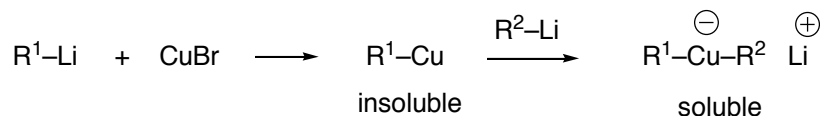


## CHEM 330

### Topics Discussed on Nov. 4

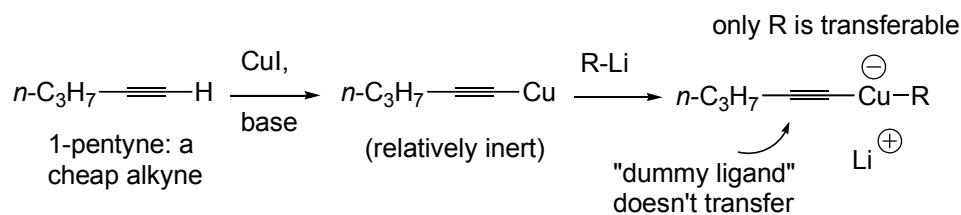
Mixed cuprates: organometallic agents of formula  $R^1-Cu(-)R^2 Mt^+$  ( $Mt = Li, MgBr, \text{etc.}$ ) that are prepared as shown below; e.g.:



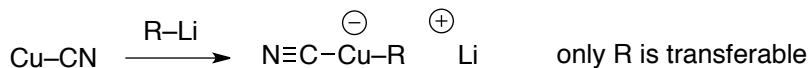
Relative rate of transfer of alkyl groups connected to the Cu atom in a cuprate:  $sp^2$  alkyls (vinyls, phenyls, etc.) >  $sp^3$  alkyls (Me, Et, etc.)  $\gg$   $sp$  alkyls (acetylides)

Methods to suppress the wasteful loss of one of the two alkyl ligands of a cuprate:

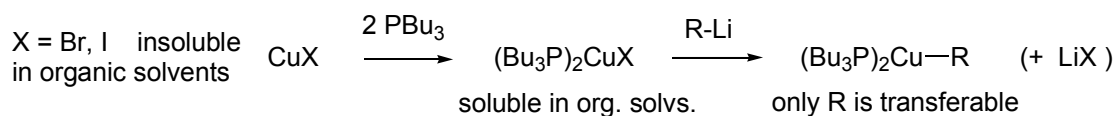
- Use of a mixed cuprate carrying a non-transferable "dummy ligand" such as an acetylide (no longer popular these days because of safety issues associated with Cu(I) acetylides):



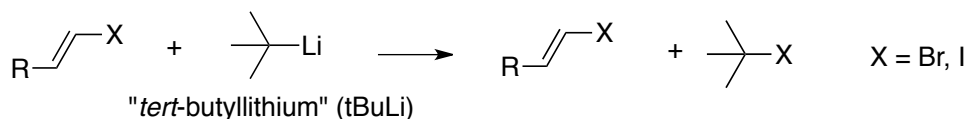
- Use of cyanocuprates (widely used in modern synthetic technology):



- Use of Noyori organocopper agents (widely used; note: these are not "cuprates", because they are not "ate" complexes).



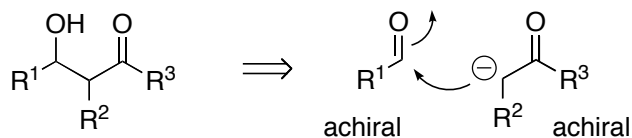
Preparation of organometallics by the **halogen-metal exchange reaction**, e.g.:



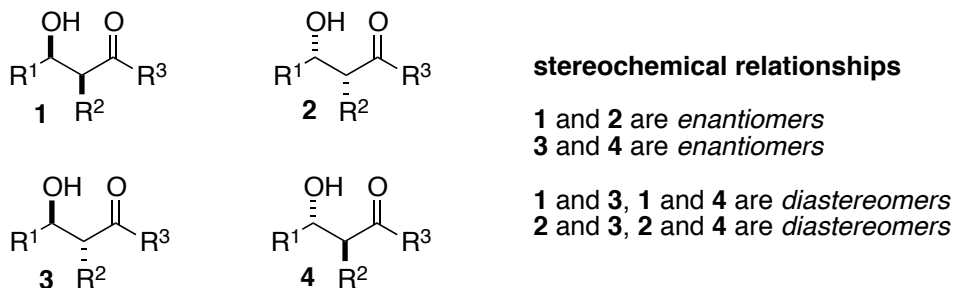
Greater reactivity of tertiary organolithium reagents such as tert-BuLi ( $pK_a \approx 55$ ) relative to secondary ( $pK_a \approx 52$ ) or primary ( $pK_a \approx 50$ ) organo-Li species



