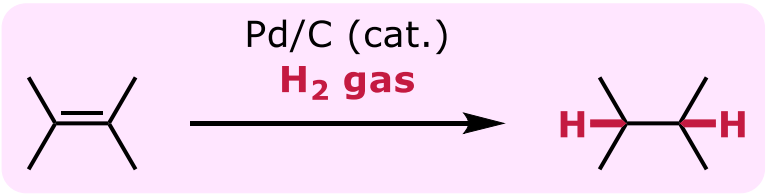
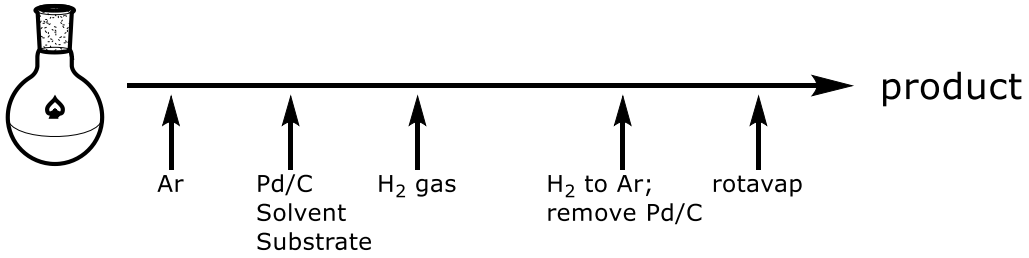
Hydrogenation (atmospheric pressure) with Pd/C

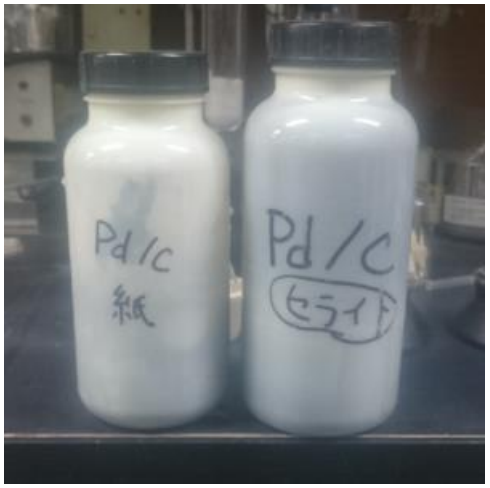




1. Put a catalyst, a solvent, and a substrate into a reaction vessel.

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 O_2 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 H_2.
7. The reaction and workup should be conducted inside a hood.



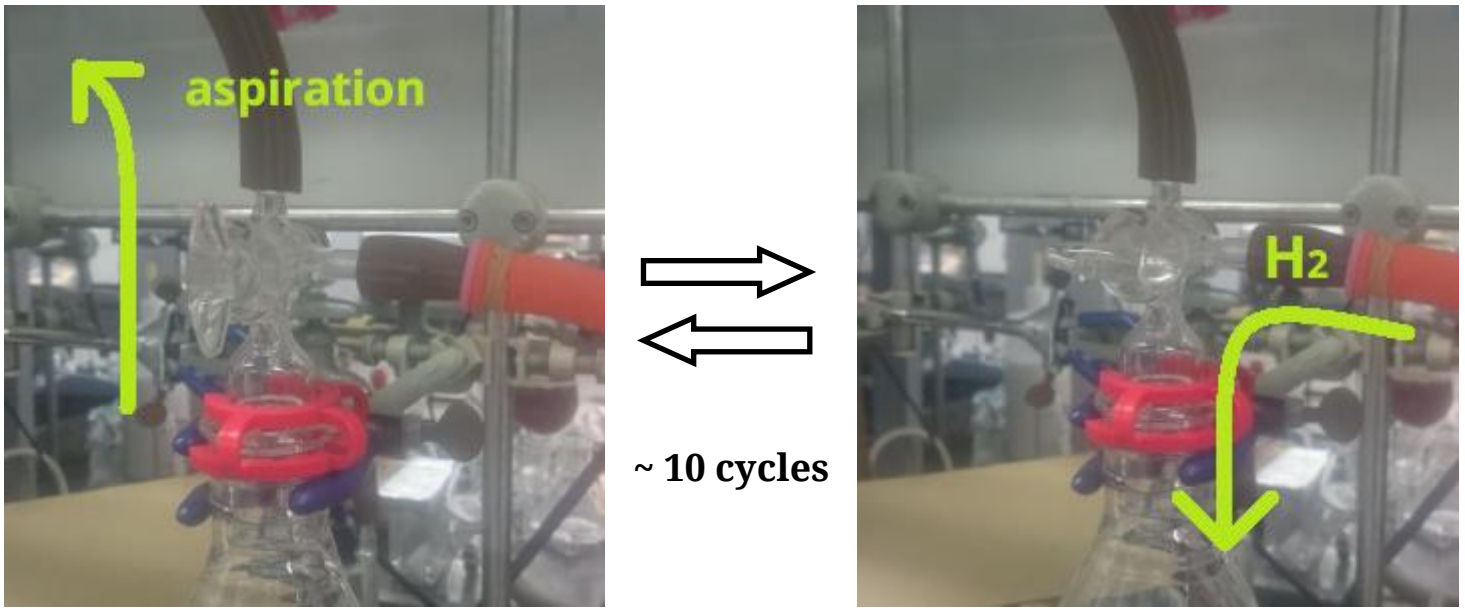
TIPS solvent effect: Generally, protic solvents (ROH, AcOH, *etc.*) accelerate the hydrogenation rates.

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, N_3, NO_2, epoxides.

