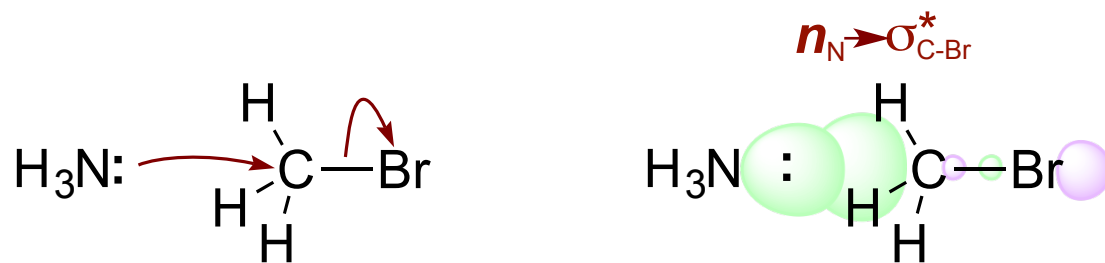


Topic 1: Arrow Pushing



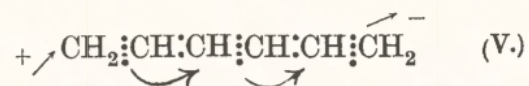
Read: I. Fleming *Molecular Orbitals and Organic Chemical Reactions*
Read the preface
Skim Ch. 1

See: the first curved arrows

O'Hagan, D.; Lloyd, D. "The iconic curved arrow." *Chemistry World* **2010**, 54-57.

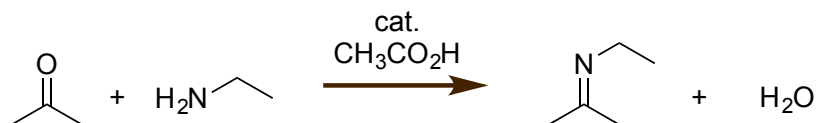
Kermack, W.O.; Robinson, R. "LI.—An explanation of the property of induced polarity of atoms and an interpretation of the theory of partial valencies on an electronic basis" *J. Chem. Soc. Trans.* **1922**, 121, 427-440.

Similarly, the conjugation of three double bonds, supposing such to occur, would be represented thus :—



The Goal of Chem 201: Plausible Arrow-Pushing Mechanisms

■ Consider the following reaction:



How many steps are there in the arrow-pushing mechanism?

Common questions:

- Why can't organic chemists agree on arrow-pushing mechanisms, even for simple reactions?
- Why doesn't my mechanism match the answer in the textbook?
- Why doesn't my mechanism match that printed in the journal article?
(My mechanism must be wrong.)

Problem: Organic chemists never agreed on rules for arrow-pushing mechanisms.

■ We have two learning goals for Chem 201

1. **Break complex mechanisms into a series of elementary reactions**
2. **Add curved arrows**

■ Properties of elementary reactions:

- a single transition state
- microscopically reversible

“kinetic” mechanism:

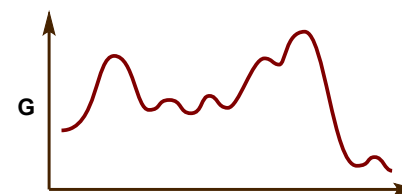
Hine *JACS* **1972**, *94*, 190.

$$k_{ct} = \left(\frac{2K_{im}}{K_{ic}} - \frac{\beta}{\alpha} \right) \ln \frac{K_{ic}\gamma a_0 + \alpha}{K_{ic}\gamma a + \alpha} + \frac{\beta}{\alpha} \ln \frac{a_0}{a}$$

where

$$\alpha = \sqrt{(\delta K_{ic} + \gamma)^2 + 4K_{ic}\gamma[A]_0}$$

$$\beta = \frac{K_{im}}{K_{ca}} \left[\gamma + \delta K_{ca} + \frac{K_{ca}(\alpha - \delta K_{ic} - \gamma)}{K_{ic}} \right]$$



