1. What is a reaction mechanism?
   1. description of conversion of reactants to products
   2. includes important intermediates and transition states
   3. should show timing of bond changes
   4. single step has one transition state (TS), no intermediates
   5. multistep has more than one TS, intermediates between TS
   6. **products can be modified rationally** if the mechanism (intermediates and transition states) can be identified
2. What is the dominant reaction?
   1. Favored by energetics (Grxn) and/or kinetics (G\*)
   2. Grxn: free energy difference between reactants (R) and products (P)
   3. G\*: free energy difference between reactants and transition state (TS)
3. Determination of energetics (Grxn): how far the reaction goes
   1. 
   2. , 2.303RT = 1.4 kcal/mol at 300 K
   3. , if kcal/mol then K = 102
   4. H = ΣBDEreactants - ΣBDEproducts
      1. assume G = H when ⏐TS⏐ is small
      2. S depends on change in available degrees of freedom: translations, vibrations, rotations
      3. chlorination of methane: *H*RXN = -25 kcal/mol ≈ *G*RXN

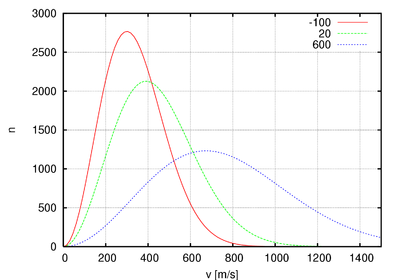
|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| CH3-H | + Cl-Cl | → | CH3-Cl | + H-Cl |
| 104 | 58 |  | 84 | 103 |

* 1. examples where ⏐S⏐ is not small
     1. CH3CH2CH3 → CH3CH=CH2 + H2 *H*RXN = 30 kcal/mol
     2. 
     3. S > 0, reactions are more favorable at higher temperatures: T*S*RXN
     4. bimolecular reaction is typically -20 to -30 eu (cal/K) ⇒ T*S* ≈ -6 to -9 kcal/mol at RT

1. Kinetics
   1. reaction coordinate: change in structure for R to P as a function of energy
      1. highest TS determines how fast a reaction goes
      2. reactions often have many steps

* + 1. the highest step = is the rate determining step, why?
    2. only a fraction of the molecules have correct orientation
    3. only a fraction have E > TS, Maxwell-Boltzmann distribution



* + 1. energy comes from collisions
    2. All other points prior to TS lower in energy (those points form faster)
  1. Kinetic versus thermodynamic control
     1. Lower temperature (irreversible reaction, kinetic control)
        1. two competing reaction: G\*1 < G\*2
        2. enough energy to go forward, reverse TS too high
        3. reaction with lowest TS faster and P1 dominates



* + 1. high temperature (reversible reaction, thermodynamic control)
       1. enough kinetic energy to go forward and backward
       2. P1 is formed faster, but reverts to reactant and eventually P2
       3. G2 < G1
    2. reaction won’t be favorable at all unless G2 < 0
       1. Note: if you start at P1 it is really a reactant and R is an intermediate.
  1. estimation of rates (calculation of activation energies)
     1. G\* determined from rate constants at different T
     2.  (Eyring equation)
     3.  (at 300 K, units = kcal/mol)
        1. if*G*\*= 14 kcal/mol then logk = 12.6 - 10 = 2.6 ( is assumed to be 1.00)
        2. k = 102.6 s-1 ≈ 103 s-1 ⇒ ms lifetime (since k ≈ 1/
        3. if *G*\*= 28 kcal/mol then logk = 12.6 - 20 = -7.4
        4. k ≈ 10-7 s-1 ⇒ 4 months lifetime
  2. ~~Calculation of activation parameters~~
     1. ~~rearrange , divide by T and take log, separate G terms~~
     2. ~~~~
     3. ~~plot log(k/T) versus 1/T, slope yields activation enthalpy~~
     4. ~~intercept yields activation entropy~~
  3. determination of rate laws (mechanisms)
     1. determine rate law empirically/compare with rate laws for proposed mechanisms
        1. dependence of rate on reactants, products, catalysts/reagents
        2. corresponds to composition of species leading to transition state
     2. rate law can distinguish between mechanisms

|  |  |  |  |
| --- | --- | --- | --- |
| [H+] | [A] | [B] | rate |
| 0.001 | 0.1 | 0.1 | 1 x 10-4 |
| 0.001 | 0.2 | 0.1 | 2 x 10-4 |
| 0.001 | 0.1 | 0.2 | 4 x 10-4 |
| 0.004 | 0.1 | 0.1 | 2 x 10-4 |

