



# **Pt(0) EnCat™ 40**

## **User Guide**



## Pt(0) EnCat™ 40

### User Guide

#### CONTENTS

| Contents  | Page |
|---|------|
| Introduction                                    | 3    |
| Preparation and Characteristics of the Catalyst | 3    |
| <b>Hydrogenation Reactions</b>                  |      |
| Hydrogenation of Nitro Compounds                | 4    |
| Platinum Contamination                          | 6    |
| Catalyst Recycling                              | 7    |
| Reductive Amination                             | 8    |



## Introduction

Pt(0) EnCat™ 40 is a microencapsulated heterogeneous platinum hydrogenation catalyst offering key advantages over traditional supported Pt(0) catalysts. For example, Pt(0) EnCat™ 40 offers improved chemoselectivity over hydrogenations using other metal catalysts. These include hydrogenation of aryl nitro groups in the presence of halides, reductive amination of benzaldehydes without formation of benzyl alcohols, and selective dearomatisation of heteroaryl rings.

The catalyst has a Pt metal content of approx. 2.3 wt%, corresponding to a Pt loading of 0.06-0.14 mmol/g, and consists of polymeric beads with an average particle size range of 100-350µm.

Benefits of Pt(0) EnCat™ 40 include:

- Safety - non pyrophoric
- Simple and easy removal of catalyst from reactor
- Very low metal contamination of product (typically < 5 ppm)
- No Pt(0) contamination of reactor vessel
- Excellent catalyst recyclability
- Very high metal recovery
- Highly chemo selective hydrogenations
- Excellent batch to batch activity
- Low absorption of product/reagents
- No license required

## Catalyst Preparation

For ease of handling, Pt(0) EnCat™ 40 is supplied as a water-wet solid with water content of approximately 50 % w/w.

It is recommended that the catalyst is washed just before use with an organic solvent (e.g. MeOH) to remove water giving the most active catalyst, followed by a single wash with reaction solvent of choice.

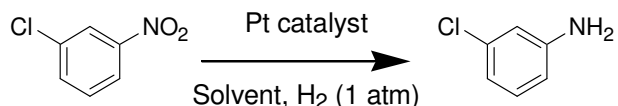
Note the catalyst can be conveniently washed in the reaction flask by decanting the wash solvent from the beads.



## Hydrogenations of Aryl Nitro Compounds

### Comparison with Other Hydrogenation Catalysts

Pt(0) EnCat™ 40 shows high activity and good selectivity in the reduction of aryl nitro groups.



| Catalyst (mol%)                    | Solvent | Time (h) | Products (% conversion) |         |        |
|------------------------------------|---------|----------|-------------------------|---------|--------|
|                                    |         |          | 3-Chloroaniline         | Aniline | Others |
| 5% Pd/C (1)                        | MeOH    | 0.5      | 1                       | 96      | 3      |
| 5% Pt/C (5)                        | MeOH    | 0.5      | 57                      | 27      | 16     |
| 5% Pt/C (1)                        | MeOH    | 0.5      | 84                      | 11      | 5      |
| Pt(0) EnCat™ 40 (5)                | MeOH    | 0.5      | 94                      | 6       | 0      |
| Pt(0) EnCat™ 40 (2)                | MeOH    | 1        | 93                      | 7       | 0      |
| Pt(0) EnCat™ 40 (1)                | MeOH    | 1.5      | 90                      | 10      | 0      |
| Pt(0) EnCat™ 40 (2)                | IMS     | 2        | 91                      | 9       | 0      |
| Pt(0) EnCat™ 40 (2)                | EtOAc   | 4        | 96                      | 4       | 0      |
| Pt(0) EnCat™ 40 (5)<br>(water wet) | MeOH    | 0.5      | 89                      | 11      | 0      |

**General Procedure:** Nitro compound (0.5 mmol) and catalyst (washed with MeOH then reaction solvent) were combined in solvent (5 ml) and stirred under a hydrogen atmosphere at room temperature until GCMS analysis indicated maximum conversion.

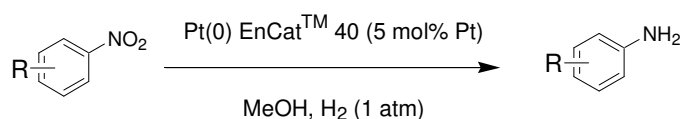
**Table 1: Comparison of Pt(0) EnCat™ 40 with carbon supported catalysts**

Platinum catalysts show clear advantages over palladium on carbon for selective hydrogenation of nitro functionality in the presence of halides. Reaction rates of Pt(0) EnCat™ 40 are comparable to platinum on carbon.

