



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.¹ 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:

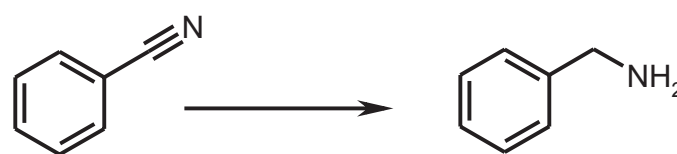
- 1) Take the optimum reaction temperature and pressure achieved using the H-Cube® and apply these to the H-Cube Midi™.
- 2) Start the reaction at a flow-rate of 10 mL/min and a concentration of 0.15 M. Take a sample and note conversion.
- 3) Alter the flow rate until 100% conversion is achieved.
- 4) 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.

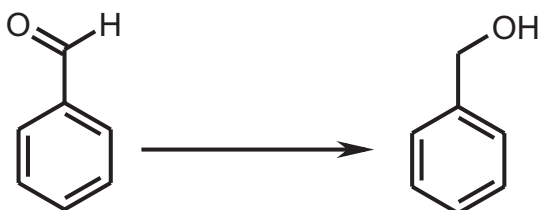
SCALE UP OF BENZONITRILE REDUCTION



Conditions	H-Cube®	H-Cube Midi™
Catalyst	20% Pd(OH) ₂ /C	20% Pd(OH) ₂ /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

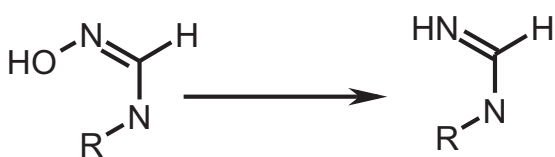


SCALE UP OF BENZALDEHYDE REDUCTION



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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