2. Fill the reaction vessel with H_2 gas.

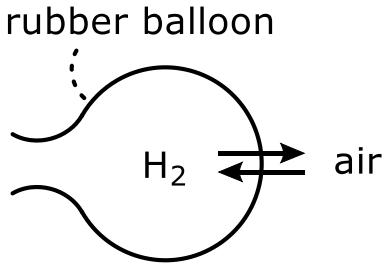
To make the vessel full of H_2, repeat around 10 times **“aspirate the gas inside => let H_2 gas inside”**.



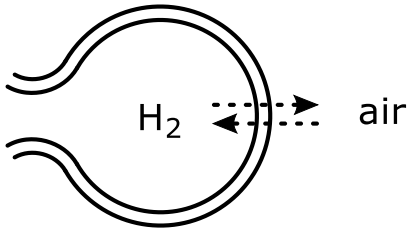
CAUTION! H_2 gas is explosive. To avoid a fire/explosion:

1. Excess H_2 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 H_2 with Ar in advance (H_2 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.

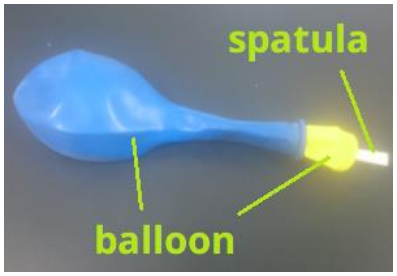
TIPS You should prepare double-layered balloons to keep H_2 inside for longer time.



H_2 easily pass through a single layer of a rubber balloon.



H_2 stays longer inside with a double-layered balloon.



One balloon put into another with a spatula.

You can keep H_2 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.

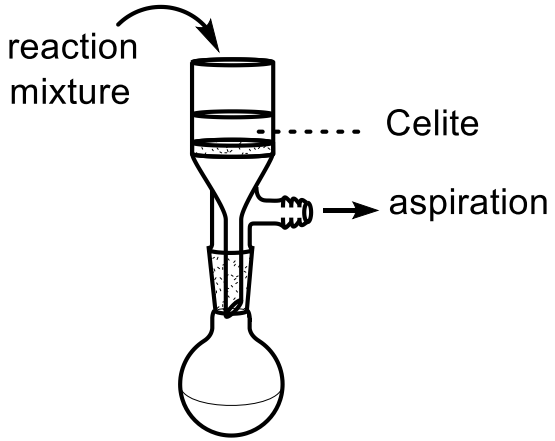
TIPS You can use beach balls (= vinyl balloons) instead of rubber balloons.
H_2 stays longer inside beach balls than inside double-layered rubber balloons. If you are concerned about H_2/air exchange, you can try beach balls.
*Rubber balloons have tension, and can apply more pressure of H_2 to the reaction mixture than beach balls. This characteristic is a trade-off.

TIPS MS is useful when TLC gives no information whether hydrogenation finishes or not.

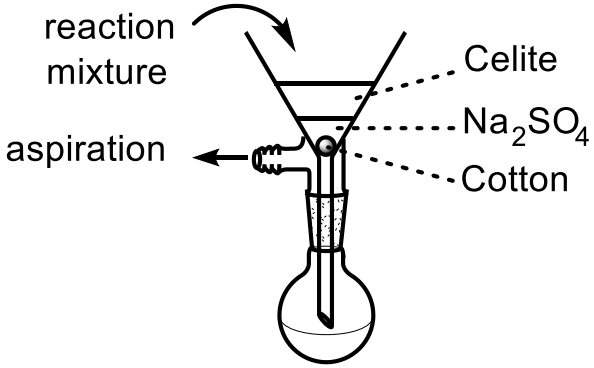
3. Removal of Pd/C — Celite filtration

CAUTION! Pd/C adsorbing H_2 is more flammable than new Pd/C. You must not dry it out.

You detach the balloon and release H_2 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 (CH_2Cl_2, CH_3Cl) are nonflammable. They are safe when you wash Pd/C on Celite.

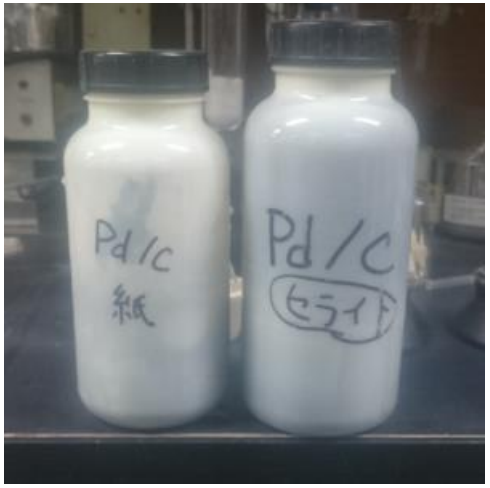


Glass filter



funnel

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

Starting Material	Product	Pd/C	Pd/C(en)	Pd/Fib	Pd/PEI
alkynes	alkanes	●	●	●	●
azides	amines	●	●	●	
olefins	alkanes	●	●	●	
Ar–NO_2	Ar–NH_2	●	●	●	
Ar–X	Ar–H	●	●		
Ar–NH-Cbz	Ar–NH_2	●	●		
R–CO_2Bn	R–CO_2H	●	●		
R–NH–Cbz	R–NH_2	●			
epoxides	alcohols	●			
R/Ar–OBn	R/Ar–OH	●			
R/Ar–OTBS/OTES	R/Ar–OH	●			

en: ethylenediamine, Fib: fibroin, PEI: polyethyleneimine; cf. http://www.wako-chem.co.jp/siyaku/product/chemical/kouso/pdf/4.pdf