

# Utilising the substance handling capability of Chemspeed's Swing platform for library synthesis

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## Introduction

Whilst efficiency is extremely important when conducting any form of parallel synthesis, library synthesis in support of medicinal chemistry programs can add considerable challenges due to the wide scope of the chemistry utilised. Any automated system will need to be very flexible to be able to support this. Chemspeed's Swing platform meets the flexibility and efficiency needs of such automated medicinal chemistry library synthesis departments by combining efficient liquid handling with a huge range of potential formats (including custom developments) for housing reagents and conducting reactions. Herein we describe the synthesis of libraries from 96 to 720 compounds using a range of chemical transformations (Figure 1).

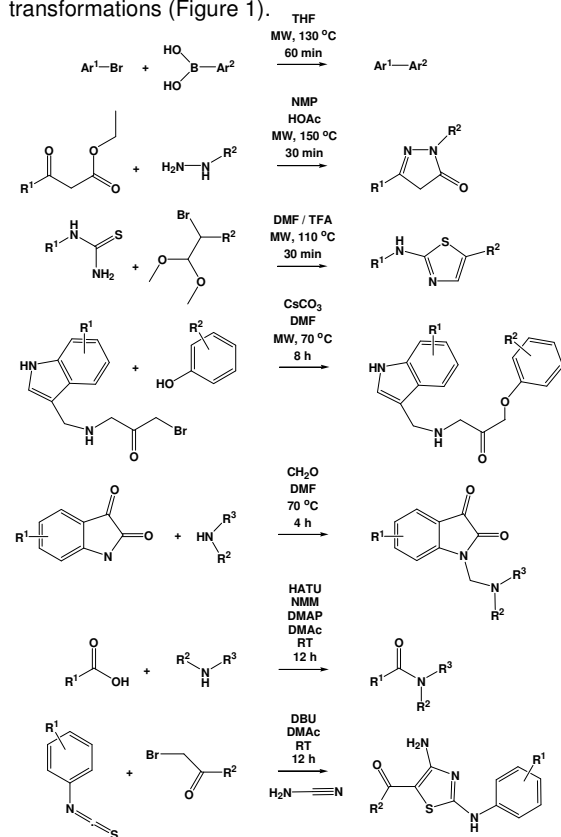


Figure 1. The diversity of typical chemical transformations routinely carried out on the Swing platform.

## Experimental

Reactions are carried out on a 0.1 and 0.3 mmol scale, all reagents are handled as solutions and dispensed with Chemspeed's 4-needlehead (Figure 2). The tray of the Swing is laid out (Figure 2) with reagent storage in 360 x 8 mL vials for building blocks, 30 x 60 mL vials for scaffolds and 6 x 1000 mL for larger volume reagents. Reaction vessels are either standard 48 well MTP, or custom racks containing 48 x 6 mL vials (again with a MTP footprint) for microwave synthesis. Reactions are carried out off-line on dedicated heater / shakers or in

microwave reactors allowing greater throughput. Once the system has done its pipetting into 2 MTPs they can be removed and undergo reaction whilst other blocks are being prepared.

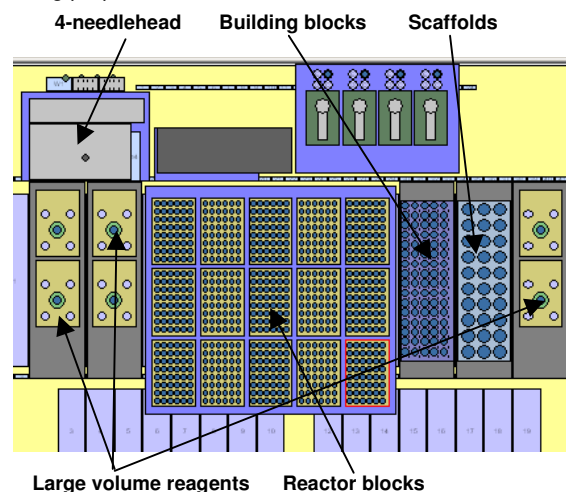


Figure 2. The set up of the Swing tray for reaction preparation.

After the reactions are complete as little preparatory work as possible is done before HPLC analysis (Figure 3). If reactions are conducted in HPLC compatible solvents and contain no solid material, the plates can be loaded directly onto HPLC autosamplers. Whilst incompatible solvents are evaporated and the residue redissolved in up to 5 mL of DMSO. Samples containing solids are filtered using 48-well filter plates.

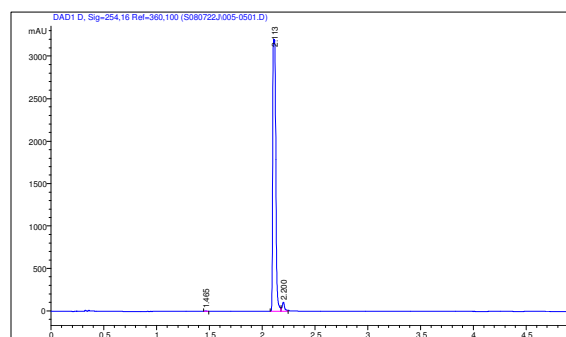


Figure 3. An example HPLC trace.

## Conclusions

The efficient production of compound libraries only becomes possible when all the bottlenecks in the process are ironed out. Chemspeed's Swing platform is an excellent solution for relieving such bottlenecks in reaction preparation. And combined with a large reagent repository, microwave synthesis capability, high throughput work up and analysis, and appropriate data management software, can contribute to output of around 3500 compounds per person per year.<sup>1</sup>

## References

1. M. Koppitz., *J. Comb. Chem.*, **2008**, 10, 573-579