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Correspondence on Microwave Effects in Organic Synthesis

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microwave chemistry · microwave effects · microwave heating · organic synthesis · temperature monitoring

Angewandte Chemie recently published an unusual Essay by Prof. C. Oliver Kappe and co-workers entitled, "Microwave Effects in Organic Synthesis—Myth or Reality?"[1] The major point of discussion is an Edge Article we published last year in the RSC journal *Chemical Science* entitled, "On the Rational Design of Microwave-Actuated Organic Reactions."[2] The *Angewandte* Essay is unusual in its inclusion of 38 pages of experimental details in the Supporting Information,[3] 30 of which describe unpublished data from original experiments pertaining to our work. These data are interpreted as conflicting with our report. We reject their alternative interpretations of our experiments, and we discuss here how the new data from their experiments in fact align with our conclusions.

In our article, we provided an example of a microwave (MW)-actuated reaction system, which we define as one for which MW irradiation provides a synthetic advantage over conventional heating at the same temperature. We designed an extreme reaction system—an ionic benzyl-transfer reagent in a nonpolar aromatic solvent[4]—and subjected it to extreme conditions: constant MW irradiation at high power (300 W). Our design of this chemical system was predicated on the concept of selective heat storage in the domains existing around microwave-absorbing solutes in nonabsorbing media at fixed (and typically high) applied microwave powers. The design rationale aligns with an understanding of selective microwave heating obtained from fundamental dielectric relaxation studies carried out by Richert and Huang.[5] In such a system, the selective absorption of microwave energy by the solute will result in localized energy in the solvation domain (i.e. effective temperature) that is higher than the surrounding medium. The solute then acts as a molecular radiator,[6] transferring thermal energy to the bulk solution.[7] If convective heat transfer out of the domains is slow compared to the build-up of thermal energy within the solute domains, then the thermal energy of the solute will exceed what would be predicted based on the measured temperature of the bulk solution. As an extension of that work, one can hypothesize that a microwave-absorbing *reactant* in a nonabsorbing medium can potentially realize product formation at rates in excess of what would be expected from conventional heating at the same measured bulk temperature. Indeed, we observed reactivity enhancements under MW heating compared to conventional oil-bath heating in a benzylation of [D_{10}]*p*-xylene (Figure 1).

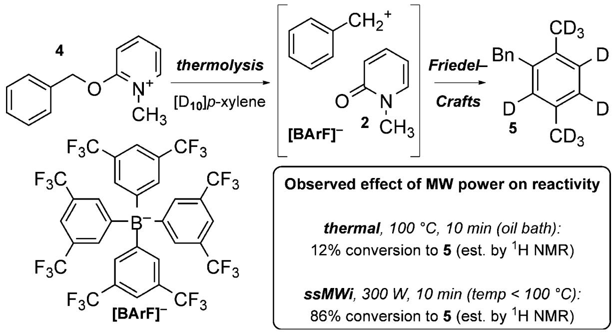

Figure 1. Scheme 2 from reference [2]. ssMWi = steady-state MW irradiation.

Prof. Kappe and co-workers have challenged our observations and the underlying rationale. In the Table of Contents text accompanying their Essay, for example, they describe the existence of so-called specific microwave effects as "highly doubtful."[8] They later conclude that our hypothesis, at least as articulated in the Essay, "ultimately proved to be unfounded." In light of the extensive discussion and criticism of our work,[9] we take this opportunity to reply and address some of the issues that they raise. First, however, I (G.B.D.) would like to thank Prof. Kappe and Dr. Gölitz for sharing and discussing this Essay with me prior to its acceptance and again in advance of the Essay appearing in print. I was permitted to comment on the initial submission, and the manuscript was revised to address some (but not all) of my concerns. The object of this Correspondence is to raise and discuss the residual concerns. In the interests of brevity, we focus on three.

