of electromagnetic radiation: λ_o - wavelength in free space, $W = h\nu$ quantum energy, ν_r - lowest resonance frequency in the rotational spectrum of water, ν_p - plasma frequency of the ionosphere. Reprinted with the permission from [2].

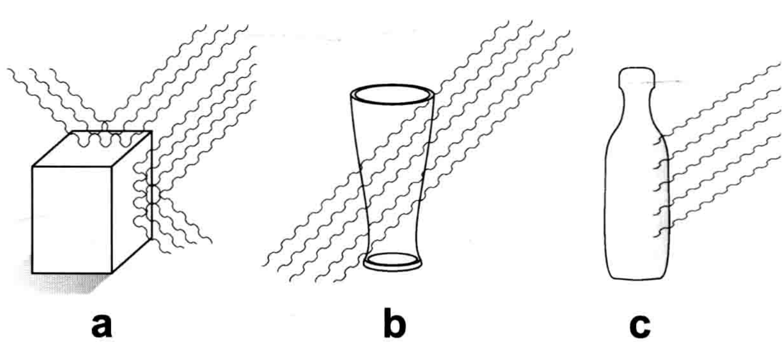

Figure 1.2. Interaction of microwaves with different materials: (a) - electrical conductor, (b) - isulator, (c) - lossy dielectric.

passage of microwave radiation which is electromagnetic in nature can give rise to absorption of microwave energy and heat generation due to the so called dielectric heating mechanism (Fig. 1.2c). Dependent on the frequency the dipole may move in time to the field, lag behind it or remain apparently unaffected. When the dipole lags behind the field (polarization losses) then interactions between the dipole and the field leads to an energy loss by heating (i.e., by dielectric heating mechanism), the extent of which is dependent on the phase difference of these fields.

In practice, most good dielectric materials are solid and examples include ceramics, mica, glass, plastics, and the oxides of various metals, but some liquids and gases can serve as good dielectric materials as well. For example, distilled water is a fairly good dielectric; however, possesing polar molecules (i.e., a dipol moment) can couple efficiently with microwaves to lead to heat generation due to polarization losses. Thus, such substances that are counted among dielectrics but exhibit some polarization losses that result in the dielectric heating are also called dielectric lossy materials or in general lossy materials. On the other hand, n-hexane, which having a symmetrical molecule, does not possess a dipole moment and does not absorb microwaves.

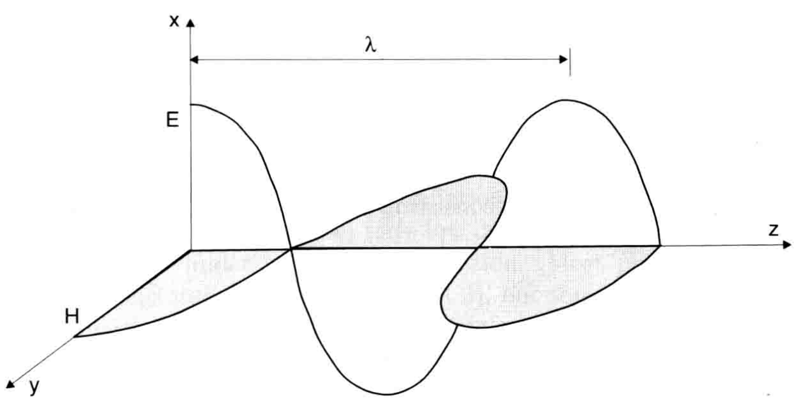

Figure 1.3. Electric (E) and magnetic (H) components during the propagation of electromagnetic waves. Reprinted with the permission from [1].

Microwave radiation, as all radiation of an electromagnetic nature, consists of two components, i.e. magnetic and electric field components (Fig. 1.3). The electric field component is responsible for dielectric heating mechanism since it can cause molecular motion either by migration of ionic species (conduction mechanism) or rotation of dipolar species (dipolar polarization mechanism). In a microwave field, the electric field component oscillates very quickly (at 2.45 GHz the field oscillates 4.9×10^9 times per second), and the strong agitation, provided by cyclic reorientation of molecules, can result in an intense internal heating with heating rates in excess of 10°C per second when microwave radiation of a kilowatt-capacity source is used [1]. Therefore, to apply microwaves to organic reactions, it is most important to find at least one reaction component that is polarizable and whose dipoles can reorient (couple) rapidly in response to changing electric field of microwave radiation. Fortunately, a number of organic compounds and solvents fulfill these requirements and are the best candidates for microwave applications.

