

Microwave-Assisted Reactions in Organic Synthesis—Are There Any Nonthermal Microwave Effects?

Response to the Highlight by N. Kuhnert

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In his recent Highlight,^[1] mentioned in the title, Kuhnert presented “two representative examples of microwave chemistry” that he claimed, “illustrate the confusion caused by an uncritical consideration of published results and lead to an overestimate of the capabilities of the method”. In subsequent sections, he outlined the benefits of modern microwave reactors and discussed recent results by Kappe and Stadler^[2, 3] who had employed such systems to allow one, in Kuhnert’s words, to “cautiously” conclude “that all speculation of special and nonthermal effects in microwave heating has no basis”. Kuhnert summarized that through the recent “thorough work of Kappe’s group, the comparison of thermal- and microwave-heating methods is possible for the first time”.

Although others also appear to have cause for grievance about the Highlight, the purpose of this Correspondence is to address misrepresentations and omissions with regard to our work and also to contextualize the two publications of Stadler and Kappe, mentioned above, as contributions to a body of literature rather than as the definitive work that Kuhnert had portrayed.

In order to “illustrate the confusion” about the existence or otherwise of “special and nonthermal effects in microwave heating”, Kuhnert cited the intramolecular Claisen–Schmidt condensation of hexane-2,5-dione with 0.05 % aqueous NaOH at 200 °C to afford 3-methylcyclopent-2-enone, that we had reported.^[4] He commented that “as no direct comparison with a thermal procedure under comparable conditions was undertaken, some room remains for speculation about nonthermal effects”. To the best of our knowledge, for this particular reaction, no confusion had been expressed previously and no speculation by others had occurred. Indeed, what grounds were there for confusion or speculation? In contrast with Kuhnert’s assertion, we had reported not only the reaction conducted by microwave heating in a batch

reactor (MBR) of our own design,^[5] but also with a commercial prototype continuous microwave reactor (CMR) embodied by our patent^[6, 7] and with conventionally heated autoclaves both on the 500-mL scale and the 3-L scale! Contrary to our being criticized by Kuhnert for failure to undertake comparative studies, single reports of the use of such a diverse array of equipment for carrying out one specific reaction are rare. We concluded^[4] that the result with the autoclave “was similar to that obtained with the MBR and agreed with earlier findings that the kinetics of microwave-heated and conventionally heated reactions do not differ significantly if the temperature is known and the solution is thermally homogeneous”. The earlier findings to which we had referred were presented in our 1993 paper entitled *A Comparison of Reaction Kinetics Observed under Microwave Irradiation and Conventional Heating*.^[8] (The publication year quoted is not a misprint.) In that work, we had measured for the first time the kinetics of microwave-heated and conventionally heated reactions. The paper contained theoretical discussion and repudiated findings of other groups who had claimed a nonthermal microwave effect. Unfortunately, Kuhnert’s Highlight did not refer to that work or to an even earlier paper that had led us to the same conclusion.^[9] Nor did it refer to a 1996 paper entitled *Reactions of Allyl Phenyl Ether in High-Temperature Water with Conventional and Microwave Heating*^[10] in which we had concluded on p. 7359, “These findings indicate that if the microwave conditions can be adequately mimicked (a proviso that may not always hold) conventional heating will produce a comparable outcome”.

Although our invited review^[11] was cited (as reference [8] in the Highlight^[1]), Kuhnert did not appear to take into account the section entitled *Rate Studies and Investigations into “Microwave Effects”* in which we summarized and critically evaluated the literature up to 1995 on those aspects.

Many studies into the effects of microwave heating on reaction outcomes (including the reports of Kappe and Stadler, mentioned above) have concerned conversions or yields obtained by microwave and conventional heating under apparently comparable conditions within a given time. Measurement of the kinetics of reactions, though, requires more rigorous experimental regimes and far more

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time and effort. An Arrhenius plot for a single reaction conducted by a specific heating method, for example, may be obtained only after 50 experiments or so. For a carefully conducted comparative study of microwave and conventional heating, data from about 100 experiments would be needed. To measure kinetics in a microwave environment in the early 1990s, major technical difficulties first had to be overcome. Dedicated reactors were required. Our paper entitled *A New Microwave Reactor for Organic Synthesis and Kinetics Studies*^[13] provided a basis not only for our kinetics studies but also for the present commercially available pressurized microwave batch reaction systems that Kuhnert advocated in his Highlight. To underscore this point, even Kappe and Stadler's work was conducted with a reactor of our design (see reference [6] in the portrayed paper by Kappe and Stadler^[3])!

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