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1. Our Conclusions Are Misstated in the Essay and Their Conclusions Are Inconsistent

Prof. Kappe and co-workers argue against the existence of "nonthermal/specific microwave effects", supposedly in order to refute our claims.[10] However, we make no such claims. We are convinced that nonthermal MW effects (as defined by Prof. Kappe) have never been observed and are highly unlikely to exist.[11] The authors are making what is known as a "straw man" argument[12] here, in which they attempt to impugn our credibility by assigning to us an incorrect position and then arguing against it. The word "nonthermal" does not appear in our manuscript, but it is used 22 times in the Essay and twice more in the Supporting Information.[13] In the Table of Contents text, for example, the authors conclude that, "the existence of so-called nonthermal or specific microwave effects is highly doubtful." In the Supporting Information, however, they conclude that our results are explained by the "well-known" specific microwave effect of solvent superheating.[14] **These conclusions are mutually exclusive**.[15] Invoking a specific microwave effect to explain their observations requires suspending any doubt as to the existence of specific microwave effects. The answer to the Essay's titular question, "Microwave Effects in Organic Synthesis—Myth or Reality?" is the latter. The more appropriate question is, can microwave-specific effects be exploited?

The actual conclusions presented in our manuscript are that MW-actuated thermal reactivity can exceed temperature-based expectations,[16] and that MW energy is a variable in this extreme reaction system. We rule out "solvent superheating" as a significant factor (see below) and instead focus on the effects of *solute* heating, taking advantage of the differential energy transfer properties of microwaves.

2. Our Experimental Conditions Were Not Appropriately Replicated

Prof. Kappe and co-workers claim to have repeated our experiments, "duplicating the reaction conditions and experimental setups", and that "no evidence for any type of specific *or nonthermal* microwave effects could be obtained" (italics added[17]). *We dispute these claims and contend that the following are true*:

- Most of their experiments are different than the ones we reported.
- The changes they made to our experimental designs result in the suppression of specific MW effects.
- In the reflux experiments discussed below, the changes were *explicitly intended* to suppress a specific MW effect.

Where their experiments correlate with ours, their observations align with ours. We stand by our original conclusions.

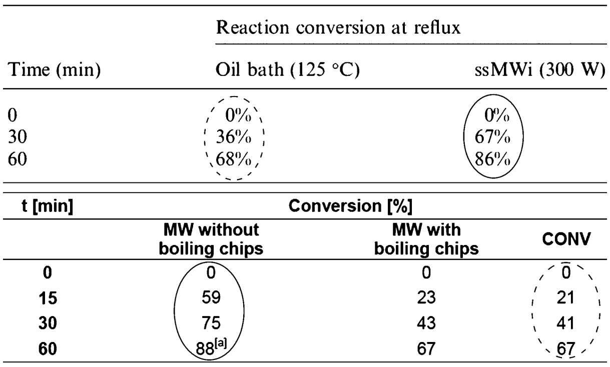
The central experiments on which we based our conclusions are recounted briefly here (cf. Figure 1). Through a trial-and-error process, we arrived at a reaction system that, at least using our equipment, heated very *in*efficiently under MW irradiation.[2,4] We irradiated this system at full power (300 W) for 30 min and observed that the ratio of product (benzylxylene **5**) to remaining starting material was $\geq 95:5$ by ^{1}H NMR analysis. The measured temperature[18] of the system steadily increased at first and then stabilized but did not reach 100 °C. We then immersed an identical system in an oil bath (preheated at 102 °C) for 30 min and observed that the ratio of product to remaining starting material was approximately 25:75 by ^{1}H NMR analysis. It is important to emphasize here that we used the constant power setting on our MW instrument, not the constant temperature setting, for the MW heating experiments. We concluded that there was a significant difference in the chemical behavior of the two systems, and we attributed this difference to the application of steady-state MW irradiation (ssMWi) at high power in the former case.

