



# How to scale up hydrogenation reactions using the H-Cube Midi™

The difficulties involved with scaling up reactions from laboratory to process scale are well known.<sup>1</sup> The H-Cube Midi™ is designed so that the scale up of reactions from the milligram scale on the H-Cube® to 100s of grams is easy and non-problematic. Using several industrial examples, this application note will describe how reactions were scaled up.

## WHERE TO START?

The H-Cube Midi™ is capable of reacting compounds at 150°C, 100 bar, and 25 mL/min. Temperature, pressure, and flow rate may be changed during the reaction for fast optimization. Concentrations of up to 0.4 M may also be used. With this wide range of potential conditions, it may be difficult for the user to know where to start. The recommended scale up procedure for the H-Cube Midi™ are the following:

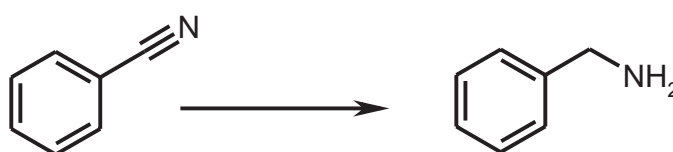
- 1) Take the optimum reaction temperature and pressure achieved using the H-Cube® and apply these to the H-Cube Midi™.
- 2) Start the reaction at a flow-rate of 10 mL/min and a concentration of 0.15 M. Take a sample and note conversion.
- 3) Alter the flow rate until 100% conversion is achieved.
- 4) Increase the flow rate with temperature and/or pressure to see if production rate can be increased.
- 5) Repeat the procedure at higher concentrations if necessary.
- 6) Once the optimum conditions have been found, leave the system to run to generate the required amount of compound.



## SCALE UP EXAMPLES

The following 3 examples illustrate how the H-Cube Midi™ was used to scale up reactions performed on the H-Cube®. The reactions were performed by one of ThalesNano's industrial partners using their own compounds.

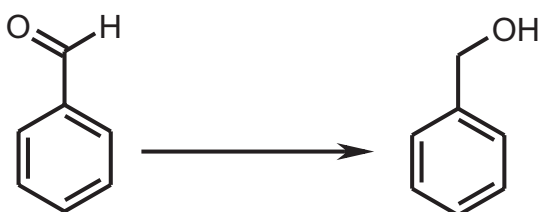
### SCALE UP OF BENZONITRILE REDUCTION



Conditions	H-Cube®	H-Cube Midi™
Catalyst	20% Pd(OH) <sub>2</sub> /C	20% Pd(OH) <sub>2</sub> /C
Temperature	60°C	60°C
Pressure	50 bar	50 bar
Flow Rate	1 mL/min	12 mL/min
Concentration	0.05 M	0.15 M
Conversion	100%	100%
Production Rate	300 mg/hour	10 g/hour

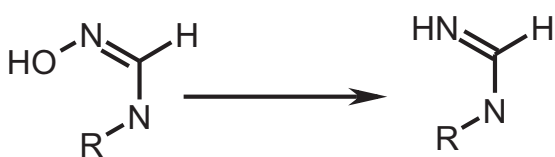


### SCALE UP OF BENZALDEHYDE REDUCTION



Conditions	H-Cube®	H-Cube Midi™
Catalyst	Raney Ni	Raney Ni
Temperature	60°C	60°C
Pressure	50 bar	50 bar
Flow Rate	1 mL/min	12 mL/min
Concentration	0.05 M	0.15 M
Conversion	100%	100%
Production Rate	300 mg/hour	10 g/hour

### SCALE UP OF OXIME REDUCTION



Conditions	H-Cube®	H-Cube Midi™
Catalyst	Raney Ni	Raney Ni
Temperature	60°C	60°C
Pressure	50 bar	50 bar
Flow Rate	1 mL/min	7 mL/min
Concentration	0.05 M	0.15 M
Conversion	100%	100%
Production Rate	500 mg/hour	10 g/hour

### DISCUSSION

Each example took less than 1 hour to perform the necessary optimization experiments. All examples resulted in 100% conversion to the product. The production rate increase in the nitrile and benzaldehyde examples was 33 times that of the original H-Cube®. The oxime reduction was 20 times higher than that of the original H-Cube®.

### CONCLUSION

The examples demonstrate that the production rate of H-Cube® reactions can be increased by at least 20 times on the H-Cube Midi™ reactor. The time taken to perform the optimization process is less than 1 hour making the process much faster than standard batch reactors where the process can take weeks to optimize reactions.

### REFERENCES

1) RSC environment, health and safety committee note on Safety Issues in the Scale up of Chemical Reactions, Version 1/3/99.

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