Factors that influence non-bonding interactions

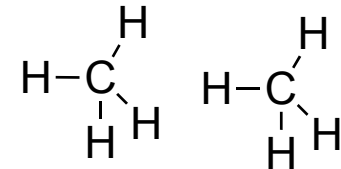
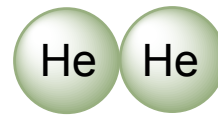
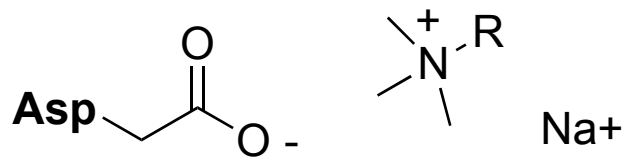
■ For non-covalent interactions, energies can be fit to an equation with three distance-dependent terms.

$$\text{Non-bonding Interaction Energy} \propto \frac{4\pi q_1 \cdot q_2}{\epsilon r} + \frac{x}{r^{12}} - \frac{y}{r^6}$$

charge-charge interactions *repulsive interactions* *attractive interactions*

van der Waals

■ This equation is good for biology (e.g., protein folding) and physical chemistry (liquid helium).

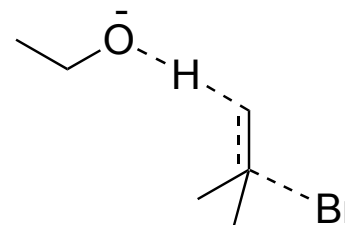
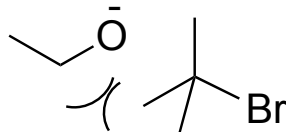
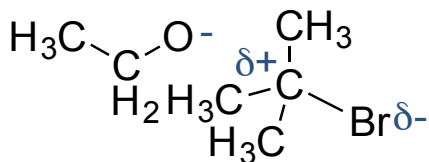


Factors that influence organic reactions

■ For organic reactions, interaction energies can be fit to an equation with three distance-dependent terms.

$$\text{Interaction Energy} \propto \frac{\text{charge-charge interactions}}{\epsilon r} + \frac{\text{repulsive interactions}}{r^n} - \sum_r^{\text{occ.}} \sum_s^{\text{unocc.}} \frac{\sum_{ab} 2(c_{ra}c_{sb}\beta_{ab})^2}{(E_s - E_r)}$$

■ Good for organic chemistry



■ Arrow pushing can not, and should not, be used to depict all three factors
(Which feature should we use curly arrows to depict?)

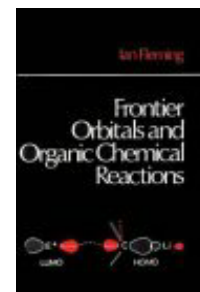
1. CHARGE is an obvious concept
2. STERICS is an obvious concept
3. **THE THIRD TERM** is mysterious and involves things that aren't seen: **molecular orbitals**.

The Central Canon of Mechanistic Arrow-Pushing

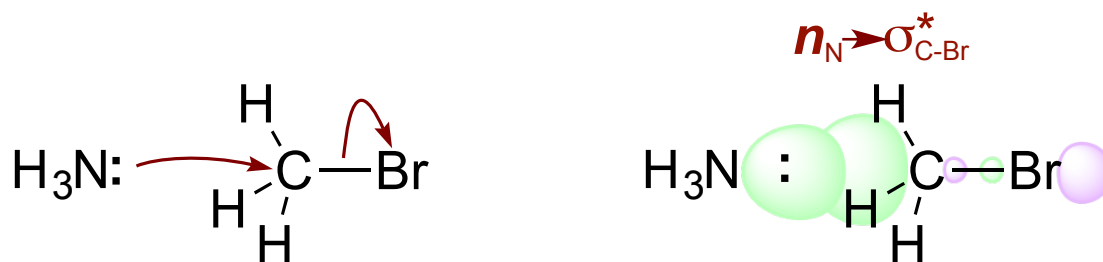
■ Our mandate comes from the original Fleming (p. 49)

However, we ought to be clear that this is a superficial argument (which fortunately works). *Curly arrows*, when used with a molecular orbital description of bonding, work as well as they do simply because they *illustrate the electron distribution in the frontier orbital*, and for reaction kinetics it is the frontier orbital that is most important. But in the present case, we are using a thermodynamic argument, for which we need to know the energy of each of the filled orbitals, and not just one of them.

