

Unraveling the Mysteries of Microwave Chemistry Using Silicon Carbide Reactor Technology

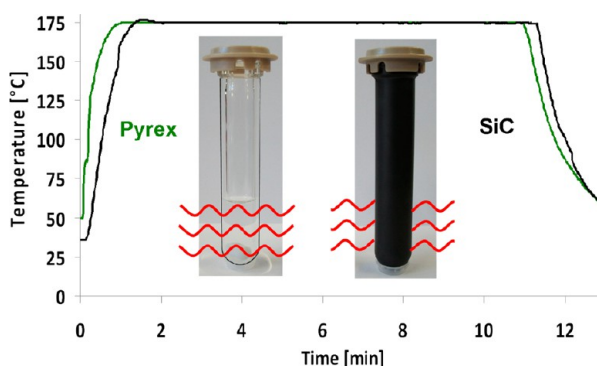
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CONSPECTUS

In the past few years, the use of microwave energy to heat chemical reactions has become an increasingly popular theme in the scientific community. This nonclassical heating technique has slowly progressed from a laboratory curiosity to an established method commonly used both in academia and in industry. Because of its efficiency, microwave heating dramatically reduces reaction times (from days and hours to minutes and seconds) and improves product purities or material properties among other advantages. Since the early days of microwave chemistry, researchers have observed rate-accelerations and, in some cases, altered product distributions as compared with reactions carried out using classical oil-bath heating. As a result, researchers have speculated that so-called specific or nonthermal microwave effects could be responsible for these differences. Much of the debate has centered on the question of whether the electromagnetic field can exert a direct influence on a chemical transformation outside of the simple macroscopic change in bulk reaction temperature.



In 2009, our group developed a relatively simple “trick” that allows us to rapidly evaluate whether an observed effect seen in a microwave-assisted reaction results from a purely thermal phenomenon, or involves specific or nonthermal microwave effects. We use a microwave reaction vessel made from silicon carbide (SiC) ceramic. Because of its high microwave absorptivity, the vessel shields its contents from the electromagnetic field. As a result, we can easily mimic a conventionally heated autoclave experiment inside a microwave reactor under carefully controlled reaction conditions. The switch from an almost microwave transparent glass (Pyrex) to a strongly microwave absorbing SiC reaction vial under otherwise identical reaction conditions (temperature profiles, pressure, stirring speed) then allows us to carefully evaluate the influence of the electromagnetic field on the particular chemical transformation.

Over the past five years we have subjected a wide variety of chemical transformations, including organic reactions, preparations of inorganic nanoparticles, and the hydrolysis of proteins, to the “SiC test.” In nearly all of the studied examples, we obtained identical results from reactions carried out in Pyrex vials and those carried out in SiC vials. The data obtained from these investigations confirm that in the overwhelming majority of cases a bulk temperature phenomenon drives the enhancements in microwave chemistry and that the electromagnetic field has no direct influence on the reaction pathway.

1. Introduction

Since the initial reports on the use of microwave irradiation to enhance organic chemical transformations by the groups of Gedye and Giguere/Majetich in 1986,¹ thousands of research articles have been published in this area.^{2,3} In many, if not in most, of the reported examples, microwave irradiation has been shown to radically reduce reaction

times and increase product yields and product purities by reducing unwanted side reactions compared to conventional heating methods.^{2–4} The advantages of this enabling technology have subsequently also been exploited in the context of medicinal chemistry/drug discovery⁵ and have additionally penetrated fields such as peptide⁶ and polymer synthesis,⁷ material sciences,⁸ nanomaterials research,⁹

and biochemical processes.¹⁰ The use of microwave irradiation in chemistry has therefore rapidly moved from being a laboratory curiosity in the 1980s and 1990s to a well-established scientific technique in the 21st century. Many academic and industrial laboratories today utilize this nonclassical form of heating in a routine manner, which undoubtedly is aided by the growing availability of carefully designed scientific microwave reactors, dedicated for use in chemical applications.

Despite the undisputed success of microwave chemistry in the past decades, there still exists some controversy on the exact reasons why microwave irradiation is able to enhance, or otherwise influence, chemical reactions. Much of the debate has centered around the issue if the observed effects can in all instances be rationalized by purely thermal Arrhenius-based phenomena (thermal microwave effects), as a consequence of the rapid heating and high bulk reaction temperatures that can be attained using microwave dielectric heating in sealed reaction vessels, or whether some effects are connected to so-called specific or nonthermal microwave effects.^{11,12} Nonthermal microwave effects have been postulated to result from a direct, often stabilizing, interaction of the electromagnetic field with specific molecules, intermediates, or even transition states in the reaction medium, which is not connected to a macroscopic change in reaction temperature.^{11,12} Specific microwave effects, on the other hand, have been suggested to be caused by the uniqueness of the microwave dielectric heating mechanisms and include, for example the selective heating of strongly microwave absorbing heterogeneous catalysts or reagents in a less polar reaction medium.^{11,12} Specific as well as nonthermal microwave effects can be largely independent of bulk reaction temperature and, at least in theory, should be influenced by the electromagnetic field strength: the higher the field strength the more pronounced the effect.¹² Today, it is generally agreed upon by most scientists in the field that in the majority of cases the experimentally observed effects in microwave chemistry are the result of purely (bulk) thermal phenomena, involving neither specific nor nonthermal microwave effects.^{11,13}