Under the pretense of replicating these experiments, the Kappe lab employed MW heating at constant temperature, not constant MW power, in stark contrast to the central hypothesis of our work. More importantly, they used relatively low average MW power to heat their system, and they got results similar to those obtained for heating in the absence of MW power. A key factor in trying to exploit selective heat storage is MW power (energy/time). The more MW energy is absorbed by the solute within a given timeframe, the greater the potential for accumulating excess thermal energy in the solvation domains. Alternatively, reducing the MW power is likely to reduce the effects of MW energy. The Essay authors acknowledged using much lower MW power than we did, but they failed to address the significance of this change with respect to microwave-specific effects. Their rationale for changing the design was that their system heated more efficiently than ours.[19] We offered repeatedly to work with them to resolve this discrepancy, but to no avail.[20] Regardless, the differences in experimental design (high constant power vs. low variable power) mean that their experiments cannot be equated (or even directly compared) with ours.[21]

Their observation of lower reactivity at lower MW power specifically correlates with one of our control experiments. As described in our manuscript, we engulfed an identical system in a propylene glycol jacket, which results in efficient MW heating by means other than direct interaction with the solute. This jacketed system was subjected to microwave heating at 100 °C. Foreshadowing what the Kappe lab later observed, we showed that rapid heating with a lower average applied MW power suppresses the reactivity that is observed at high MW power.[22] *All of these experiments reinforce our conclusion of the link between MW power and chemical reactivity in this system*.

3. The Text of the Essay Does Not Match the Supporting Information

We conducted a separate set of experiments in which we used reflux to define the solution temperature. As before, we saw significantly higher conversion under MW-induced reflux than when reflux was maintained by conventional heating (Figure 2, top). The Kappe lab performed similar reflux experiments and *also* saw significantly higher conversion under MW heating than under conventional heating, although



	Reaction conversion at reflux	
Time (min)	Oil bath (125 °C)	ssMWi (300 W)
0	0%	0%
30	36%	67%
60	68%	86%

t [min]	Conversion [%]		
	MW without boiling chips	MW with boiling chips	CONV
0	0	0	0
15	59	23	21
30	75	43	41
60	88[a]	67	67

Figure 2. Top: Table 1 from reference [2]. Bottom: Table S3 from the Supporting Information for reference [1].

these observations are revealed only in the Supporting Information (Figure 2, bottom). In fact, their data are similar to ours, as indicated by the ovals added to Figure 2.

In the main text of the Essay, the authors present an incomplete truth: "conversions… [achieved using MW heating] were more or less identical to those achieved using conventional heating…" The tables reproduced in Figure 2 present a more complete picture. Microwave heating (solid ovals) resulted in significantly higher conversions than oil-bath heating (dotted ovals) *in both of our studies*.[23] We concluded that this effect is real, and that MW energy is an important variable in this system. The Essay authors do not argue this point; they conclude, as we do, that there is an effect. They attribute these observations to solvent superheating,[14] which they describe as "a well-known phenomena (a specific microwave effect)" (p. 30 in the Supporting Information). According to them, this specific microwave effect can be quite dramatic in that, "the superheating temperature can be up to 40 °C above the classical boiling point of the solvent."[24]

Later in the Essay, the authors note, "Key to achieving *comparable* conditions…was the use of boiling chips that prevent superheating under microwave conditions" (italics added[25]). In other words, they altered our experimental design—by adding boiling chips—explicitly to prevent what they describe as "a specific microwave effect". It is incorrect for them to conclude that, "in our hands no evidence for any type of specific or nonthermal[17] microwave effect could be obtained." [26] In fact, they *did* obtain such evidence. They just did not present the evidence in the main text of the Essay.

