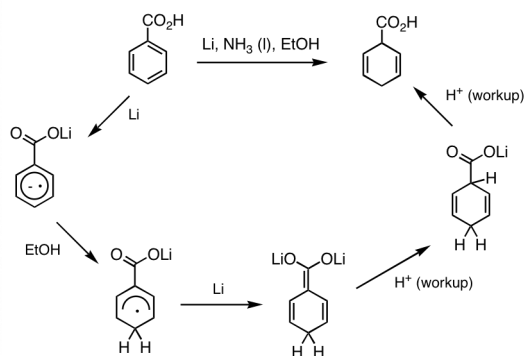
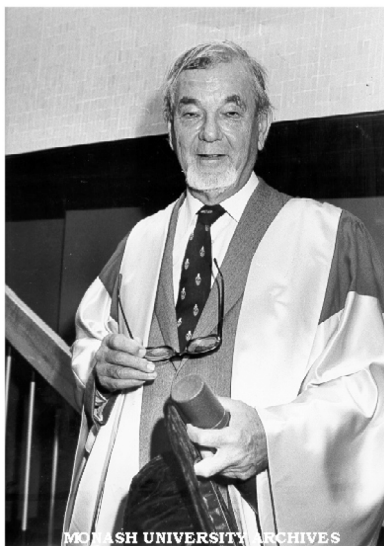
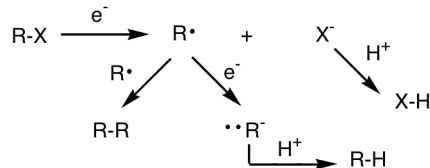


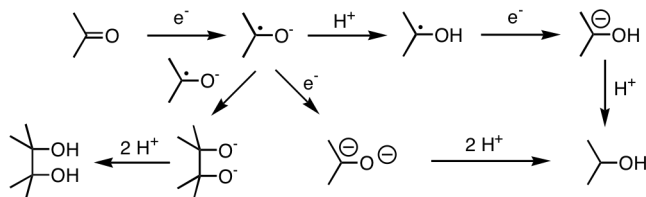
## 4. Birch and other (Dissolving) Metal Reductions



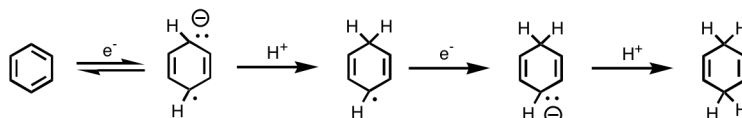
Mechanism of bond fission of single bonds with lithium-ammonia illustrated for alkyl halides:



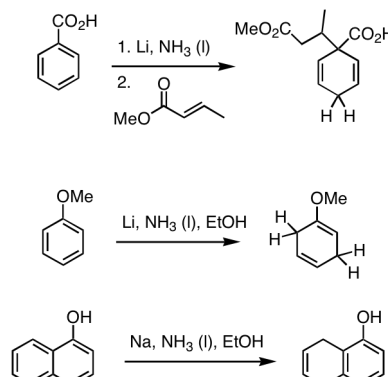
Mechanism of multiple bond saturation with lithium-ammonia illustrated for ketones:



Mechanism of Birch reduction of benzene:



Regioselectivity in the Birch reduction of aromatic rings:

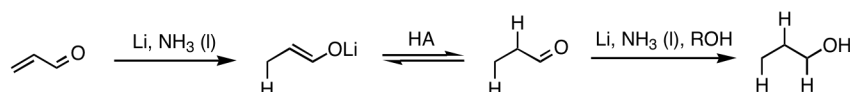


The radical and anion sites are always para to one another and tend to localize at sites on the ring that stabilize charge. Regioselectivity is therefore controlled by the substituents on the ring. Electron-withdrawing groups stabilize the negative charge generated during the course of the reaction and increase the rate, leading to reduction at the position on the aromatic ring bearing the stabilizing group. In contrast, electron donors are deactivating and direct protonation toward the unsubstituted *ortho*- and *meta*-positions.

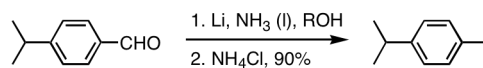
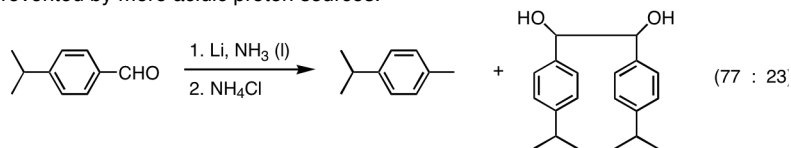
Ring-fusions and electron-withdrawing groups have more influence in polysubstituted systems in directing reduction than electron-donating groups. Of the electron-donating groups, the directing effects of functional groups containing N or O outweigh alkyl groups. The empirical order of directing power is carboxyl > amino, alkoxy > alkyl. Hydrogen addition is *para* to an electron-withdrawing group and *meta* to the most strongly deactivating group, but preferentially not at a position occupied by a deactivating substituent.