The issue of microwave effects has fascinated our research group from the very beginning when we started to get involved in microwave chemistry in 1998.¹⁴ With the implementation of the Christian Doppler Laboratory for Microwave Chemistry at the University of Graz in 2006, our research in this area has significantly intensified as one of the main scientific tasks of this 7 year research grant was to establish the true nature of microwave effects. What we have realized early on was that the main problem in

investigating microwave effects is the fact that it is rather difficult to perform appropriate control experiments comparing microwave with conventionally heated processes using oil baths or autoclave devices, since in order to be scientifically meaningful both sets of experiments have to be conducted at the exact same temperature, including a careful adjustment of heating and cooling profiles.^{15–17} We have also recognized that the standard practice of using external infrared (IR) temperature sensors in microwave reactors that record the outer surface temperature of the reaction vessel, not the internal reaction temperature, is highly problematic when reliable temperature data are required.^{15–18} Internal fiber-optic (FO) temperature probes are far better suited to accurately monitor the actual reaction temperature during the microwave irradiation process.^{15,18} Notably, other processing parameters such as vessel geometry and stirring speed must also be closely matched in order to ensure scientifically valid results.^{15–18} In our opinion, most scientists do not fully appreciate the experimental difficulties in performing adequate control experiments between microwave and conventionally heated reactions. This has led to a situation where the literature is now full of erroneous reports and false claims of specific/nonthermal microwave effects that have failed independent verification.¹¹

In 2009, our group has developed technology that makes it possible to rapidly evaluate whether an observed enhancement/effect experienced in a microwave-assisted chemical transformation is the result of a purely (bulk) thermal phenomenon, or whether specific or nonthermal microwave effects are involved.¹⁹ Key to this protocol is the use of a microwave reaction vessel produced from silicon carbide (SiC) ceramic, which owing to the high microwave absorptivity of SiC will shield the contents of the reaction vessel from the electromagnetic field. Used in combination with a dedicated microwave reactor with an internal FO temperature probe, this in essence allows mimicking a conventionally heated autoclave experiment under carefully controlled reaction conditions. A simple change from a nearly microwave transparent glass (Pyrex) to a strongly microwave absorbing SiC reaction vial in the same microwave reactor platform then allows to investigate the influence of the electromagnetic field on the particular chemical transformation and thus to distinguish between thermal and specific/nonthermal microwave effects.¹⁹ In this Account, the development of this technology and its significance for the investigation of microwave effects in a variety of different fields ranging from organic synthesis to nanotechnology are discussed.

2. Microwave Dielectric Heating and Silicon Carbide

Microwave chemistry generally relies on the ability of the reaction mixture to efficiently absorb microwave energy, taking advantage of microwave dielectric heating phenomena such as dipolar polarization or ionic conduction mechanisms.²⁰ This produces efficient internal heating (in-core volumetric heating) by direct interaction of electromagnetic irradiation with the molecules that are present in the reaction mixture.²⁰ The ability of a specific solvent (or other material) to convert microwave energy into heat is determined by the so-called loss tangent ($\tan \delta$). In general, a reaction medium with a high $\tan \delta$ is required for good absorption and, consequently, for efficient heating. Solvents used for microwave synthesis can be classified as high ($\tan \delta > 0.5$), medium ($\tan \delta 0.1-0.5$), and low microwave absorbing ($\tan \delta < 0.1$).²¹

For microwave irradiation to penetrate to the reaction mixture, reaction vessels employed in microwave chemistry are typically made out of low microwave absorbing or microwave transparent materials such as borosilicate glass (Pyrex). This of course is not unlike heating for example a cup of milk in a kitchen microwave. While the microwave absorptivity of food to be heated or thawed in a kitchen microwave is in most instances high enough to allow sufficient microwave dielectric heating to the desired temperature, this is not always the case for chemistry applications. Notably, microwave chemistry in low-absorbing or microwave transparent solvents ($\tan \delta < 0.1$) is often not feasible, unless either the substrates or some of the reagents/catalysts are strongly polar and therefore microwave absorbing, raising the overall dielectric properties of the reaction medium to a level that allows sufficient heating by microwaves. Since this is not always the case, many nonpolar solvents, that have proven to be very useful and are popular in conventional chemistry, are potentially precluded from use as solvents in microwave synthesis.