A Closer Look at the Question of Sustained Superheated Boiling

Can our observations be explained by the specific microwave effect of superheated boiling, as suggested in the Essay? The general phenomenon of solvent superheating and the MW-specific effect of superheated boiling are mentioned in references [25] and [26] of our publication,[2] respectively, but we did not consider them to be determining factors. The general phenomenon of solvent superheating can occur upon heating of unstirred liquids, but it does not persist once boiling is initiated.[27] The MW-specific phenomenon of superheated boiling, in which reflux is maintained above the solvent boiling point, also is suppressed by stirring.[28] However, the Kappe lab reports "an extremely fluctuating temperature profile ≈ 10 °C above the standard boiling point of toluene… *even applying vigorous stirring*" (p. 14 in the Supporting Information, italics added).

To our knowledge, this claim is without precedent. Several groups have studied MW-specific superheated boiling[28,29] or nucleation-limited boiling,[30] but none of the papers cited in the Essay describe a significant effect in a *stirred* liquid. Superheated boiling is known, but it is only significant in unstirred liquids. For example, a comprehensive study by Chemat and Esveld revealed that "[f]or many solvents, the superboiling temperature under microwave irradiation can be 10 °C to nearly 40 °C above the classical boiling point", but superheated boiling is suppressed by stirring, boiling stones, and to a lesser degree by fiber-optic probes and other mild perturbations, as illustrated unambiguously in Table 2 of their paper.[28] In the words of Chemat and Esveld, "The action of stirring…practically removes all super-heating."[28]

We now have precise measured temperature data that correlate with the Chemat study and that unequivocally rule out both solvent superheating and superheated boiling as confounding variables in our stirred reflux reaction systems. We acquired an appropriate fiber-optic temperature probe and used it to monitor the internal temperature of reflux reactions in toluene (Figure 3).[31] Identical mixtures of 75 mg of salt **4** and 15 mL of toluene were heated at reflux using a microwave reactor under three sets of conditions: 1) no stirring, 2) stirring, and 3) stirring in the presence of boiling chips.[32] The *unstirred* solution (top line) initially shows evidence of superheating,[27] then sustained superheated boiling with measured temperatures hovering around 126 °C. However, stirring the solution (as we did in all of

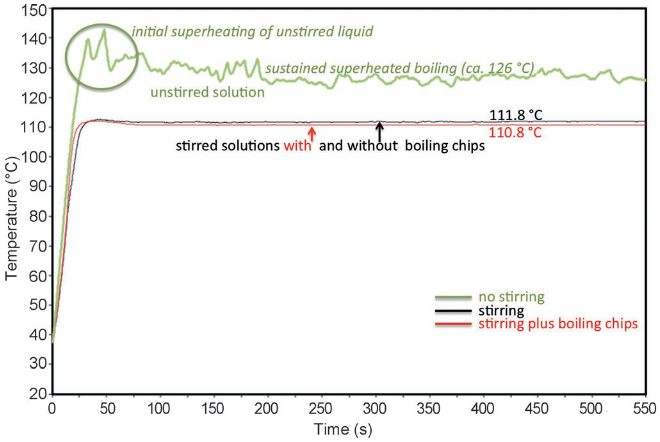


Figure 3. Measured internal reflux temperatures of toluene under MW heating (300 W) without stirring (top line) and with stirring (with or without boiling chips, bottom two lines). Temperatures were measured using a Neoptix Reflex internal fiber-optic thermometer, calibrated between 150 °C and room temperature with a NIST traceable thermocouple with a precision of ± 0.001 °C.

our original experiments) "practically removes all superheating"[28] and results in a sustained measured reflux temperature of 111.8 °C. The stirred solution with boiling chips was measured at 110.8 °C. The specific microwave effect of superheated boiling may offer insights into other microwave heating phenomena, but it does **not** explain the observed reactivity of this system (cf. Figure 2). Because our offers to work with the Kappe lab were declined, we can only speculate on the origins of their "fluctuating temperature profile".[33]

It is important to understand that these temperature measurements, regardless of their precision, must be interpreted thoughtfully, because the system is not at thermal equilibrium.[34] As a consequence of selective MW heating, individual solution components respond differently to steady-state MW irradiation (ssMWi). The measured temperature reflects the average kinetic molecular energies of all solution components, but to a first approximation, only the solute absorbs MW energy, and only the solvent evaporates and condenses. The measured solution temperature—a weighted average—overestimates the thermal energy of the solvent and underestimates the thermal energy of the solute.[35] In this case, the measured solution temperature is slightly above the boiling point of the solvent, and the observed solute reactivity significantly exceeds what would be expected based on the solution temperature.

