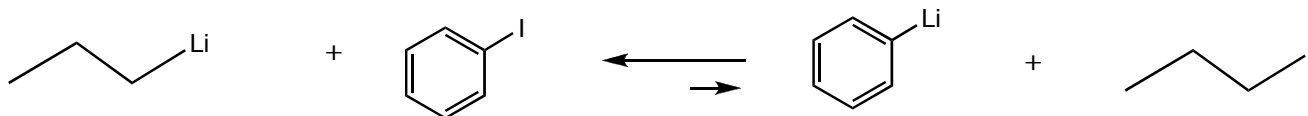
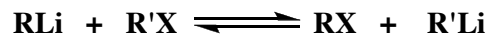


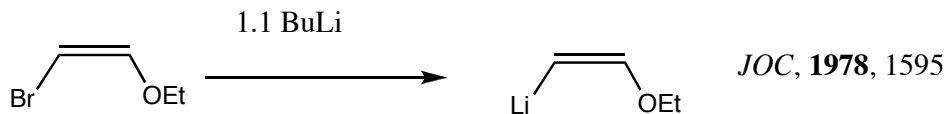
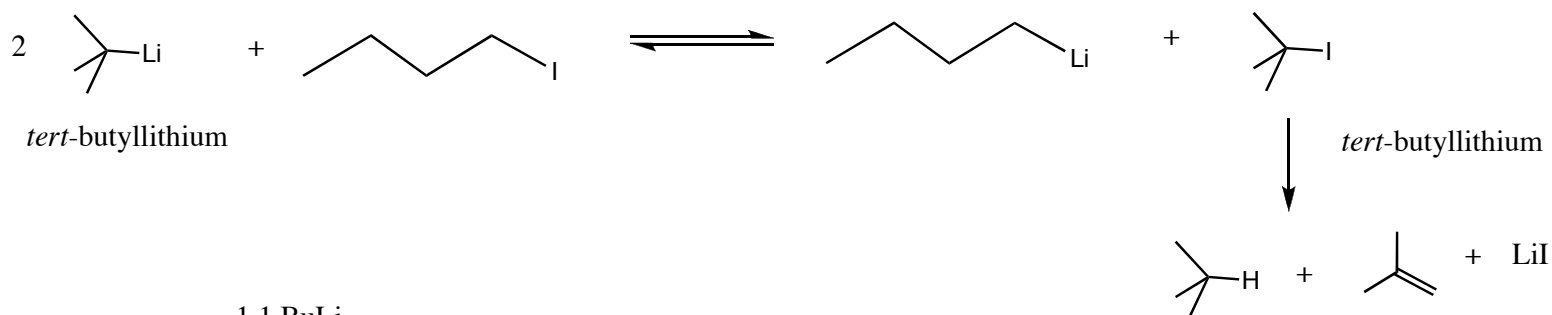
Organolithiums - Preparation and Reactivity

Lithium-Halogen exchange is an equilibrium process, and the position of the equilibrium varies with the stability of the carbanion intermediate:

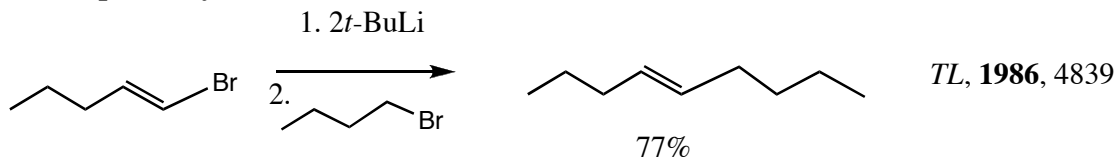


Stability: $sp > sp^2 > sp^3$

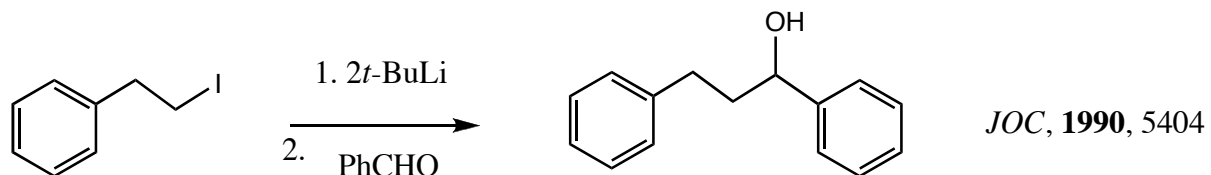
Alkyl iodides are more reactive than bromides and chlorides are inert.



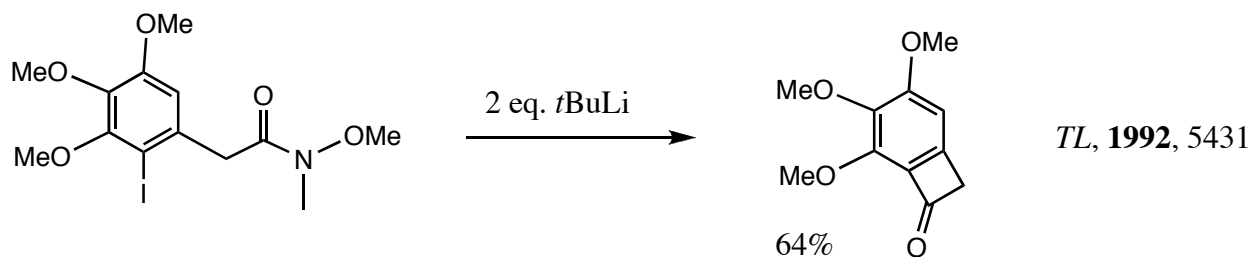
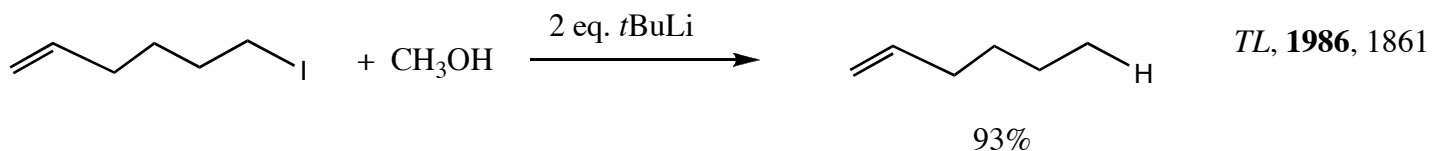
Stereospecificity:



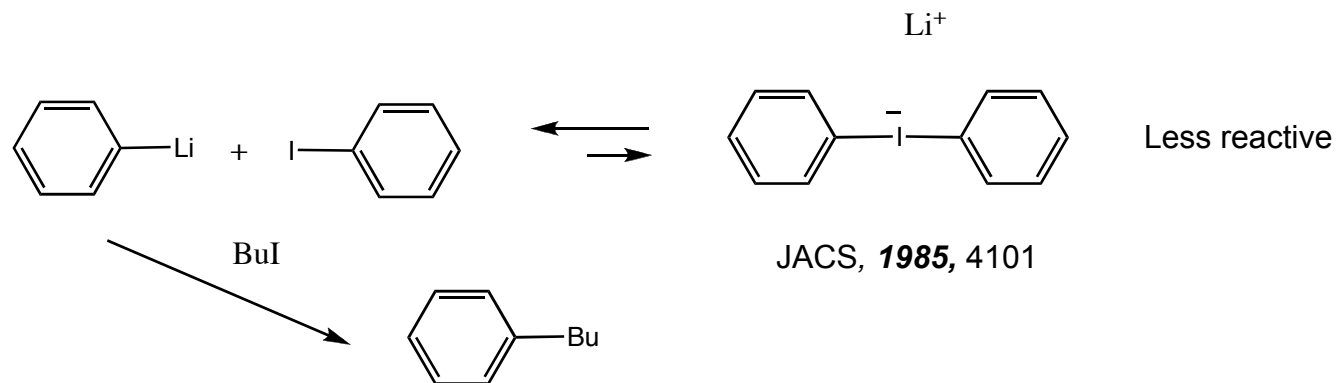
Organolithiums - Preparation and Reactivity



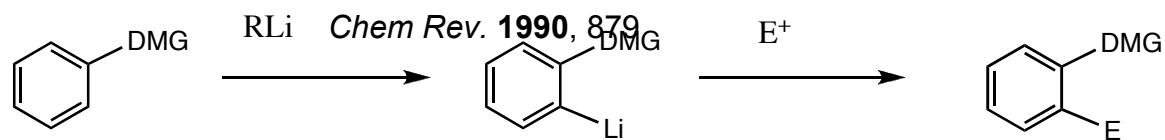
Note: lithium-halogen exchange is faster than the rate of proton transfer!



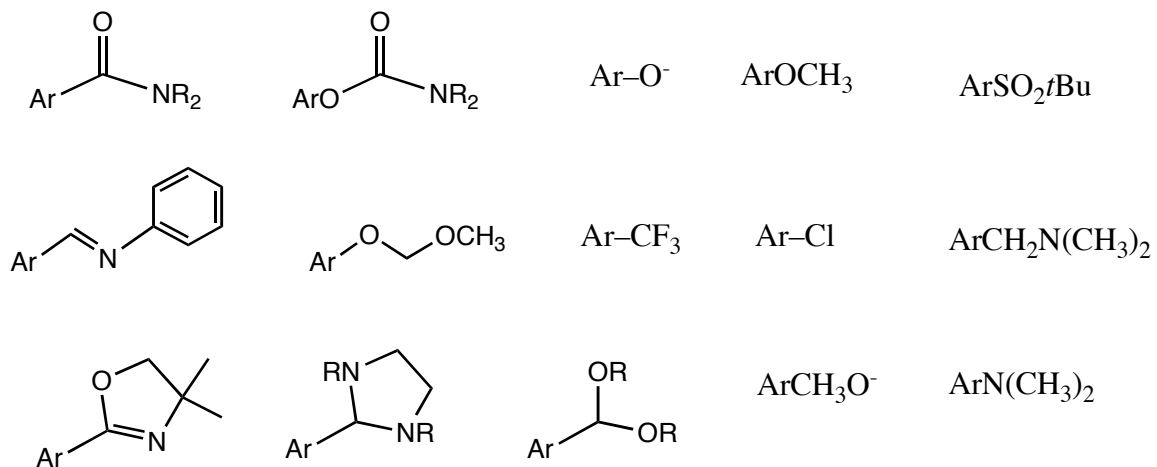
Mechanism of lithium-halogen exchange: "ate" complexation



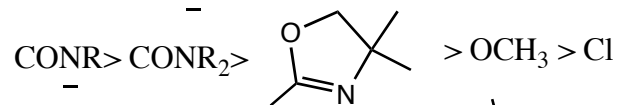
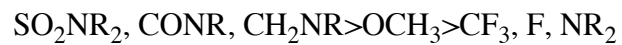
Directed Ortho Metallation



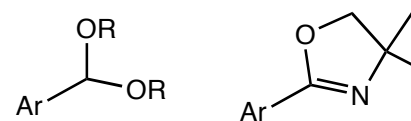
DMG's:



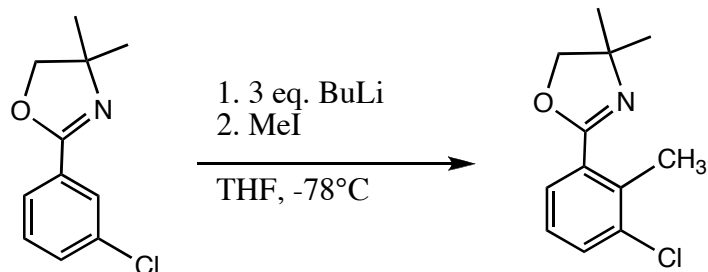
Relative Rates of directed metalation:



Protecting groups serving as DMG's

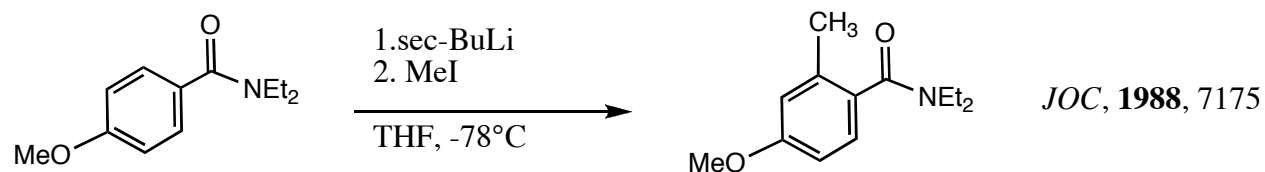


JOC, **1982**, 34
Tet, **1983**, 1983

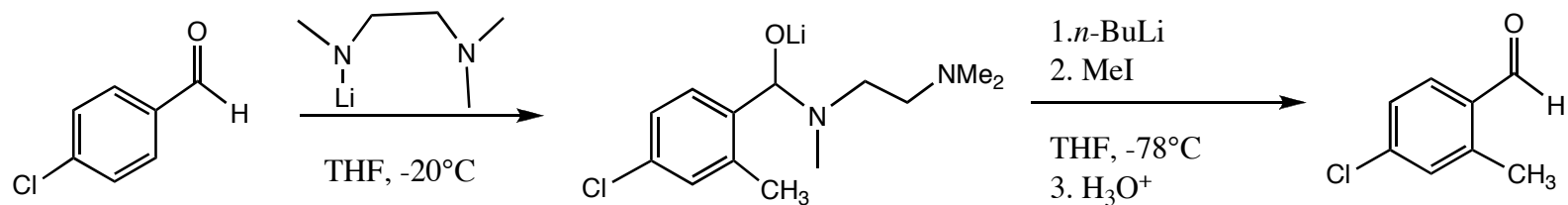


Directed Ortho Metallation

Lithiation occurs ortho to the better directing group:

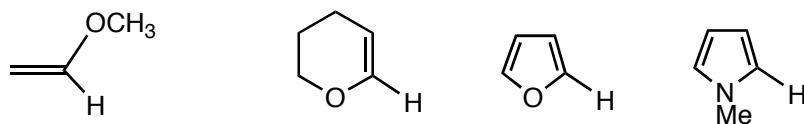


Aldehydes can be transiently protected:

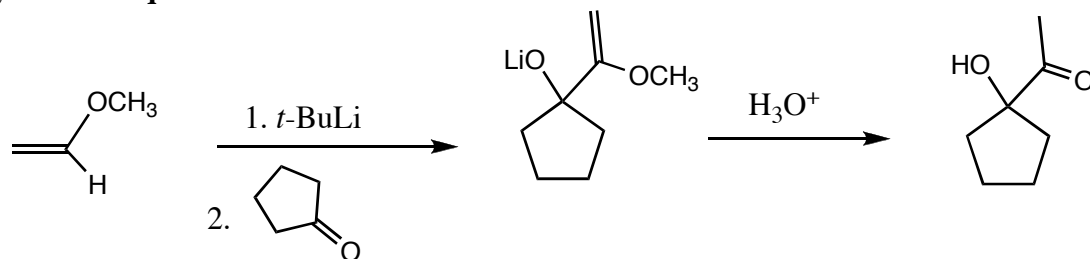


JOC, **1984**, 1078

Metalation of vinyl ethers and heterocycles:



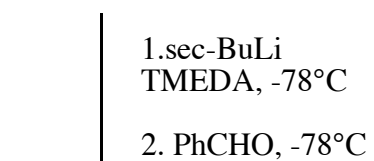
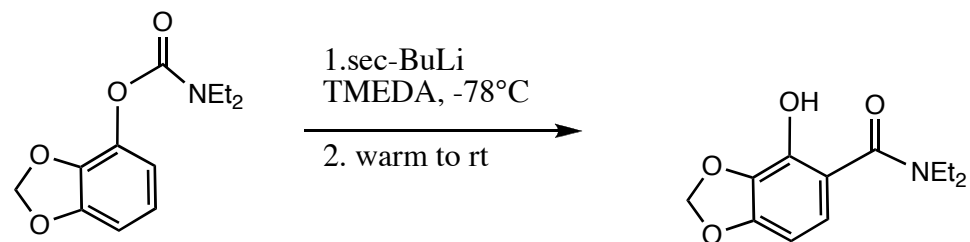
Acyl Anion Equivalent:



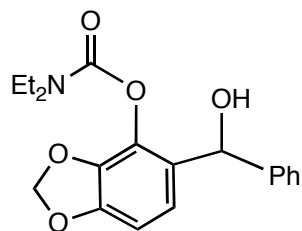
JACS, **1974**, 7125

Directed Ortho Metallation

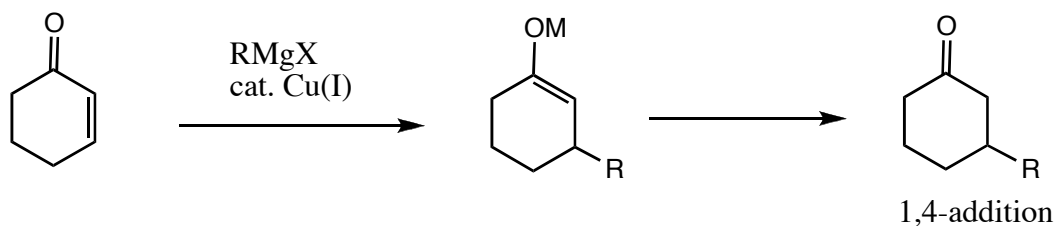
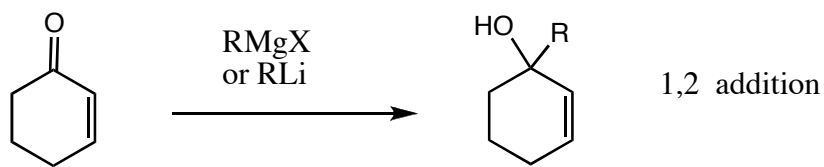
Carbamate directing groups can rearrange upon warming:



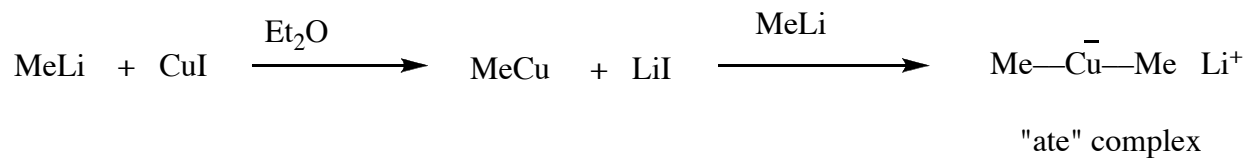
JACS, **1989**, 4829



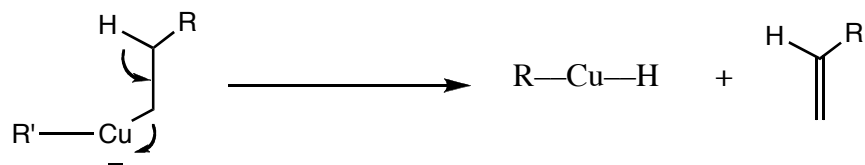
Organocuprates



Stoichiometric organocuprates:



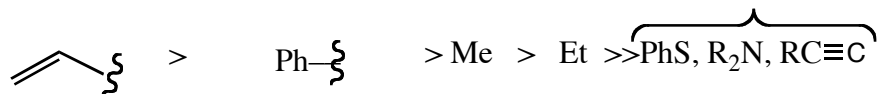
Cuprates other than vinyl, phenyl, or methyl are subject to β -Hydride elimination; must be handled at or below -40°C



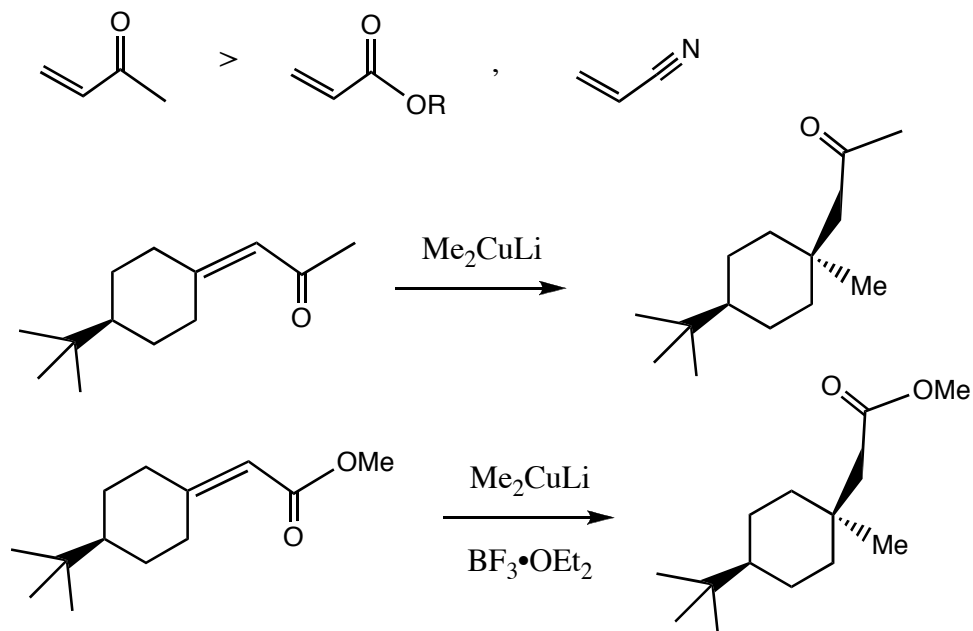
Organocuprates

Ease of ligand transfer:

Dummy ligands; non-transferable

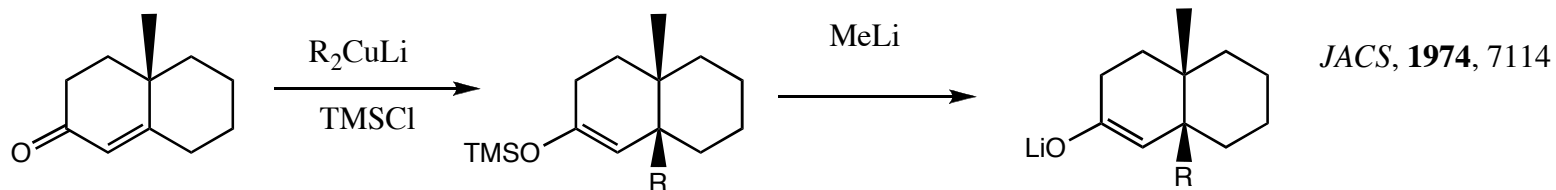


Order of reactivity of Substrates:



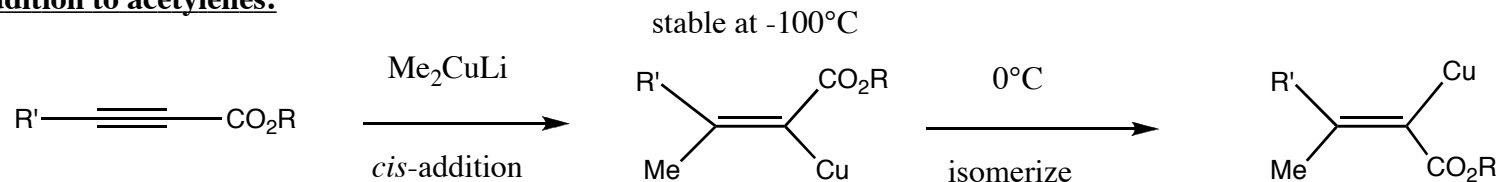
unreactive substrates will react if
Lewis acids are added to activate the substrate
toward nucleophilic addition

Regiospecific Enolate Trap

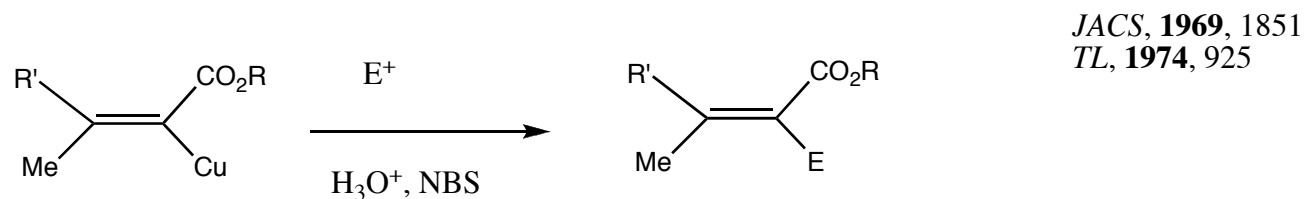


Organocuprates

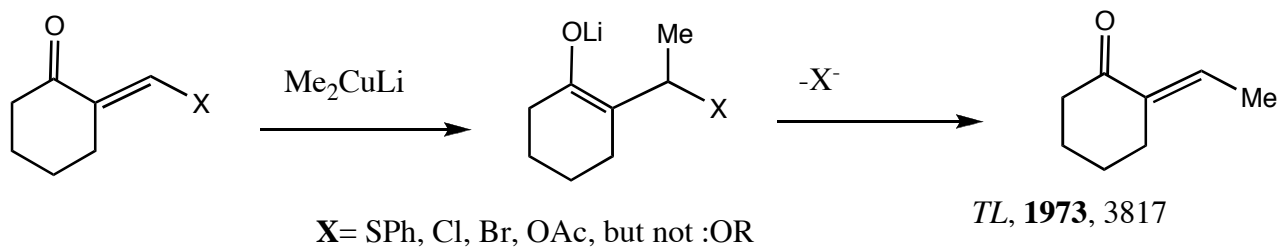
Addition to acetylenes:



Alkenyl Coppers can be trapped:

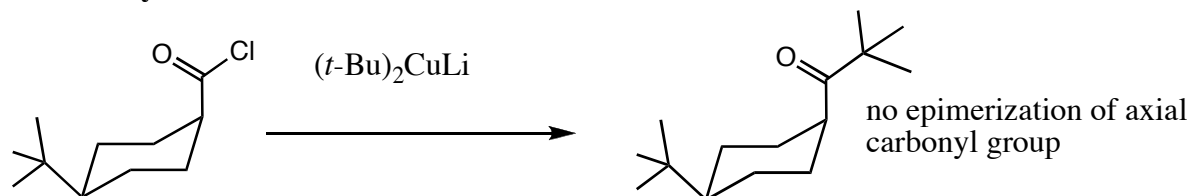


Leaving Group Displacement:



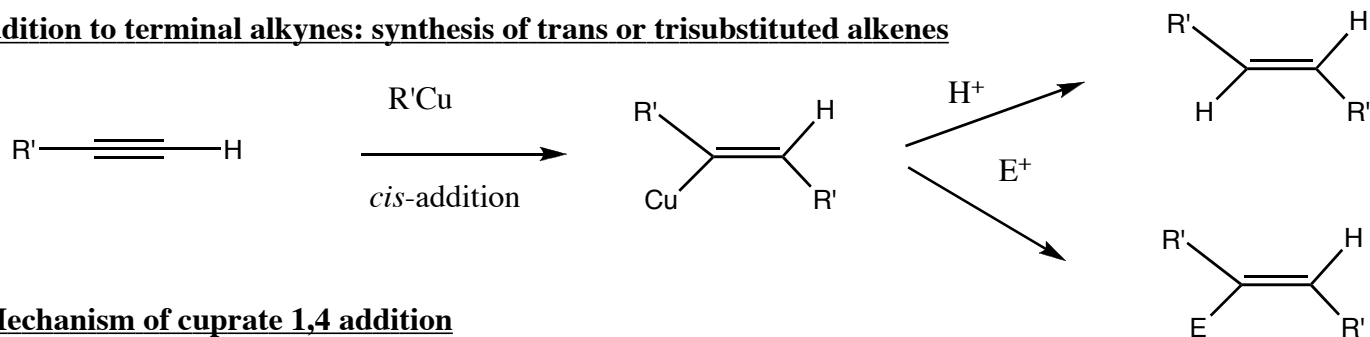
mechanism: *cis* addition, *trans* elimination, net retention of stereochemistry