■ Here is a re-statement of Fleming's casual observation



***Use curly arrows
to depict the interaction
of filled orbitals with un-filled orbitals***

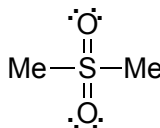
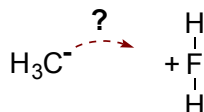
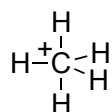
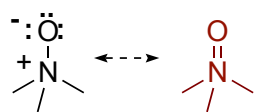


■ DO NOT use curly arrows to depict the motion of atoms

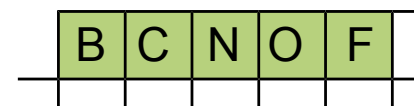
■ DO NOT use curly arrows to depict the interaction of charges

1. CORRECT LEWIS STRUCTURES

■ Obey the octet rule



...only for 2nd row atoms



■ Draw every substituent on every atom except carbon.

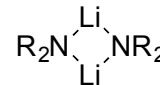
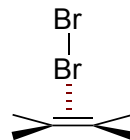
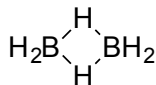
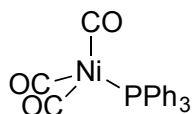
■ Show every charge

■ DRAW THE LONE PAIRS



■ **Don't make or break dative bonds using arrow-pushing.** Dative bonds *do not account for charges*; Convert dative structures to charge-separated ylides *before* pushing arrows.

Useless for arrow-pushing:



wrong charges

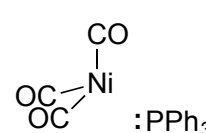
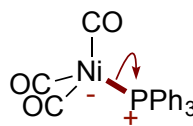
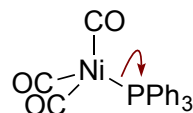
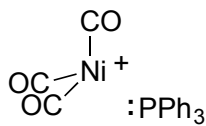


dative bonds

Lewis structure



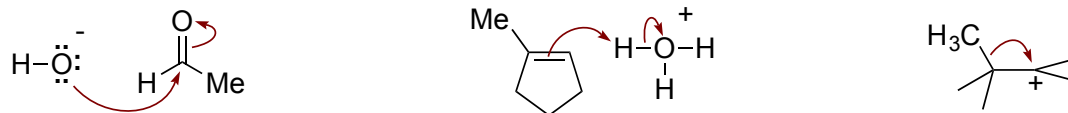
right charges



You don't have to convert every dative bond to an ylide bond, just the bonds that break.

2. MAKE ARROWS START WITH BONDS OR LONE PAIRS

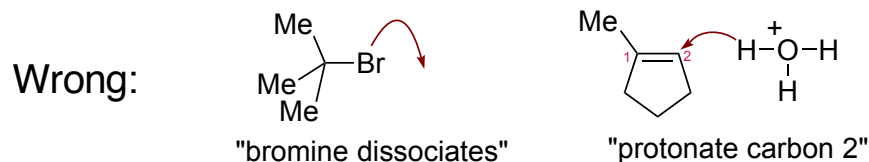
■ Three canonical types of **FILLED ORBITALS** = lone pairs, pi bonds, and sigma bonds.
Every arrow must start with one of these



■ **Arrows do not start on charges** (Charges don't form bonds; electrons do)
The charges on Lewis structures don't correlate electrostatic charges.