It was not our intention to parse the relative contributions of specific MW effects, none of which is well understood, in our initial publication. Considerably more work is needed, including perhaps development of new theoretical models, to quantify the impact of MW energy. Such work is now in progress. Our original objective was to demonstrate an effect: that different chemical behaviors can be observed from otherwise identical chemical systems depending on whether conventional or microwave heating is employed. In this regard our results are clear: MW energy is an important variable in promoting thermal reactivity in the specific system that we studied.

In conclusion, the new experiments that Prof. Kappe and co-workers report in an unusual Essay published in *Angewandte Chemie*[1] are, by our interpretation, consistent with our experiments published last year in *Chemical Science*.[2] We rationally designed a system with the expectation (hypothesis) of observing enhanced reactivity under ssMWi compared to conventional heating. We observed compelling evidence of reactivity that we described as "microwave-actuated",[36] and concluded that our now-validated hypothesis "can provide a foundation for the rational design of new microwave-actuated organic reactions for strategic applications in chemical synthesis." Continued research in this direction should be fruitful.

Additional Comments from the Co-Author, Prof. Dr. Al Stiegman

It is certainly the case that a significant number of prior studies that claimed a microwave-specific effect were flawed due to the problem of accurate temperature measurement, and Prof. Kappe, quite correctly, pointed this out in a number of publications, although it is important to note that recognition of the problem greatly precedes Prof. Kappe's entrance into this field.[37] For this reason, the problem of temperature measurement, which is typically due to the use of external IR thermometers, is now well known in the field, and the number of claims in the literature that are flawed by this error have diminished. In the particular case of our paper, which unambiguously discussed and experimentally addressed the temperature problem, Prof. Kappe's conceit that we were somehow blithely ignorant of the problems of external IR thermometers is, to say the least, disingenuous. More importantly, the fact that a number of studies claiming a microwave-specific effect have been shown to be faulty is a necessary but certainly not sufficient condition to dismiss the existence of such an effect. The fact is, microwaves heat in a manner that is intrinsically different from convective heating, and mechanisms exist, consistent with the fundamental physics of microwave heating, by which a "specific microwave effect" can potentially manifest itself. This effect is thermal in nature and arises from the selective heating of molecules in solution. Our benzylation paper was an attempt to find reaction conditions under which such an effect could be observed. Our reported enhancement of reactivity in the microwave is correct and represents a direct observation of microwave-specific rate enhancement. As we outlined in this rebuttal, Prof. Kappe's attempt to "debunk" our effort is without merit, as he neither accurately duplicated our deliberately chosen experimental conditions nor accurately determined the temperature in our refluxing solution. In my view, the problem with setting out to "debunk" a result rather than replicate it is that objectivity is discarded and science is little served.

Final Thoughts from the Corresponding Author

This Correspondence must not be viewed as a general criticism of Prof. Kappe or the bulk of his work in the area of MW chemistry.[38] It is rather a defense of our work, which has been misrepresented in this *Angewandte* Essay.[39] More importantly, it is a defense of a controversial hypothesis that may have been prematurely dismissed by many in the synthetic community: that synthetic chemists can harness MW energy strategically in ways not yet fully appreciated. This hypothesis runs counter to the current conventional wisdom in microwave-assisted organic synthesis, and it warrants further investigation as we seek better ways to exploit the alternative heating properties of microwaves.

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[1] C. O. Kappe, B. Pieber, D. Dallinger, *Angew. Chem.* **2013**, *125*, 1124–1130; *Angew. Chem. Int. Ed.* **2013**, *52*, 1088–1094.