Ketone Synthesis

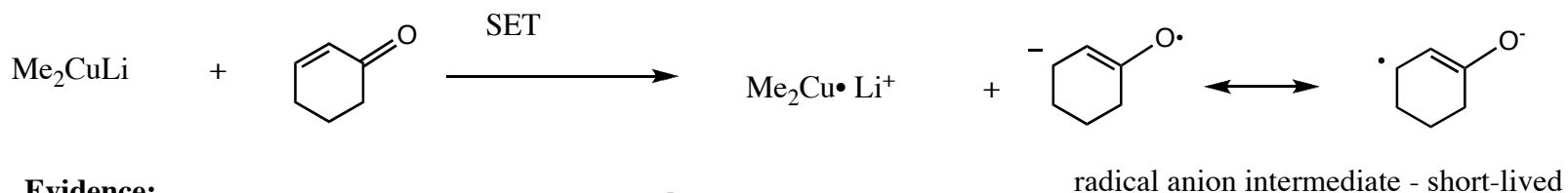


Organocuprates

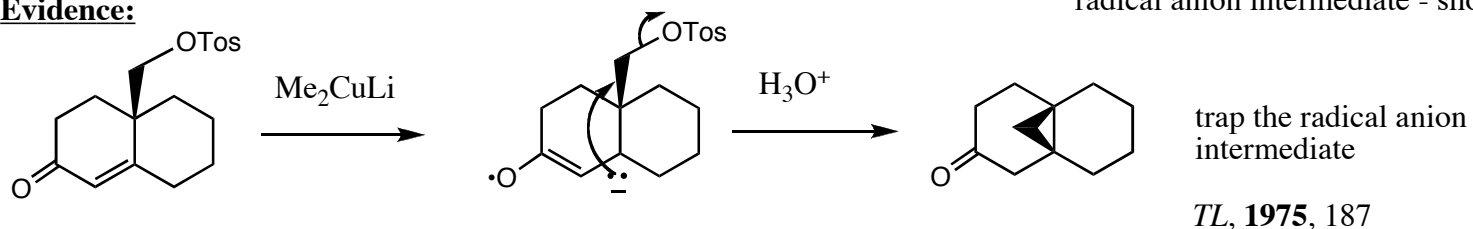
Addition to terminal alkynes: synthesis of trans or trisubstituted alkenes



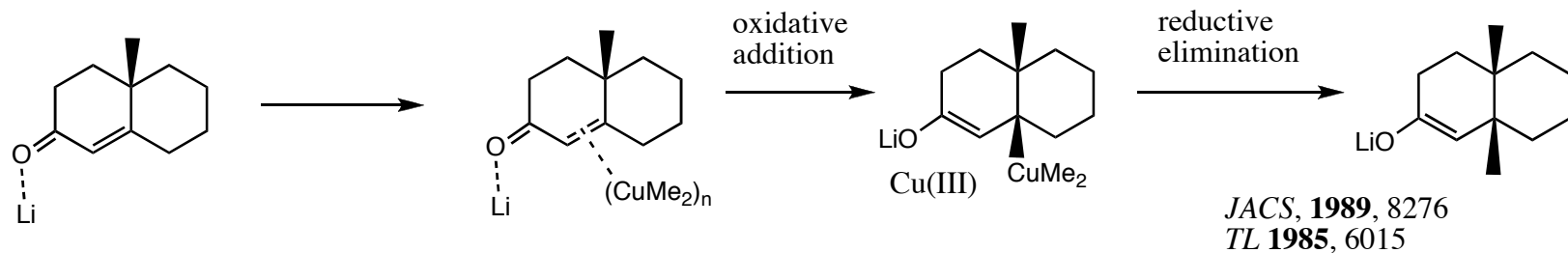
Mechanism of cuprate 1,4 addition



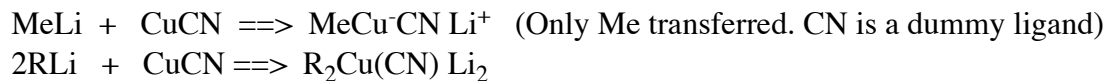
Evidence:



Possible mechanism

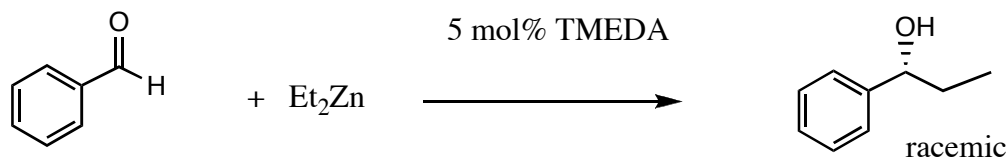


Higher Order Cuprates: More reactive toward a range of substrates:

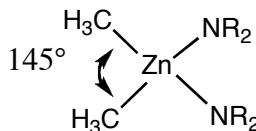
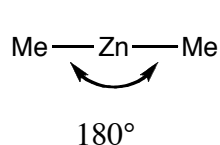


OrganoZincs

Organozinc reagents are low reactive organometallics. Et_2Zn doesn't add to benzaldehyde at room temperature, but the addition of TMEDA (a diamine) promotes addition at RT

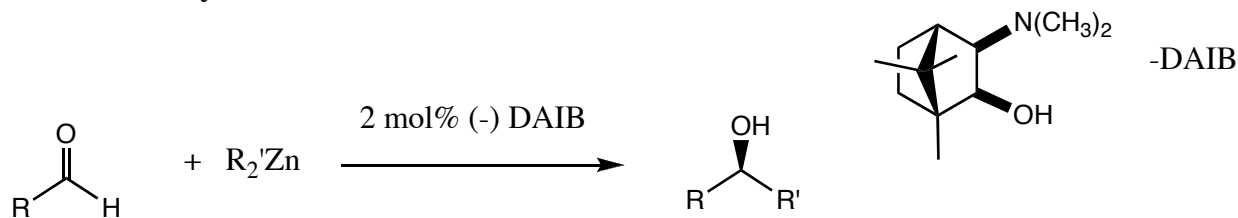


ordinarily in the presence of a diamine



increase in Zn-C bond length (1.95Å to 1.98Å) and decrease in bond angle makes methyls more nucleophilic in the presence of the coordinating diamine