To address this issue, we have some time ago (2006) introduced so-called passive heating elements (PHEs) made out of sintered SiC that aid in the microwave heating of weakly absorbing or transparent reaction mixtures.²² SiC is a strongly microwave absorbing chemically inert ceramic material that can be utilized at extremely high temperatures due to its high melting point (~ 2700 °C) and very low thermal expansion coefficient.²³ Microwave irradiation induces a flow of electrons in the semiconducting SiC that heats the material very efficiently through resistance (ohmic) heating mechanisms.²³ The cylindrical SiC PHEs can be utilized in combination with standard 10 mL Pyrex microwave

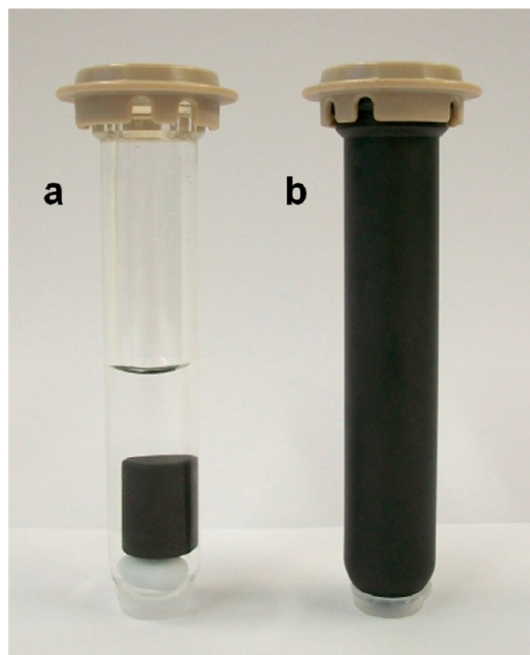


FIGURE 1. (a) 10 mL Pyrex microwave vessel containing a stir bar and a cylindrical SiC passive heating element. (b) Reaction vial made entirely from sintered SiC. Both vials have identical geometry and a wall thickness of 2.85 mm and are fitted with a thermoplastic snap cap and PTFE-coated silicone septa to be used in a Monowave 300 (Anton Paar GmbH) single-mode microwave instrument at up to 300 °C and 30 bar pressure.

vials (Figure 1a). In essence, these heating inserts will absorb microwave energy and subsequently transfer the generated thermal energy via conduction phenomena to the surrounding reaction mixture. This technique therefore allows the heating of even fully microwave transparent solvents or reaction mixtures to very high temperatures using sealed vessel microwave processing.²²

It became evident to us after employing this technology in a variety of different applications that by using the strongly microwave absorbing PHEs, most of the “microwave heating” in an experiment of this type essentially occurs by conventional conduction and convection heat transfer principles from the SiC surface, resembling a classical oil bath experiment.^{22,24} In particular, for low and medium microwave absorbing reaction mixtures, there is only a very limited possibility for genuine dielectric heating of the reaction mixture since most of the energy will be absorbed by the heating element and not by the surrounding solution.^{22,24}

Based on our experience with PHEs made from SiC we then wondered if it would be possible to manufacture a microwave reaction vial made entirely out of SiC ceramic. We hypothesized that owing to the strong microwave absorptivity of SiC, any material contained inside the vial

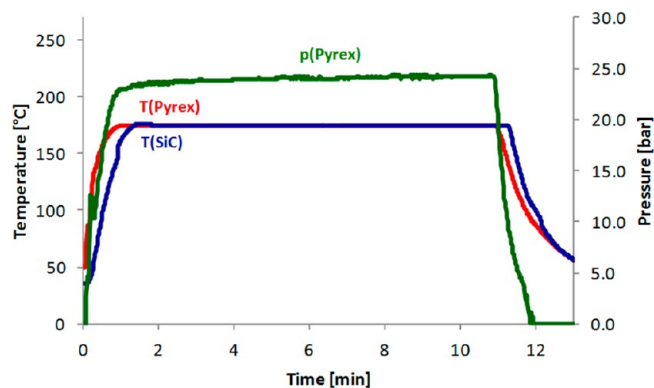


FIGURE 2. Comparison of internal FO temperature (T) profiles for the heating of methanol ($\tan \delta$ 0.659) to 175 °C performed in Pyrex and SiC vials. In both experiments, the desired target temperature is maintained for exactly 10 min, with very similar heating and cooling profiles. The pressure profile (p) for the Pyrex experiment is also shown.