[2] M. R. Rosana, Y. Tao, A. E. Stiegman, G. B. Dudley, *Chem. Sci.* **2012**, *3*, 1240–1244.

[3] According to the *Angewandte Chemie*'s Author Guidelines on writing an Essay: "Use of unpublished results from original research should be extremely limited."

[4] Our system featured a dilute homogeneous solution comprising an ionic substrate and nonpolar solvent in a quartz (not Pyrex) vial. Only one component of this system—the reaction substrate—interacts with MW radiation, so any heat generated within the system arises from the MW-actuated reactant.

[5] a) W. Huang, R. Richert, *J. Phys. Chem. B* **2008**, *112*, 9909 – 9913; b) W. Huang, R. Richert, *J. Chem. Phys.* **2009**, *130*, 194509; c) A. C. Metaxas, R. J. Meredith, *Industrial Microwave Heating*, IET, **1983**.

[6] a) N.-F. K. Kaiser, U. Bremberg, M. Larhed, C. Moberg, A. Hallberg, *Angew. Chem.* **2000**, *112*, 3741 – 3744; *Angew. Chem. Int. Ed.* **2000**, *39*, 3595 – 3598; b) E. Van der Eycken, P. Appukkuttan, W. De Borggraeve, W. Dehaen, D. Dallinger, C. O. Kappe, *J. Org. Chem.* **2002**, *67*, 7904 – 7907.

[7] According to Prof. Kappe, "The formation of 'molecular radiators' by direct coupling of microwave energy to specific reagents in homogeneous solution" is a specific MW effect.

[8] The same descriptor is simultaneously attached to nonthermal effects. As we note below (see Ref. [10]), there is a clear distinction between so-called nonthermal effects and specific microwave effects, and any attempt to associate them will result in confusion.

[9] This Essay better meets the criteria for an *Angewandte* Correspondence, except that our article was published in a different journal. The Author Guidelines state: "Manuscripts that critically comment on publications in *Angewandte Chemie* can be published as Correspondences if they make an important contribution to the scientific discussion. The author of the publication to which the Correspondence pertains will have the opportunity to reply."

[10] We contend that it is not appropriate to discuss nonthermal effects in the same context as specific MW effects, much as no one discusses vitalism in the context of drug design. The nonthermal effects discussed in the Essay were postulated early in MW chemistry, but less so now as the field has matured and understanding of the underlying physics has improved. Specific MW effects may be rare and difficult to design successfully into experiments at this time, but there is no reason to doubt at this point that they are possible.

[11] For an excellent theoretical discussion, see: a) D. Stuerga, *J. Microw. Power Electromagn. Energy* **1996**, *31*, 87 – 100; b) D. Stuerga, *J. Microw. Power Electromagn. Energy* **1996**, *31*, 101 – 113.

[12] a) "The straw man fallacy": D. Walton in *Logic and Argumentation* (Eds.: J. van Bentham, F. H. van Eemeren, R. Grootendorst, F. Veltman), Royal Netherlands Academy of Arts and Sciences, Amsterdam, **1996**, pp. 115 – 128; b) See also http://en.wikipedia.org/wiki/Straw_man (accessed 5 April 2013).

[13] The Supporting Information (p. S15) includes an explicit example of the attempt to paint our research as a misguided quest for nonexistent, nonthermal microwave effects: "reflux… should ensure a consistent internal temperature and therefore present more or less ideal conditions *to verify/falsify a nonthermal microwave effect. For this reason*, the Dudley group has performed the reaction of BnOP-BArF **1** in refluxing toluene" (italics added). This is their reasoning, not ours. We have no interest in the quest to verify/falsify so-called nonthermal effects, as we see no physical rationale for their existence.

[14] We repeat the use of the term "superheating" here to be consistent with the Essay. However, we and others prefer the terms "superheated boiling", "superboiling", or "nucleation-limited boiling", because the term "superheating" has already been applied to a different physical phenomenon that is not microwave-specific. These effects are discussed in more detail below and in references [27–30].