The acidity of the proton source used in the first protonation step is important to the outcome of the reduction. Sometimes, a more acidic proton source than  $\text{NH}_3$  ( $\text{pK}_a = 35$ ) is advantageous. According to House, *Modern Synthetic Reactions*, alcohols ( $\text{pK}_a = 16-19$ ) or ammonium salts ( $\text{pK}_a = 10$ ) may be added to the reaction mixture. Generally, the more acidic the proton source, the faster the reduction. If the protonation of the radical anion is the rate limiting step,  $\text{NH}_3$  can be too weak an acid to allow reaction. An unactivated benzene ring is only slowly reduced without an added proton donor.

Reduction of an  $\alpha,\beta$ -unsaturated ketone in  $\text{NH}_3$  stops at the saturated ketone stage; in the presence of an added proton source, the saturated alcohol is obtained.

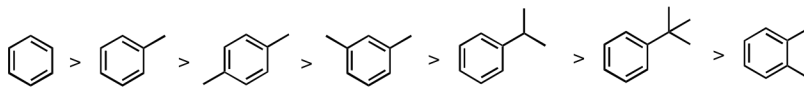


The formation of dimerization products of the intermediate radical anion can be prevented by more acidic proton sources.



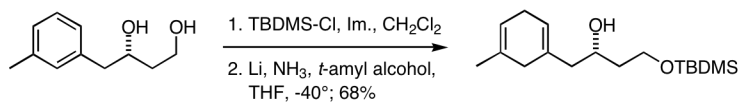
Quenching: To avoid further reduction during the quenching step,  $\text{NH}_4\text{Cl}$  or another acidic salt is used (not alcohol).

The presence of bulky substituents on an aromatic ring retards reduction, presumably because of steric interference with solvation of the radical anion. The order of stability for the anion radical from alkyl substituted benzenes is:



Stork, G.; Schulenberg, J. W. *J. Am. Chem. Soc.* **1962**, *84*, 284. Synthesis of dehydroabietic acid.

Wipf, P.; Lim, S. *Chimia* **1996**, *50*, 157.



## Chemoselectivity:

Ando, M.; Sayama, S.; Takase, K.  
*Chem. Lett.* **1981**, 377.



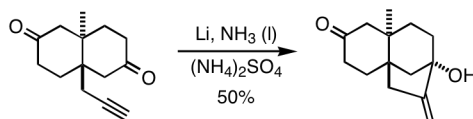
## Stereoselectivity:

Huang, P. Q.; Arseniyadis, S.; Husson, H.-P. *Tetrahedron Lett.* **1987**, 28, 547.

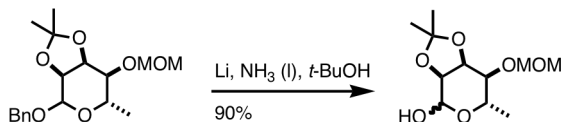
Truce, W. E.; Breiter, J. J. *J. Am. Chem. Soc.* **1962**, 84, 1623.

Boeckman, R. K.; Thomas, E. W. *J. Am. Chem. Soc.* **1977**, 99, 2805.

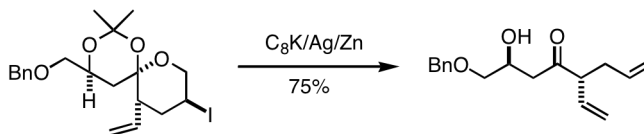
Stork, G.; Malhotra, S.; Thompson, H. *J. Am. Chem. Soc.* **1965**, 87, 1148.



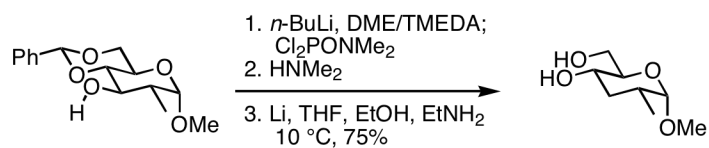
Ireland, R. E.; Anderson, R. C.; Badoud, R.; Fitzsimmons, B. J.; McGarvey, G. J.; Thaisrivongs, S.; Wilcox, C. S. *J. Am. Chem. Soc.* **1983**, 105, 1988.



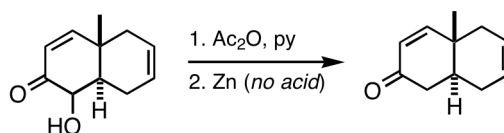
Ireland, R. E.; Wipf, P.; Miltz, W.; Vanasse, B. *J. Org. Chem.* **1990**, 55, 1423. Use of a masked aldol unit.



Deoxygenation: Ireland, R. E.; Wipf, P. *Tetrahedron Lett.* **1989**, 30, 919.



Zinc reduction: Woodward, R. B. et al. *J. Am. Chem. Soc.* **1952**, 74, 4223.



**McMurry Coupling:** Corey, E. J.; Kania, R. S. *Tetrahedron Lett.* **1998**, 39, 741.  
Reductive pinacol coupling.