would be completely shielded from the electromagnetic field. Such a reaction vessel would thus ideally be suited to investigate the significance of specific and nonthermal microwave effects since by a simple switch from a microwave transparent Pyrex to a strongly microwave absorbing SiC vial any effects of the electromagnetic field on the reaction mixture could be eliminated, while retaining the sealed vessel capabilities, rapid heating/cooling and excellent process control features inherent to modern microwave reactors. Ultimately, a 10 mL SiC reaction vial of the exact same geometry as a standard microwave-transparent Pyrex vial was obtained (Figure 1b), that allowed sealed vessel microwave processing at temperatures up to 300 °C and 30 bar pressure in a commercially available microwave reactor capable of simultaneous temperature measurement and control by both an external IR and internal FO sensor.^{19,25} Gratifyingly, excellent internal control of reaction temperature in both the Pyrex and SiC vessels could be obtained for all evaluated solvents/reaction mixtures (see, for example, Figure 2), thus ensuring that the intended comparison experiments could indeed be performed under virtually identical reaction conditions.^{19,25}

3. Microwave Field Strength Inside the SiC Vials

The fact that the electric field strength and the power density inside the SiC vial must be comparatively low could be easily derived from several experiments. First of all, the heating profiles obtained for solvents with vastly different loss tangents ($\tan \delta$) at constant power provide clear evidence that the SiC vial provides efficient shielding of its contents from the microwave field.²⁵ The fact that nearly microwave transparent hexane ($\tan \delta = 0.02$) is heated at a similar same rate as strongly microwave absorbing ethanol ($\tan \delta = 0.941$)

clearly indicates that the microwave field inside the SiC vial must be extremely low, and that heating occurs in essence via conventional heat-transfer mechanisms from the wall and not by dielectric heating effects (Figure 3a).²⁵ This is in stark contrast to the identical experiment carried out in Pyrex vials where genuine microwave dielectric heating occurs and solvents with higher $\tan \delta$ values are heated more rapidly (Figure 3b).²⁵ Because of the unusually high thermal conductivity of SiC (~ 100 times higher compared to Pyrex) the heat flow through the SiC wall of the reaction vessel is exceptionally fast. In addition, due to its extremely high thermal effusivity (a measure for the ability to exchange thermal energy with its surroundings) the contents inside the SiC reaction vial are also heated in a very efficient manner, at an equal rate if not faster than using a Pyrex vessel.

In a complementary set of experiments, the four solvents used in the experiments shown in Figure 3 were heated in temperature control mode to a specific target temperature.²⁵ Notably, the applied magnetron microwave power for all four solvents was virtually identical. Even for a completely empty vial, the same magnetron power was used, strongly suggesting that heating of the SiC vial is largely independent of its contents, which again points to the strong shielding effect of the SiC vessel. Additional support for the strong shielding characteristics of the SiC vials have been derived from electromagnetic field simulations,²⁶ and experiments with electrodeless discharge lamps.²⁵ In the presence of a microwave field, these devices will illuminate and emit UV/visible light. In contrast to the use of Pyrex vials it was virtually impossible to induce a gas discharge in SiC reaction vessels.²⁵

Based on the obtained evidence, it can be safely concluded that the use of SiC vials in a single-mode microwave reactor will provide an almost complete shielding of the contents inside from the electromagnetic field. In essence, this technology therefore allows to use a standard microwave reactor platform to perform a noncontact heating autoclave experiment under very carefully controlled and monitored conditions (heating and cooling ramp, final set temperature, pressure, stirring speed). This type of experiment, although performed in a microwave reactor, does not involve electromagnetic field effects on the chemistry, since the SiC vial is effectively preventing microwave irradiation to penetrate to the reaction mixture.

4. Investigating Microwave Effects

Since the invention of the SiC vial concept in 2008/2009, we have routinely used this technology in our microwave chemistry projects, comparing the outcome of chemical transformations

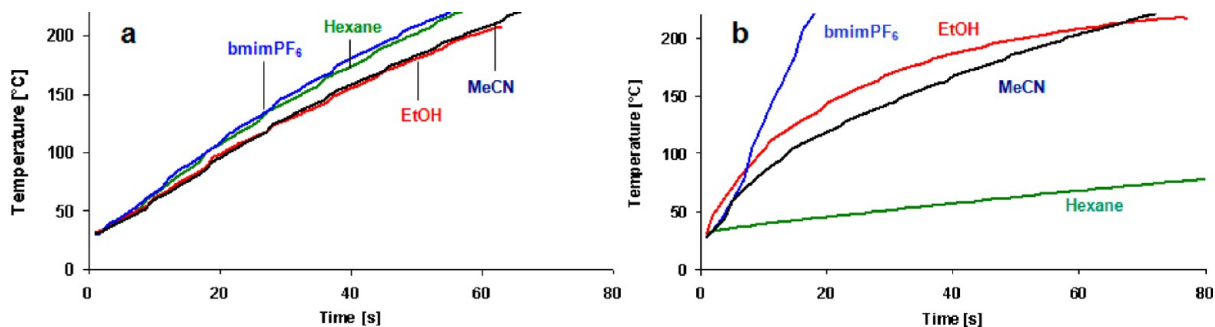


FIGURE 3. Heating profiles for 3 mL samples of hexane, MeCN, EtOH, and the ionic liquid 1-butyl-3-methylimidazolium hexafluorophosphate (bmimPF₆) at 130 W constant magnetron power (a) in a 10 mL SiC vial and (b) in a 10 mL Pyrex vial. Adapted with permission from Wiley-VCH, ref 25.