[15] Also, neither claim is supported by the data. As discussed herein, we contend that microwave superheated boiling is neither well understood nor relevant to the observed effects in our vigorously stirred system. Moreover, the existence of one effect does not negate the possibility of other effects.

[16] The authors may be confusing thermal effects with temperature effects. Heat and temperature are different, just like mass and weight are different. We note the distinction between heat and temperature in our manuscript, and we will elaborate on this important point in the context of microwave heating in a forthcoming publication.

[17] Nonthermal effects are inconsistent with the current understanding of microwave heating, so it is not clear what Prof. Kappe and co-workers would consider to constitute evidence of a nonthermal effect. We make no mention of nonthermal effects in our paper, as noted above.

[18] We used a noninvasive external IR sensor to monitor system temperature, with repeated multipoint calibration to ensure correlation with solution temperature. Our manuscript includes a discussion of the strengths and limitations of this technology and why it was the appropriate choice for our experiments, and a control experiment showing that the IR sensor is sufficiently reliable to support our conclusions. The Essay authors acknowledge that our discussion is correct, but they insist that we should have used an internal fiber-optic probe anyway. They are entitled to their opinions here, and we do not wish to belabor a moot point. As we discuss in more detail later, what they describe as the "genuine reaction temperature" is not physically defined for multicomponent solutions under steady-state MW irradiation.

[19] They attribute the different behavior of our respective systems to "a serious hardware or temperature measurement problem in the Dudley experiments." (p. 29 in the Supporting Information) We contend that other explanations, like differential release of heat to the surroundings, should be considered here, perhaps resulting from a seemingly trivial change in the experiment setup. The shape, size, and thickness of the vials used and any other physical impediments between the system and surroundings will impact heat transfer, and we spent considerable time optimizing our specific system to achieve the heat-transfer profile we needed to conduct the experiments. We offered and would have been more than happy to advise them on a similar optimization of their system, but they repeatedly declined these offers.

[20] We also suggested that they lower the concentration of the solute (such that less heat is generated), rather than reduce the incident MW power, to remain faithful to the design principles that we set forth in our publication.

[21] The reflux experiments described below are easier to compare, and in these experiments their data aligned very closely with ours.

[22] This control experiment also demonstrates the ability of the properly calibrated external IR sensor to regulate system temperature, despite the fact that this system is more prone to rapid temperature fluctuations; cf. reference [18].

[23] We did not use boiling chips in our experiments. The new data in the Essay table in the column labeled "MW with boiling chips" is discussed below.

[24] No citation was provided here, and we cannot find relevant literature to connect this effect to our experiments. Such a 40 °C temperature differential *in an unstirred liquid* is reported in a **2001** Chemat paper entitled, "Microwave Super-Heated Boiling of Organic Liquids: Origin, Effect, and Application." See reference [28]. We discuss this and related papers on superheated boiling in the following section.

