Debenzylation Reactions with Pd(0) EnCat™ 30NP Catalyst

Introduction

Pd(0) EnCat™ 30NP is a chemically produced, well defined and characterised 'nano-particulate' palladium zero catalyst for use in chemo selective hydrogenationation and transfer hydrogenations reactions. Typical features of this catalyst include:

- Easy and safe to handle vs Pd/C
- Non pyrophoric
- Ative transfer hydrogenation catalyst
- Fast simple recovery of catalyst from process vessel
- Very low metal contamination of product
- Excellent catalyst recycle properties
- High chemo selectivity in both transfer hydrogenations and hydrogenations
- Pd(0) loading on dry catalyst is 4.3% by weight
- Catalyst supplied as water wet free flowing powder (water content 45%)
- Excellent storage stability

For ease of handling the Pd(0) EnCat™ 30NP is supplied as a water wet free flowing solid. It may be necessary to remove the water from the catalyst just prior to use. This can best be achieved by washing the catalyst several times with a water miscible solvent:

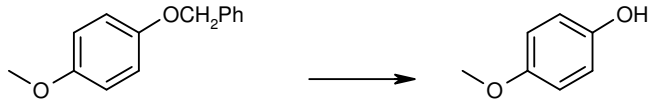
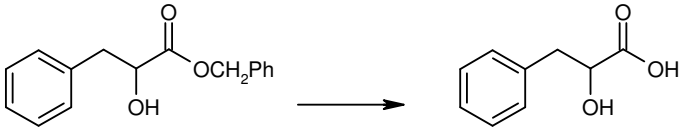
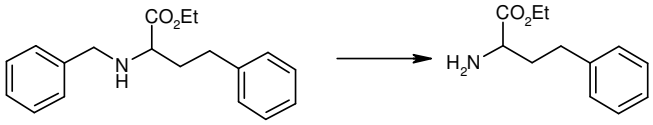
Experimental Method for Removing Water from the Catalyst Prior to Use

Pd(0) EnCat™ 30NP is washed thoroughly on a sinter with ethanol or IMS to remove water (supplied as a water wet solid with water content 45%w/w) followed by a single wash with the reaction solvent of choice.

Debenzylation Reactions Using Hydrogen Gas

Pd(0) EnCat™ 30NP can be an efficient catalyst for the selective reductive hydrogenation of aryl benzyl ethers, benzyl esters, and benzyl amines leaving other sensitive groups intact.

Alkyl benzyl ethers, are not reduced under hydrogen balloon with Pd(0) EnCat™ 30NP.

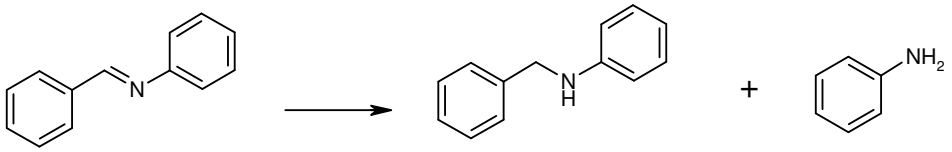
Reaction	Conversion(%)
	100
	100
	100

Experimental Procedure

All reactions were performed on a 1 mmol scale. The substrate was generally dissolved in 10 ml of EtOH, 10 mol% of the catalyst (water wet) was added and the mixture degassed twice under vacuum (using a water pump) and replacing each time the vacuum by hydrogen. The reaction mixture was left at room temperature overnight connected to a double layer balloon of hydrogen. Next day the catalyst was filtered off and washed with EtOH. The filtrated was concentrated to give a crude which was submitted for ^{1}H-NMR analysis to determine the conversion.

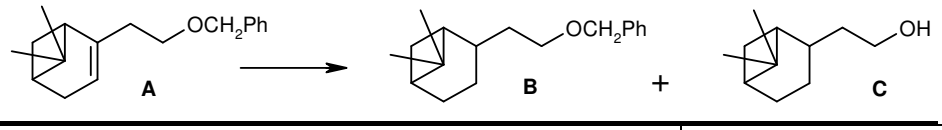
Aryl Imine Reduction Under Hydrogen Balloon.

Hydrogenation of aryl imines with Pd(0) EnCat™ 30NP leads to some cleavage of the C-N bond under hydrogen balloon. Best yields of the seconday amine were obtained when the catalyst was solvent washed to remove water before use.