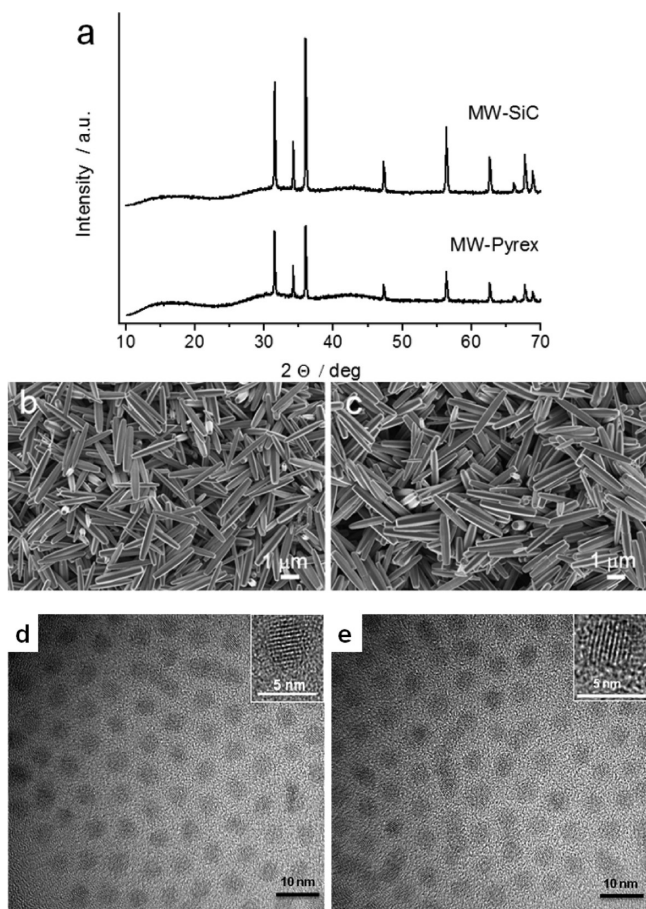


FIGURE 4. (a) X-ray diffraction patterns of ZnO samples prepared from Zn(NO₃)₂ and urea in an ethylene glycol/water (3:1) mixture in Pyrex and SiC microwave experiments obtained after 10 min at 150 °C; (b, c) scanning electron microscopy (SEM) micrographs of the same ZnO samples synthesized in Pyrex (b) and SiC (c) vessels. (d, e) Transmission electron microscopy (TEM) images of CdSe nanocrystals synthesized from Cd-myristate, SeO₂, 1,2-hexadecanediol, and oleic acid in 1-octadecene after 16.5 min overall processing time at 240 °C in a Pyrex (d) and SiC (e) vessel. Reproduced with permission of Wiley-VCH, ref 28c, and the Royal Society of Chemistry, ref 28d.

performed in a Pyrex vessel with the outcome of the analogous experiment using a SiC vessel under otherwise strictly identical