[25] In fact, the heterogeneous systems described in the main text of the Essay are *not comparable* to our homogeneous system. Changes in homogeneity impact the transfer of energy and heat, and surface effects of the additives must also be considered. The heterogeneous additives cannot be assumed to be inert. We have begun to examine systems like the ones they describe. Preliminary indications are that crushed glass, for example, accelerates benzylation under conventional heating. For leading references on heterogeneous and surface catalysis (e.g., of Friedel–Crafts reactions), see: a) *Fine Chemicals through Heterogeneous Catalysis* (Eds.: R. A. Sheldon, H. van Bekkum), Wiley-VCH, **2008**; b) M. A. Keane, *J. Mater. Sci.* **2003**, *38*, 4661 – 4675.
[26] A related claim by Prof. Kappe and co-workers in the main text that "it is not possible to superheat the solvent above its boiling point" is also undermined by their data and cited literature, although it is true that solvent superheating is minimal at best with proper stirring.
[27] "Bumping" of unstirred liquids during distillation is a common manifestation of this effect. For discussions on superheated liquids with leading references, see: a) V. G. Baidakov, *Explosive Boiling of Superheated Cryogenic Liquids*, Wiley-VCH, **2009**; b) P. G. Debenedetti, *Metastable Liquids*, Princeton University Press, **1996**.
[28] F. Chemat, E. Esveld, *Chem. Eng. Technol.* **2001**, *24*, 735 – 744.
[29] R. Saillard, M. Poux, J. Berlan, M. Audhuy-Peaudecerf, *Tetrahedron* **1995**, *51*, 4033 – 4042.
[30] D. R. Baghurst, M. P. Mingos, *J. Chem. Soc. Chem. Commun.* **1992**, 674 – 677.
[31] We thank Jacob Hunt and Anthony Ferrari (Stiegman lab) for assisting with these temperature measurements.
[32] We used ceramic boiling chips made from crushed Büchner funnels as the Essay authors describe, as well as the same amounts of reagent and solvent as they report.
[33] Our measured reflux temperatures fall within a few degrees at most of the boiling point, so what could explain "an extremely fluctuating temperature profile" in their experiments? Superheated boiling of *unstirred* systems depends on myriad factors (reference [28]), and their experimental setup differed from ours in several ways: less reagent, less solvent, smaller flask, and probably a smaller reflux condenser. Perhaps the parameters of their smaller system enabled them to produce unprecedented levels of stirred superheated boiling, although our data (cf. Figure 3) suggest otherwise. Alternatively, perhaps their reflux condenser was too small for the task at hand, and the solvent they report seeing trapped in the condenser created "an extremely fluctuating" pressure profile; see also reference [19].
[34] "Temperature" is only defined for a system at thermal equilibrium. Strictly speaking, temperature cannot be measured for a multicomponent system under ssMWi, because thermal equilibrium between individual components is perturbed as a function of differential interactions with the incident MW energy. The "measured temperature" data provided by the thermometer has empirical value but requires a nuanced interpretation.
[35] Our central design hypothesis was based on the premise that ssMWi at high power results in differential average kinetic molecular energy between the solute and solvent. A more detailed discussion of the underlying physics will be included in future manuscripts; our initial study was focused on securing experimental support for the hypothesis.
[36] Specific MW effects are unequivocally observed in this system. However, the nature of the effects and opportunity to exploit them remain as open questions.
[37] a) E. G. E. Jahngen, R. R. Lentz, P. S. Pesheck, P. H. Sackett, *J. Org. Chem.* **1990**, *55*, 3406 – 3409; b) R. Laurent, A. Laporterie, J. Dubac, J. Berlan, S. Lefeuvre, M. Audhuy, *J. Org. Chem.* **1992**, *57*, 7099 – 7102; c) K. D. Raner, C. R. Strauss, F. Vyskoc, L. Mokbel, *J. Org. Chem.* **1993**, *58*, 950 – 953; d) K. C. Westaway, R. N. Gedye, *J. Microw. Power Electromagn. Energy* **1995**, *30*, 219 – 230.
[38] As we discovered during the course of our studies, however, Pyrex is not MW-transparent, so the systematic comparison of reactions conducted in silicon carbide and Pyrex vials would have more appropriately featured quartz vials: a) D. Obermayer, B. Gutmann, C. O. Kappe, *Angew. Chem.* **2009**, *121*, 8471 – 8474; *Angew. Chem. Int. Ed.* **2009**, *48*, 8321 – 8324; b) B. Gutmann, D. Obermayer, B. Reichart, B. Prekodravac, M. Irfan, J. M. Kremsner, C. O. Kappe, *Chem. Eur. J.* **2010**, *16*, 12182 – 12194.
[39] It is also my opinion that the Kappe lab should have offered to work with us to resolve our experimental differences before submitting the Essay. The interests of science would have been better served by cooperation here.