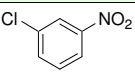
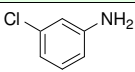
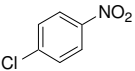
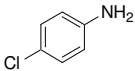
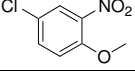
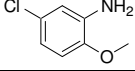
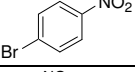
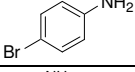


Although most studies with Pt(0) EnCat™ 40 have been carried out at 5 mol% Pt, loadings of 1 mol% Pt also give good reactivity and conversion. Pt(0) EnCat™ 40 has been found to be effective in a range of common hydrogenation solvents. The catalyst also showed similar reactivity when used water-wet.

### Hydrogenation of Nitro Compounds

Pt(0) EnCat™ 40 demonstrates selectivity for the reduction of nitro groups in the presence of other sensitive functionalities such as halogens and benzyl ethers. A range of aryl nitro substrates were reduced with good to excellent conversions and isolated yields.





| Substrate   | Product   | Conversion (%) | Time (h) |
|---|---|----------------|----------|
|  |  | 94             | 0.5      |
|  |  | 84             | 0.5      |
|  |  | 96             | 1        |
|  |  | 45             | 1        |
|  |  | 92             | 0.5      |

**General Procedure:** Nitro compound (0.5 mmol) and Pt(0) EnCat™ 40 (5 mol% Pt, MeOH washed) were combined in methanol (5 ml) and stirred under a hydrogen atmosphere until GCMS analysis indicated maximum conversion.

**Table 2: Pt(0) EnCat™ 40 Catalysed Hydrogenation of Aryl Nitro Compounds**

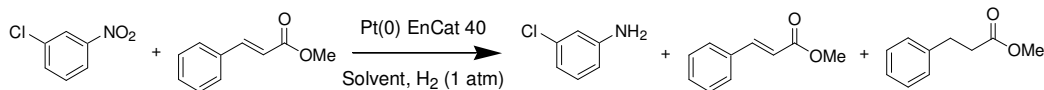
#### Experimental Example: Hydrogenation of 4-Chloro-2-nitroanisole

4-Chloro-2-nitroanisole (0.470 g, 2.5 mmol) and MeOH washed Pt(0) EnCat™ 40 (0.83 g, 4 mol% Pt) were stirred in MeOH (15 ml) and placed under a hydrogen atmosphere using a balloon. The reaction mixture was stirred at room temperature until GCMS analysis showed complete consumption of starting material in 0.5 h. The catalyst was removed by filtration and solvent evaporated from the filtrate gave the pure isolated product 4-chloro-2-aminoanisole (0.34 g, 87 %).



### Hydrogenation of Aryl Nitro Groups in the Presence of Multiple C-C Bonds

Selectivity of nitro group reduction over carbon-carbon multiple bonds with Pt(0) EnCat™ 40 was tested, by competitive hydrogenation experiments, using a mixture of 3-chloronitrobenzene and *trans*-methyl cinnamate. A 1:1 molar mixture of the two compounds was subjected to standard hydrogenation conditions and initially gave only limited selectivity: however, by optimisation of catalyst loading and reaction solvent choice, acceptable conversions of 70% nitro reduction could be obtained with almost 90% of the cinnamate left unreacted.



| Catalyst        | Solvent | Time (h) | 3-Chloroaniline (% conversion) | <i>trans</i> -Methylcinnamate (% remaining) |
|-----------------|---------|----------|--------------------------------|---|
| 2 mol% Pt EnCat | MeOH    | 2        | 95                             | 43  |
| 5 mol% Pt EnCat | MeOH    | 1        | 97                             | 60  |
| 5 mol% Pt EnCat | THF     | 2        | 78                             | 48  |
| 2 mol% Pt EnCat | THF     | 2        | 71                             | 87  |

**General Procedure:** 3-Chloronitrobenzene (0.08 g, 0.5 mmol), *trans*-methylcinnamate (0.08 g, 0.5 mmol) and Pt(0) EnCat™ 40 (50 wt% water-wet) were stirred in solvent (5 ml) and placed under a hydrogen atmosphere using a balloon. The reaction mixture was stirred at r.t. and analysed by GCMS to ascertain conversion to products.

