Topic 4: Selectivity





Hatch, L. F.; Alexander, H. E.; Randolph, J. D. *J. Org. Chem.* **1950**, *15*, 654.

■ In irreversible reactions, you get the product that forms fastest = lowest energy transition state

• ΔG^{\ddagger} = free energy of the transition state, we are usually concerned with differences in ΔG^{\ddagger} , often designated $\Delta \Delta G^{\ddagger}$. We depict the energetic consequences using *reaction coordinate energy diagrams*.

Don't worry about the X-axis.

Each factor of 10 in k corresponds to 1.4 kcal/mol in $\Delta\Delta G^{\ddagger}$



■ In sophomore organic chemistry you were taught that more stable carbocations form faster. That was a special case. The less stable products frequently form faster

■ Transition state theory pretends that the S.M. is in equilibrium with the T.S. Therefore, the free energy of activation can be used determine how fast the reaction will occur.

Rxn rate =
$$k$$
[S.M.] $\Delta G^{\ddagger} = -RT \ln \frac{k}{k^{\ddagger}} \Leftrightarrow fastest poss.$ For a typical 8 hr rxn $\Delta G^{\ddagger} = -RT \ln \frac{k}{k^{\ddagger}} \Leftrightarrow fastest poss.$ $\Delta G^{\ddagger} \sim 23$ kcal/mol

Rule of thumb: Each 10 °C rise in temperature will double the reaction rate

■ You rarely know the absolute value of *k*, but there are limits.

 \blacksquare Limits on the rate constants (k^{\ddagger}) for elementary reaction steps

1. Unimolecular reaction:
$$10^{-8} \text{ s}^{-1} < \mathbf{k} < 10^{13} \text{ s}^{-1} = \mathbf{k}^{\ddagger}$$

bond vibration



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2. Bimolecular reaction: 10^{-9} \text{ M}^{-1}\text{s}^{-1} < k < 10^{9} \text{ M}^{-1} \text{ s}^{-1} = k^{\ddagger}
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3. Termolecular reaction: no practical examples

■ If your TLC looks like this after 2 h, when will it be done?



Most reactions are first order in starting material. It takes about 8 half lives to reach completion.



Note: Some metal-catalyzed reactions that don't involve reagents in the RDS exhibit linear product buildup.

■ For organizing your time, **half lives are intuitive** - rate constants aren't. For unimolecular reactions or bimolecular reactions run at 1 M concentration

$$A \longrightarrow B \qquad t_{1/2} \approx \frac{1}{k}$$

Selectivity in Equilibrium Reactions is Determined by ΔG°

If products or intermediates equilibrate rapidly on the time scale of the reaction, then their ratio Is determined by ΔG° .

■ In the following example, the product that forms fastest is less stable than the product that forms slowest



Deslongchamps, P. *et. al. Can. J. Chem.* **1975**, *53*, 1601.



■ Yields don't tell you about rates. Reaction temperature and reaction time do. *Caution: lazy chemists allow reactions to proceed long after they are done.*

So how can one know which elementary reactions are fast and which elementary reactions are slow?



■ There are very few tabulated listings of reaction rates for interesting processes.

Mayr*, H.; Bug, T.; Gotta, M. F.; Hering, N.; Irrgang, B.; Janker, B.; Kempf, B.; Loos, R.; Ofial, A. R.; Remennikov, G.; Schimmel, H. "Reference Scales for the Characterization of Cationic Electrophiles and Neutral Nucleophiles" *J. Am. Chem. Soc.* **2001**, *123*, 9500.

Reaction Temperature Is a Clue to Rates of Elementary Reactions

For reactions you cool: EVERY ELEMENTARY STEP in the mechanism must be fast



■ For reactions you heat: AT LEAST ONE ELEMENTARY STEP is slow

