

CONTINUOUS FLOW MICROWAVE SYNTHESIS; REACTION OPTIMISATION AND SCALE-UP

Otman Benali and Martyn Deal

GlaxoSmithKline Pharmaceuticals, Technology Development, New Frontiers Science Park
(North), Third Avenue, Harlow, Essex, CM19 5AW, UK

In recent years the use of emerging techniques such as microwave heating and continuous flow reactor technology for organic synthesis has attracted considerable interest, particularly within the pharmaceutical and fine chemical communities, where the benefits associated with rate enhancement, higher yields and greater product selectivity have been reported.¹

Scale up of reactions performed in standard laboratory microwave systems on a research scale (mgs) has been identified as a current technology gap. Our results from thermal imaging of fluoro-polymer flow reactors to determine the areas of microwave absorption, and a comparison between mono-mode cavity (CEM) and a multi-mode cavity (Milestone) will be presented.

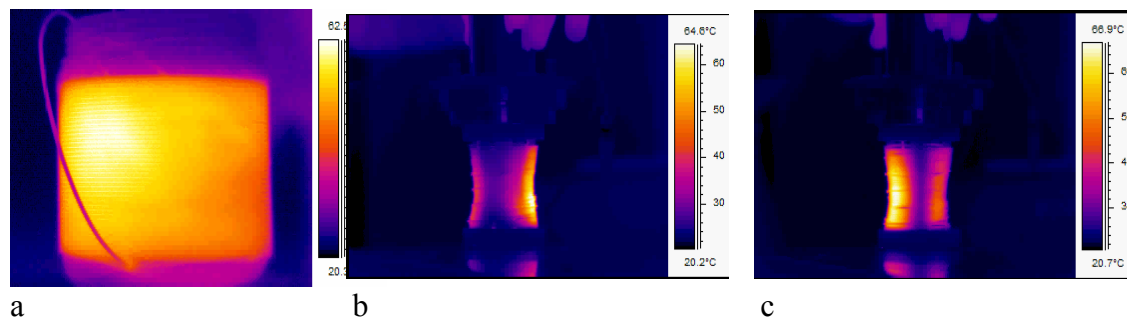
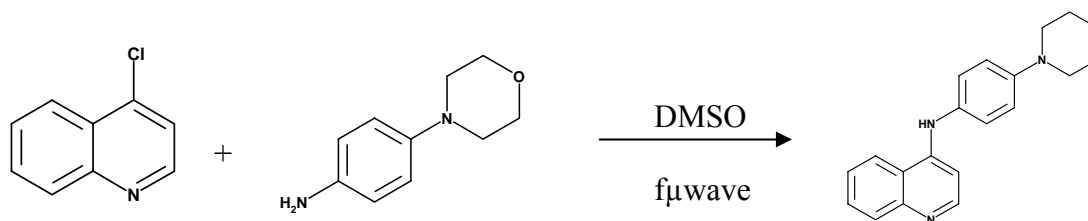


Figure 1a. Reactor (50', 0.75 mm id. PFA HP) full of water (Stopped flow) was microwaved in Ethos for 1 min at 250 w. Figure 1b,c. Reactor (20', 0.75 mm id. PFA HP) full of water (Stopped flow) was microwaved in the CEM cavity for 30 s at 10 w.

An example of reaction optimisation and subsequent scale-up, without modifying reaction conditions, in a continuous flow system, using microwave irradiation will be discussed.



Scheme 1

¹ Comer, E.; Organ, M. *J. Am. Chem. Soc.* **2005**, *127*, 8160-8167.