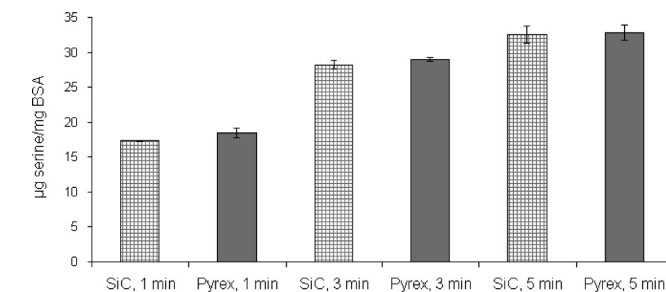
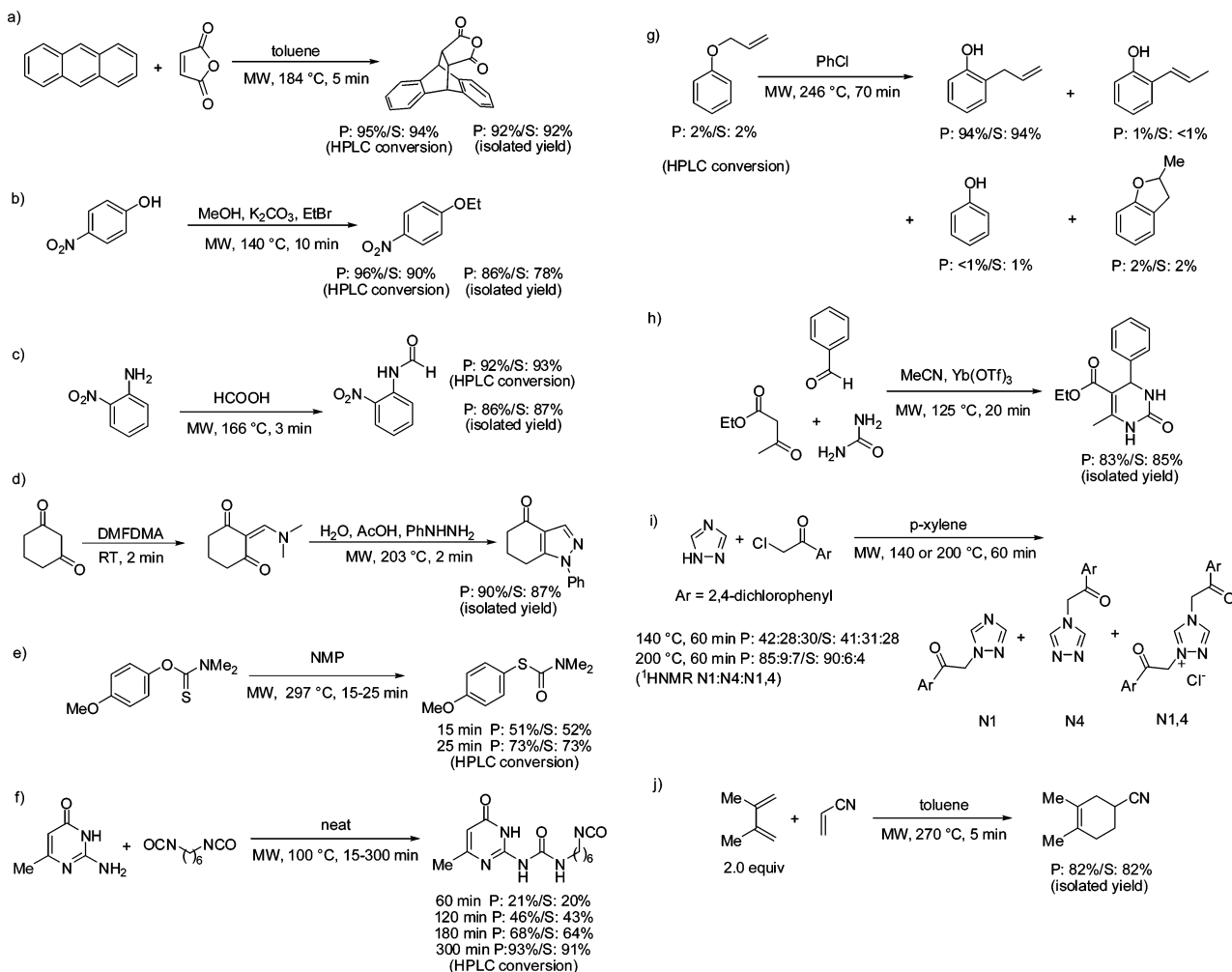


FIGURE 5. Comparison of serine recoveries in the bovine serum albumin (BSA) liquid-phase hydrolysis with 6 M HCl at 160 °C for 1, 3, and 5 min using either Pyrex or SiC vessels. Reproduced with permission from Elsevier, ref 29a.

processing conditions. In the past five years therefore, a multitude of chemical processes have been investigated in our laboratories using the SiC/Pyrex conditions in the desire to identify microwave effects that are not simply due to a purely thermal (bulk) temperature phenomenon.^{19,25,27–29} These transformations involved not only synthetic organic chemistry (see Schemes 1 and 2),^{19,25,27} but also the preparation of inorganic nanomaterials (Figure 4)²⁸ and several biochemical/bioanalytical protocols such as, for example, the acid-catalyzed hydrolysis of proteins (Figure 5).²⁹

Despite the wide range of transformations and experimental conditions, in practically all of the studied examples, virtually identical results in terms of conversion, purity profile/material property, and/or isolated yields/efficiency were obtained, comparing experiments that involved genuine microwave chemistry in Pyrex vials with “autoclave chemistry” in SiC vials. Selected examples from our publications over the past 5 years are highlighted in Schemes 1 and 2, and Figures 4 and 5 (for additional case studies and an extended discussion of individual transformations, the reader is referred to the original references).^{19,25,27–29} While in most of the examples the use of high-temperature sealed vessel microwave conditions in Pyrex vessels led to a significant