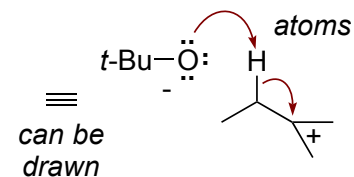
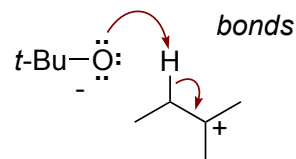
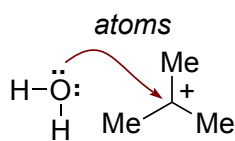
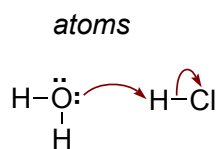


■ **Arrows do not start on atoms.** We often describe elementary reactions with suggestive terms like “dissociate” and “protonate”, but don't use arrows to show the motion of atoms.

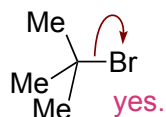
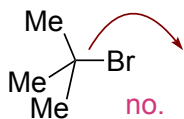


3. MAKE ARROWS END ON ATOMS OR BONDS

■ Three canonical types of **UNFILLED ORBITALS** = empty p orbitals, π^* orbitals, and σ^* orbitals. Problem: unfilled orbitals are generally not depicted in Lewis structures. We will show arrows ending on atoms or bonds.

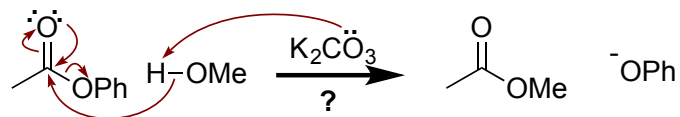


■ Arrows do not terminate in empty space



4. OBEY THE THREE-ARROW RULE

■ **Don't draw elementary steps with more than three curly arrows.** It means you probably didn't break the mechanism into elementary steps.

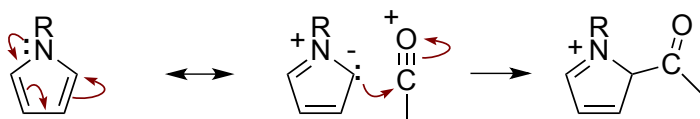


The mechanism involves three steps.

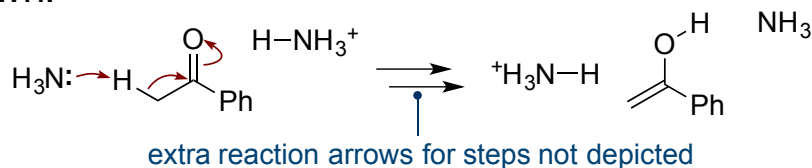
■ You are free to violate the three-arrow rule *after you finish this class*. It's just a safety device.



However, **the three arrow rule can always be accommodated** through the use of resonance structures.



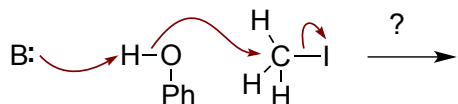
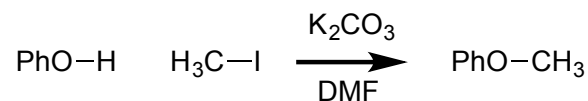
■ **A shortcut for experts:** If you are confident that the elementary steps are obvious, just show the arrow-pushing for the first step, and use stacked reaction arrows to indicate that some elementary steps are not shown.



5. DON'T DRAW TERMOLECULAR REACTIONS

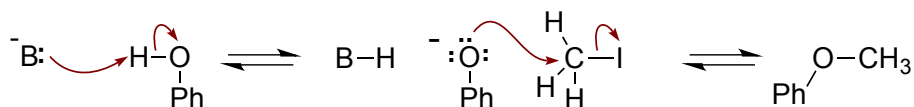
■ DON'T DRAW TERMOLECULAR ELEMENTARY REACTIONS

Where three molecules simultaneously react in one elementary step.