Noyori developed the first highly enantioselective addition to aldehydes utilizing the chiral amino alcohol (-)-DAIB as a catalyst



R	R'	% yield	ee
Ph	Et	97	98
Ph	Me	59	91
PhCH ₂ CH ₂	Et	80	90
C ₆ H ₁₃	Et	81	61

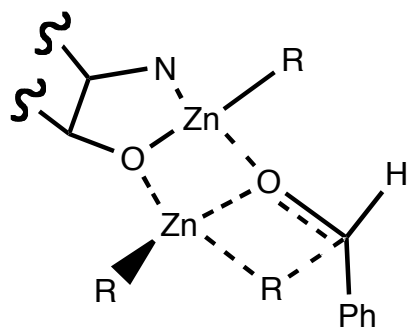
JACS, 1986, 6071

An example of Ligand-Accelerated Catalysis

Enantioselective addition of organozincs to aldehydes

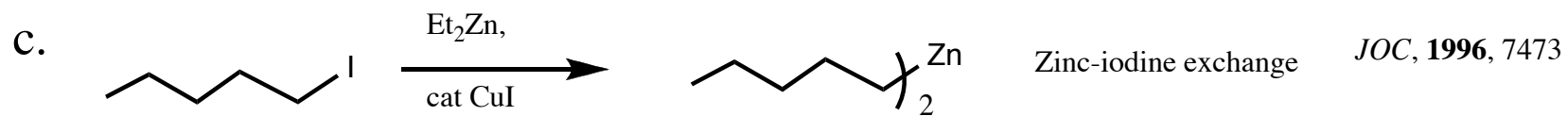
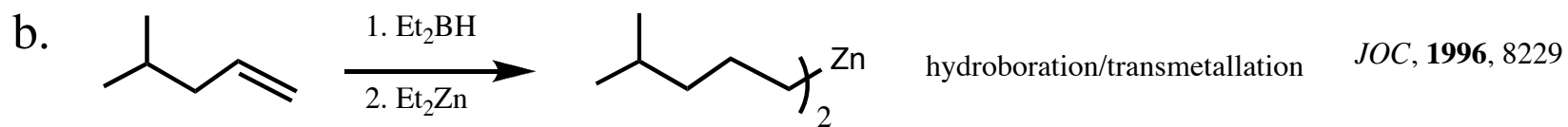
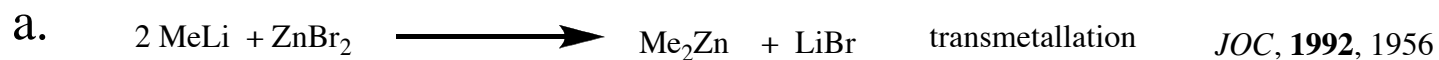
No alkylation occurs when the ratio of ligand to Et_2Zn was 1:1. Catalytic quantities of ligand were required. Proposed transition state assembly:

a dimeric zinc species containing only one chiral ligand

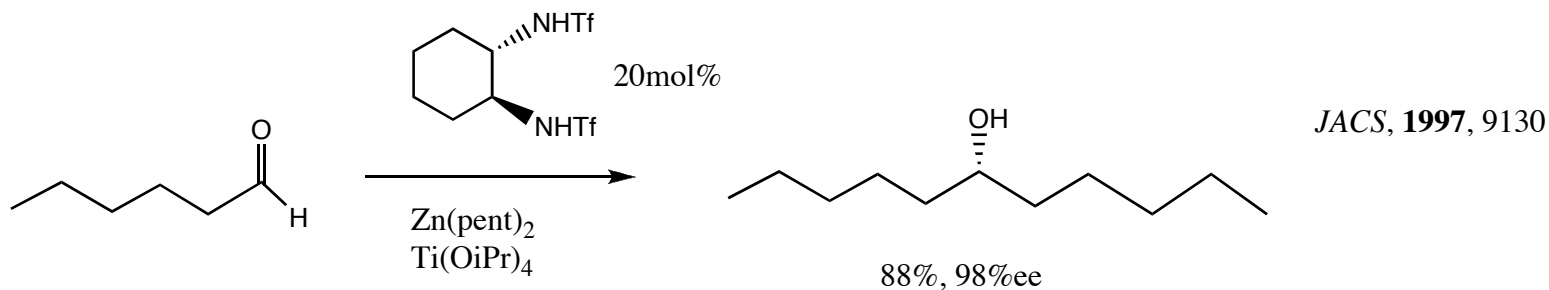


dimeric zinc species with two chiral ligands are unreactive

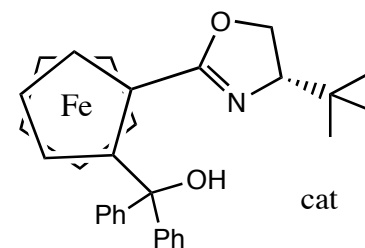
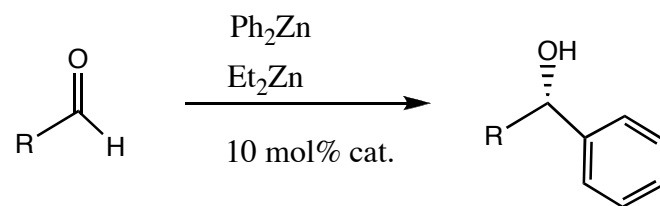
Prep of the Zinc reagents:



Enantioselective addition of organozincs to aldehydes



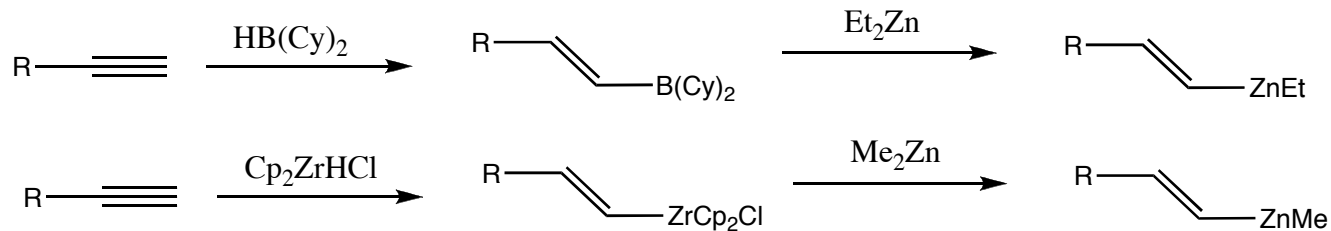
Arylzinc additions:



R	% yield	% ee
i-Pr	75	91
<i>t</i> Bu	68	94
PhCH ₂	82	83
PhCH=CH	97	90

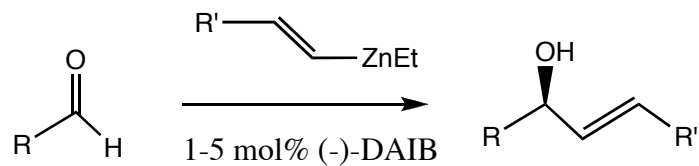
ACIEE, 2000, 3465

Prep of Alkenylzinc reagents: alkenyl and aryl ligands are transferred much faster than alkyl from zinc therefore, this allows the use of mixed alkyl alkenyl zinc species.



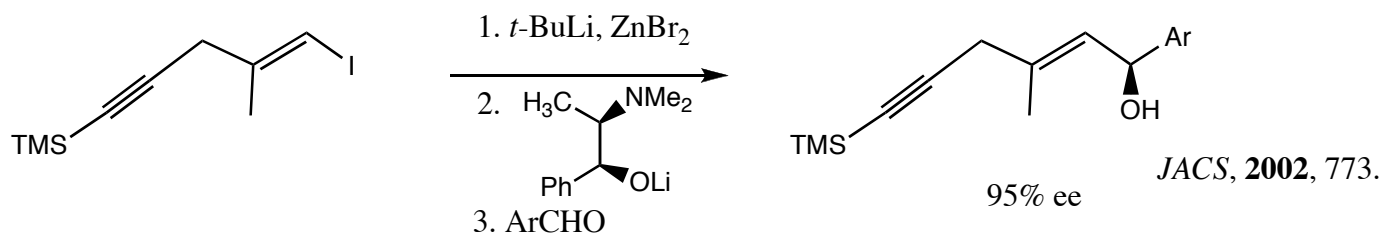
Enantioselective addition of organozincs to aldehydes

Alkenylzinc additions:

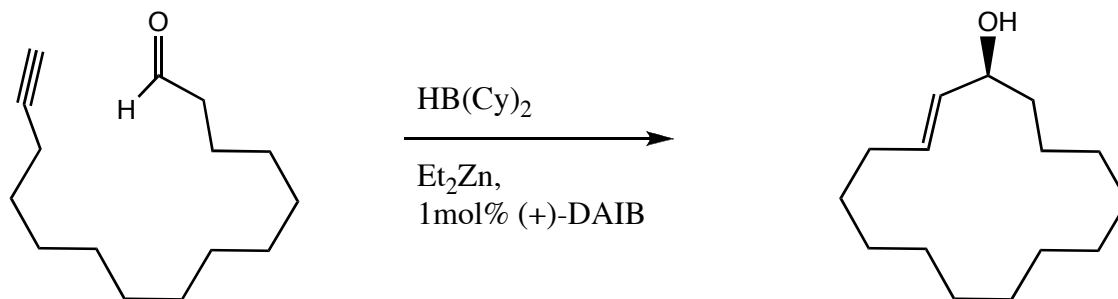


R	R'	% ee
Ph	Bu	96
Et	C ₆ H ₁₃	86
C ₆ H ₅	<i>t</i> -Bu	98

Helv. Chim. Acta, **1992**, 170



JACS, **2002**, 773.

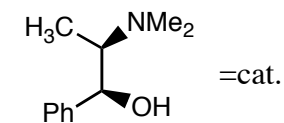
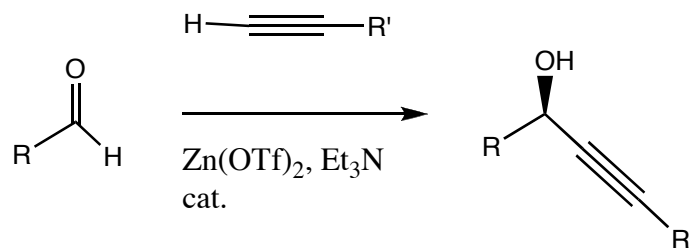


JACS **1993**, 1593

Alkynylzinc Additions to aldehydes

Alkenylzinc additions:

in situ-generated
zinc acetylide; reaction can
be rendered catalytic
at elevated temperatures
using 20mol% Zn(OTf)₂



R	R'	yield %	% ee
C ₅ H ₁₁	Ph	90	97
<i>i</i> -Pr	Ph	96	92
Ph	CH ₂ CH ₂ Ph	67	89

JACS, **2000**, 1806