Hydrogenation (atmospheric pressure) with Pd/C

1. Put a catalyst, a solvent, and a substrate into a reaction vessel.

CAUTION! Pd/C is flammable. To avoid a fire:

1. A fire distinguisher beside you.
2. Fill the reaction vessel with Ar.
3. Put Pd/C first (a vapor of the solvent can cause a fire).
4. Collect the powder paper used in weighing Pd/C in specialized bottles. Paper to ‘the bottle for paper’ (the left bottle in the right photo).
5. Remove O₂ from the solvent by sonication or Ar bubbling (if necessary).
6. Reduce the pressure moderately (water aspirator is recommended) when you replace air/Ar with H₂.
7. The reaction and workup should be conducted inside a hood.

TIPS solvent effect: Generally, protic solvents (ROH, AcOH, etc.) accelerate the hydrogenation rates.

TIPS stirring speed: The hydrogenation proceeds faster as the reaction mixture is stirred faster.

• Typical substrates: C–C double/triple bonds, benzyl ethers/esters, Cbz, N₃, NO₂, epoxides.
2. Fill the reaction vessel with H₂ gas.

To make the vessel full of H₂, repeat around 10 times “aspirate the gas inside => let H₂ gas inside”.

CAUTION! H₂ gas is explosive. To avoid a fire/explosion:

1. Excess H₂ gas should be discharged into a hood.
2. Reduce the pressure moderately (water aspirator is recommended).
3. **You must not add another amount of Pd/C, even if you replace H₂ with Ar in advance (H₂ may remain in the solvent).** Filter Pd/C out, evaporate the solvent, and try hydrogenation from the beginning again when the reaction did not finish.
4. The reaction and workup should be conducted inside a hood.
**TIPS** You should prepare double-layered balloons to keep H₂ inside for longer time.

H₂ easily pass through a single layer of a rubber balloon.  
H₂ stays longer inside with a double-layered balloon.  
One balloon put into another with a spatula.

You can keep H₂ for 6~12 hours (my feeling) with double-layered balloon.

**TIPS** You can use 2 balloons when you try a large-scale hydrogenation (the right photo).
*Water aspirator is too weak to reduce sufficiently the pressure in a large flask: a benchtop pump is better then.

**TIPS** You can use beach balls (= vinyl balloons) instead of rubber balloons.  
H₂ stays longer inside beach balls than inside double-layered rubber balloons.
If you are concerned about H₂/air exchange, you can try beach balls.
*Rubber balloons have tension, and can apply more pressure of H₂ to the reaction mixture than beach balls. This characteristic is a trade-off.

**TIPS** MS is useful when TLC gives no information whether hydrogenation finishes or not.
3. Removal of Pd/C — Celite filtration

**CAUTION!** Pd/C adsorbing H₂ is more flammable than new Pd/C. You must not dry it out.

You detach the balloon and release H₂ into a hood, then replace the gas inside with Ar. After that you remove Pd/C from the reaction mixture by Celite filtration.

*Chlorinated solvents (CH₂Cl₂, CH₃Cl) are nonflammable. They are safe when you wash Pd/C on Celite.

The waste Celite containing Pd/C is collected in specialized bottles in the same way as paper adsorbing Pd/C. Celite to ‘the bottle for Celite’ (the right bottle in the right photo).
4. Appendix

<table>
<thead>
<tr>
<th>Starting Material</th>
<th>Product</th>
<th>Pd/C</th>
<th>Pd/C(en)</th>
<th>Pd/Fib</th>
<th>Pd/PEI</th>
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<tr>
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<td>R/Ar–OH</td>
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