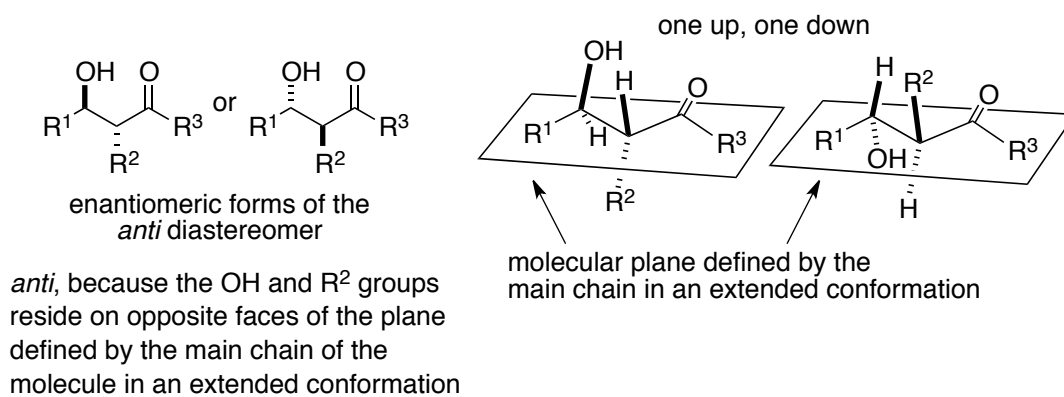
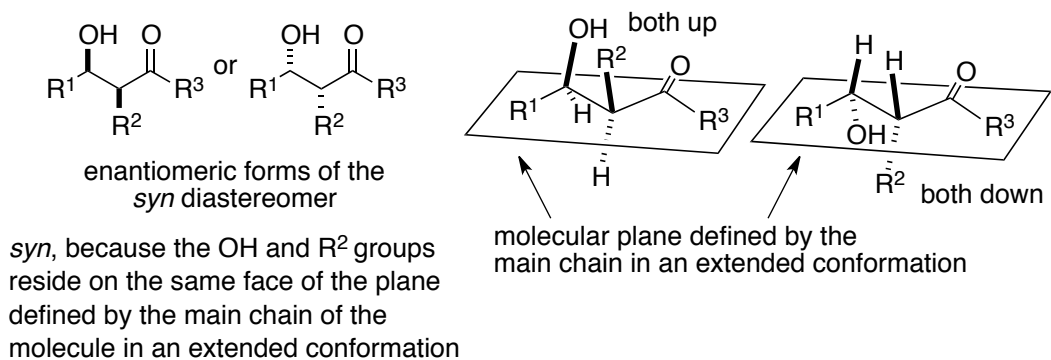
The problem of assembling 1,3-hydroxycarbonyl compounds by an aldol reaction of an achiral aldehyde with an achiral enolate:



Existence of four stereoisomeric forms of the above 1,3-hydroxycarbonyl compound:



*Syn* and *anti* aldol diastereomers:



Reminder:      enantiomers have identical thermodynamic properties  
                   diastereomers have distinct thermodynamic properties

Principle: it is not going to be possible to achieve selective formation of a particular *enantiomer* of the product during the foregoing aldol reaction, because the thermodynamic properties of two enantiomers are identical, but it may be possible to achieve selective formation of a particular *diastereomer* of the product (*syn* or *anti*), because the thermodynamic properties of two diastereomers differ.

The aldol reaction as a potentially *diastereoselective*, but not *enantioselective*, process

Principle: good diastereoselectivity in aldol reactions is often observed if:

- (i) the process occurs under kinetic control (= conditions of irreversibility), and
- (ii) the carbonyl enolate contains a strongly oxophilic metal

Oxophilic metals: small, Lewis acidic ions with a strong charge density and orbitals that interact readily with the orbitals of oxygen, e.g.: Li, B, Ti, Zr....

Existence of metal enolates as two possible geometric isomers: *E* and *Z* enolates



**note:** by convention, the O-Mt substituent takes priority over  $\text{R}^3$  when defining the geometry of an enolate, and this even if  $\text{R}^3$  were of higher Cahn-Ingold-Prelog priority

Principle: *E* and *Z* metal enolates are configurationally stable and do not interconvert, especially if they are generated and maintained at low temperature ( $-78^\circ\text{C}$ ) and if Mt is strongly oxophilic