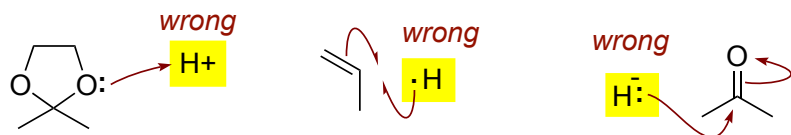
■ **Collision theory:** in solution, molecules collide with frequencies around 10^{11} sec^{-1} , but only a tiny fraction of the collisions lead to bond changes. It is rare for two molecules to collide with the correct alignment for a chemical reaction, so *the chance of three molecules simultaneously colliding with correct alignment is vanishingly small.*

■ Break the reaction into **discrete** bimolecular steps.

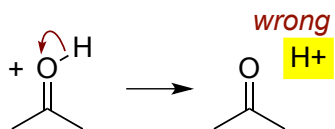


6. H IS ALWAYS ATTACHED TO SOMETHING

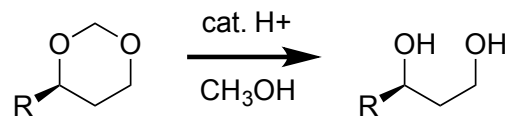
- The terms **proton**, **hydride**, and **hydrogen atom**, refer to functional groups, NOT free species. H^+ , H^- , and $H\cdot$ have no role in solution phase chemistry.



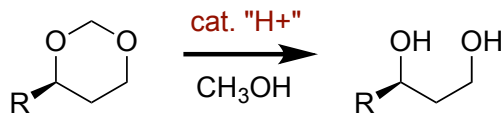
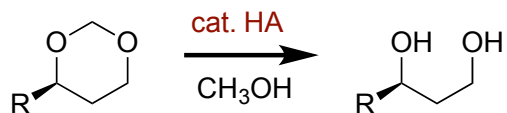
- Avoid the following...



- Avoid writing H^+ as a reagent

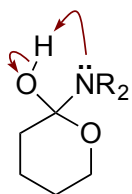


Instead, consider the following sophisticated alternatives

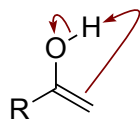


7. AVOID PROTON TRANSFER THROUGH 4-MEMBERED TRANSITION STATES

■ Intermolecular proton transfers reactions are usually very fast. Don't draw intramolecular proton transfers if they involve 4-membered ring transition states.



slow



impossible

■ Instead, use acid-catalyzed or base-catalyzed proton transfers

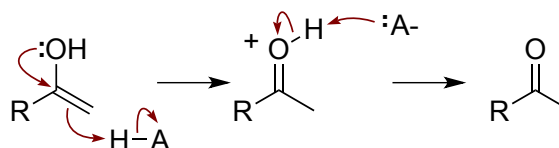
Step 1: **decide if conditions are acidic or basic**

Step 2: write the mechanism **using symbolic acids and symbolic bases**

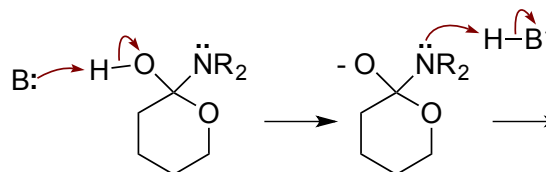
H-A and A⁻ under acidic conditions

B-H⁺ and B: under basic conditions

Under **acidic conditions**: use H-A and A⁻



Under **basic conditions**: use B-H⁺ and B:



Don't mix H-A and B or B-H and A-

Summary of Rules for Mechanistic Arrow-Pushing

- **RULE #1: DRAW CORRECT LEWIS STRUCTURES**
- **RULE #2: MAKE ARROWS START WITH BONDS OR LONE PAIRS**
- **RULE #3: MAKE ARROWS END ON ATOMS OR BONDS**
- **RULE #4: OBEY THE THREE ARROW RULE**
- **RULE #5: DON'T DRAW TERMOLECULAR ELEMENTARY REACTIONS**
- **RULE #6: H IS ALWAYS ATTACHED TO SOMETHING**
- **RULE #7: AVOID PROTON TRANSFER THROUGH 4-MEMBERED TRANSITION STATES**