SCHEME 1. Examples of Miscellaneous Organic Reactions Performed in Pyrex (P) or SiC (S) Reaction Vials under Otherwise Identical Reaction Conditions^a

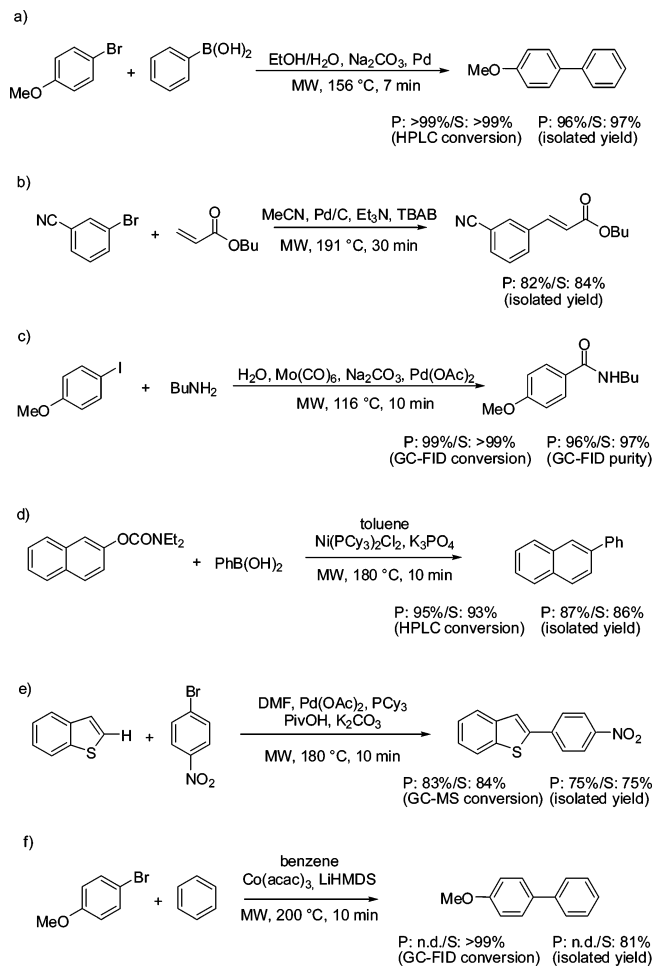
^aFor details, see ref 25 (a–i) and 27a (j).

reduction of processing times compared to conventional flask conditions performed at a much lower reaction temperature (i.e., at the boiling point of the reaction mixture), the control experiments using the SiC vessel allowed reproducing the microwave Pyrex results quite easily. In our opinion, the data obtained from these SiC/Pyrex comparison experiments therefore strikingly confirm that it is simply a bulk temperature effect which is responsible for the typically observed enhancements in microwave chemistry (thermal microwave effect) and that the electromagnetic field itself has no direct influence on the reaction pathway.¹³ The conclusions reached from applying the SiC vessel protocol are therefore in good agreement with our earlier investigations on microwave effects using a variety of different experimental techniques.^{11,14–18} It should be emphasized, however, that the “SiC test” is much easier to perform than other methods

(i.e., involving an oil bath or autoclave), since the experiment is performed in the same microwave reactor as the Pyrex experiment and requires only a simple switch from one vial type to the other under otherwise identical conditions. Notably, all processing parameters are monitored and controlled on the same platform with the identical probe (most importantly temperature) which reduces experimental error.

5. Additional Characteristics of SiC Reaction Vessels

Our original motivation for the development of the SiC microwave reaction vessel was exclusively connected to the investigation of microwave effects and the influence of the electromagnetic field on chemical transformations. We subsequently realized, however, that there are numerous inherent advantages associated with the use of a reaction

SCHEME 2. Examples of Transition-Metal Catalyzed Reactions Performed in Pyrex (P) or SiC (S) Reaction Vials under Otherwise Identical Reaction Conditions^d

^dFor details, see ref 25 (a–c), 27c (d), 27e (e), and 27f (f).

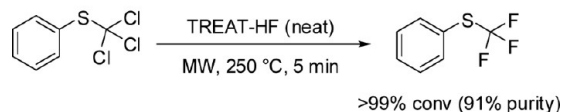
vessel made from strongly microwave absorbing SiC in conjunction with a dedicated microwave reactor. A very practical advantage of using SiC vials in microwave chemistry is that low absorbing ($\tan \delta < 0.1$) or even completely microwave transparent solvents or reaction mixtures can be efficiently heated to high temperatures, which would be virtually impossible utilizing standard Pyrex vials. The C–H activation chemistry using benzene as reagent/solvent at 200 °C shown in Scheme 2f is one such example where a traditional Pyrex experiment is extremely difficult to perform.^{27f} On the other hand, because of the high thermal conductivity and effusivity of the SiC material the heat flow through the wall of the SiC vessel is exceptionally fast in both directions. This means that the cooling efficiency by compressed air at the end of a reaction is at least as high as when using a Pyrex vial (see Figure 2). More importantly, the use of a SiC reaction vessel can aid in the prevention of exotherms,

thermal runaways and temperature overshoots as the heat generated during a microwave-assisted chemical reaction can be more efficiently exchanged with the comparatively cool air in the microwave cavity via the SiC ceramic.²⁵ A case in point is the synthesis of ionic liquids via alkylation of nitrogen-containing heterocycles, which is notoriously difficult to control under microwave conditions.^{18a}