* + 1. example: rate = ko + k[H+]1/2[A][B]2
    2. order of mechanism is 3 1/2, 1/2 in [H+], 1st in [A] and 2nd [B] (sum of exponents)
    3. compare experimental rate law with rate law of a proposed mechanism
  1. How do you determine mechanism for expt. rate law: (1) propose mechanism (2) derive its rate law
     1. compare derived rate laws with experimental rate law
     2. , : first-order process
     3. , ; second-order process
     4. 
        1. 
        2. : steady state assumption
        3. , substitute above
        4. 
  2. product analysis: mechanism must explain product distribution

 (at least three plausible mechanisms)

* 1. mechanism must include important intermediates
  2. mechanism predicts of isotopic labeling

* 1. correct mechanism predicts kinetic isotope effects
     1. bond energies are different for different isotopes
     2. kH/kD >2 if cleavage occurs in rate determining step (primary isotope effects)
     3. What is kH/kD for the elimination of HBr? – show arbitrary rate equation.



1. Predictions of reaction products
   1. Determined by fastest reaction and/or most stable product
   2. barriers to reaction?
      1. Broken bonds? What does it take to break a bond?
      2. heterolytic or homolytic?
      3. Typical gas phase bond energies? (Chemist Companion)
      4. substitution of chloromethane with sodium hydroxide (gas phase)



* + 1. Which steps are slow? Fast?
       1. don’t know G\*
       2. G\* ≥ G for single step. Why?
       3. steps that form bonds but don’t break bonds are usually fast
    2. Ignoring first step in each case, which pathway is preferred?
    3. Are conditions conducive to formation of anions, cations, or radicals?
    4. solvation lowers energy of ions
    5. concerted process may lower TS: simultaneous bond making/breaking

1. Mechanistic predictions based on “reactivity”
   1. identify reagent reactive sites (functional groups)
      1. **electronegativity differences** determine likelihood of attack by acids (electrophiles, **electron sinks**) or bases (nucleophiles, **electron sources**)
      2. **electron sources**: lone pairs,  electrons and  electrons (normal order of reactivity)
      3. **charge** increases effectiveness of nucleophile (negative) or electrophile (positive)
      4. **weak bonds** – bond cleavage to form radicals or atom abstraction
         1. herteroatom-heteroatom single bonds: ROOR → 2RO•, Cl-Cl → 2Cl•
         2. stabilized products: R-N=N-R → 2R• + N2.
   2. survey **known reactions** of reagent functional groups
      1. what are the similarities to current reaction reagent
   3. role of solvent, temperature, pressure
   4. follow the path of reactivity: test a step, sequentially determine the behavior of each species,
2. common reaction types
   1. composed of fundamental processes (can you determine electron count?)
      1. dissociation – heterolytic, homolytic, consider alternative first step?





* + 1. addition – heterolytic, homolytic

 proton addition very fast!!! Why???

* + 1. migration – 1-2, 1-3, 1-4 (usually to electron deficient atoms: heterolytic)



* 1. displacement (first reaction is not a single step)



* 1. 1,2-addition (sometimes single step, usually two steps)



* 1. 1,2-elimination



* 1. rearrangements (1st = dissociation, 2nd = rearrangement (migration?) 3rd = addition)



* 1. radical abstraction
  2. radical addition

1. cannot prove a mechanism
   1. disprove mechanism: show mechanism inconsistentwith evidence
   2. show mechanism is consistent with available evidence
   3. new evidence could disprove accepted mechanism
2. Ground rules for mechanisms
   1. reaction arrows, charge balance, electron source arrows, show all proton transfers, strongest acid and base react
   2. bisulfate or bromide versus water as bases, methyl and primary carbocations never form in solution. K (equilibrium) versus k (rate)?