To consider the application of microwave irradiation for organic synthesis, the first step is to analyze the reaction components together with their dielectric properties among which of the greatest importance is dielectric constant (ϵ_r) sometimes called electric permeability. Dielectric constant (ϵ_r) is defined as the ratio of the electric permeability of the material to the electric permeability of free space (i.e., vacuum) and its value can derived from a simplified capacitor model (Fig. 1.4).

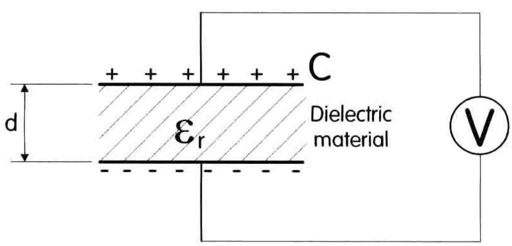

Figure 1.4. An electrical capacitor consisting of two metal plates separated by an insulating material called a dielectric.

When the material is introduced between two plates of a capacitor, the total charge (C_o) stored in the capacitor will change (C)(Eq. 1.1). The change depends on the ability of the material to resist the formation of an electric field within it and, finally, to get polarized under the electric field of the capacitor.

$$\epsilon_r = \frac{C}{C_0} \tag{1.1}$$

where:

- C_o - the capacitance of the capacitor with vacuum
- C - the capacitance of the capacitor with the material

Thus, dielectric constants(ϵ_r) that determine the charge holding ability of the materials are characteristic for each substance and its state, and vary with temperature, voltage, and, finally, frequency of the electric field. Dielectric constants for some common materials are given in Table 1.1.

Table 1.1
Dielectric constants (ϵ_r) of some common materials at 20°C .

Material	Dielectric constant(ϵ_r)	Material	Dielectric constant (ϵ_r)
Vacuum	1	Titanium Dioxide	100
Air(1 atm)	1.00059	Water	80
Air(100 atm)	1.0548	Acetonitrile	38
Glass	5 - 10	Liquid ammonia(-78°C)	25
Quartz glass	5	Ethyl Alcohol	25
Porcelain	5 - 6	Benzene	2
Mica	3 - 6	Carbon Tetrachloride	2
Rubber	2 - 4	Hexane	2
Nylon	3 - 22	Plexiglass	3
Paper	1 - 3	Polyvinyl chloride	3
Paraffin	2 - 3	Polyethylene	2
Soil (dry)	2.5 - 3	Teflon	2
Wood (dry)	1 - 3	Polystyrene (foam)	1.05

Air has nearly the same dielectric constant as vacuum (ϵ_r = 1.00059 and 1, respectively). Polar organic solvents (i.e., water, acetonitrile, ethyl alcohol) are characterized by relatively high values of dielectric constants and, in turn, can be heated by dielectric heating mechanism under microwave irradiation. Non-polar organic solvents (i.e., benzene, carbon tetrachloride, n-hexane) have low dielectric constants and, in fact, show negligible heating effects under microwave irradiation. Most plastics range in the low values of dielectric constants (i.e., between 2 and 3), but some of these materials besides glass and quartz glass are used to manufacture reaction vessels for microwave application due to their good chemical as well as temperature resistance (e.g., Teflon, PET, PEEK).

However, in the case of highly oscillating electric fields and microwave applications, dielectric constant is turned into complex permeability ($\epsilon^* = \epsilon' - j * \epsilon''$), which is a measure of the ability of dielectric materials to absorb and to store electrical potential energy. Like dielectric constant(ϵ_r), which is commonly used to describe good isolators, the real permeability (ϵ') component characterizes the ability of the material to be polarized by the electric field and thus the ability of microwaves to propagate into the material. At low frequencies this value reaches its maximum (i.e., ϵ_r) since the maximum amount of energy can be stored in the material. The imaginary part of the complex electric permeability (ϵ'') is usually called the loss factor and indicates the ability of the material to dissipate the energy i.e. the efficiency of conversion of electromagnetic radiation into heat. The loss factor (ϵ'') reaches the maximum when the real permittivity (ϵ') gradually decreases (Fig. 1.5). Obviously, it depends on the molecular structure of the material, on the frequency at which ϵ'' reaches its maximum and how distinctly this maximum is exhibited.