



# Simple, Fast, And Safe Hydrogenation Using H-Cube Tutor™

**This application note details how the H-Cube Tutor™ may be used as part of an undergraduate practical session. The chemistry examples shown also demonstrate the reactor's suitability for real research and development.**

## INTRODUCTION

Hydrogen is highly explosive, therefore it is rarely used in academic research labs and never in teaching laboratories. However, approximately 5-10% of reactions in the chemical industry as a whole involve catalytic hydrogenation. The lack of practical experience of this fundamental technique is a hindrance to undergraduates. The H-Cube® technology which generates small amounts of Hydrogen insitu eliminates the hazards associated with using it as a reagent. This technology opens the door on a highly useful and expanding area of chemistry, allowing chemists and chemistry students greater freedom to use its full potential.

## STANDARD EXPERIMENTAL PROTOCOL

Switch on the H-Cube Tutor™ and the HPLC pump. Fill the water reservoir with de-ionized water. Place the Cat-Cart® into the CatCart® holder. Set the flow rate (3 mL/min max) and temperature (100°C max) respectively. Put about 200 mL of the appropriate solvent for the reaction being performed into a conical flask containing the pump inlet tube with the Teflon filter. Start the pump and run pure solvent through the system to remove any air. Press the START button to generate hydrogen. After a short time, Hydrogen will be released into flow system and mixed with the solvent at the set temperature. When the Hydrogen is seen bubbling from the reaction line, change the pump inlet line from solvent reservoir to the substrate vial. When most of the substrate solution has been taken up by pump, add the same volume again of pure solvent to flush it through the system. When the additional solvent has been pumped into the system replace the inlet line into the solvent reservoir. It is imperative that transfer operations are performed quickly to avoid air being pumped into the system.



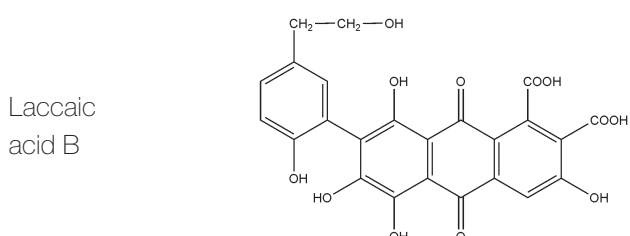
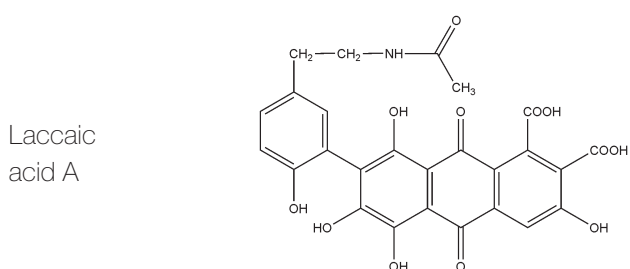
## EXAMPLES OF AVAILABLE CATALYSTS

- 10% Pt/C
- 5% Rh/Al<sub>2</sub>O<sub>3</sub>
- 20% Pd(OH)<sub>2</sub>/C
- CuO/Al<sub>2</sub>O<sub>3</sub>
- Ru black

## INCOMPATIBLE SOLVENTS

- Dichloromethane
- Tetrahydrofuran
- Dimethyl sulfoxide
- Triethylamine

## 1. REDUCTION OF NATURAL RED 25





Natural red is used for colouring material of vegetable/animal origin. The Natural red 25 is sourced from *Coccus laccae*, an insect living in South Asia. Natural red 25 also known as Lac dye or laccaic acid has two major components; laccaic acids A. and B. Lac dye is a yellowish powder. Lac dye is both photo- and thermo- stable, it melts at 180°C. Dissolving Natural red 25 in water or ethanol results in a dark red solution which on reduction becomes colourless.

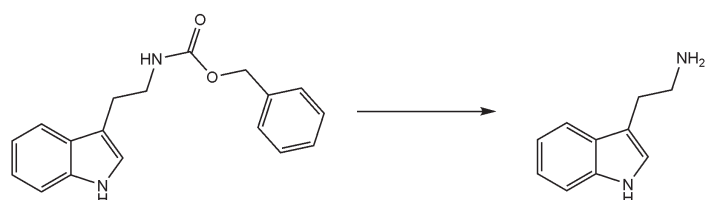
### EXPERIMENTAL PROTOCOL 1

Natural red 25 (10 mg) was dissolved in 20 mL ethanol (0,05 M) in a substrate vial (deep red colour observed). The H-Cube Tutor™ was set up using the standard experimental protocol above and a RaneyNi CatCart®. Set the reaction parameters to 50°C; flow rate of 1 mL/min. Press the START button to generate hydrogen. When Hydrogen is observed bubbling from the delivery tube, transfer it rapidly to the substrate vial. After 3 minutes, the product will emerge from the delivery line and can be collected in vials.

### RESULTS

The product of the reduction is colourless therefore a colourless eluent indicates the reaction is complete.

## 2. DEPROTECTION OF CBZ-TRYPTAMINE



Protecting group strategy is widely used in multistep organic synthesis to minimise side product formation and improve the yield of final product. Benzyloxy-carbonyl (CBZ) is a protecting group which can be removed by hydrogenation, which does not affect acid or base labile protecting groups.

### EXPERIMENTAL PROTOCOL 2

0,29 g CBZ-tryptamine was dissolved in 20 mL ethanol:ethyl-acetate 1:1 (0,05 M). Set up the H-Cube Tutor using the standard experimental protocol above and a 10% Pt/C CatCart®.

Set the reaction parameters to 60°C and flow rate of 0,5 mL/min. Press the START button to generate hydrogen. When Hydrogen is observed bubbling from the delivery tube, transfer it rapidly to the substrate vial. After 6 minutes, the product will emerge from the delivery line and can be collected in vials.

### RESULTS

The reaction was repeated 15 times and LCMS analysis indicated yields between 94-100% and selectivity between 96-99%.

### CONCLUSIONS

These two reactions demonstrate the speed, facility and safety of the H-Cube Tutor™. The reaction mixture in this system is easy to sample and monitor with simple techniques such as colour change and TLC or more sophisticated analysis such as LCMS.

### REFERENCES

Konkachuichay, P.; Shitangkoon, A and Chinwongamorn, N; Studies on Dyeing of Silk Yarn with Lac Dye: Effect of Mordants and Dyeing Conditions; *Science Asia*; **2002**; 28; 161-166  
Jones R., Godorhazy L., Varga N., Szalay D., Urge L., and Darvas F., Continuous-Flow High Pressure Hydrogenation Reactor for Optimization and High-Throughput Synthesis, *J. Combi. Chem.*, **2006**, 8(1), 110-116.

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