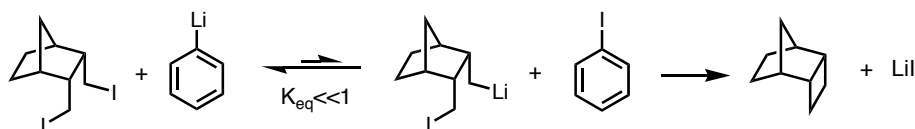
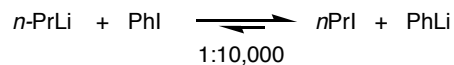
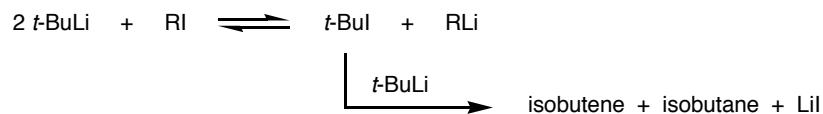


- Lithium-halogen exchange reactions are kinetically controlled. The position of the equilibrium varies with the stabilities of the carbanion intermediates involved ($sp \gg sp_2 \gg sp_3$).

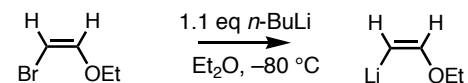


- In the above example, internal trapping of the newly formed alkyllithium reagent by alkylation drives an otherwise unfavorable exchange reaction.

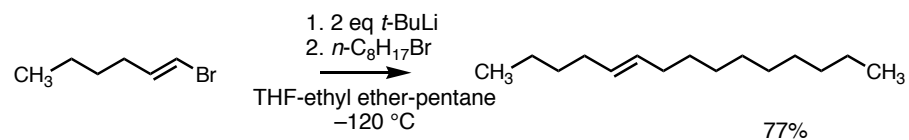
- Alkyl iodides are more reactive than the corresponding bromides. Alkyl chlorides are essentially inert.



- Lithium-halogen exchange reactions using $t\text{-BuLi}$ typically employ two or more equivalents of $t\text{-BuLi}$. The first equivalent is used for the exchange and the second equivalent reacts with the $t\text{-BuI}$ produced, to form isobutene, isobutane, and lithium iodide.

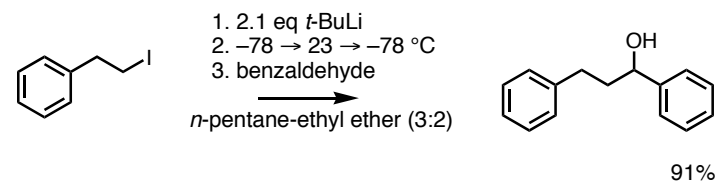


Lau, K. S.; Schlosser, M. *J. Org. Chem.* **1978**, *43*, 1595.



Neumann, H.; Seebach, D. *Tetrahedron Lett.* **1976**, *52*, 4839.

- Lithium-halogen exchange of vinyl halides is stereospecific, proceeding with retention of configuration.



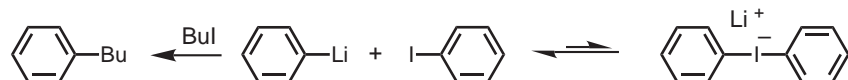
Bailey, W. F.; Punzalan, E. R. *J. Org. Chem.* **1990**, *55*, 5404.

- Aliphatic alkyllithium reagents are normally prepared from the corresponding primary iodides at low temperature in a pentane-ether solvent system.

Mechanism of Lithium-Halogen Exchange:

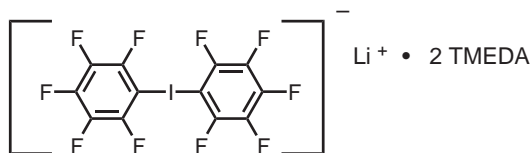
Review:

Bailey, W. F.; Patricia, J. J. *J. Organomet. Chem.* **1988**, 352, 1.



Reich, H. J.; Phillips, N. H.; Reich, I. L. *J. Am. Chem. Soc.* **1985**, 107, 4101.

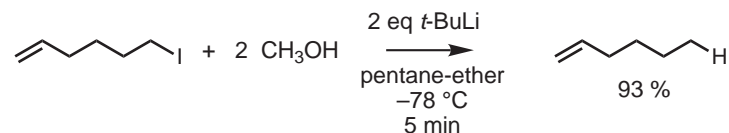
- Added phenyl iodide slows the reaction of butyl iodide with phenyllithium, providing evidence for the intermediacy of a less reactive "ate-complex".



Farnham, W. B.; Calabrese, J. C. *J. Am. Chem. Soc.* **1986**, 108, 2449.

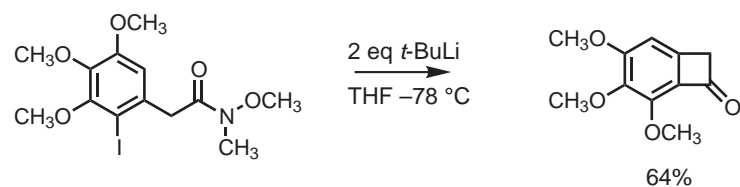
- An X-ray crystal structure of lithium bis(pentafluorophenyl) iodinate complexed with TMEDA has been obtained, providing support for the intermediacy of ate complexes during lithium-halogen exchange.

- Lithium-halogen exchange is extremely fast. In some instances, the rate of lithium-halogen exchange can exceed the rate of proton transfer.