One of the most striking benefits of the SiC vessel in microwave chemistry is derived from the corrosion resistance of this ceramic material. The corrosion resistance of sintered SiC is, like most ceramics, far better than of metals and even aggressive media such as concentrated acids or bases, HF, or chlorine gas have negligible impact in terms of corrosion.³⁰ The high-temperature fluorine–chlorine exchange reaction using triethylamine trihydrofluoride (TREAT-HF) as a reagent shown in Scheme 3 is an example where in a microwave-assisted process using a standard Pyrex vessel a significant amount of corrosion of the borosilicate glass was noticeable.³¹ In stark contrast, the SiC vial proved to be completely corrosion resistant to TREAT-HF even at 250 °C for prolonged periods of time (no measurable weight loss).³¹ A similar effect was noticeable for nitrile hydrolysis reactions employing 20% aqueous KOH in a temperature range of 150–190 °C.²⁵

An additional feature of using a reaction vial made out of a high-temperature/high-pressure resistant material in microwave chemistry is that vessel failures can be essentially eliminated. SiC has a melting point of ~ 2700 °C, and the 10 mL SiC reaction vial shown in Figure 1 is mechanically extremely robust. While standard Pyrex microwave process vials for microwave chemistry have an approved pressure rating of 20–30 bar, the SiC tube could not be destroyed even at 200 bar pressure. In particular, vessel failure due to deposition of strongly microwave absorbing materials on the inner vessel wall can be eliminated. Such catastrophic vessel failures are sometimes observed using Pyrex microwave vessels, most notably in transition-metal catalyzed processes where inadvertently formed zerovalent metal deposits can cause melting of the Pyrex glass or will lead to arcing phenomena.³² As the electromagnetic field strength inside the SiC vial is practically zero, the possibility for arcing phenomena is minimized. Therefore, safe microwave processing even in the presence of metals or other strongly microwave absorbing materials becomes possible using SiC reaction vessels.

In addition to the use of SiC reaction vessels designed for single-mode microwave reactors, we and others have extensively used microtiter plates made out of SiC material in multimode microwave instruments. The main purpose of

SCHEME 3. Fluorination Reaction Involving Triethylamine Trihydrofluoride (TREAT-HF) Using a Corrosion Resistant SiC Vial⁴

⁴The inset shows the strong corrosion effect of TREAT-HF on a standard Pyrex microwave vessel comparing a broken vial before (left) and after (right) exposure at 250 °C for 30 min.

these designs is to allow the parallelization and miniaturization of sealed vessel microwave chemistry in the context of high-throughput synthesis. The results of these investigations have recently been reviewed.³³

6. Conclusion and Outlook

The results of our research over the past 5 years using SiC reaction vessels in microwave chemistry essentially demonstrate two important issues: (1) Using a SiC reaction vessel inside a microwave reactor simulates a conventionally heated autoclave experiment. (2) Comparison studies between experiments performed in SiC and Pyrex reaction vessels under otherwise identical conditions can rapidly establish that for the overwhelming majority of cases¹³ the effects seen in microwave chemistry are the result of a purely (bulk) temperature phenomenon and are not related to so-called specific or nonthermal microwave effects. So the obvious question then becomes: what really is the difference between a microwave-heated reaction and an autoclave experiment? Based on the arguments presented in this Account, the answer may simply be: Convenience! If the electromagnetic field strength has no direct influence on the chemistry and all effects in microwave-assisted transformations related to more rapid conversions, higher yields/purities, and so forth can be explained by bulk temperature phenomena, there is no strictly scientific reason to favor a sealed vessel microwave reactor over a more traditional autoclave.³⁴ One therefore has a difficult time disagreeing with a quote from a recently published book on microwave chemistry: "Heating is just that – heating, be it in an microwave or an oil bath".³⁵ Ultimately, it must be stressed, however, that the ability to rapidly superheat reaction mixtures far above their boiling points in an operationally simple and safe manner with

exquisite online and rapid control over reaction temperature and pressure (unlike in a typical autoclave!) will ensure that modern microwave reactors are here to stay and will not easily be replaceable by other technologies in the future.

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BIOGRAPHICAL INFORMATION

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FOOTNOTES

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The authors declare no competing financial interest.

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