

# RAPID PHASE SPACE SURFACE GENERATION USING AN INTEGRATED MICROFABRICATED DEVICE REACTION DETECTION SYSTEM AND AUTOMATED CONTROL

Christopher Cullen,<sup>1</sup> Siva Krishnadasan,<sup>1</sup> John C. deMello,<sup>1</sup> Robert C.R. Wootton,<sup>2</sup> and Andrew J. deMello<sup>1</sup>

<sup>1</sup>Department of Chemistry, Imperial College London, South Kensington, London, SW7 2AZ, UK. <sup>2</sup>Department of Pharmacy and Chemistry, Liverpool John Moores University, Byrom Street, Liverpool, L3 3AF, UK.  
Phone: +44 207 5945866, Fax: +44 207 5945834

## Abstract

The optimisation of reaction conditions is a vital process in the establishment of viable industrial synthetic routes. This paper shows a method for the rapid generation of high resolution chemical surfaces illustrating the effects on the reaction rates of the variation of ratios of reactants on imine formation.

**Keywords:** microreactor, reaction kinetics, reaction optimisation

## 1. Introduction

Conventionally the acquisition of information relating to reaction kinetics is a slow process with the reaction data typically measured by titrations. Even some of the more recent integrated methods of analysis have a limited scope for the rapid variation of reactant concentrations. Recently, it has been shown that continuous flow systems with integrated analysis can rapidly generate large amounts of reaction data.[1] [2]

The novel approach described herein allows the simultaneous alteration of the ratio of the reagents at fixed reaction times to generate phase space surfaces. These are generated using a continuous flow microfluidic reactor with online UV/vis spectroscopic detection. By automating control of hydrodynamic flow within the system phase space surfaces may be generated in a rapid and reproducible manner.

## 2. Experimental

The planar glass microfluidic reactor used in the current studies was fabricated using conventional wet etching techniques. The formation of benzylidene-phenylamine from aniline and benzaldehyde (Figure 1) is monitored with 0.5 mM reactant solutions in ethanol.

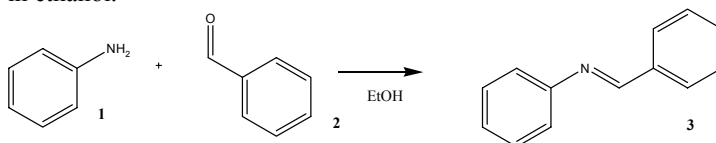


Figure 1. Reaction of aniline **1** and benzaldehyde **2** to form benzylidene-phenyl-amine **3**.

The reaction is well known to proceed readily at room temperature with the product demonstrating an absorption maximum at 310 nm. This is suitably resolved from the spectroscopic features of the reactants, allowing simple generation of phase space surface data. The variation in the extent of reaction is observed in real time by the transmittance of monochromatic light (at 310 nm) through a commercially available 1 mm path length flow cell in series with the microfluidic reactor. The hydrodynamic infusion of reagents is controlled by a LabView programme which allows incremental changes in pumping rates and the concentration ratios of reagents.

### 3. Results and discussion

Initial experiments with proportional incremental increases in the flow rates of both reagents were compared to stopped-flow and steady state experiments. The stopped-flow measurement show the reactions progress when the flow rate through the observation cell is suddenly stopped. The static point or steady state reaction profile was made with a series of transmittance readings at fixed flow rates, each corresponding to a fixed reaction time. The ramped method with incremental increases in flow rate of  $0.1 \mu\text{min}^{-1}$  each second gives a very dense set of data, with readings of transmittance every second unaffected by the short equilibrium times.

The kinetic traces for all three experimental modes are illustrated in Figure 2, and using calculations of the dead volume of the microreactor, showed good agreement with less than a 3 % variation.

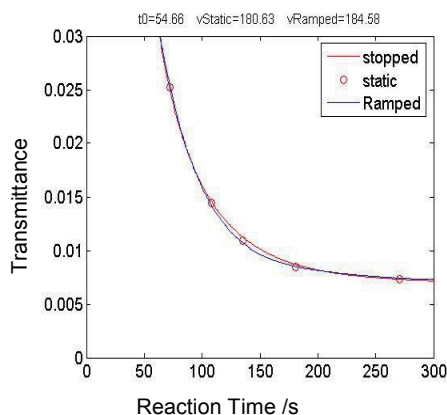


Figure 2. Reaction profiles of aniline with 1 equivalent of benzaldehyde to produce benzylidene-phenyl-amine measured by stopped-flow, static point and ramped methods

Subsequently a set of data obtained at fixed ratios of reactants with a gradual increase in volumetric flow rate (inversely proportional to reaction times) was used to generate a surface of reaction data (Figure 3). Data were also obtained at fixed flow rates with incremental variations in reactant concentration (Figure 4). The two space phase surface plots obtained independently by varying differing reaction parameters correspond closely showing the accuracy of this method.

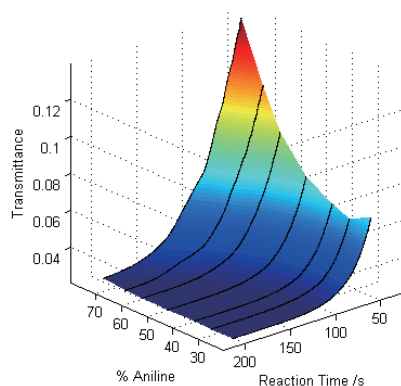


Figure 3. Phase surface plot generated from varying the reaction times at fixed ratios of reactants.

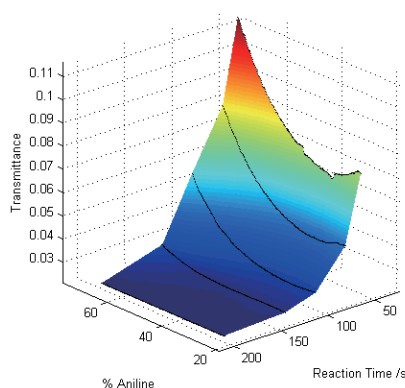


Figure 4. Phase surface plot generated from varying the ratios of reactants at fixed reaction times.

#### 4. Conclusion

In conclusion, we have shown that reproducible and accurate high resolution chemical phase space surfaces can be generated from reactions within microfluidic devices using online UV/vis spectroscopy detection. The frequent and small incremental variations in flow rates allow a high density of data to be collected showing the effects of both reaction time and reactant concentrations on the efficiency of product formation, thus allowing the optimisation of reaction conditions. The automated reloading of syringes from reactant reservoirs means many runs can be sequentially programmed, providing a system capable of extruding a high density of reaction data very rapidly. A reaction surface can be generated within the period of a working day with a density of data that would take weeks-months using traditional titration methodologies.

#### Acknowledgements

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#### References

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