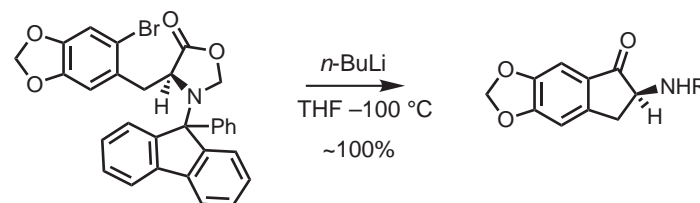


Bailey, W. F.; Patricia, J. J.; Nurmi, T. T.; Wang, W. *Tetrahedron Lett.* **1986**, 27, 1861.

- Lithium-halogen exchange is typically more rapid than addition reactions that might compete.



Aidhen, I. S.; Ahuja, J. R. *Tetrahedron Lett.* **1992**, 33, 5431.

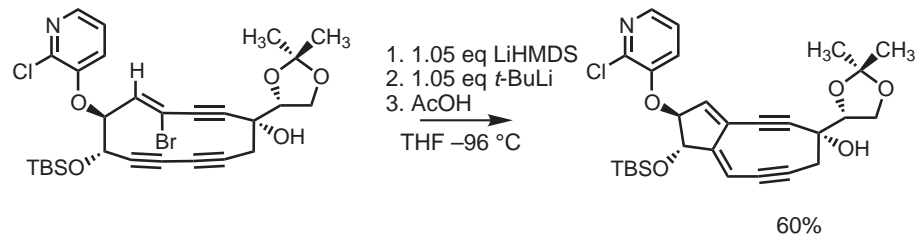
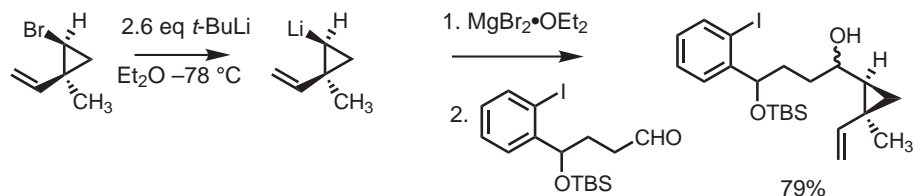


Paleo, M. R.; Castedo, L.; Dominguez, D. *J. Org. Chem.* **1993**, 58, 2763.

- The 9-phenylfluorenyl protecting group is particularly useful in minimizing the rate of epimerization of adjacent labile centers, such as the α -amino ketone above.

Lubell, W. D.; Rapoport, H. *J. Am. Chem. Soc.* **1987**, 109, 236.

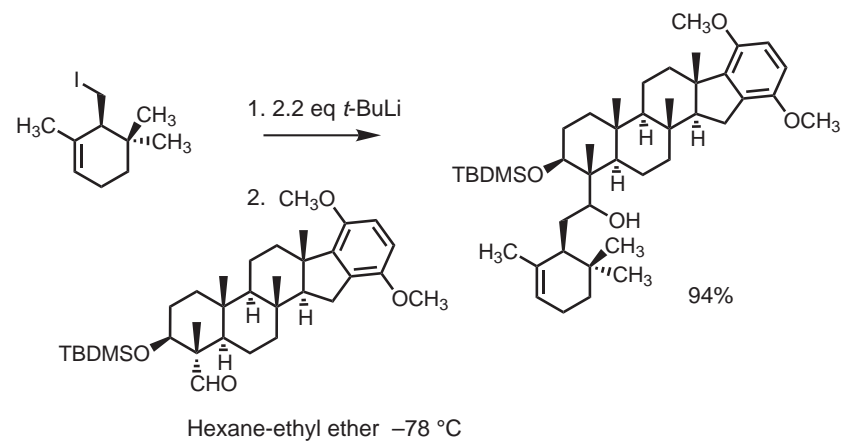
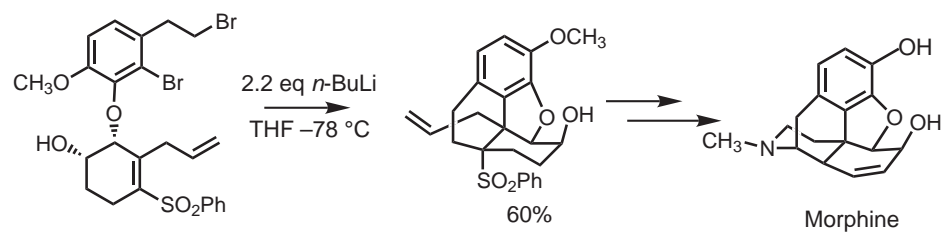
Examples of Lithium-Halogen Exchange in Synthesis:



Overman, L. E.; Ricca, D. J.; Tran, V. D. *J. Am. Chem. Soc.* **1997**, *119*, 12031.

Myers, A. G.; Goldberg, S. D. *Angew. Chem., Int. Ed. Engl.* **2000**, *39*, 2732.

- Cyclopropyl bromides, unlike normal aliphatic bromides, can be reliably converted to the corresponding organolithium reagents. Pretreatment of the cyclopropyl anion with magnesium bromide ethyl etherate in the example above prevents a second, unwanted lithium-halogen exchange reaction from occurring between the cyclopropyllithium reagent and the aryl iodide.



Bogenstatter, M.; Limberg, A.; Overman, L. E.; Tomasi, A. L. *J. Am. Chem. Soc.* **1999**, *121*, 12206.

Toth, J. E.; Fuchs, P. L. *J. Org. Chem.* **1986**, *52*, 473.

- Consider the relative rates of the processes that must occur in the above transformation.