Method	*Conversion (%)*	
	B	C
Pd(0) EnCat™ 30NP (10 mol%), used water wet Hydrogen balloon, CH_3CN, RT, 16 hours	69	31
Pd(0) EnCat™ 40NP (10 mol%), pre washed with EtOH Hydrogen balloon, CH_3CN, RT, 16 hours	89	11

Alkyl Benzyl Ether Reduction Under Hydrogen Balloon

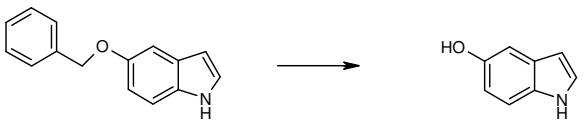
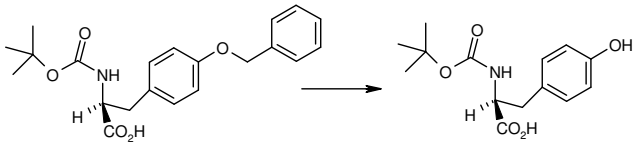
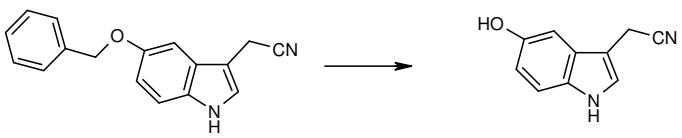


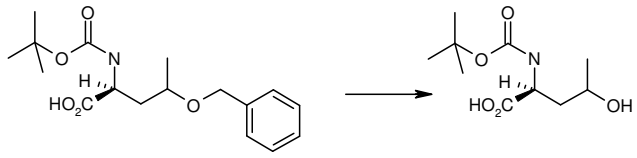
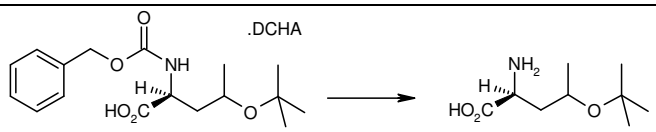
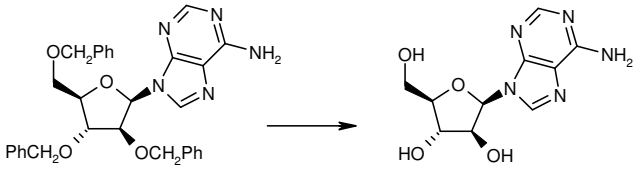
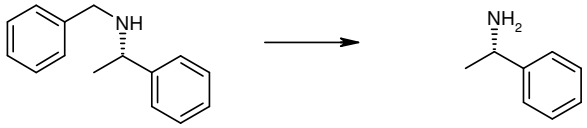
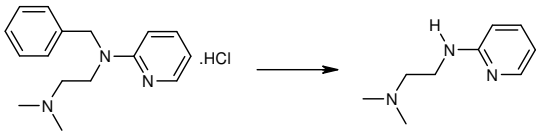
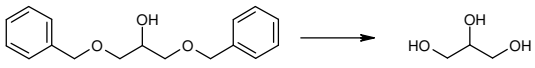
Method	Conversion (%)		
	A	B	C
Pd(0) EnCat™ 30NP (10 mol%), used water wet Hydrogen balloon, EtOH, RT, 16 hours	—	86	14
Pd(0) EnCat™ 30NP (10 mol%), used water wet Hydrogen balloon, EtOH, 76°C, 16 hours	—	65	35
Pd(0)EnCat™ 30NP (10 mol%), pre washed with EtOH Hydrogen balloon, RT, EtOH, 16 hours	18	82	—
Pd(0) EnCat™ 30NP (10 mol%), used water wet Hydrogen balloon, EtOAc, RT, 16 hours	40	60	—

Denbenzylation Reactions Under Transfer Hydrogenation Conditions

Under transfer hydrogenation conditions we have observed efficient debenzylation of O-aryl benzyl ethers but we have not observed debenzylation of alkyl benzylethers, Z groups, or benzyl amines.

The selection of hydrogen donor is also important. Cyclohexene is preferred for debenzylations but no reaction takes place without the presence of acetic acid. Formic acid was not an efficient donor for the debenzylation reaction.

Reaction	Conversion (%)
	quantitative
	86%
	Quantitative

Reaction	Conversion (%)
	No reaction
	No reaction
	No reaction
	No reaction
	No reaction
	No reaction

Experimental Method:

Before use the Pd(0) EnCat^{TM} 30NP (0.55g, 10mol%) was washed thoroughly with ethanol to remove water (supplied as a water wet solid with water content 45%w/w). To 5-benzyloxyindole (0.22g, 1 mmol) in cyclohexene (9.1ml, 90mmol) was added the pre-washed Pd(0) EnCat^{TM} 30NP. Ethanol (5 ml) and acetic acid (1ml, 6%v/v) were added to the reaction mixture which was then heated at 85 ^{o}C until the reaction was judged complete (TLC). Samples were analysed by RP-HPLC which showed that after 20 hours reaction 5.5% of 5-benzyloxyindole remained and after 38 hours 1.4% of 5-benzyloxyindole remained with the only other peak being the hydroxyindole product.