**Table 3: Hydrogenation of Nitro Groups in the presence of  $\alpha,\beta$ -Unsaturated Esters**

#### Experimental Example:

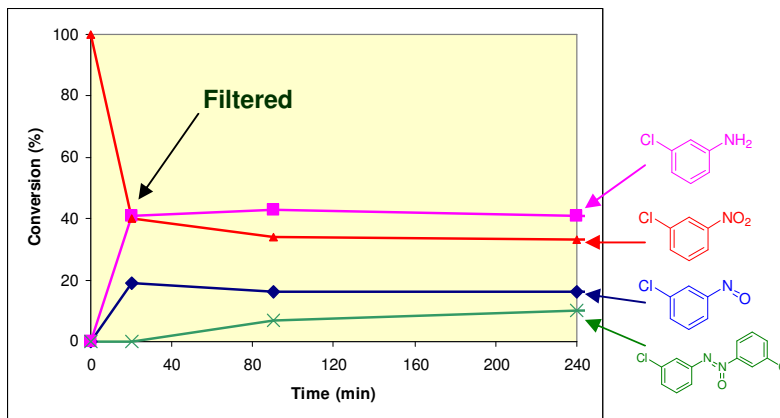
##### Selective Hydrogenation of 3-Chloronitrobenzene over *trans*-Methylcinnamate

3-Chloronitrobenzene (0.08 g, 0.5 mmol), *trans*-methylcinnamate (0.08 g, 0.5 mmol) and MeOH, then THF, washed Pt(0) EnCat™ 40 (0.4 g, 50 % water wet, 2 mol% Pt) were stirred in THF (5 ml) and placed under a hydrogen atmosphere using a balloon. The reaction mixture was stirred at room temperature until GCMS analysis showed optimum conversion to the chloroaniline product after 1 h (71 % chloroaniline, 87 % cinnamate remaining).

#### Platinum Contamination

A key advantage of encapsulated catalysts is the low levels of metal contamination in reaction products compared with traditional Pt/C. The leaching of platinum metal from Pt(0) EnCat™ 40 was investigated by two approaches:

a. The presence of solution phase catalytic platinum species was tested by the removal of the Pt(0) EnCat™ 40 by filtration from a hydrogenation reaction at partial completion. The filtrate was returned to the reaction conditions and monitored for additional conversion which would imply active platinum was leached from the EnCat™ beads; no further reduction was found, strongly suggesting low levels of platinum contamination.



#### Filtration Test for Pt(0) EnCat™ 40

After removal of the bulk catalyst no additional product forms. The relative amounts of other component changes slightly due to reaction of the chloroaniline with the nitroso intermediate.

b. Analysis of the platinum content in a crude reaction product was measured by ICP; a platinum content of less than 2 ppm in the product confirmed an exceedingly low level of metal loss from Pt(0) EnCat™ 40.

#### Catalyst Recycling

The simple reuse of Pt(0) EnCat™ 40 was demonstrated by a recycling experiment using the standard hydrogenation of 3-chloronitrobenzene.

| Run            | 1   | 2   | 3   | 4   |
|----------------|-----|-----|-----|-----|
| Conversion (%) | 100 | 100 | 100 | 100 |
| Purity (%)     | 93  | 93  | 91  | 90  |
| Time (h)       | 1   | 1   | 1   | 1   |

Table 4: Recycling Test with Pt(0) EnCat™ 40

In the experiment, the same catalyst was reused four times with minimal change in activity and in each case giving complete consumption of the starting material in 1 hour. The catalyst was recovered by simple decanting of the reaction mixture followed by three washes with the reaction solvent and the resulting solvent wet catalyst was used directly in the next run.



## Reductive Amination

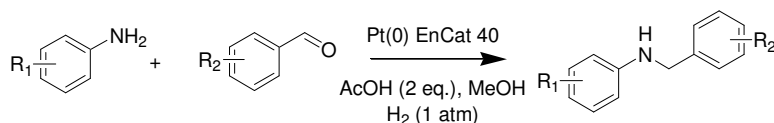
The reductive condensation of amines with aldehydes and ketones is an important method for the formation of secondary and tertiary amines. Successful reductive aminations require a reducing agent which selectively reduces the imine formed in the condensation step over the aldehyde or ketone, or any other sensitive functionality, in the starting materials.

The use of Pt(0) EnCat™ 40 as a catalyst for reductive aminations was investigated with focus on substrates where the selectivity of the catalyst provided advantages.

### Anilines and Benzaldehydes

Pt(0) EnCat™ 40 efficiently formed N-benzyl anilines from anilines and benzaldehydes with no formation of benzyl alcohols and minimal loss of labile substituents such as chlorine. Comparable conversions and reaction times to the same loading of Pt/C were observed. The addition of 2 equivalents of acetic acid was found to enhance rate and maximum conversion in most cases.

Reactions were carried out by simply placing the starting materials and catalyst under hydrogen; an additional step to pre-form the imine was not necessary.



| Amine | Aldehyde | Catalyst               | Time (h) | Conversion (%) |
|-------|----------|------------------------|----------|----------------|
|       |          | 1 mol% Pt/C            | 1        | 87             |
|       |          | 5 mol% Pt/C            | 1        | 74             |
|       |          | 5 mol% Pt(0) EnCat™ 40 | 1        | 85             |
|       |          | 5 mol% Pt(0) EnCat™ 40 | 1        | 83             |
|       |          | 5 mol% Pt(0) EnCat™ 40 | 1.5      | 71             |
|       |          | 5 mol% Pt(0) EnCat™ 40 | 1        | 66             |

**General Procedure:** Aniline (0.5 mmol) and aldehyde (0.5 mmol) were combined in solvent (5 ml) with Pt(0) EnCat™ 40 (5 mol% Pt) and stirred under a hydrogen atmosphere until GCMS analysis indicated maximum conversion.

**Table 5: Pt(0) EnCat™ 40 Catalysed Reductive Aminations of Anilines and Aldehydes**

### Experimental Example: Synthesis of 3-Chloro-N-(4-fluorobenzyl)-aniline

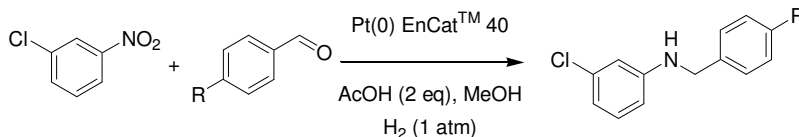
To MeOH washed Pt(0) EnCat™ 40 (0.50 g, 50 % water wet, 5 mol% Pt) in MeOH (5 ml) was added 3-chloroaniline (0.064 g, 0.5 mmol), 4-fluorobenzaldehyde (0.062 g, 0.5 mmol) and acetic acid (0.060 g, 1 mmol). The reaction mixture was stirred and placed under a hydrogen atmosphere using a balloon. Analysis by GCMS showed complete consumption of starting materials after 1 h with a conversion to product of 83%.





### One-Pot Nitro Reduction/Reductive Amination

The high selectivity of Pt(0) EnCat™ 40 for the reduction of nitro groups and imines in the presence of aryl aldehydes has allowed its use in one-pot reductive aminations starting with the nitro compound.



| Aldehyde | Catalyst                  | Time (h) | Conversion (%) |
|----------|---------------------------|----------|----------------|
|          | 5 mol% Pt(0)<br>EnCat™ 40 | 1        | 66             |
|          | 5 mol% Pt(0)<br>EnCat™ 40 | 1.5      | 74             |
|          | 5 mol% Pt(0)<br>EnCat™ 40 | 3        | 65             |

4-Chloro, 4-fluoro and 4-methoxybenzaldehyde reacted with 3-chloronitrobenzene, to give the reductive amination product, with comparable yields and rates to the direct process from the aniline.

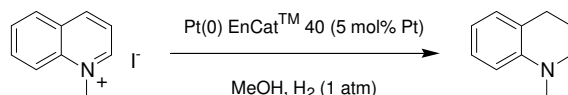
#### Experimental Example: Synthesis of 3-Chloro-N-(4-fluorobenzyl)-aniline

To MeOH washed Pt(0) EnCat™ 40 (0.50 g, 50 % water wet, 5 mol% Pt) in MeOH (5 ml) was added 3-chloronitrobenzene (0.079 g, 0.5 mmol), 4-fluorobenzaldehyde (0.062 g, 0.5 mmol) and acetic acid (0.060 g, 1 mmol). The reaction mixture was stirred and placed under a hydrogen atmosphere using a balloon. Analysis by GCMS showed complete consumption of starting materials after 1.5 h with a conversion to product of 74%.



### Heteroaromatic Reduction

Platinum catalysed reduction of heteroaromatic systems are generally carried out under high pressures and elevated temperatures, conditions which have yet to be investigated with Pt(0) EnCat™ 40. However, certain activated heteroaromatic systems, such as N-alkylated pyridinium species, are known to undergo hydrogenation with much milder conditions.<sup>1</sup>



The starting material was selectively reduced to N-methyl-1,2,3,4-tetrahydroquinoline under atmospheric pressure of hydrogen at room temperature using Pt(0) EnCat™ 40 as catalyst. Conversions of up to 90% were obtained for overnight reaction, with a small amount N-demethylation without dearomatisation. Similar results were obtained using N-methyl pyridinium iodide.

### Experimental Example: Synthesis of N-methyl-1,2,3,4-tetrahydroquinoline

N-Methyl quinolinium iodide and MeOH washed Pt(0) EnCat™ 40 (0.50 g, 50 % water wet, 5 mol% Pt) in MeOH (5 ml) were stirred and placed under a hydrogen atmosphere using a balloon. After 22 h, GCMS analysis indicated a 89 % conversion to N-methyl-1,2,3,4-tetrahydroquinoline, the remaining material being identified as quinoline.

<sup>1</sup> Hönel, M., Vierhapper, F. W., *J. Chem. Soc. Perkin Trans. I*, 1982, 2607.